

# Immunisation Handbook

2024

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# Anaphylaxis

## response/management

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**CALL FOR HELP – send for professional assistance (ambulance, doctor).**  
**Never leave the individual alone.**

**ASSESS FOR ANAPHYLAXIS** (see Table 2.10 for full details)

**Airway and breathing**

Noisy breathing due to airways obstruction; or respiratory arrest

**Circulation/shock**

Tachycardia; hypotension; dysrhythmias; circulatory arrest

**Skin changes**

Red, raised and itchy rash; swollen eyes and face; generalised rash

**If cardiac arrest** – commence age-appropriate CPR and life support measures

**LAY THE PATIENT DOWN** (do not allow them to stand)

If they have breathing difficulties, elevate the head and chest.

**ADMINISTER ADRENALINE** by deep IM injection into outer thigh

Adrenaline dosage for 1:1,000 formulation is 0.01 mL/kg up to a maximum of 0.5 mL.

For those under 10 kg or if weight is not known, use the following guidelines:

Age	Dose
under 2 years	0.1 mL
2–4 years	0.2 mL
5–11 years	0.3 mL
12 years and over	0.5 mL
Adult	0.5 mL

You can expect to see some response to the adrenaline within 1–2 minutes. If necessary, adrenaline can be repeated at 5–15-minute intervals, while waiting for assistance.

**ADMINISTER OXYGEN**, if available, at high flow rates when there is respiratory distress, stridor or wheeze.

**IF HYPOTENSIVE, ELEVATE LEGS.**

**RECORD VITAL SIGNS** every 5–10 minutes. All observations and interventions need to be clearly documented in medical notes and should accompany the individual to hospital.

**ADMIT TO HOSPITAL** – all cases of anaphylaxis should be admitted to hospital for observation. Rebound anaphylaxis can occur 12–24 hours after the initial episode.

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Note: IV adrenaline should only be used with extreme caution by medical staff. It is not appropriate as a first-line management

# National Immunisation Schedule

Antigen(s)	DTaP-IPV-HepB/Hib	PCV13	MenB	RV1	MMR	Hib-PRP	VV	DTaP-IPV	Tdap	HPV9	Influenza	rZV
Brand name	Infanrix-hexa	Prevenar 13	Bexsero	Rotarix	Priorix	Act-HIB	Varilrix	Infanrix-IPV	Boostrix	Gardasil 9	Influvac Tetra	Shingrix
Pregnancy									Tdap		Influenza	
6 weeks	DTaP-IPV-HepB/Hib	PCV13 <sup>a</sup>		RV1								
3 months	DTaP-IPV-HepB/Hib		MenB <sup>b</sup>	RV1								
5 months	DTaP-IPV-HepB/Hib	PCV13	MenB									
12 months		PCV13	MenB		MMR							
15 months					MMR	Hib-PRP	VV					
4 years								DTaP-IPV				
11 or 12 years									Tdap	HPV9 (2 doses)		
45 years									Tdap			
65 years									Tdap		Influenza (annually)	rZV (2 doses)

**Key:** D = diphtheria; T = tetanus; aP = acellular pertussis; IPV = inactivated polio vaccine; HepB = hepatitis B; Hib = *Haemophilus influenzae* type b; PCV13 = 13-valent pneumococcal conjugate vaccine; RV1 = rotavirus vaccine (monovalent); MenB = meningococcal B vaccine; MMR = measles, mumps and rubella; VV = varicella vaccine; d = adult diphtheria; ap = adult acellular pertussis; HPV9 = human papillomavirus (9 serotypes); rZV = herpes zoster vaccine.

- For children at high risk of pneumococcal disease, an additional dose of PCV13 is given at age 3 months.
- An alternative approved schedule for MenB given at 8 weeks (2 months), 4 months and 12 months is available.

All individuals aged from 5 years are eligible to receive two doses of a COVID-19 vaccine. Additional doses are also available to different groups

# Funded vaccines for special groups

As described in chapter 4, certain vaccines may be given in addition to or instead of the routine Schedule vaccines as part of an extended immunisation programme for special groups.

Vaccine	Individuals eligible for funded vaccine
Hib	Post-HSCT or chemotherapy; pre- or post-splenectomy or with functional asplenia; pre- or post-solid organ transplant (SOT), pre- or post-cochlear implants, renal dialysis and other severely immunosuppressive regimens. Testing for primary immune deficiency.
Hep A	Transplant patients. Children with chronic liver disease. Close contacts of hepatitis A cases.
HepB and HBIG	HepB and HBIG at birth for babies of mothers with chronic HBV infection. HepB for: household or sexual contacts of HBsAg-positive patients; children <18 years who have not achieved positive serology and who require additional vaccination; HIV- or hepatitis C-positive patients; following non-consensual sexual intercourse; following immunosuppression; SOT; post-HSCT; following needle-stick injury; dialysis and liver or kidney transplant.
HPV	Individuals aged 9–26 years: with confirmed HIV infection; transplant (including stem cell) patients; post-chemotherapy.
Influenza	Pregnant women. Individuals aged 6 months to <65 years with certain medical conditions.
MMR	For (re-)vaccination following immunosuppression.
MenC, MenACWY and MenB	Pre- or post-splenectomy or with functional asplenia; with HIV, complement deficiency (acquired or inherited) or pre- or post-SOT; close contacts of meningococcal cases; prior meningococcal disease (any group); HSCT patients; prior to planned immunosuppression; following immunosuppression.
Pertussis-containing vaccine	Tdap for pregnant women, recommended from 16 weeks' gestation of every pregnancy, preferably in the second trimester, but at least two weeks before birth. (Funded when given any time in second or third trimester.) Tdap is funded for parents or primary caregivers of infants admitted to a Neonatal Intensive Care Unit or Specialist Care Baby Unit for more than 3 days.  Tdap, DTaP-IPV-HepB/Hib or DTaP-IPV for (re-)vaccination: post-HSCT or chemotherapy; pre- or post-splenectomy; pre- or post-SOT, renal dialysis and other severely immunosuppressive regimens.
PCV13 and 23PPV	Children and adults with eligible conditions. PCV13 and 23PPV for testing for primary immune deficiency.
IPV	For (re-)vaccination following immunosuppression.
Tdap	For (re-)vaccination following immunosuppression; boosting of patients with tetanus-prone wounds; testing for primary immune deficiency.
BCG	Infants and children <5 years at increased risk of TB.
Varicella	Varicella non-immune patients: with chronic liver disease who may need a transplant in the future; with deteriorating renal function before transplant; prior to SOT; prior to elective immunosuppression; for post-exposure prophylaxis of immune-competent in-patients; HIV-positive with mild or moderate immunosuppression, on advice of their specialist. Patients at least 2 years after HSCT or at least 6 months after completion of chemotherapy, on advice of their specialist. Patients with inborn errors of metabolism at risk of major metabolic decompensation, with no clinical history of varicella. Household members with no clinical history of varicella: of paediatric patients who are immunocompromised or undergoing a procedure leading to immunocompromise; of adult patients who have no clinical history of varicella and who are severely immunocompromised or undergoing a procedure leading to immunocompromise.
Zoster	Individuals aged from 18 years who are pre/ post HSCT or cellular therapy; pre/post SOT; with haematological malignancies; with poorly controlled HIV infection; individuals with certain rheumatological diseases receiving DMARDs; with end-stage CKD 4 or 5; or primary immunodeficiencies.

For details by vaccine and special groups, see the most current IMAC factsheet '*Funded vaccines for special groups*' (available at [immune.org.nz/resources/factsheets](http://immune.org.nz/resources/factsheets)).

Also, see the Pharmaceutical Schedule ([pharmac.govt.nz](http://pharmac.govt.nz)) for the number of funded doses and any changes to the funding decisions.

# Introduction

The purpose of the *Immunisation Handbook 2024* (the *Handbook*) is to provide clinical guidelines for health professionals on the safest and most effective use of vaccines in their practice. These guidelines are based on the best scientific evidence available at the time of publication, from published and unpublished literature.

The information contained within the *Handbook* was correct at the time of publication. This edition of the *Handbook* will remain current unless amended electronically via the Health New Zealand | Te Whatu Ora website until the next edition or update is published.

## Changes to the *Handbook* since 2024

The following changes have been made for the 2024 edition.

- In the notifiable disease chapters, public health measures have been edited and where relevant referred to the Communicable Disease Control Manual website.
- Chapter 4 Immunisation of special groups – continues to be updated as funded indications change
- Chapter 5 Coronavirus disease (COVID-19) continues to be updated.
- Chapter 9 Hepatitis B, changes to non-responder protocol recommendations to give additional doses of HepB via intradermal administration
- Chapter 12 Measles, infants vaccinated given a first dose of MMR at the age of 11 months (ie from 11 months to under 12 months) are considered to have received MMR dose 1.
- Chapter 13 Meningococcal, access to broader protection for infants aged under 12 months.
- Chapter 14 Mpox – addition of new chapter
- Chapter 19 Respiratory syncytial virus - addition of new chapter
- Chapter 25 Zoster – eligibility for funded vaccine for certain special groups



# The National Immunisation Schedule

The National Immunisation Schedule (the Schedule) is the series of publicly funded vaccines available in New Zealand (see Table 1). Some vaccines are also offered as part of an extended immunisation programme for targeted special groups in response to a recognised need (see Table 2). See also section 2.1.7 for a summary of the primary immunisation requirements for adults (funded) and other funded and unfunded recommendations for this age group.

On 1 July 2012, the management and purchasing of vaccines transferred from the Ministry of Health to PHARMAC. All publicly funded vaccines are now listed on PHARMAC's Pharmaceutical Schedule (see [pharmac.govt.nz](https://www.pharmac.govt.nz)), and the districts are responsible for funding these once PHARMAC has listed them.

PHARMAC considers medicine and vaccine funding applications from pharmaceutical suppliers, health professionals, consumer groups and patients. Usually, manufacturers/suppliers decide whether to make an application for funding. Normally this will follow registration and approval of the medicine or vaccine by Medsafe. PHARMAC will generally only consider an application for a medicine or vaccine to be funded once it has been registered and approved by Medsafe.

Following a vaccine funding application, PHARMAC will assess the vaccine, seek clinical input (for vaccines this may be from the immunisation subcommittee of the Pharmacology and Therapeutics Advisory Committee [PTAC] or from PTAC itself), and conduct an economic analysis. The recommendations from the immunisation subcommittee are then considered by PTAC, which will provide advice to PHARMAC. PHARMAC then decides what priority the application has for funding and consults with Health New Zealand | Te Whatu Ora on capacity and implementation issues that may be associated with introducing a new vaccine. Depending on the outcome of that process, PHARMAC may then negotiate with the supplier. If an agreement is reached, PHARMAC will consult with the health sector on a funding proposal.

Health New Zealand | Te Whatu Ora remains responsible for and manages the National Immunisation Programme, which:

- aims to prevent disease through vaccination and to achieve coverage that prevents outbreaks and epidemics
- is accountable for achieving the Immunisation Coverage targets
- monitors disease burden and those at risk
- provides guidance to the sector on immunisation, cold chain and resources
- ensures immunisation providers deliver services that meet the needs of their population
- implements the National Immunisation Schedule
- delivers trusted and effective vaccine programmes
- provides immunisation resources, including the *Immunisation Handbook*
- improves information and data systems



- manages the Aotearoa Immunisation Register (AIR) (see section 2.3.5).

Health New Zealand | Te Whatu Ora works with PHARMAC to ensure there is a strong link between vaccine purchasing decisions and the management and implementation of the National Immunisation Programme.

Although funding decisions will be communicated to the sector, vaccinators are advised to regularly check the Pharmaceutical Schedule and any online updates (see [pharmac.govt.nz](https://www.pharmac.govt.nz)) for changes to funding decisions, and the *Handbook* for the latest immunisation information.

## Changes to the National Immunisation Schedule in 2024

Table 1 shows the 2024 National Immunisation Schedule, and Table 2 shows the vaccines funded for special groups at higher risk of some diseases.

Changes to vaccine funding in 2024 are as follows:

- The quadrivalent inactivated influenza vaccine (Influvac Tetra; see chapter 11 'Influenza') will be the Schedule vaccine for eligible individuals, including pregnant women and adults aged 65 years and older.

**Table 1: National Immunisation Schedule, commencing 1 October 2020 (revised 1 March 2023)**

Antigen(s)	DTaP-IPV-HepB/Hib	PCV13	MenB	RV1	MMR	Hib-PRP	VV	DTaP-IPV	Tdap	HPV9	Influenza	rZV
Brand	Infanrix-hexa	Prevenar 13	Bexsero	Rotarix	Priorix	Act-HIB	Varilrix	Infanrix-IPV	Boostrix	Gardasil 9	Influvac Tetra	Shingrix
Manufacturer	GSK	Pfizer	GSK	GSK	GSK	Sanofi	GSK	GSK	GSK	Seqirus / MSD	Viartis	GSK
Pregnancy									• <sup>a</sup>		•	
6 weeks	•	• <sup>b</sup>		•								
3 months	•		• <sup>c</sup>	•								
5 months	•	•	•									
12 months		•	•		•							
15 months					•	•	• <sup>d</sup>					
4 years								•				
11 or 12 years <sup>e</sup>									•	•		
										2 doses <sup>e</sup>		
45 years									• <sup>f</sup>			
65 years									•		•	•
											annually	2 doses

a. Tdap is for women during every pregnancy, from 16 weeks' gestation, preferably in the second trimester.

b. For infants at high risk of pneumococcal disease, an additional dose of PCV13 is given at age 3 months.

c. An alternative approved schedule for MenB can be offered at ages 8 weeks, 4 months and 12 months.

d. VV is funded for children born on or after 1 April 2016.

e. HPV is funded for individuals aged 26 years and under: 2 doses are recommended for individuals who receive the first dose before their 15th birthday, even if they are 15 years or older at the time of the second dose; 3 doses are recommended for those aged 9–26 years with certain medical conditions, plus an additional dose post-chemotherapy.

f. Funded for adults from 45 years who have not received 4 previous doses of tetanus vaccine

All individuals aged from 5 years are eligible to receive a primary course of a COVID-19 vaccine. Additional doses are also available to certain groups (see Chapter 5).

# Changes to extended immunisation programme for special groups

Vaccines funded for special groups are described in Table 2 below. Changes to existing programmes in 2024 are as follows.

- A single dose of meningococcal ACWY vaccine (MenACWY) and two doses of meningococcal B vaccine (MenB) are funded for individuals aged between 13 and 25 years entering or in their first year of living in boarding school hostels, tertiary education halls of residence, military barracks, youth justice residences or prisons. This includes children who turn 13 years while living in boarding school hostels.
- Meningococcal B vaccine (MenB) and quadrivalent meningococcal vaccine (MenACWY) are funded for certain special groups at increased risk of meningococcal disease, including those who have previously had meningococcal disease of any group. MenC vaccine has been replaced with MenACWY vaccine for certain infants aged 6 weeks to under 12 months.
- Zoster vaccine, certain individuals aged from 18 years with severe immunocompromise are eligible for funded vaccine.
- DTaP-IPV-HepB/Hib is funded for the revaccination of children up to age 18 years post-haematopoietic stem cell transplantation.

**Table 2: Extended immunisation programme for special groups – vaccines funded in addition to the routine schedule**

Note: Vaccinators are advised to regularly check the Pharmaceutical Schedule and any online updates ([pharmac.govt.nz](http://pharmac.govt.nz)) for changes to funding decisions for special groups. See also chapter 4 'Immunisation of special groups'.

Vaccine	Individuals eligible for funded vaccine
<i>Haemophilus influenzae</i> type b (Hib-PRP) (chapter 7)	<p>For (re)vaccination of patients who are:</p> <ul style="list-style-type: none"> <li>• post-haematopoietic stem cell transplant (HSCT) or chemotherapy</li> <li>• pre- or post-splenectomy or with functional asplenia</li> <li>• pre- or post-solid organ transplant</li> <li>• pre- or post-cochlear implants</li> <li>• undergoing renal dialysis and other severely immunosuppressive regimens</li> </ul> <p>For use in testing for primary immune deficiency<sup>a</sup></p>
Hepatitis A (HepA) (chapter 8)	<p>Transplant patients</p> <p>Children with chronic liver disease</p> <p>Close contacts of hepatitis A cases</p>
Hepatitis B (HepB) (chapter 9)	<p>Household or sexual contacts of patients with acute or chronic hepatitis B virus (HBV) infection</p> <p>Babies of mothers with chronic HBV infection need both hepatitis B vaccine (HepB) and hepatitis B immunoglobulin (HBIG) at birth</p> <p>Children aged under 18 years who have not achieved positive serology and who require additional vaccination</p> <p>HIV-positive patients</p> <p>Hepatitis C-positive patients</p> <p>Following non-consensual sexual intercourse</p> <p>Prior to any planned immunosuppression<sup>b</sup></p> <p>Patients following immunosuppression<sup>b</sup></p> <p>Solid organ transplant patients, including liver or kidney transplant</p> <p>Post-HSCT patients</p> <p>Following needle-stick injury</p> <p>Dialysis patients</p>
Human papillomavirus (HPV) (chapter 10)	<p>People aged 9 to 26 years inclusive who are:</p> <ul style="list-style-type: none"> <li>• confirmed with HIV infection</li> <li>• transplant (including stem cell) patients</li> <li>• post-chemotherapy</li> </ul>

*Continued overleaf*

Vaccine	Individuals eligible for funded vaccine
Annual influenza vaccine (chapter 11)	<p>Patients aged 6 months to &lt;65 years who:</p> <ul style="list-style-type: none"> <li>• have any of the following cardiovascular diseases: <ul style="list-style-type: none"> <li>– ischaemic heart disease</li> <li>– congestive heart failure</li> <li>– rheumatic heart disease</li> <li>– congenital heart disease</li> <li>– cerebrovascular disease</li> </ul> </li> <li>• have either of the following chronic respiratory diseases: <ul style="list-style-type: none"> <li>– asthma, if on a regular preventative therapy</li> <li>– other chronic respiratory disease with impaired lung function</li> </ul> </li> <li>• have diabetes</li> <li>• have chronic renal disease</li> <li>• have any cancer, excluding basal and squamous skin cancers if not invasive</li> <li>• have any of the following other conditions: <ul style="list-style-type: none"> <li>– autoimmune disease</li> <li>– immune suppression or immune deficiency</li> <li>– HIV</li> <li>– transplant recipients</li> <li>– neuromuscular and central nervous system diseases/disorders</li> <li>– haemoglobinopathies</li> <li>– are children on long-term aspirin</li> <li>– have a cochlear implant</li> <li>– errors of metabolism at risk of major metabolic decompensation</li> <li>– pre- and post-splenectomy</li> <li>– Down syndrome</li> </ul> </li> <li>• are pregnant</li> <li>• are children aged 4 years and under who have been hospitalised for respiratory illness or have a history of significant respiratory illness, including children age under 5 who were hospitalised with measles</li> <li>• are currently accessing secondary or tertiary mental health and addiction services</li> <li>• have any of the following serious mental health conditions: <ul style="list-style-type: none"> <li>– schizophrenia</li> <li>– major depressive disorder</li> <li>– bipolar disorder</li> <li>– schizoaffective disorder</li> </ul> </li> </ul>
Measles, mumps and rubella (MMR) (chapters 12, 14 and 21)	(Re)vaccination of patients prior to planned or following immunosuppression <sup>b</sup>

*Continued overleaf*

Vaccine	Individuals eligible for funded vaccine
Meningococcal conjugate quadrivalent vaccine (MenACWY) and meningococcal B vaccine (MenB) (chapter 13)	<ul style="list-style-type: none"> <li>• Pre- and post-splenectomy or with functional or anatomical asplenia</li> <li>• HIV</li> <li>• Complement deficiency (acquired or inherited)</li> <li>• Pre- or post-solid organ transplant</li> <li>• Close contacts of meningococcal case</li> <li>• HSCT (bone marrow transplant) patients</li> <li>• Prior to any planned immunosuppression<sup>b</sup></li> <li>• Following immunosuppression<sup>b</sup></li> <li>• Individuals who have had previous meningococcal disease (any group)</li> <li>• Individuals aged between 13 and 25 years entering or in their first year of living in boarding school hostels, tertiary education halls of residence, military barracks, youth justice residences or prisons. This includes children who turn 13 years while living in boarding school hostels.</li> </ul>
Pertussis-containing vaccines (chapter 16)	<p>Pregnant women – recommended to be given from 16 weeks' gestation of every pregnancy, preferably in the second trimester. (Funded when given any time in second or third trimester)</p> <p>Tdap is funded for parents or primary caregivers of infants admitted to a neonatal intensive care unit or special care baby unit for more than 3 days, who had not been exposed to maternal vaccination at least 14 days prior to birth</p> <p>(Re)vaccination of patients who are:</p> <ul style="list-style-type: none"> <li>• post-HSCT or chemotherapy</li> <li>• pre- or post-splenectomy</li> <li>• pre- or post-solid organ transplant</li> <li>• undergoing renal dialysis or other severely immunosuppressive regimens</li> </ul>

*Continued overleaf*

Vaccine	Individuals eligible for funded vaccine
13-valent pneumococcal conjugate vaccine (PCV13) and 23-valent pneumococcal polysaccharide vaccine (23PPV) (chapter 17)	<p>For (re)vaccination of high-risk children, PCV13 for patients aged under 5 years and 23PPV for patients aged under 18 years:</p> <ul style="list-style-type: none"> <li>• prior to planned or on immunosuppressive therapy or radiotherapy (vaccinate when there is expected to be a sufficient immune response)</li> <li>• with primary immune deficiencies</li> <li>• with HIV infection</li> <li>• with renal failure or nephrotic syndrome</li> <li>• who are immune-suppressed following organ transplantation (including HSCT)</li> <li>• with cochlear implants or intracranial shunts</li> <li>• with cerebrospinal fluid leak</li> <li>• receiving corticosteroid therapy for more than 2 weeks, and who are on an equivalent daily dosage of prednisone of 2 mg/kg per day or greater, or children who weigh more than 10 kg on a total daily dosage of 20 mg or greater</li> <li>• with chronic pulmonary disease (including asthma treated with high-dose corticosteroid therapy)</li> <li>• preterm infants, born before 28 weeks' gestation</li> <li>• with cardiac disease, with cyanosis or failure</li> <li>• with diabetes</li> <li>• with Down syndrome</li> <li>• who are pre- or post-splenectomy, or with functional asplenia</li> </ul> <p>PCV13 and 23PPV for (re)vaccination of patients aged 5 years and older:</p> <ul style="list-style-type: none"> <li>– with HIV infection</li> <li>– pre- or post-HSCT<sup>c</sup> or chemotherapy<sup>c</sup></li> <li>– pre- or post-splenectomy or with functional asplenia</li> <li>– pre- or post-solid organ transplant</li> <li>– undergoing renal dialysis</li> <li>– with complement deficiency (acquired or inherited)</li> <li>– with cochlear implants, intracranial shunts<sup>d</sup> or cerebrospinal fluid leaks<sup>d</sup></li> <li>– with primary immune deficiency</li> </ul> <p>PCV13 and 23PPV for use in testing for primary immune deficiency.<sup>a</sup></p>
Inactivated polio vaccine (IPV) (chapter 18)	(Re)vaccination of patients prior to planned or following immunosuppression <sup>b</sup>
Tetanus, diphtheria and pertussis (Tdap) (chapter 22)	(Re)vaccination of patients prior to planned or following immunosuppression <sup>b</sup> Boosting of patients with tetanus-prone wounds For use in testing for primary immune deficiency <sup>a</sup>
Bacillus Calmette–Guérin (BCG) (chapter 23)	For infants at increased risk of tuberculosis (TB): <ul style="list-style-type: none"> <li>• living in a house or family with a person with current or past history of TB; or</li> <li>• having one or more household members or carers who within the last 5 years lived in a country with a rate of TB <math>\geq 40</math> per 100,000 for 6 months or longer; or</li> <li>• who, during their first 5 years, will be living 3 months or longer in a country with a rate of TB <math>\geq 40</math> per 100,000</li> </ul>

Vaccine	Individuals eligible for funded vaccine
Varicella vaccine (VV) (chapter 24)	<p>Non-immune patients:</p> <ul style="list-style-type: none"> <li>• with chronic liver disease who may in future be candidates for transplantation</li> <li>• with deteriorating renal function before transplantation</li> <li>• prior to solid organ transplant</li> <li>• prior to any planned immunosuppression<sup>b</sup></li> <li>• for post-exposure prophylaxis of immune-competent hospital in-patients</li> </ul> <p>Patients at least 2 years after bone marrow transplantation, on advice of their specialist</p> <p>Patients at least 6 months after completion of chemotherapy, on advice of their specialist</p> <p>HIV-positive patients with mild or moderate immunosuppression who are non-immune to varicella, on advice of their HIV specialist</p> <p>Patients with inborn errors of metabolism at risk of major metabolic decompensation, with no clinical history of varicella</p> <p>Household members of paediatric patients who are immunocompromised, or undergoing a procedure leading to immunocompromise, where the household members has no clinical history of varicella</p> <p>Household members of adult patients who have no clinical history of varicella and who are severely immunocompromised or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella</p>
Zoster (rZV) (chapter 25)	<p>Individuals aged from 18 years, including those aged 66 years and over,</p> <ul style="list-style-type: none"> <li>• pre- and post-haematopoietic stem cell transplant or cellular therapy</li> <li>• pre- or post-solid organ transplant</li> <li>• with haematological malignancies</li> <li>• living with poorly controlled HIV infection</li> <li>• prior to planned or receiving disease-modifying anti-rheumatic drugs (DMARDs – targeted synthetic, biologic, or conventional synthetic) for polymyalgia rheumatica, systemic lupus erythematosus or rheumatoid arthritis</li> <li>• with end-stage kidney disease (CKD 4 or 5)</li> <li>• with primary immunodeficiency.</li> </ul>

- a. Upon the recommendation of an internal medicine physician or paediatrician.
- b. The period of immunosuppression due to steroid or other immunosuppressive therapy must be longer than 28 days.
- c. PCV13 is funded pre- or post-HSCT or chemotherapy. 23PPV is only funded post-HSCT or chemotherapy.
- d. Only PCV13 is funded for these indications; 23PPV is recommended but not funded.



# Eligibility for publicly funded vaccines

Only vaccines given according to the Schedule are available free of charge, unless there is a specific funded programme in response to a recognised need (see Table 2). The immunisation benefit is paid by districts to providers for the administration of:

- all childhood Schedule vaccines
- influenza vaccine to eligible children and adults (ie, those at higher risk of disease)
- zoster vaccine to individuals aged 65 years
- tetanus-diphtheria-pertussis (Tdap) boosters given at ages 45 and 65 years (now funded)
- hepatitis A, hepatitis B, Hib-PRP, human papillomavirus (HPV), inactivated polio vaccine (IPV), MMR, meningococcal conjugate, pertussis, pneumococcal conjugate and/or polysaccharide, varicella and zoster vaccines only, for eligible children and adults (ie, at higher risk of disease) as part of an extended immunisation programme for special groups.

The *Health and Disability Services Eligibility Direction 2011* (the Eligibility Direction) issued by the Minister of Health sets out the eligibility criteria for publicly funded health and disability services in New Zealand. Only people who meet the eligibility criteria defined in the Eligibility Direction can receive publicly funded (ie, free or subsidised) health and disability services.

Regardless of their immigration and citizenship status, all children aged under 18 years are eligible to receive Schedule vaccines, and providers can claim the immunisation benefit for administering the vaccines. All children are also eligible for Well Child Tamariki Ora services.

Non-residents who were aged under 18 years when they commenced HPV vaccination are currently funded to complete the course, even if they are aged 18 years or older when they complete it.

Further information on eligibility can be found on the Health New Zealand | Te Whatu Ora website ( <https://www.tewhatauora.govt.nz/our-health-system/eligibility-for-publicly-funded-health-services>).

As part of the COVID-19 pandemic response the preferred vaccine, mRNA-CV, is available for certain children aged 6 months to 4 years, all children aged from 5 years and all adults in New Zealand, regardless of eligibility for publicly funded health and disability services.

## Notifiable diseases

All diseases preventable by vaccines on the Schedule (or as part of a targeted programme) are notifiable, except for HPV, seasonal influenza, rotavirus, varicella and herpes zoster.

Note: Rotavirus infections presenting as gastroenteritis are notifiable as acute gastroenteritis.

It is a legal requirement (under the Health Act 1956) that health professionals notify their local Medical Officer of Health of any notifiable disease they suspect or diagnose so that appropriate action (eg, public health prevention and control activities) can be undertaken.

Notification processes, and the diseases to which they relate, have been updated in the Health Act and supporting Health (Infectious and Notifiable Diseases) Regulations 2016. See the Ministry of Health's 2017 document *Guidance on Infectious Disease Management under the Health Act 1956* (available at [www.health.govt.nz/publications/guidance-on-infectious-disease-management-under-the-health-act-1956](http://www.health.govt.nz/publications/guidance-on-infectious-disease-management-under-the-health-act-1956)) for an explanation, as well as the processes and forms for notifiable diseases.

The case definitions used by the medical officer of health to classify the notified case for surveillance purposes (and to assist in identifying appropriate prevention and control activities) and the laboratory tests required to confirm the diagnosis can be found in the *Communicable Disease Control Manual*. For the most up-to-date information, refer to the online version (available at <https://www.tewhātuora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/>).

# 1 General Immunisation principles

It is not necessary to have an in-depth knowledge of the immune system to understand the first principles of vaccinology. The immune system is an extremely complex inter-connected system, but understanding certain aspects involved in the process of inducing specific immunity through vaccination inform vaccination practice.

As protective immunity develops over time, the timing of vaccine doses, along with a basic understanding of the different types of vaccines, becomes important.

## 1.1 Immunity and immunisation

Immunity is the biological state of being able to resist disease or a toxin: the primary objective of vaccination is to induce an immunological memory against specific diseases, so that if exposure to a disease-causing pathogen occurs, the immune response will neutralise the infection or toxins it releases before disease can occur.

### 1.1.1 Immune recognition

One of the primary ways in which the immune system achieves elimination of pathogens and other unwanted foreign material is being able to distinguish 'self' from 'non-self'. Each cell in the body is equipped with a type of molecule that identifies the individual from any other, much like a 3D barcode. Pathogens not only lack the individual's 'self' marker, they also contain 'virulence factors' that alert the immune system to danger.

Antigens (*antibody generators*) are the drivers of the specific immune response. Antigens are molecular shapes, such as part of a protein or glycoprotein, that the immune system recognises as foreign and can trigger an adaptive immune response. While some vaccines contain the entire weakened or attenuated organism (live viral vaccines like measles, mumps and rubella vaccines), increasingly, newer vaccines contain purified or recombinant protein antigens (as in acellular pertussis, HPV or pneumococcal vaccines).

The first process that occurs when a foreign antigen, such as a vaccine antigen, is introduced to the body is the recognition that the antigen is non-self by triggering an inflammatory response. The antigen is taken up at the local site (such as the injection site) by specialist phagocytic cells called antigen-presenting cells – macrophages and dendritic cells. Once inside the antigen-presenting cells, the foreign protein (or microbe) is dismantled into tiny fragments that are displayed on cell surface alongside a 'self' molecule. These antigen-presenting cells carry the antigen to through the lymph to the local lymph node where the adaptive immune response is initiated.

## 1.1.2 Induction of the adaptive immune response

The response that occurs the first time an antigen is 'seen' by the immune system is called the primary immune response.

The adaptive immune responses occur in lymphoid tissue, primarily in the spleen and in the 500–600 lymph nodes distributed throughout the body.

The adaptive immune response to most vaccines occurs at the draining lymph node proximal to the site of injection. The spleen and lymph nodes are densely populated with important effector lymphocytes of the immune response: T-cells and B-cells. In the lymph node, the vaccine antigen is presented to the specific T-cells and B-cells.

Among the trillions of specific T and B lymphocytes (there are  $\sim 10^{16}$  possibilities), there usually exists a match for the antigen. Cells that recognise the antigen are activated through communication with the antigen presenting cell and the primary immune response can be initiated. This process and the response matures over a period of four to six weeks.

An early outcome of the interaction between these antigen-presenting cells and T and B lymphocytes is the production of antibody-producing B-cells. Antibody can be measured in the blood as soon as 4–7 days after this interaction, but is usually more effectively measured weeks to months later. Initially, this is low in quantity and of low affinity for the antigen (it binds weakly to the antigen), and primarily consists of the antibody subtype immunoglobulin M (IgM), often referred to as 'early antibody'. It peaks at around 10 days then declines relatively quickly (see Figure 1.1).

For most vaccine-preventable diseases this process is too slow following infection, and disease occurs before an effective immune response can be mounted. Injecting a part or a weakened version of the pathogen in the form of a vaccine, readies the immune system so that it can mount a more rapid and effective response when the wild disease is encountered.

## 1.1.3 Development of immune memory and the secondary response

The response that occurs the second time an antigen is 'seen' by the immune system is called the secondary immune response.

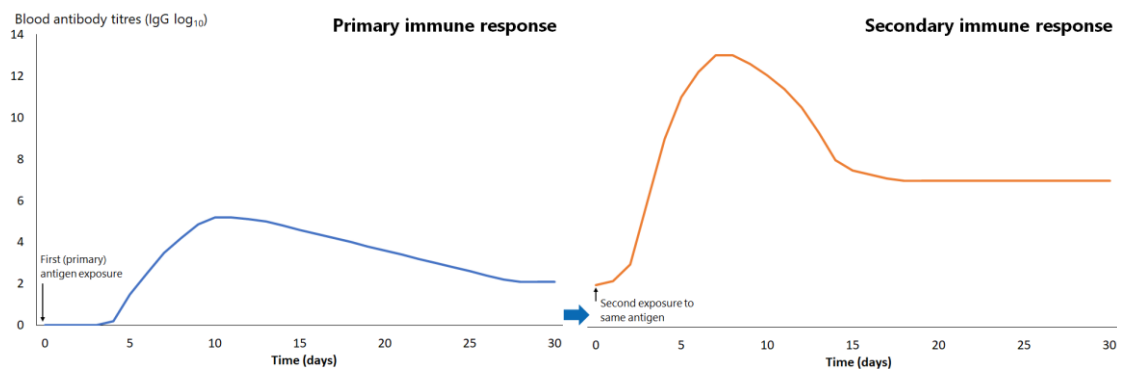
During the primary immune response, over a period of around two months, cells that are less specific for the specific antigen are deleted, and those that are highly specific are retained and multiply within the lymph node. Antibody production also switches from IgM to more specific IgG or IgA subtypes. During this time immunological memory cells also develop, but it takes around four months, after the initial antigen is cleared, to fully form immune memory.

The next time the same antigen is introduced, either as a pathogen component or as a further dose of vaccine, the immunological memory cells that recognise it will be activated and begin to proliferate. Highly specific antibody (primarily of the IgG subtype, but also IgA) is rapidly produced in large amounts. The lag phase is much shorter than the primary immune response (see Figure 1.1), at just 1–4 days; the antibody level peaks very quickly and lasts much longer.

The immune system has been readied by the vaccine; if the actual disease pathogen enters the body, then it is recognised promptly and neutralised by the immune system preventing it from causing disease.

### Figure 1.1: Comparison of primary and secondary immune responses to protein-containing vaccines

Secondary responses are faster (peaking at day 7) than the primary immune response and the antibody titres are higher, more prolonged and of higher neutralising capacity.

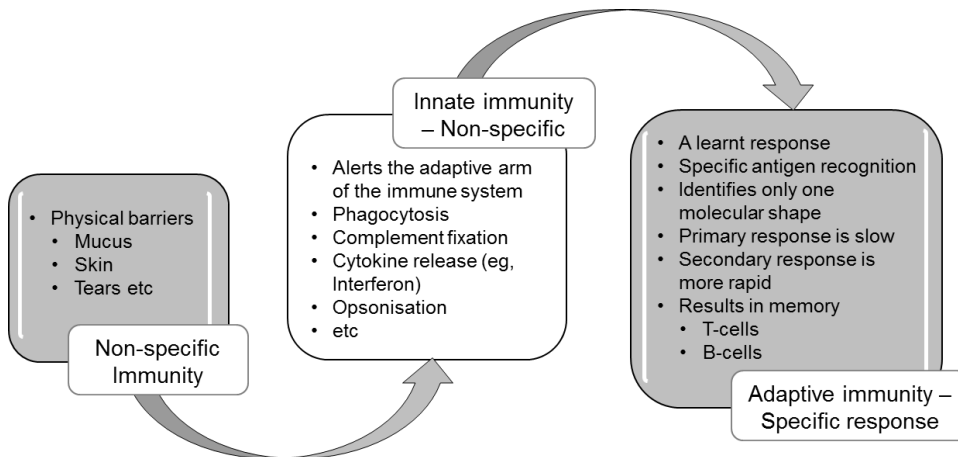


## Innate immunity

Most infectious microbes (also known as micro-organisms) are prevented from entering the body by barriers such as skin, mucosa, cilia and a range of anti-microbial enzymes. Any microbes that breach these surface barriers are then attacked by other components of the innate immune system, such as polymorphonuclear leucocytes (neutrophils), macrophages and complement.

This innate immune response is a pre-programmed non-specific response that does not involve learnt or adaptive mechanisms. The cells and proteins of the innate immune system can recognise common microbial markers or virulence factors and can kill microbes without the need for prior exposure. The chemical messages (cytokines) and cells of the innate immune system also interact with the cells of the adaptive immune system (eg, lymphocytes) to induce a cascade of events that leads to adaptive, antigen-specific immunity and immune memory, as summarised in Figure 1.2.

**Figure 1.2: Summary of non-specific innate and adaptive (specific) immunity**



## 1.1.4 Acquisition of adaptive immunity

Specific immunity can be actively produced by directly responding to an antigen. This is termed adaptive or learnt immunity, in which the immune system learns to respond to specific antigens. Passive immunity is provided by transferring antibody from an immune person to temporarily protect another.

### Naturally acquired immunity

Naturally acquired immunity occurs either actively by experiencing the infection or passively through the transfer of maternal antibodies from mother to fetus or infant (transplacentally or in breastmilk).

### Artificially acquired immunity

'Artificially' acquired immunity occurs either actively through vaccination or passively through administration of immunoglobulin (IG) (see Appendix 6).

While actively acquired immunity lasts from years to life, passively acquired immunity lasts from weeks to months as the transferred antibodies decay and are not renewed.

## 1.1.5 Maternally derived immunity

The passive transfer of antibody from mother to fetus provides an opportunity to provide protection to the neonate against several diseases before they are old enough to be vaccinated themselves. Maternal vaccination boosts the immunity of the mother, inducing high levels of maternal antibody. This antibody is actively transported across the placenta to concentrate at protective levels by birth (in term infants).

Important diseases that maternal vaccination is effective at preventing include neonatal tetanus, influenza and pertussis in the infant for the first weeks or months of life (see section 4.1 and the relevant disease chapters).

## 1.1.6 Summary

- Successful immune responses occur following the recognition of, and appropriate response to, a foreign antigen.
- Specialised but non-specific cells, called antigen-presenting cells, take up, transport and present the vaccine antigen to antigen-specific T-cells and B-cells within the lymph nodes and spleen.
- The first wave of antibodies produced are short lived and of low affinity.
- Immune memory takes at least four months to fully develop, but the antibody and memory cells that arise are of high affinity.
- Immune memory can be boosted. This is called a secondary immune response.
- Adaptive immunity is learnt and acquired actively through disease or vaccination.
- Passive immunity is acquired through maternal transfer and administration of IG.
- Maternal vaccination offers passive protection to infants for the first weeks or months of life.

## 1.2 From personal protection to community (herd) immunity

By protecting individuals, vaccination can also protect the wider community. This herd immunity occurs when the vaccine coverage is high, meaning an infectious case is unlikely to encounter susceptible contacts, so transmission stops.

The whole population benefits when a vaccine prevents carriage and transmission of a human-only pathogen, such as polio virus, measles virus or *Streptococcus pneumoniae*, and circulation of these pathogens can be reduced and even eliminated. This phenomenon, called herd or community immunity, can prevent infections spreading and therefore protect vulnerable members of the population, such as the very young, the very old, or those with underlying conditions that increase their risk from infectious diseases (ie, the immunocompromised). These individuals may not themselves be able to receive some vaccines (eg, live vaccines) or may not mount a sufficiently effective immune response to other vaccines.

The population benefits depend on the disease itself, the nature of the vaccine and the proportion or target group of the population needed to be immunised to prevent the disease from spreading. A recent example of herd immunity in New Zealand is the significant reduction in rotavirus hospital discharge rates in children aged under 5 years following the July 2014 introduction of rotavirus vaccine for infants (see section 20.3.2).

### 1.2.1 Reproduction number and herd immunity threshold

A measure of the infectiousness of a disease is the basic reproduction number ( $R_0$ ). This is the number of secondary cases generated by a typical infectious individual when the rest of the population is susceptible. In other words,  $R_0$  describes the spreading potential of an infection in a population.<sup>1</sup> Measles is one of the most infectious diseases, with an  $R_0$  of 12–18 (Table 1.1). In other words, one person with measles is likely to infect up to 18 other susceptible people. Pertussis is similarly infectious.

If a significant proportion of the population are immune, then the chain of disease transmission is likely to be disrupted. The herd immunity threshold (H) is the proportion of immune individuals in a population that must be exceeded to prevent disease transmission. For example, to prevent measles or pertussis transmission, 92–94 percent of the population must be immune (Table 1.1).



$R_0$  must remain above 1 for an infection to continue to exist. Once  $R_0$  drops below 1 (such as in the presence of an effective vaccination programme), the disease can be eliminated. The greater the proportion of the population that is immune to the infection, the lower the  $R_0$  will be. For example, data<sup>2</sup> indicates that a quadrivalent HPV vaccine programme with 70 percent coverage in young women may lead to the near disappearance of genital warts from the heterosexual population because the  $R_0$  for HPV types 6 and 11 (causing genital warts) falls to below 1 (see 'Herd immunity and population impact' in section 10.4.2).

**Table 1.1: Approximate basic reproduction numbers (in developed countries) and implied crude herd immunity thresholds<sup>a</sup> for common vaccine-preventable diseases<sup>b</sup>**

Infection	Basic reproduction number ( $R_0$ )	Crude herd immunity threshold, H (%)
Diphtheria	6–7	83–85
Influenza <sup>c</sup>	1.4–4	30–75
Measles	12–18	92–94
Mumps	4–7	75–86
Pertussis	5–17	80–94
Polio <sup>d</sup>	2–20	50–95
Rubella	6–7	83–85
Varicella	8–10	Not defined

Notes

- The herd immunity threshold (H) is calculated as  $1 - 1/R_0$ .
- The values given in this table are approximate: they do not properly reflect the range and diversity among populations, nor do they reflect the full immunological complexity underlying the epidemiology and persistence of these infections.
- The  $R_0$  of influenza viruses varies among subtypes.
- This is complicated by uncertainties over immunity to infection and variation related to hygiene standards.

Adapted from: Fine P, Mulholland K, Scott J, et al. 2018. Community Protection. In: Plotkin S, Orenstein W, Offit P, et al (eds). *Plotkin's Vaccines (7th edition)*. Philadelphia, US: Elsevier. Table 77.2.

## 1.2.2 Summary

- Not only do vaccines provide individual protection, but for many of the diseases we vaccinate against, there is also a population effect called herd/community immunity.
- Some diseases are extremely infectious and require a very high proportion of the community to be immune to prevent transmission (particularly measles and pertussis).

## 1.3 The importance of immunisation coverage

High immunisation coverage means more individuals are protected; it is also vital for achieving herd immunity. High coverage reduces the spread of disease to those who have not been vaccinated for medical reasons (eg, children with leukaemia while receiving treatment) or because of age (eg, infants who are too young to respond to some vaccines). High coverage also reduces the spread of disease to those who may not mount an effective immune response to vaccines because of an underlying condition (eg, those on immunosuppressive regimes).

The World Health Organization (WHO) and the New Zealand government target for immunisation coverage (since 2017/18) is for at least 95 percent of children to be fully vaccinated by age 2 years. The New Zealand target includes a marker for on-time immunisation of 95 percent by age 8 months, as well as at ages 2 years and 5 years.

This target is based on the need for:

- on-time immunisation coverage, particularly three doses of pertussis-containing vaccine for infants in the primary series and the first dose of measles vaccine at age 12 months
- achieving high herd immunity, particularly to prevent measles transmission.

For the three months ending 31 March 2020, 91 percent of New Zealand children were fully immunised by age 8 months and 92 percent were fully immunised by age 2 years. Up-to-date national and district immunisation coverage data is available at the Health New Zealand | Te Whatu Ora website (<https://www.tewhatoru.govt.nz/for-the-health-sector/vaccine-information/immunisation-coverage/>).

## 1.4 Classification of vaccines

There are two broad categories of vaccine type: live attenuated (weakened) and non-live, which includes inactivated or whole killed, subunit and nucleic acid vaccines. Examples of the different types of vaccines are summarised in Table 1.2.

**Table 1.2: Classification of vaccines, with examples**

Live attenuated	Non-live Inactivated or whole killed	Subunit	Nucleic acid	Non-replicating viral vector
Measles	Poliomyelitis (IPV)	Toxoid:	COVID-19 (mRNA-CV)	COVID-19 (Ad26-CV and ChAd-CV)
Mumps	Hepatitis A	<ul style="list-style-type: none"> <li>diphtheria</li> <li>tetanus</li> </ul>		
Rubella	Some influenza vaccines	Polysaccharide:		
Varicella		<ul style="list-style-type: none"> <li>pneumococcal (23-valent)</li> </ul>		
Rotavirus		Conjugate:		
Tuberculosis (BCG)		<ul style="list-style-type: none"> <li>pneumococcal (10- and 13-valent)</li> <li><i>Haemophilus influenzae</i> type b</li> <li>meningococcal C and ACWY</li> </ul>		
Zoster		Recombinant:		
		<ul style="list-style-type: none"> <li>COVID-19 (rCV)</li> <li>hepatitis B</li> <li>human papillomavirus</li> <li>meningococcal B</li> <li>zoster (rZV)</li> </ul>		
		Other subunit:		
		<ul style="list-style-type: none"> <li>pertussis, acellular</li> <li>influenza</li> </ul>		

Note: Travel vaccines have been omitted from the above table.

## 1.4.1 Live attenuated vaccines

Live vaccines contain pathogens, usually viruses, which have been weakened (attenuated) so that they are able to replicate enough to induce an immune response but not cause disease. Immunity from live vaccines is usually very long-lived. The live vaccines on the National Immunisation Schedule are MMR, varicella, BCG and rotavirus vaccines.

## 1.4.2 Non-live vaccines: Whole killed and inactivated vaccines

Killed vaccines contain whole bacteria that have been killed. The whole-cell pertussis vaccine is an example of a killed vaccine. There are no killed vaccines on the Schedule.

Inactivated vaccines contain viruses that have been inactivated in some way, such as splitting, so they are unable to replicate or cause disease. Examples of inactivated vaccines are influenza, hepatitis A and polio vaccines.

## 1.4.3 Non-live vaccines: Subunit vaccines

Subunit vaccines contain microbial fragments or particles that can induce an immune response which protects against disease. These are produced using a range of methods including recombinant engineering, detoxification processes and splitting and purification.

### Toxoid vaccines

In some bacterial infections (eg, diphtheria and tetanus), the clinical manifestations of disease are caused not by the bacteria themselves but by the toxins they secrete. Toxoid vaccines are produced by harvesting a toxin and altering it chemically (usually with formaldehyde) to convert the toxin to a toxoid. The toxoid is then purified. Toxoid vaccines induce antibodies that neutralise the harmful exotoxins released from these bacteria.

### Recombinant vaccines

Recombinant vaccines, such as those used against COVID-19 (rCV), hepatitis B virus (HBV) and human papillomavirus (HPV), are made using a gene from the (disease-causing) pathogen. The gene is inserted into a cell system capable of producing large amounts of the protein of interest. The protein produced can generate a protective immune response. For example, the gene for the hepatitis B surface antigen (HBsAg) is inserted into yeast cells, which replicate and produce large amounts of HBsAg. This antigen is purified and used to make vaccine. The advantage of this approach is that it results in a very pure vaccine that is efficient to produce.

### Polysaccharide and conjugate vaccines

Polysaccharides are strings of sugars. Some bacteria, such as *Streptococcus pneumoniae* and *Neisseria meningitidis*, have large amounts of polysaccharide on their surface, which encapsulate the bacteria. The polysaccharide capsules protect the bacteria from the host's immune system and can make the bacteria more virulent. Historically, it has been difficult to stimulate an effective immune response to these polysaccharide capsules using vaccines, particularly in children aged under 2 years.

First-generation capsular polysaccharide vaccines contained antigens isolated from the different polysaccharide capsules (eg, 23PPV, see chapter 17). Polysaccharide vaccines

are poorly immunogenic, and they only induce a primary immune response. They produce low affinity antibodies (which do not bind well to the antigen) and, because they do not elicit T-cell responses, immune memory is not strong. Multiple priming doses (even a single dose) can cause hyporesponsiveness in both children and adults to further doses. There is also concern that repeated doses could result in 'clonal deletion' where the specific B-cell pool becomes depleted due to successive primary responses.

Polysaccharide conjugate vaccines (eg, Hib-PRP, PCV13 and MenACWY) contain carrier proteins that are chemically attached to the polysaccharide antigens. Attaching relatively non-immunogenic polysaccharides to the highly immunogenic carrier proteins results in activation of a T-cell response; in this way, conjugate vaccines induce both high-affinity antibodies against the polysaccharide antigens, and immune memory, and can be used in infants.

Examples of carrier proteins and vaccines that use them are:

- tetanus toxoid, used in *Haemophilus influenzae* type B vaccine (Hib-PRP) and meningococcal ACWY (MenACWY; MenQuadfi)
- a non-toxic recombinant variant of diphtheria toxin (CRM197), used in the 13-valent pneumococcal conjugate vaccine (PCV13; Prevenar 13)

These conjugate vaccines are limited by the number of polysaccharides that can be covalently linked to the carrier molecule, so there is still a role for polysaccharide vaccines to broaden the number of serotypes recognised. For example, PCV13 has 13 serotypes, compared to 23PPV with 23 serotypes. Polysaccharide vaccines are expected to be phased out eventually with improvements to conjugate vaccine technology and other vaccine technologies.

## Principles and implications for using polysaccharide and conjugate vaccines

- Because of their improved immune response, where possible use polysaccharide-protein conjugate vaccines in preference to polysaccharide-only vaccines.
- To ensure broad protection against disease, use a conjugate vaccine to prime the immune system before using the polysaccharide vaccine to increase the number of serotypes recognised. For example, high-risk children are primed with PCV13 then boosted with 23PPV (see section 17.5.2).
- To avoid or minimise hyporesponsiveness, individuals should have a maximum of three lifetime doses of polysaccharide vaccine.
- Children aged under 2 years should not receive polysaccharide vaccines as they are likely to be ineffective in young children.

### 1.4.4 Non-live vaccines: Nucleic acid vaccines

Recent developments in vaccine technology have allowed the use of messenger ribonucleic acid (mRNA) to deliver the genetic code to our dendritic cells make specific

viral proteins. Since mRNA is easily destroyed by ubiquitous ribonuclease enzymes, it is protected inside a lipid nanoparticle that also facilitates uptake by the dendritic cells. Inside the dendritic cell, ribosomes and vaccine mRNA generate the viral protein which is then presented to the T and B cells in the lymph nodes. For example, the mRNA COVID-19 vaccine (mRNA-CV) provides the instructions to make the SARS-CoV-2 virus spike protein and induces an effective humoral and cellular immune responses against this virus.

### 1.4.5 Non-live vaccines: Non-replicating viral vector vaccines

Another recent development in vaccine design is the use of adenoviruses as a vector to deliver the instructions to human cells to make antigens. The adenovirus is genetically modified to be unable to replicate (non-replicating or replication deficient), and as such are non-live vaccines, but can deliver its double-stranded DNA into the cell's nucleus as would normally occur during an adenovirus infection. The viral DNA contains a transgene, a portion that codes for the target antigen protein. Only this portion of the viral DNA can be expressed, thus preventing the vector from reproducing. The presence of the adenovirus triggers an immune response killing the infected cell and thereby releasing the new protein (antigen) to activate a specific immune response. For example, ChAdOx1 vector COVID-19 vaccine (ChAd-CV) uses a chimpanzee adenovirus and the Ad26 vector COVID-19 vaccine (Ad26-CV) uses a human adenovirus (Ad26) to produce SARS-CoV-2 spike proteins.

### 1.4.6 Summary

- Vaccines introduce antigens to the immune system in the form of live and non-live vaccines.
- Non-live vaccines include killed/inactivated, subunit or nucleic acid vaccines.
- Polysaccharide vaccines do not induce immune memory and have been associated with hyporesponsiveness to later doses. Polysaccharide conjugate vaccines overcome these problems.
- Nucleic acid vaccines and viral vector vaccines provide the instructions for our own cells to make the target antigen.

## 1.5 Vaccine ingredients

In addition to the antigen, a vaccine may contain a range of other substances; for example, an immune enhancer (adjuvant) and/or a preservative. Traces of residual components from the manufacturing process may also be present in the vaccine. For further information on vaccine content, see the vaccine sections within the disease chapters of this *Handbook*.

## 1.5.1 Adjuvants

Adjuvants are substances that enhance the immune response to an antigen through a range of mechanisms, including improving the delivery of the antigen to the innate immune system and to the lymphoid organs. Use of adjuvants also means that less antigen, which can be difficult to produce, is needed (this is called antigen sparing).

Adjuvants licensed for human use include aluminium salts (eg, aluminium hydroxide and aluminium phosphate), oil-in-water emulsions (MF59, Seqirus; AS03, GSK), saponin-based liposomal suspension (AS01<sub>B</sub>, GSK; Matrix-M, Novavax) and a bacterial endotoxin (AS04, GSK). Most non-live vaccines require an adjuvant, and most vaccines still use aluminium adjuvants. The amount of aluminium contained in a vaccine is very small compared with that present in our daily intake from food and water, including breastmilk.

## 1.5.2 Preservatives

Preservatives prevent the contamination of vaccines, particularly in multi-dose vials. 2-phenoxyethanol is an example of a preservative used in some vaccines. It is also used in many cosmetics and baby care products. Many vaccines do not contain a preservative. Mercury-based preservatives (thiomersal/thimerosal) are not used in vaccines on the New Zealand National Immunisation Schedule, and multi-dose vials are not used for Schedule vaccinations.

## 1.5.3 Stabilisers

Stabilisers protect the vaccine from adverse conditions (such as exposure to heat), inhibit chemical reactions and prevent components from separating. Examples include sucrose, lactose, albumin, gelatin, glycine and monosodium glutamate (MSG).

## 1.5.4 Surfactants/emulsifiers

These are wetting agents that alter the surface tension of a liquid, like a detergent does. Surfactants assist particles to remain suspended in liquid, preventing settling and clumping. One commonly used surfactant is polysorbate 80, made from sorbitol (sugar alcohol) and oleic acid (an omega fatty acid). It is also commonly used in foods such as ice-cream.

## 1.5.5 Residuals

Residuals are traces of substances that remain in the vaccine as an inevitable consequence of the manufacturing process. Regulatory bodies vary as to which trace substances must be specified. Residuals may include virus-inactivating agents (such as



formaldehyde), antibiotics and other substances used in the manufacturing process, such as ovalbumin (an egg protein) and gelatin.

## 1.6 Safety monitoring of vaccines in New Zealand

### 1.6.1 The approval of vaccines for use in New Zealand

Vaccines, like all medicines, have benefits and risks of harm. Before a medicine or vaccine is approved for use, it must be tested in a series of clinical trials to determine its immunogenicity, efficacy and safety profile. The data from these trials is assessed and scrutinised by regulatory authorities, such as Medsafe in New Zealand, the European Medicines Agency and the Food and Drug Administration in the US, before the medicine or vaccine is approved for use.

Known information about each medicine and vaccine is published for health professionals in a manufacturer's data sheet, available on the Medsafe website ([medsafe.govt.nz](https://www.medsafe.govt.nz)). Consumer medicine information is usually also published.

Once the vaccine is used widely (ie, outside of the clinical trials), more information is collected on its safety profile and effectiveness. Some adverse reactions are rare and may not be seen until a very large number (thousands or even millions) of people have received the medicine or vaccine. This is one of the reasons why it is important to monitor all medicines and vaccines after they have been approved (registered). Note that some vaccines that are approved for use by Medsafe may not have been made available for distribution by the manufacturer or supplier.

Most countries (including New Zealand) have a safety monitoring system, which includes a voluntary spontaneous reporting scheme, to help identify any possible safety concerns. These reporting systems feed into the WHO Collaborating Centre for International Drug Monitoring, called the Uppsala Monitoring Centre in Sweden. This means that international data, often covering millions of doses, is available for Medsafe, which is the medicines regulator responsible for monitoring information to ensure that approved vaccines remain acceptably safe for use in New Zealand. Vaccine safety is never reviewed in isolation from the expected benefits of the vaccine; it is always looked at in terms of the risk–benefit balance.

In addition, the WHO plays an important role in monitoring vaccine safety through its Strategic Advisory Group of Experts on Immunization and the Global Advisory Committee on Vaccine Safety.



## 1.6.2 The New Zealand spontaneous reporting scheme

Two terms are used to describe spontaneous reports in the context of vaccination. *Adverse events* are undesirable events experienced by a person, which may or may not be causally associated with the vaccine. *Adverse reactions* are undesirable effects resulting from medicines or vaccines (ie, they are causally associated).

Spontaneous reports are case reports of adverse events that people have experienced while or after taking a medicine or having a vaccine. Medsafe contracts the collection, review and analysis of this information to the New Zealand Pharmacovigilance Centre at the University of Otago in Dunedin.

Health care professionals and consumers are encouraged to report adverse events following immunisation (AEFIs) to the Centre for Adverse Reactions Monitoring (CARM), which is part of the New Zealand Pharmacovigilance Centre. Pharmaceutical companies also submit adverse event reports.

Further information about suspected adverse reactions (and events following immunisation) reported in New Zealand can be found in the *Suspected Medicine Adverse Reaction Search* on the Medsafe website ([www.medsafe.govt.nz/safety/safety-monitoring.asp](http://www.medsafe.govt.nz/safety/safety-monitoring.asp)). See below for details about how to report to CARM and what information should be reported.

## 1.6.3 AEFI reporting process – notifying CARM

When obtaining consent for immunisation, vaccinators should also seek consent to report any adverse events that may occur, because AEFI reporting is considered part of immunisation programme quality control monitoring and public safety.

### How to report to CARM

Adverse events may be reported to CARM through:

- the electronic adverse reaction reporting tool available in practice management software programmes
- online reporting at <https://pophealth.my.site.com/carmreportnz/s/>

For support with completing a CARM report please call: 0800 400569.

To submit a clinical document or if enquiring about a submitted report, please send an email to: [CARMreport@health.govt.nz](mailto:CARMreport@health.govt.nz)

In terms of guidance, the sort of information the reporting form generally requires is a patient identifier (gender, age, initial), a medicine, a reaction and the reporter's contact details.

This information can also be accessed from the Medsafe website (revised 28 August 2023; [www.medsafe.govt.nz/safety/report-a-problem.asp](http://www.medsafe.govt.nz/safety/report-a-problem.asp)).

## What should be reported?

Health professionals/vaccinators should report:

- all serious suspected AEFI and other reactions of clinical concern to established vaccines, such as those described in Table 1.3 below. The AEFIs should be reported regardless of whether they consider the event to have been caused by the vaccination, and they should still be reported even if the effect is well recognised
- all suspected adverse reactions (including minor reactions) to newly introduced vaccines, or those being used for new indications or being delivered by a different route.

Individuals or parents/guardians should be encouraged to notify vaccinators of any AEFI that they consider may have been caused by the vaccination. Alternatively, individuals or parents/guardians may wish to notify CARM themselves, or they can contact their general practice or the Immunisation Advisory Centre (IMAC) on 0800 IMMUNE/0800 466 863 to help with notification.

**If in doubt, report it.**

**Table 1.3: Examples of AEFIs to be reported**

Timeframe	Event
<b>All vaccines</b>	
Within 24 hours of vaccination	Anaphylactic reaction (acute hypersensitivity reaction) Anaphylaxis Persistent inconsolable screaming (more than 3 hours) Hypotonic-hyporesponsive episode Fever >40°C
Within 5 days of vaccination	Severe local reaction Sepsis Injection-site abscess
Within 12 days of vaccination	Seizures, including febrile seizures Encephalopathy
Within 3 months of vaccination	Acute flaccid paralysis* (AFP), including Guillain–Barré syndrome (GBS) Brachial neuritis (can occur around 2–28 days after tetanus-containing vaccine) Thrombocytopenia (can occur around 15–35 days after MMR)
Between 1 and 12 months after BCG vaccination	Lymphadenitis Disseminated BCG infection Osteitis/osteomyelitis
No time limit	Intussusception after rotavirus vaccine Any death, hospitalisation or other severe or unusual events of clinical concern that are thought by health professionals or the public to possibly be related to vaccination

*Continued overleaf*

### **Newly introduced vaccines, or those with new indications or being delivered by a different route**

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No time limit	All suspected adverse reactions
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\* AFP in children is also monitored by the New Zealand Paediatric Surveillance Unit as part of polio eradication surveillance (see chapter 18).

## Seriousness of AEFIs

Reports of suspected adverse reactions or AEFIs can be categorised as serious or non-serious. This categorisation system is a tool used to try and prioritise safety concerns. It is not a reflection of the importance of the events to the consumer or their health care professional. Because a report is defined as serious based on what is reported, it is possible to have both serious and non-serious cases reporting the same type of event; for example, headache.

International convention defines the seriousness of reports based on the outcome or nature of the reported event as documented in the report, *irrespective of whether there is any association to the medicine or vaccine*.

Serious events are based on the following international criteria:

- hospitalisation (or prolonged hospitalisation) of the patient
- life-threatening event
- persisting disability of the patient
- intervention required to prevent permanent impairment
- congenital anomaly
- death of the patient.

## CARM assessment of causality

The WHO recommends that individual reports of adverse reactions to vaccines are assessed for causality. This assessment is a tool used to help detect new safety concerns; it is not a determination of whether a vaccine caused an adverse reaction.

The person reporting the event will receive a letter of response from CARM commenting on the adverse effect, the causal relationship and the number of other similar events, and advice about future use of the vaccine in the individual. Also, where applicable, CARM will provide a validated AEFI code to the AIR.

The information provided by CARM:

- needs to be communicated to the individual and parent/guardian (if applicable)
- must be entered in the medical notes
- will help to identify those individuals who should receive follow-up vaccination in a controlled environment, such as a hospital.

## 1.6.4 What does Medsafe do with this information?

Medsafe and CARM analyse spontaneous reports in conjunction with other information to determine whether there are any new potential safety signals. Medsafe seeks the advice of independent experts through the Medicines Adverse Reactions Committee or may form working groups of experts to provide advice. Medsafe works closely with other regulatory authorities from around the world.

Medsafe undertakes a risk–benefit assessment of safety signals to decide if action is required. Further information on risk–benefit assessment is provided on the Medsafe website ([www.medsafe.govt.nz/Consumers/Safety-of-Medicines/Medsafe-Evaluation-Process.asp](http://www.medsafe.govt.nz/Consumers/Safety-of-Medicines/Medsafe-Evaluation-Process.asp)).

Most safety signals are not supported by any additional information, and no action is taken, although Medsafe may continue to monitor the issue closely. A small number of possible safety signals are confirmed as real. In these cases, Medsafe has several regulatory actions it can take, including withdrawing the product.

In New Zealand, it is less likely that any rare new side-effects to vaccines will be detected because of the small number of people immunised compared to other countries. Therefore, Medsafe uses international data available from the WHO, other regulators and pharmaceutical companies to help assess any reports of rare events following immunisation and to determine if they may be new events linked to immunisation.

## 1.6.5 Advantages and limitations of spontaneous reports

Spontaneous reports have been shown to be a very simple way of identifying potential or possible safety signals with medicines, and over 90 countries have a spontaneous reporting system. They can be used to monitor the safety of medicines in real-life use over the lifetime of the medicine, and for all types of people.

The limitations of using spontaneous reports include under-reporting, a lack of reliable information on the extent of use of the medicine and wide variations in the clinical details provided about the event and the history of the patient. Spontaneous reports are heavily subject to reporting bias, such as media or other attention on an issue. They are also not very effective at detecting adverse reactions that occur a long time after starting the medicine.

For these reasons, such reports are only used to identify safety signals. These signals require further formal epidemiological study before they can be validated or discounted. Information obtained from spontaneous reports needs to be interpreted with caution.

## Understanding vaccine safety and spontaneous reporting

Spontaneous report patterns can be variable, and they depend on many factors. Summaries of reported events following immunisation *are not* lists of known or proven adverse reactions to vaccines. They cannot be used to determine the frequency of adverse reactions to vaccines in the whole population, and they cannot be used to directly compare the relative safety of vaccines. They must not be interpreted and used as such.

Health care professionals and consumers are encouraged to report any suspicions that an event they have experienced may have been caused by vaccination. Therefore, reports sent to CARM may be:

- real adverse reactions to the vaccine
- anxiety or nervousness about needles or the process of vaccination
- coincidental events that would have occurred anyway.

With any vaccine, the adverse events that are generally reported include:

- injection-site reactions
- well-recognised events, such as headaches, dizziness, muscle aches, mild fever and tiredness
- mild allergic reactions, such as mild rashes and itching
- rare but serious allergic reactions, called anaphylaxis, which can occur in response to any medicine or vaccine and some foods – health care professionals giving vaccines are trained to recognise the symptoms of serious allergic reactions and promptly treat them
- immunisation stress-related responses due to fear or anticipation of the needle injection (eg, fainting or hyperventilation)
- coincidental medical conditions
- new adverse events (ie, those not already listed in the prescribing information [data sheet]).

There will always be a few coincidental events reported because vaccines are given to large sections of the population. In some cases, vaccines are specifically targeted at people with underlying medical conditions (eg, the influenza vaccine). The challenge is to be able to distinguish these coincidental 'background' events from those that may have been caused by the vaccine. There are a range of research methods for assessing the risk of an event after a vaccine compared with the risk with no vaccine exposure.

The time between immunisation and an event can be important in determining whether the event was coincidental. Most reactions to vaccines occur within a very short time of immunisation, usually within days.

Another important approach taken when assessing vaccine safety is comparing the number of reports for a specific event with the expected background rate for that event. When doing this, it is important to ensure that definite diagnoses of the events reported were made and to adjust the background rate for any differences in population groups and seasonal variations.<sup>3</sup>

## References

1. Fine P, Mulholland K, Scott J, Edmunds W. 2018. Community Protection, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
2. Read TR, Hocking JS, Chen MY, et al. The near disappearance of genital warts in young women 4 years after commencing a national human papillomavirus (HPV) vaccination programme. *Sexually Transmitted Infections*, 2011. 87(7): p. 544-7.
3. Sexton K, McNicholas A, Galloway Y, et al. Henoch-Schönlein purpura and meningococcal B vaccination. *Archives of Disease in Childhood*, 2009. 94(3): p. 224-6.

# 2 Processes for safe immunisation

This chapter provides information about:

- Pre-vaccination: cold chain management, informed consent, pre-vaccination screening, contraindications, spacing of doses, catch-up, and adult vaccination (section 2.1)
- Vaccine administration: preparation, route, vaccination techniques by age, and multiple injections (section 2.2)
- Post-vaccination: post-vaccination advice, pain and fever recommendations, anaphylaxis and emergency management, and documentation and insurance (section 2.3).

## **Who can administer a vaccine?**

Vaccines can be administered by:

- a nurse practitioner
- a medical practitioner
- a registered midwife
- a designated prescriber (which includes a registered nurse fulfilling the designated prescriber criteria)
- a person authorised to administer the medicine in accordance with a prescription or a standing order
- a registered pharmacist and a registered intern pharmacist (who has completed approved training on vaccinations)
- a person who is authorised by either the Director-General of Health or a Medical Officer of Health under Regulation 44A or 44AB of the Medicines Regulations 1984 (see A3.6)
- a person authorised as a vaccinating health worker by either the Director-General of Health or the national Medical Officer of Health under Regulation 44AB of the Medicines Regulations 1984 (see A3.6).

The vaccines a person may administer will vary depending on the lawful basis upon which they can administer a vaccine or vaccines (see A3.6).

## 2.1 Pre-vaccination

The 'Immunisation standards for vaccinators' and the 'Guidelines for organisations storing vaccines and/or offering immunisation services' apply to the delivery of all Schedule vaccines and those not on the Schedule. See Appendix 3.

The vaccinator is responsible for ensuring all the vaccines they are handling and administering have been stored at the recommended temperature range of +2°C to +8°C at all times (see section 2.1.1 '**Cold chain management**' below and *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at <https://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines>).

Information on vaccine presentation, preparation and disposal can be found in Appendix 7.

Vaccinators are expected to know and observe standard occupational health and safety guidelines to minimise the risk of spreading infection and needle-stick injury (see Appendix 7).

All vaccinations on the New Zealand National Immunisation Schedule are given parenterally (by injection) except for the rotavirus vaccine which is given non-parenterally (orally). For non-parenteral vaccine administration, follow the manufacturer's instructions.

### 2.1.1 Cold chain management

All vaccines must always be stored and/or transported within the recommended temperature range of +2°C to +8°C.

See Health New Zealand | Te Whatu Ora Cold chain standards for vaccines website for further details on vaccine storage and the *National Standards for Vaccine Storage and Transportation for Immunisation Providers* (available at <https://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines>).

The 'cold chain' is defined as 'the system of transporting and storing vaccines within the recommended temperature range of +2°C to +8°C from the place of manufacture to the point of vaccine administration (the individual)'. The integrity of the cold chain is dependent not only on the equipment used for storage, transportation and monitoring but also on the people involved and the processes/practices they undertake.



**Table 2.1: Key points for cold chain management**

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All vaccinators are responsible for ensuring the vaccines they administer have been stored correctly.

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All immunisation providers storing vaccines must use a pharmaceutical refrigerator.

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The pharmaceutical refrigerator minimum and maximum temperatures must be monitored and recorded at the same time each working day.

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All immunisation providers must monitor the refrigerator with an electronic temperature recording device (eg, a data logger) that records and downloads data on a weekly basis. This should be compared with the daily minimum/maximum recordings.

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**All** immunisation providers who store vaccines and/or offer immunisation services must achieve Cold Chain Accreditation.

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Each immunisation provider must have a written cold chain management policy in place and ensure their policy is reviewed and updated annually. Each vaccinator is responsible to ensure they are able to access this policy, as it will contain important practice information on vaccine storage.

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**If the vaccine refrigerator temperature goes outside the recommended +2°C to +8°C range**

- Label the vaccines 'not for use'.
  - If the refrigerator is currently running within the +2°C to +8°C range, leave the labelled vaccines in your refrigerator.
  - If the refrigerator is not within the +2°C to +8°C range, look for obvious reversible causes (door open, power interruption). If no cause found, pack your labelled vaccines into a chilly bin, with a temperature monitoring device and consider transporting to your back-up provider (details for this are in your cold chain policy).
- Download the data logger and check for inconsistencies or temperature fluctuations; note any temperature fluctuations outside the +2°C to +8°C range, and the time-period
- Breaches of less than 30 minutes, under 12°C with a known cause can be documented but you do not need to report to local immunisation coordinator. If the cause is unknown, or multiple events occur on the same day, seek advice.
- Contact your local immunisation coordinator for advice and further actions.
- Document the steps and actions you have taken.

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## 2.1.2 Informed consent

### What is informed consent?

Informed consent is a fundamental concept in the provision of health care services, including immunisation. It is based on ethical obligations that are supported by legal provisions (eg, the Health and Disability Commissioner Act 1994, Code of Health and Disability Services Consumers' Rights 1996, Health Information Privacy Code 2020, Privacy Act 1993 and Privacy Amendment Act 2013).

Providing meaningful information to enable an informed choice and to seek informed consent is a duty that all health and disability providers must meet to uphold the rights of health and disability consumers. Informed consent includes the right to be honestly and openly informed about one's personal health matters. The right to agree to treatment carries with it the right to refuse and withdraw from treatment.

Informed consent is also an external expression of a health care provider's pivotal ethical duty to uphold and enhance their patient's autonomy by respecting the patient's personhood in every aspect of their relationship with that individual.

## The informed consent process

Informed consent is a process whereby the individual or parent/guardian are appropriately informed in an environment and manner that are meaningful. Having been well informed, they are willing and able to agree to what is being suggested without coercion.

Regardless of age, an individual and/or their parent/guardian must be able to understand:

- that they have a choice
- why they are being offered the treatment/procedure
- what is involved in what they are being offered
- the probable benefits, risks, side-effects, failure rates and alternatives, and the risks and benefits of not receiving the treatment or procedure.

To make an informed choice and give informed consent for vaccination, the individual or parent/guardian needs to understand the benefits and risks of vaccination, including those to the child and community.

Consent for patients who are incompetent (individuals who do not have the capacity to consent) may be given by:

- a welfare guardian appointed under the Protection of Personal and Property Rights Act 1988
- an attorney under an activated enduring power of attorney in respect of care and welfare.

If there is no welfare guardian or attorney under an enduring power of attorney, treatment may be provided under Right 7(4) of the Code of Health and Disability Services Consumers' Rights if:

- the treatment is in the best interests of the patient; and
- attempts have been made to find out what the patient would have wanted if s/he were competent; or
- if it is not possible to find out what the patient would have wanted, the views of people interested in the patient's welfare have been considered.

The essential elements of the informed consent process are effective communication, full information and freely given competent consent. The specific rights in the Code of Health and Disability Services Consumers' Rights that represent these three elements are:

- Right 5: Right to effective communication
- Right 6: Right to be fully informed
- Right 7: Right to make an informed choice and give informed consent.<sup>1</sup>

For example, section 7(1) of the Code states that ‘services may be provided to a consumer only if that consumer makes an informed choice and gives informed consent, except where any enactment, or the common law, or any other provision of the Code provides otherwise.’ Information on the Code of Health and Disability Services Consumers’ Rights can be found on the Health and Disability Commissioner’s website ([hdc.org.nz](http://hdc.org.nz)).

Health professionals have legal obligations to obtain informed consent prior to a procedure and prior to data collection (eg, data collected for the AIR). Unless there are specific legal exceptions to the need for consent, the health professional who acts without consent potentially faces the prospect of a civil claim for exemplary damages, criminal prosecution for assault (sections 190 and 196 of the Crimes Act 1961), complaints to the Health and Disability Commissioner and professional disciplining.

Ensuring that an individual has made an informed choice regarding treatment options has been included in the Health Practitioners Competence Assurance Act 2003. This Act ensures that health practitioners are, and remain, competent and safe to practise. For example, the Nursing Council of New Zealand competencies for the Registered Nurse Scope of Practice, Competency 2.4, ‘ensures the client has adequate explanation of the effects, consequences and alternatives of proposed treatment options’ (see the Nursing Council of New Zealand website, [nursingcouncil.org.nz](http://nursingcouncil.org.nz)).

## Privacy and control over personal information

The right to authorise, or to exert some control over, the collection and disclosure of personal information about oneself is a right closely allied to that of consent to treatment and is also relevant to personal integrity and autonomy.

The Health Information Privacy Code 2020 requires health agencies collecting identifiable information to be open about how and for what purpose that information will be used and who will be able to see it (Rule 3).

In addition to providing information about collection by the vaccinating agency, people should be advised that vaccination information will be recorded in the Aotearoa Immunisation Register (AIR) maintained by Health New Zealand and directed to the online privacy statement for the AIR at [tewhatauora.govt.nz/air-privacy](http://tewhatauora.govt.nz/air-privacy). This includes information on their choices with respect to control over their information.

The Health Information Privacy Code 2020 also gives people the right to access, and seek correction of, health information about them (Rules 6 and 7). Parents and guardians have a similar right of access to information about their children. Further information about privacy and health information can be found on the Privacy Commissioner’s website ([privacy.org.nz](http://privacy.org.nz)).

## Immunisation consent in primary care

Parents should be prepared during the antenatal period for the choice they will have to make about their child’s vaccination. During the third trimester of pregnancy, the lead maternity carer must provide Ministry of Health information on immunisation and the

AIR. This is a requirement under clause DA21(c) of the Primary Maternity Services Notice 2007, pursuant to section 88 of the New Zealand Public Health and Disability Act 2000.

## Vaccine hesitancy

Vaccine hesitancy refers to delay in acceptance or refusal of vaccines despite availability of vaccination services. Vaccine hesitancy is complex and context specific, varying across time, place and vaccines. It includes factors such as complacency, convenience and confidence.

WHO: Addressing Vaccine Hesitancy

Effective communication and active listening are key components of the informed consent process, especially when health care providers are working with vaccine-hesitant individuals/parents/guardians. In this situation, providers should:

- be willing to initiate the conversation, and avoid leaving it to others
- tailor content to the needs of the individual
- ensure respect and acknowledgement of concerns
- use plain language, open-ended questions and active listening
- avoid medical jargon, or ensure it is explained
- offer resources
- finish with an effective immunisation recommendation.

## Information for parents, guardians and health care providers

Health care providers must offer information without individuals or parents/guardians having to ask for it. The depth of information offered or required may differ, but it should at least ensure that the individual or parent/guardian understands what the vaccine is for and the possible side-effects, as well as information about the vaccination programme, the AIR and the risks of not being vaccinated (see chapter 3).

Every effort should be made to ensure that the need for information is met, including extra discussion time, use of an interpreter and alternative-language pamphlets. Health New Zealand | Te Whatu Ora immunisation pamphlets are produced in several languages, and are available from the local authorised provider or can be ordered, viewed and/or downloaded from the HealthEd website ([healthed.govt.nz](https://healthed.govt.nz)).

Issues to discuss with individuals or parents/guardians about immunisation include:

- the vaccine-preventable diseases
- the vaccines used on the Schedule (ie, the funded vaccines that are available)
- how vaccines work, known risks and adverse events, and what the vaccine is made of, in case of known allergies
- the collection of immunisation information on the AIR from birth, or as part of a targeted immunisation programme (eg, the information that will be collected, who will have access to it and how it will be used; see section 2.3.5 for more information on the AIR)

- the choice to vaccinate.

Informed consent is required for each immunisation episode or dose. Presentation for an immunisation event should not be interpreted as implying consent. Individuals and parents/guardians have the right to change their mind at any time. Where consent is obtained formally but not in writing, the provider should document what was discussed, and that consent was obtained and by whom.

### Health New Zealand | Te Whatu Ora information

Health New Zealand | Te Whatu Ora immunisation information is available for parents and guardians on the Health New Zealand | Te Whatu Ora website ([info.health.nz/immunisations/](https://info.health.nz/immunisations/)). Parents and guardians may also order, view or download Health New Zealand | Te Whatu Ora immunisation information from the HealthEd website ([healthed.govt.nz](https://healthed.govt.nz)) or from the local authorised resource provider, including:

- Immunise Your Child on Time (leaflet, available in English [HE1327] and other languages)
- Childhood Immunisation (health education booklet [HE1323]).

Further immunisation consent information for health care providers is also available in Appendix 3 'Immunisation standards for vaccinators and guidelines for organisations offering immunisation services'. Responses to commonly asked questions and suggestions for addressing myths and concerns are available in chapter 3.

### Other information sources

- Sharing Knowledge About Immunisation (SKAI) is an Australian suite of online resources and tools to support vaccination communication designed to aid conversations about childhood immunisation for parents and health care providers ([www.ncirs.org.au/our-work/sharing-knowledge-about-immunisation](http://www.ncirs.org.au/our-work/sharing-knowledge-about-immunisation)).
- Offit PA, Moser C. 2011. *Vaccines and Your Child – Separating fact from fiction*. New York, NY: Columbia University Press.
- Vaccine manufacturers' data sheets, available on the Medsafe website ([medsafe.govt.nz](https://medsafe.govt.nz)). Consumer and health care provider versions are available.
- Other recommended immunisation-related websites (see Appendix 8).

Alternatively, contact:

- the Immunisation Advisory Centre on freephone 0800 IMMUNE/0800 466 863, or see the IMAC website ([immune.org.nz](https://immune.org.nz))
- your local immunisation coordinator (a list of regional contacts are available at [immune.org.nz](https://immune.org.nz)).

## Immunisation consent in other settings (eg, schools)

In mass immunisation campaigns, such as those undertaken at schools, the consent requirements are different from those that apply to the vaccination of individuals in primary care. The parent/guardian may not be with the child on the day of immunisation, so immunisation should proceed only after the parent/guardian has had the opportunity to read the immunisation information and discuss any areas of concern. Consent forms are provided for immunisations given in schools by public health nurses and may also be used in mass vaccination settings. For children aged under 16 years who are being immunised at school, written consent must be obtained from the parent/guardian. Individuals who are aged 16 years or older may self-consent.

## Consent and children

Under the Code of Rights, every consumer, including a child, has the right to the information they need to make an informed choice or to give informed consent. The law relating to the ability of children to consent to medical treatment is complex. There is no defined age at which all children can consent to all health and disability services. The presumption that parental consent is necessary to give health care to those aged under 16 years is inconsistent with common law developments and the Code of Rights.

The Code of Rights makes a presumption of competence (to give consent) in relation to children, although New Zealand is unusual in this respect (ie, the obligations regarding consent of minors are greater in New Zealand than in many other jurisdictions).

A child aged under 16 years has the right to give consent for minor treatment, including immunisation, providing he or she understands fully the benefits and risks involved. In 2002 the Health and Disability Commissioner provided an opinion of a child's consent to a vaccine, whereby the Commissioner was satisfied that a 14-year-old was competent to give informed consent for an immunisation event due to an injury where a tetanus toxoid vaccine would be commonly given. More details of this opinion can be found on the Health and Disability Commissioner's website ([hdc.org.nz/](http://hdc.org.nz/) – Case: 01HDC02915).

Further information on informed consent can be found on the Health and Disability Commissioner's website ([hdc.org.nz](http://hdc.org.nz/)).

### 2.1.3 Pre-vaccination screening

Prior to immunisation with *any* vaccine, the vaccinator should ascertain if the vaccine recipient (child or adult) has a condition or circumstance which may influence whether a vaccine is given, deferred or contraindicated. Table 2.2 below provides a checklist of conditions or circumstances to screen for, along with the appropriate action to take and a rationale.

The vaccinator will also need to determine which vaccines are due, assess the vaccine recipient's overall current vaccination status and address parental concerns. The vaccinator also needs to advise the individual/parent/guardian they will need to remain for 20 minutes post-vaccination.

**Table 2.2: Pre-vaccination screening and actions to take**

Condition* or circumstance	Action	Rationale
Is unwell today: <ul style="list-style-type: none"> <li>• fever &gt;38°C</li> <li>• acute systemic illness</li> </ul>	Defer all vaccines until afebrile. Note: Children with minor illnesses (without acute symptoms/signs) should be vaccinated.	To avoid an adverse event in an already unwell child, or to avoid attributing symptoms to vaccination.
Is a preterm infant and had apnoea following immunisation in hospital (at 6-week and/or 3-month event)	Re-admission for the next infant immunisation and respiratory monitoring for 48 to 72 hours may be warranted, <sup>2</sup> but do not avoid or delay immunisation.  Babies born <28 weeks' gestation and other preterm babies who develop chronic lung disease will require PCV13 plus 23PPV at 2 years (see section 4.2.2).	There is a potential risk of apnoea in infants born before 28 weeks' gestation.  Preterm infants may be at increased risk of vaccine-preventable diseases (eg, invasive pneumococcal disease).
Previously had a severe reaction to any vaccine	Careful consideration will be needed depending on the nature of the reaction. If in doubt about the safety of future doses, seek specialist advice.	Anaphylaxis to a previous vaccine dose or any component of the vaccine is an absolute contraindication to further vaccination with that vaccine.
Anaphylaxis to vaccine components (eg, gelatin, neomycin)	Refer to the relevant vaccine data sheet ( <a href="http://www.medsafe.govt.nz">www.medsafe.govt.nz</a> ) for the components.  If an individual has had anaphylaxis to any component contained in a vaccine, seek specialist advice.  Note: Egg allergy, including anaphylactic egg allergy, is not a contraindication to MMR or influenza vaccination (see sections 11.6.3 and 12.6.3).	Vaccinators need to be aware of the possibility that allergic reactions, including anaphylaxis, may occur after any vaccination without any apparent risk factors (see section 2.3.3).  Delayed hypersensitivity to a prior vaccine dose or a component of a vaccine is not a contraindication to further doses, but it is important to distinguish this from anaphylaxis.
Appropriate spacing between doses of the same vaccine (when was the last vaccination, and what was it?)	See section 2.1.5 and check the relevant disease chapters and catch-up schedules.  (See below for live parenteral vaccines.)	The general rule is for a minimum of 4 weeks between doses of a primary series and 4 months between the priming dose(s) and the booster.

*Continued overleaf*



Condition* or circumstance	Action	Rationale
Had a live parenteral vaccine within the last 4 weeks – if in doubt, check the individual's immunisation status on the AIR	Delay further live attenuated parenteral vaccines to 4 weeks. Note that this does not apply to rotavirus vaccine, which is an oral vaccine.	The antibody response to the first dose may interfere with the response to the second. They may be given on the same day.
Had an injection of immunoglobulin or a blood transfusion within the last year and is now due for a live vaccine	Check which product the person received and the interval since administration. See Table A6.1. Delay vaccination if necessary.	Live virus vaccines should be given at least 2 weeks before or deferred. The interval will be determined by the blood product and dose received.
Has a disease that lowers immunity, is receiving treatment that lowers immunity or is an infant of a mother who received immunosuppressive therapy during pregnancy	See chapter 4 'Immunisation of special groups'. In some cases, specialist advice may need to be sought before vaccination. Note: Persons living with someone with lowered immunity should be fully vaccinated, including with live viral vaccines (see section 4.3.1).	The safety and effectiveness of the vaccine may be suboptimal in persons who are immunocompromised. Live attenuated vaccines may be contraindicated.
Is planning a pregnancy	See section 4.1.1 'Women planning pregnancy'. Ensure women and household members have received all vaccines recommended for their age group. Women should know if they are immune to measles (section 12.8.3), rubella (section 21.5.3) and varicella (section 24.5.4). Advise women not to become pregnant within 4 weeks of receiving live viral vaccines.	Vaccinating before pregnancy may prevent maternal illness, which could affect the infant, and may confer passive immunity to the newborn.
Is pregnant	See sections 4.1.2 'During pregnancy' and 4.1.3 'Breastfeeding and post-partum'. COVID-19, influenza and Tdap vaccines are recommended.	Vaccinating (with inactivated or subunit vaccines) during pregnancy may prevent maternal illness, which could affect the infant, and confers passive immunity to the newborn.
	Live vaccines should be avoided until after the delivery.	Deferring administration of live vaccines until after delivery is a precautionary safety measure. Studies of women who inadvertently received a live vaccine during pregnancy and their infants have not identified any adverse effects.

*Continued overleaf*



Condition* or circumstance	Action	Rationale
Unstable neurological condition (for pertussis-containing vaccines only)	Seek specialist advice.	Vaccination is recommended for children with unstable neurological conditions as they may be at high risk of severe pertussis complications. Individual cases should be discussed with a specialist.
Thrombocytopenia or bleeding disorders	Administer intramuscular vaccines with caution: <ul style="list-style-type: none"> <li>use a 23-gauge or smaller needle and apply firm pressure to the injection site (without rubbing) for at least 10 minutes. (see section 2.2.3).</li> </ul>	A haematoma may occur following intramuscular administration. In some cases, subcutaneous is preferred where datasheet allows. Seek specialist advice as appropriate.
Individuals who are currently being treated with immune checkpoint inhibitors, as well as those who have discontinued treatment within the past 6 months.	Contraindication for live vaccines.	There is a theoretical risk that vaccines may trigger an autoimmune response in these individuals. See the 'Immune checkpoint inhibitor (immunostimulant) therapy' discussion in section 4.3.8.
History of myocarditis or pericarditis	If unrelated to vaccination, continue vaccination (for COVID-19 and mpox vaccines, continue once cardiac inflammation has resolved).	To reduce potential risk of exacerbating underlying condition
	Defer further doses if individual develops myocarditis/pericarditis after any dose of mRNA-CV or rCV. Seek specialist immunisation advice regarding future COVID-19 vaccination doses.	To consider risk of recurrent myocarditis/pericarditis against risk of severe COVID-19
	Any further doses of MPV (mpox) vaccine are contraindicated if myocarditis or pericarditis is considered related to a previous dose.	
History of Guillain–Barré syndrome (GBS)	The risks and benefits of withholding vaccination should be considered on an individual basis.	Consider the risk of recurrent GBS following influenza infection.

\* See chapter 4 for more information about pregnancy and lactation and for information about infants with special immunisation considerations, immune-deficient and immunosuppressed individuals, immigrants and refugees, travel, and occupational and other risk factors.

Adapted from: Australian Technical Advisory Group on Immunisation (ATAGI). 2018. *Australian Immunisation Handbook* Canberra: Australian Government Department of Health URL: <https://immunisationhandbook.health.gov.au> (accessed 30 June 2020).

## 2.1.4 Contraindications

No individual should be denied vaccination without serious consideration of the consequences, both for the individual and for the community. Where there is any doubt, seek advice from the individual's general practitioner (GP), a public health medicine specialist, medical officer of health, consultant paediatrician or IMAC.

Anaphylaxis to a previous vaccine dose or any component of the vaccine is an absolute contraindication to further vaccination with that vaccine. (Note that egg-related anaphylaxis and influenza vaccine or MMR are exceptions.)

**For more detail on anaphylaxis, see section 2.3.3.**

Live viral vaccines should not be given to pregnant women, nor, in general, to immunosuppressed individuals and those treated within the last 6 months with immune checkpoint inhibitors (see chapter 4).

See the relevant disease chapter section for more specific vaccine contraindications.

### Conditions that are not contraindications to immunisation

The conditions in Table 2.3 are not contraindications to the immunisation of children and adults (see also section 3.1).

**Table 2.3: Conditions that are not contraindications to immunisation**

Individuals with these conditions should be vaccinated with all the recommended vaccines.

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Mildly unwell, with a temperature  $\leq 38^{\circ}\text{C}$

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Asthma, hay fever, eczema, 'snuffles', allergy to house dust

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Receiving treatment with antibiotics or locally acting steroids

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A breastfeeding mother or a breastfed child

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Neonatal jaundice

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Low weight in an otherwise healthy child

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The child being over the usual age for immunisation – use age-appropriate vaccines, as per the catch-up schedules in Appendix 2 (the exception is rotavirus vaccine: see section 20.5.2)

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A previous hypotonic-hyporesponsive episode (see section 2.3.3)

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Clinical history of pertussis, measles, mumps or rubella infection – clinical history without laboratory confirmation cannot be taken as proof of immunity (even when an individual is proven to be immune to one or two of either measles, mumps or rubella, there is still the need for immunisation against the other/s: see relevant chapters)

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Prematurity, but an otherwise well infant – it is particularly important to immunise these children, who are at higher risk of severe illness if infected; immunisation is recommended at the usual chronological age (see 'Preterm and low birthweight infants' in section 4.2.2)

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Stable neurological conditions, such as cerebral palsy or Down syndrome

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Contact with an infectious disease

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Egg allergy, including anaphylaxis, is not a contraindication to MMR (see section 12.6.3) or influenza vaccine (see section 11.6.3)

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*Continued overleaf*

Family history of vaccine reactions

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Family history of seizures

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Family history of sudden unexpected death in infancy (SUDI)

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Child's mother or household member is pregnant or immunocompromised

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## 2.1.5 Spacing of doses

In general, follow the recommendations in the manufacturers' data sheets.

### Principles for spacing of doses of the same vaccine

The immune response to a series of vaccines depends on the time interval between doses. The general rule is for a minimum of four weeks between doses of a primary series; however, the immune response may be better with longer intervals. A repeat dose of the same vaccine given less than four weeks after the previous dose may result in a reduced immune response. Specific recommendations for a rapid schedule by the manufacturer may apply for some vaccines.

Generally, a minimum interval of four to six months between priming dose(s) and the booster dose allows affinity maturation of memory B cells, and thus higher secondary responses (see section 1.1).

It is not necessary to repeat a prior dose if the time elapsed between doses is more than the recommended interval.

### Spacing of different vaccines

Two or more parenterally administered live vaccines may be given at the same visit; for example, MMR and VV. However, when given at different visits, a minimum interval of four weeks is recommended. This interval is to avoid the response to the second vaccine being diminished due to interference from the response to the first vaccine.

**Note that no interval is required between administration of Bacillus Calmette–Guérin (BCG) and rotavirus vaccines.**

Unless there is a specific recommendation against it, a subunit vaccine can be administered either simultaneously or at any time before or after a different subunit or live vaccine.

### Concurrent administration of vaccines

Changing the timing of visits or increasing the number of visits to avoid multiple injections delays protection against potentially serious diseases and may also lead to incomplete immunisation. Best practice is to follow the Schedule.

Where different injectable vaccines are given on the same day, they must be administered in separate syringes, at different sites.

## 2.1.6 Catch-up programmes for unimmunised or partially immunised children

The objective of a catch-up programme is to complete a course of vaccinations that provides adequate protection. Catch-up programmes should be based on documented evidence of previous vaccination (eg, the child's *Well Child Tamariki Ora My Health Book*, AIR, or overseas immunisation records).

When children have missed vaccine doses, it is important to bring them up to date as quickly as possible. Where more than one vaccine is overdue, it is preferable to give as many as possible at the first visit. For children aged 12 months and older, MMR is the priority.

See Appendix 2 for determining catch-up requirements and planning a catch-up programme.

If the vaccinator is uncertain about how to plan a catch-up programme, they should contact the local immunisation coordinator, IMAC, medical officer of health or public health service.

Once catch-up is achieved, vaccination for the child should continue as per the Schedule.

### Vaccination of children with inadequate vaccination records

It is recommended that children *without a documented history of vaccination* have a full course of vaccinations appropriate for their age. It is preferable, and safe, for the individual to receive an unnecessary dose rather than to miss out a required dose(s) and not be fully protected.

## 2.1.7 Adult vaccination (aged 18 years and older)

Whenever adults are seen in general practice or by immunisation providers, there is an opportunity to ensure they have been adequately protected against the following diseases and have received at least a primary immunisation course as described in Table 2.4. If the requisite number of doses has not been received, catch-up vaccination is recommended and funded (see Appendix 2).

Women of childbearing age should know whether or not they are immune to measles (see chapter 12), rubella (see chapter 21) and varicella (see chapter 24).

Refer to the PHARMAC schedule for further details on vaccines funded for adults (available at [pharmac.govt.nz](http://pharmac.govt.nz)).

**Table 2.4: Funded immunisation for adults**

Vaccine	Number of vaccine doses
Tdap	3 doses <sup>a</sup>
Poliomyelitis (IPV)	3 doses
Measles, mumps, rubella	2 doses
HPV (aged 26 years and under)	3 doses <sup>b</sup>
Influenza	1 dose annually (for eligible groups)
COVID-19 (mRNA-CV)	2 doses <sup>c</sup> (additional doses for eligible groups)
Zoster (rZV, at age 65 years)	2 doses

- Although pertussis protection is included in the Tdap vaccine as part of protection against Tetanus and diphtheria, if a patient is missing this antigen only but is otherwise fully vaccinated, no further vaccines are required unless the patient is pregnant.
- Individuals who were under age 27 years when they commenced HPV vaccination are currently funded to complete the 3-dose course, even if they are older than 27 years when they complete it.
- Includes all adults, regardless of eligibility to health and disability services. One other COVID-19 vaccine is available (see section 5.4.2).

See Table 2.5 for additional adult vaccination recommendations, including vaccinations recommended for special groups (funded vaccines are in the shaded boxes). See also chapter 4 'Immunisation of special groups' for information about immunisation during pregnancy and lactation (section 4.1), of immunocompromised individuals (section 4.3), of immigrants and refugees (section 4.7), for those with occupational-related vaccination (section 4.8) and for travel (section 4.9).

**Table 2.5: Adult (≥18 years) vaccination recommendations, excluding travel requirements**

Vaccine	Recommended and funded	Recommended but not funded
COVID-19 (chapter 5)	All adults Three primary doses for severely immunocompromised Additional doses available	
Hib-PRP (chapters 4 and 7)	(Re)vaccination of patients post-haematopoietic stem cell transplant (HSCT) or chemotherapy; pre- or post-splenectomy or with functional asplenia; pre- or post-solid organ transplant, pre- or post-cochlear implants, renal dialysis and other severely immunosuppressive regimens	
Hepatitis A (chapter 8)	Transplant patients Close contacts of hepatitis A cases <sup>a</sup>	Patients with chronic hepatitis B or C infection; men who have sex with men; adults at occupational risk

*Continued overleaf*

Vaccine	Recommended and funded	Recommended but not funded
Hepatitis B (chapter 9)	Household or sexual contacts of patients with acute or chronic HBV infection HIV-positive patients Hepatitis C-positive patients Following non-consensual sexual intercourse Prior to or following immunosuppression <sup>b</sup> Solid organ transplant patients Post-HSCT patients Following needle-stick injury Dialysis patients Liver or kidney transplant patients	Non-immune adults at risk including occupational or other risk factors
HPV (chapter 10)	All individuals aged 9–26 years <sup>c,d</sup> Individuals aged 18–26 years who are: <sup>c,d</sup> <ul style="list-style-type: none"> <li>confirmed with HIV infection</li> <li>transplant (including stem cell) patients</li> <li>an additional dose post-chemotherapy</li> </ul>	Adults ≥27 years: <sup>c,d,e</sup> <ul style="list-style-type: none"> <li>who have had little previous exposure to HPV and are now likely to be exposed</li> <li>who are men who have sex with men</li> <li>with HIV</li> </ul>
Annual influenza vaccine (chapter 11)	Pregnant women and people Individuals aged 65 years and older Individuals aged under 65 years with eligible conditions See <a href="http://www.immune.org.nz">www.immune.org.nz</a>	Close contacts of elderly adults and other high-risk groups All other adults
MMR (chapters 12, 14 and 21)	Any individual susceptible to any one of these three diseases (Re)vaccination prior to planned or following immunosuppression <sup>b</sup>	
MenACWY and MenB (chapters 4 and 13)	For patients who are pre- or post-splenectomy or with functional asplenia; with HIV; with complement deficiency (acquired, including monoclonal antibody therapy against C5, or inherited); who are pre- or post-solid organ transplant Close contacts of meningococcal cases <sup>a</sup> Patients who have had previous meningococcal disease (any group) HSCT (bone marrow transplant) patients Patients prior to planned and following immunosuppression <sup>b</sup> Adolescents and young adults aged 13–25 years inclusively who will be living or are currently living in a boarding school hostel or university hall of residence, military barracks, youth justice residences or prison	Laboratory workers handling bacterial cultures Health care professionals in very close contact with cases

*Continued overleaf*

Vaccine	Recommended and funded	Recommended but not funded
Pertussis-containing vaccine (chapters 4 and 16)	Tdap is recommended to be given from 16 weeks' gestation of every pregnancy, preferably in the second trimester to protect both the mother and her infant from pertussis  Tdap for (re)vaccination of patients who are post-HSCT or chemotherapy; pre- or post-splenectomy; pre- or post-solid organ transplant, renal dialysis and other severely immunosuppressive regimens	Tdap if in contact with infants aged under 12 months
PCV13 and 23PPV (chapters 4 and 17)	(Re)vaccination of patients with HIV; pre- or post-HSCT <sup>f</sup> or chemotherapy; <sup>f</sup> pre- or post-splenectomy or with functional asplenia; pre- or post-solid organ transplant; renal dialysis; complement deficiency (acquired or inherited); cochlear implants; primary immune deficiency	PCV13 followed by 23PPV for those with certain conditions  PCV13 followed by 23PPV for those aged 65 years or older
IPV (chapter 18)	Any unvaccinated or partially vaccinated individual  (Re)vaccination prior to planned or following immunosuppression <sup>b</sup>	Travellers to certain high-risk countries
Tetanus (Tdap) (chapters 4 and 22)	Tdap for susceptible individuals (including following immunosuppression); boosters at 45 (if had less than 4 previous doses of tetanus vaccine) plus 65 years; boosting of patients with tetanus-prone wounds	
Varicella (chapter 24)	Non-immune patients: <ul style="list-style-type: none"> <li>with chronic liver disease who may need a transplant in the future</li> <li>with deteriorating renal function before transplantation</li> <li>prior to solid organ transplant</li> <li>prior to any planned immunosuppression<sup>b</sup></li> <li>for post-exposure prophylaxis of immune-competent hospital in-patients</li> </ul> Patients at least 2 years after bone marrow transplant <sup>g</sup> Patients at least 6 months after completion of chemotherapy <sup>g</sup> HIV-positive patients who are non-immune to varicella, with mild or moderate immunosuppression <sup>g</sup> Patients with inborn errors of metabolism at risk of major metabolic decompensation, with no clinical history of varicella Household members of paediatric patients who are immunocompromised or undergoing a procedure leading to immunocompromise, where the household member has no clinical history of varicella	Susceptible adults

*Continued overleaf*



Vaccine	Recommended and funded	Recommended but not funded
Varicella <i>continued</i>	Household members of adult patients who have no clinical history of varicella and who are severely immunocompromised or undergoing a procedure leading to immunocompromise, where the household member has no clinical history of varicella	
Zoster (chapter 25)	<p>Individuals at age 65 years.</p> <p>Individuals aged from 18 years, including those aged 66 years and over,</p> <ul style="list-style-type: none"> <li>• pre- and post-haematopoietic stem cell transplant or cellular therapy</li> <li>• pre- or post-solid organ transplant</li> <li>• with haematological malignancies</li> <li>• living with poorly controlled HIV infection</li> <li>• prior to planned or receiving disease-modifying anti-rheumatic drugs (DMARDs – targeted synthetic, biologic, or conventional synthetic) for polymyalgia rheumatica, systemic lupus erythematosus or rheumatoid arthritis</li> <li>• with end-stage kidney disease (CKD 4 or 5)</li> <li>• with primary immunodeficiency.</li> </ul>	<p>rZV may be considered, but is not funded, for individuals who are:</p> <ul style="list-style-type: none"> <li>• aged over 66 years</li> <li>• aged from 50 years at increased risk of shingles and who may benefit from being vaccinated earlier than the routine schedule</li> <li>• aged from 18<sup>h</sup> years with other immunocompromising conditions not included in funded indications.</li> </ul>

- Only 1 dose of vaccine is funded for close contacts.
- Note that the period of immunosuppression due to steroid or other immunosuppressive therapy must be longer than 28 days.
- Individuals who started with HPV4 may complete their remaining doses with HPV9.
- Individuals who were <27 years when they commenced HPV vaccination are currently funded to complete the 3-dose course, even if they are ≥27 years when they complete it.
- HPV9 vaccine is registered for use in females and males aged 9–45 years.
- PCV13 is funded pre- or post-HSCT or chemotherapy. 23PPV is only funded post-HSCT or chemotherapy.
- On the advice of their specialist.
- Available for use for certain medical conditions from age 18 years.

## 2.2 Vaccine administration

### 2.2.1 Minimising pain and distress at the time of vaccination

The WHO key recommendations for minimising pain and distress at the time of vaccination are:<sup>3, 4</sup>

- do not aspirate (draw back) when giving vaccines
- administer vaccines from the least to the most painful for all ages



- breastfeed before and during vaccine injection
- position (hold the infant/young child, individuals aged 3 years and older should sit up, parental presence)
- for infants, give oral rotavirus vaccine before injections (the vaccine contains sucrose that can reduce pain)
- use calming and supportive words at the time of vaccination; avoid language that increases anxiety
- provide appropriate distractions
- consider using topical anaesthetics (only if the cost is acceptable to the family).

See also section 2.3.2 and the IMAC factsheets *Mitigating Vaccination Pain and Distress and Fear of Needles or Needle Phobia* (available at [immune.org.nz/resources/factsheets](http://immune.org.nz/resources/factsheets)).

## 2.2.2 Preparing for vaccine administration

### **Key points for administering injectable vaccines**

Vaccines should not be mixed in the same syringe, unless the prescribing information sheet specifically states it is permitted or essential (eg, DTaP-IPV-HepB/Hib).

Careful use of a longer needle will cause less damage than a short needle.

To avoid tracking, make sure all the vaccine has been injected before smoothly withdrawing the needle.

Correct vaccine administration is important, and vaccinators have a responsibility to see that vaccines are given:

- in the optimal site as recommended in Handbook
- using the appropriate needle size for vaccine effectiveness and patient safety.

The use of alternative sites will be based on professional judgement, including knowledge of the potential risks at each site and recommendations in the manufacturer's data sheet.

The guidelines in Table 2.6 will help to make the experience less distressing for the individual, parent/guardian and/or whānau, and vaccinator.

**Table 2.6: Guidelines for vaccine administration**

<b>Preparation</b>	<b>Immunisation event</b>
Vaccinate in a private and appropriate setting.	Draw up injections out of sight, if possible. Medical equipment is commonplace to vaccinators, but it may heighten the anxiety of some individuals.
Prepare the area/room layout to suit the vaccinator and vaccination event.	Ensure the individual or parent/guardian has had the opportunity to discuss any concerns and has given informed consent.
Be familiar with the vaccines (eg, their correct preparation, administration and the potential for adverse events).	Be prepared to include other family members and whānau in the discussion; explain to older children accompanying infants why the injections are being given and what will happen.
Be aware of the individual's immunisation history (eg, submit a status query to the AIR, if the history is unknown).	Give the appropriate immunisations due and advise when the next immunisation event is due.
Ensure there are age-appropriate distractions available.	For breastfed babies, suggest that the mother breastfeeds baby before, during and after immunisation.  For children, sit them upright and talk quietly to them before and during immunisation. Make eye contact and explain what is going to happen. Even when a child is unable to understand the words, an unhurried, quiet approach has a calming effect and reassures the parent/guardian.  See also section 2.3.2.
Ensure the relevant immunisation health education resources are available.	Give written and verbal advice to the individual and parent/guardian. The advice should cover what may be expected after immunisation, and what to do in the event of an adverse event, along with advice on when to notify the vaccinator.

## Removal of air bubbles

Advice for removal of air in the syringe before vaccine administration is dependent on the vaccine presentation. For guidelines see Table 2.7.

**Table 2.7: Guidelines for management of air bubbles in a vaccine syringe**

Vaccine presentation	Management of air bubbles
Vaccines supplied in a prefilled syringe with a fixed needle	Do not expel the air
Vaccines supplied in a prefilled syringe without a fixed needle (eg, Gardasil 9)	Add an appropriate administration needle Do not expel the air
Vaccines supplied diluted in a vial	Draw up the entire vaccine volume into a syringe Expel the air until the vaccine is at the level of the syringe hub, then change the needle Do not expel the air contained in the new needle
Vaccines supplied as diluent and powder/pellet requiring reconstitution <sup>a</sup>	Reconstitute the vaccine correctly Draw up the entire vaccine volume into a syringe Expel the air until the vaccine is at the level of the syringe hub, then change the needle <sup>a</sup> Do not expel the air contained in the new needle

a. See section 5.4.5 for administration procedures of COVID-19 vaccines.

## Skin preparation

Skin preparation or cleansing when the injection site is clean is not necessary. However, if an alcohol swab is used, it must be allowed to dry for at least two minutes, otherwise alcohol may be tracked into the muscle, causing local irritation. Alcohol may also inactivate a live attenuated vaccine such as MMR.

A dirty injection site may be washed with soap and water and thoroughly dried before the immunisation event.

## Special considerations for COVID-19

In patients who have had acute COVID-19 illness or tested positive for SARS-CoV2 virus, COVID-19 vaccination is recommended to be continued from six months after recovery from acute illness, or six months from the first confirmed positive test if asymptomatic. This applies for any additional doses (see Vaccination following SARS-CoV-2 infection) For all other vaccines, commence vaccination as soon as the individual is no longer acutely unwell and when cleared to leave isolation.

## 2.2.3 Route of administration

Most Schedule vaccines are administered by intramuscular injection. The exceptions are IPV (IPOL; subcutaneously), BCG (intradermally) and rotavirus (oral). Live vaccines have previously been given via SC route and data sheets may still show this as an option, which can be helpful for those with bleeding disorders (see below).

## Needle angle, gauge and length

Intramuscular injections should be administered at a 90-degree angle to the skin plane. The needle length used will be determined by the size of the limb and muscle bulk, whether the tissue is bunched or stretched and the vaccinator's professional judgement. BCG vaccine (which can only be administered by authorised vaccinators with BCG endorsement) is given by intradermal injection. See Table 2.8.

**Table 2.8: Needle gauge and length, by site and age**

Age	Site	Needle gauge and length	Rationale
<b>Intramuscular (IM) injection</b>			
Birth	Vastus lateralis	23–25 G × 16 mm	
6 weeks	Vastus lateralis	23–25 G × 16 or 25 mm	Choice of needle length will be based on the vaccinator's professional judgement.
3–11 months	Vastus lateralis	23–25 G × 25 mm	A 25 mm needle will ensure deep IM vaccine deposition.
12 months to 3 years	Deltoid or	23–25 G × 16 mm	The vastus lateralis site may be the preferred option in young children if deltoid muscle bulk is small or multiple injections are necessary.
	Vastus lateralis	23–25 G × 25 mm	
3–7 years	Deltoid	23–25 G × 16 mm	A 16 mm needle should be sufficient to effect deep IM deposition in the deltoid in most children.
	Vastus lateralis <sup>a</sup>	21–22 G × 25 mm	
Older children (7 years and older), adolescents and adults	Deltoid	23–25 G × 16 mm, or 23–25 G × 25 mm, or 21–22 G × 38 mm	Most adolescents and adults will require a 25 mm needle to effect deep IM deposition.
	Vastus lateralis <sup>a</sup>	21–22 G × 38 mm	
Very large or obese person	Deltoid	21–22 G × 38 mm	Use clinical judgment to ensure needle length is appropriate to reach muscle. <sup>4, 5</sup>
<b>Subcutaneous injection</b>			
Subcutaneous injection	Deltoid region of the upper arm	25–26 G × 16 mm	An insertion angle of 45 degrees is recommended. The needle should never be longer than 16 mm or inadvertent IM administration could result.

*Continued overleaf*

Age	Site	Needle gauge and length	Rationale
<b>Intradermal injection: BCG vaccine – for authorised vaccinators with BCG endorsement</b>			
Intradermal injection	Slightly above the insertion of the deltoid muscle on the lateral surface of the left arm. The arm should be gently but firmly supported.	Drawing-up: Tuberculin syringe (attach a drawing-up needle), or a single-use insulin syringe with a needle attached  Administering: If using a tuberculin syringe, change the needle to a sterile 26 G × 13 or 16 mm needle (no needle change required if using an insulin syringe)	The syringe should be held with the bevel uppermost, parallel with the skin of the arm. The bevel should be fully inserted but visible under the skin. Inject the vaccine slowly and gradually to form a white 'bleb' or wheal, then gradually withdraw the needle.

- a. Consideration may be given to the vastus lateralis as an alternative vaccination site, providing it is not contraindicated by the manufacturer's data sheet.

## Intramuscular injection sites

Injectable vaccines should be administered in healthy, well-developed muscle, in a site as free as possible from the risk of local, neural, vascular and tissue injury. Incorrectly administered vaccines (incorrect sites and poor administration techniques) contribute to vaccine failure, injection-site nodules or sterile abscesses, and increased local reactions.

Careful use of a longer needle will cause less damage than a shorter needle.

The recommended sites for intramuscular (IM) vaccines (based on proven uptake and safety data) are:

- the vastus lateralis muscle on the anterolateral thigh for infants aged under 12 months – the vastus lateralis muscle is large, thick and well developed in infants, wrapping slightly onto the anterior thigh
- either the vastus lateralis or deltoid site for children aged 12 months to 3 years (see below)
- the deltoid muscle for older children, adolescents and adults.

The deltoid muscle is not routinely used in infants and young children aged under 12 months, due to the potential for deltoid or radial nerve injury. However, when there is no access to the vastus lateralis (eg, the infant is in a spica cast), the deltoid muscle is used to administer intramuscular vaccines.

The buttock should not be used for the administration of vaccines in infants or young children, because the buttock region is mostly subcutaneous fat until the child has been walking for at least 9 to 12 months. Use of the buttock is not recommended for adult vaccinations either, because the buttock subcutaneous layer can vary from 1 to 9 cm and IM deposition may not occur.

With older children and adults, consideration may be given to using the vastus lateralis as an alternative site to the deltoid.

## Subcutaneous injection sites

A subcutaneous (SC) injection should be given into healthy tissue that is away from bony prominences and free of large blood vessels or nerves. The recommended site for subcutaneous vaccine administration is the upper arm (overlying the deltoid muscle).

The principles for locating the upper arm site for an SC injection are the same as for an IM injection. *However, needle length is more critical than angle of insertion for subcutaneous injections.* An insertion angle of 45 degrees is recommended, and the needle should never be longer than 16 mm, or inadvertent IM administration could result. The thigh may be used for SC vaccination unless contraindicated by the manufacturer's data sheet. For patients with thrombocytopenia and bleeding disorders, the risk of haematoma may be reduced when given via SC route. See below for further details.

## Intramuscular versus subcutaneous administration

Health New Zealand | Te Whatu Ora recommends that parenteral live vaccines on the Schedule (MMR and varicella vaccines) be administered via intramuscular (IM) route, unless the patient is on an anticoagulant or has a bleeding disorder, in which case the preferred route is subcutaneous (SC) where the data sheet allows (see below).

Historically, live vaccines have been given subcutaneously following on from their original licensure trials. Further research has now established immunogenicity and safety when these vaccines are administered by the IM route.<sup>6</sup> There is evidence that injections given intramuscularly, rather than deep subcutaneously, are less likely to cause local reactions.<sup>8, 9, 10</sup> There are no immunogenicity concerns when MMR and varicella vaccines are given either SC or IM. BCG is required to be given intradermally.

## Thrombocytopenia, anticoagulant therapy and bleeding disorders

For patients with thrombocytopenia and bleeding disorders, the risk of haematoma may be reduced when given via SC route, where data sheet allows this option.

- Vaccines can be administered to people on anticoagulants, dabigatran (Pradaxa), enoxaparin (Clexane), heparin, ticagrelor (Brilinta) and warfarin. Subcutaneous route is preferred option where data allows, to reduce risk of haematoma. For vaccines that do not have the SC option administer IM. After vaccination, apply firm pressure over the injection site without rubbing for 10 minutes to reduce the risk of bruising.
- For patients with haemophilia receiving clotting factor replacement or a similar therapy, vaccinations should be given as soon as possible after receiving the medicine and vaccines should be given in the same way as for those on anticoagulants. Specialist advice is recommended.

## Intradermal injections

The intradermal injection technique for BCG vaccine (see section 2.2.4) requires special training, and should only be performed by an authorised vaccinator with BCG endorsement (see A3.6).

## Oral vaccine administration

The rotavirus vaccine is administered orally. Administer the entire contents of the oral applicator into the infant's mouth, towards the inner cheek (see section A7.2.4). **Do not inject oral vaccines.**

For specific oral vaccine administration instructions, refer to the vaccine data sheet (available on the Medsafe website at [medsafe.govt.nz](https://www.medsafe.govt.nz)).

## 2.2.4 Infant vaccination

Infants aged under 6 months do not need to be grasped or restrained as firmly as toddlers or older children. At this age, excessive restraint increases their fear as well as muscle tautness. The recommended positioning for an infant is in a cuddle hold with parent/guardian, breastfeeding as appropriate. The cuddle position offers better psychological support and comfort for both the infant and the parent/guardian,<sup>3</sup> and the parent/guardian should be offered this position as a first choice (Figure 2.1).

If the parent/guardian is helping to hold the infant or child, ensure they understand what is expected of them and what will take place. Most vaccinators choose to quickly administer all the injections due and soothe the infant or child afterwards (see section 2.3.2 for soothing measures).

**Figure 2.1: The cuddle position for infants**





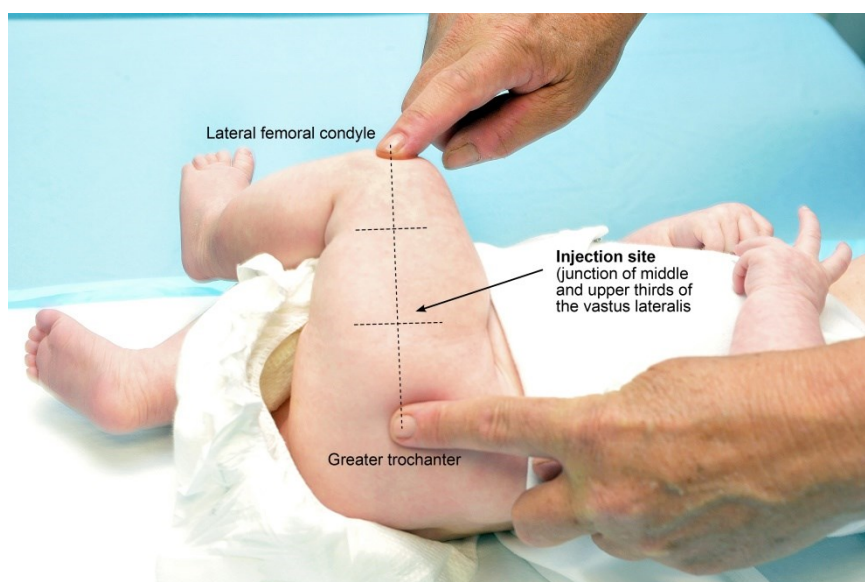
## Vastus lateralis

To locate the injection site, undo the nappy, gently adduct the flexed knee and (see Figure 2.2):

1. find the greater trochanter
2. find the lateral femoral condyle
3. section the thigh into thirds and run an imaginary line between the centres of the two markers (look for the dimple along the lower portion of the fascia lata).

The injection site is at the junction of the upper and middle thirds and slightly anterior to (above) the imaginary line, in the bulkiest part of the muscle.

**Figure 2.2: The infant lateral thigh injection site**



The needle should be directed at a 90-degree angle to the skin surface and inserted slightly anterior to (above) the junction of the upper and middle thirds. Inject the vaccine at a controlled rate. To avoid tracking, make sure all the vaccine has been injected before smoothly withdrawing the needle. Do not massage or rub the injection site afterwards. However, infants with a bleeding disorder may require firm pressure over the injection site without rubbing for at least 10 minutes.

Where three injections are required as at the 5-month immunisation event, two injections should be given into one vastus lateralis (DTaP-IPV-HepB/Hib and PCV) separated by 2 cm, and the other injection (MenB) is given into the other vastus lateralis. See Figure 2.9.

## BCG vaccine (administered by authorised vaccinators with BCG endorsement)

The reconstituted BCG vaccine is given by intradermal injection slightly above the insertion of the deltoid muscle on the lateral surface of the left arm. The infant's arm should be gently but firmly supported (see Figure 2.3(a)). The syringe should be held with the needle bevel uppermost, parallel with the skin of the arm (see Figure 2.3(b)).



**Figure 2.3: The infant BCG vaccination site, and how to support the infant's arm and hold the syringe**



(a)



(b)

Inject the vaccine slowly (see Figure 2.4(a)), then gradually withdraw the needle. The injection is given slowly to avoid leakage around the needle or vaccine being squirted. Safety glasses should be used to protect the eyes of those involved. If BCG vaccine is accidentally squirted into the eyes, wash them immediately with water. Following BCG vaccination, a white weal should appear (see Figure 2.4(b)), which should subside in approximately 30 minutes. The vaccination site requires no swabbing or dressing.

**Figure 2.4: The BCG vaccine being slowly injected, and a white weal appearing as the needle is gradually withdrawn**



(a)



(b)

## 2.2.5 Young child vaccination (vastus lateralis or deltoid)

The choice between the two sites for IM injections from 12 months of age will be based on the vaccinator's professional judgement, taking in account knowledge of the child and ease of restraint. Some vaccinators consider the vastus lateralis preferable for young children when the deltoid muscle bulk is small and because of the superficiality of the radial nerve. Discuss the options with the parent/guardian when making your decision. (See also 'The 12- and 15-month immunisation events' in section 2.2.7.)

The easiest and safest way to position and restrain a young child for a lateral thigh and/or deltoid injection is to sit the child sideways on their parent's or guardian's lap. The parent's/guardian's hand restrains the child's outer arm and the child's legs are either restrained between the parent's/guardian's legs or by placing a hand on the child's outer knee or lower leg. Alternatively, the child may face their parent/guardian while straddling the parent's/guardian's legs (see Figure 2.5 and Figure 2.6). Keeping a firm hold will help to avoid needle scratches that can result if the child moves.

**Figure 2.5: Cuddle positions for vastus lateralis or deltoid injections in children**



(a)



(b)

**Figure 2.6: The straddle position for vastus lateralis or deltoid injections in children**

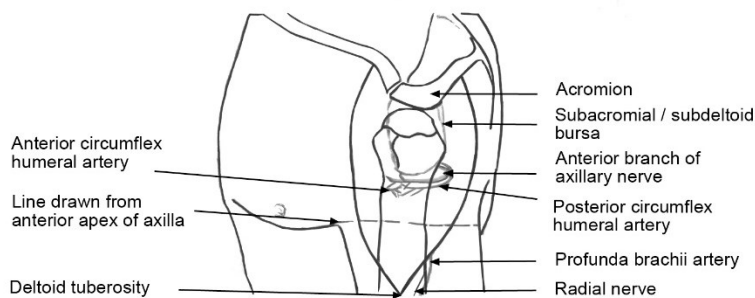


In the straddle position, both the deltoid and vastus lateralis muscle are likely to be more tense or taut, and the injection may therefore be more painful.

## 2.2.6 Older child, adolescent and adult vaccination (deltoid)

The deltoid muscle is located in the lateral aspect of the upper arm. The entire deltoid muscle must be exposed to avoid the risk of radial nerve injury (an injection at the junction of the middle and upper thirds of the lateral aspect of the upper arm may damage the nerve) (see Figure 2.7).

**Figure 2.7: Surface landmarks and structures potentially damaged by intramuscular injection in the upper limb**



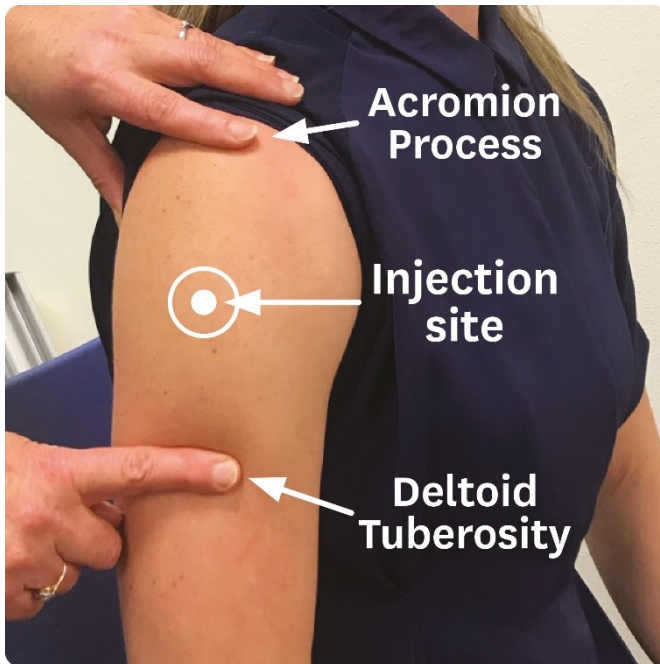
Reproduced with permission: Cook IF. 2011. An evidence-based protocol for the prevention of upper arm injury related to vaccine administration (UAIRVA). *Human Vaccines* 7(8): 845–8.

The volume injected into the deltoid should not exceed 0.5 mL in children and 1.0 mL in adults.

The vaccine recipient should be seated with their arm removed from the garment sleeve and hanging relaxed at their side. The vaccinator places their index finger on the vaccine recipient's acromion process (the highest point on the shoulder) and their thumb on the vaccine recipient's deltoid tuberosity (the lower deltoid attachment point).<sup>7</sup>

The injection site is midway between these anatomical landmarks. The vaccine should be deposited at the bulkiest part of the muscle, which usually in line with the axilla (Figure 2.8).

**Figure 2.8: How to locate the deltoid site**



## 2.2.7 Multiple injections at the same visit

A well-prepared and confident vaccinator will reassure the parent/guardian or whānau that giving concurrent vaccines is a safe and appropriate practice, avoiding multiple visits.

When more than one vaccine is scheduled at the same visit, it is recommended that vaccinators give all the scheduled vaccines at that visit. This particularly applies to the 12- and 15-month events (see below), when three vaccines are scheduled.

Multiple vaccines should not be mixed in a single syringe unless specifically licensed and labelled for administration in one syringe. A different needle and syringe should be used for each injection.

### The 12-month and 15-month immunisation events

MMR1, PCV and MenB are the vaccines are scheduled at the 12-month immunisation event. It is preferable to give vaccines into separate sites. If the deltoid bulk is considered insufficient for IM injection, then two injections can be given into one vastus lateralis (MMR and PCV), and the MenB given into the other leg. Local tenderness is a potential reaction to MenB, such that, if given in the vastus lateralis may temporarily affect the infant's mobility.

Suggested options for 12-months immunisation are given below.

<i>Sufficient deltoid mass:</i>	<i>Insufficient deltoid mass:</i>
MMR: IM left leg (vastus lateralis)	MMR: IM left leg (vastus lateralis)
MenB: IM left arm (deltoid)	PCV: IM left leg (vastus lateralis)
PCV: IM right leg (vastus lateralis)	MenB: IM right leg (vastus lateralis)

To give two injections in the same limb, the vastus lateralis is preferred because of its greater muscle mass (see Figure 2.9). The injection sites should be on the long axis of the thigh and *separated by at least 2 cm* so that potential localised reactions will not overlap.

MMR2, varicella and Hib-PRP vaccines are scheduled at the 15-month event. When giving these vaccines, it is preferable to give one in each vastus lateralis and the third in the deltoid. When a fourth injection is required (eg, MenB catch-up), this should be given in the other deltoid.

The recommended vaccine administration sequence and location is:

1. Hib-PRP: IM in left leg (vastus lateralis)
2. Varicella: IM in left arm (deltoid)
3. MMR: IM in right leg (vastus lateralis).

If parents/guardians request to split the vaccines given at the 15-month event, then providers are advised to give MMR and VV at the first visit, followed by Hib-PRP at the second visit.

**Note:** there is a risk that the patient may not return for the second visit when the 15-month vaccines are split.

If MMR and VV are not given at the same visit (concurrently), then there should be an interval of at least four weeks between them. This interval is to avoid the response to the second vaccine being diminished due to interference from the response to the first vaccine (see section 2.1.5).

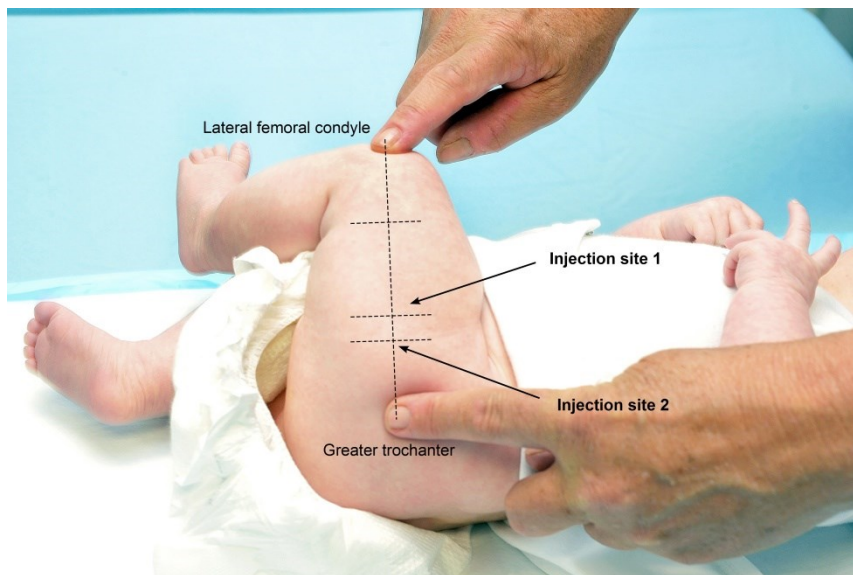
## Multiple injections in the same muscle

When two injections are to be given in the same limb, the vastus lateralis is preferred because of its greater muscle mass (see Figure 2.9). The injection sites should be on the long axis of the thigh and *separated by at least 2 cm* so that localised reactions will not overlap.

If multiple injections in the deltoid are required, the sites should be separated by at least 2 cm.<sup>8</sup>



**Figure 2.9: Suggested sites for multiple injections in the lateral thigh**



## 2.3 Post-vaccination

### 2.3.1 Post-vaccination advice

Post-vaccination advice should be given both verbally and in writing. The advice should cover:

- which vaccines have been given and the injection sites, and whether the injections were IM or SC
- potential vaccine responses following immunisation (see Table 2.9) and what to do if these occur (eg, measures for relieving fever, when to seek medical advice)
- when the individual or parent/guardian should contact the vaccinator if they are worried or concerned
- contact phone numbers (including after-hours phone numbers).

**Table 2.9: Potential vaccine responses**

Vaccine	Potential vaccine responses
DTaP- or Tdap-containing vaccine	Localised pain, redness and swelling at injection site Mild fever Being grizzly and unsettled Loss of appetite, vomiting, and/or diarrhoea Drowsiness Extensive limb swelling after multiple doses of a DTaP-containing vaccine
Hib-PRP	Localised pain, redness and swelling at the injection site Mild fever Being grizzly and unsettled

Vaccine	Potential vaccine responses
Hepatitis B	Very occasionally pain and redness at the injection site Nausea or diarrhoea
HPV	Fainting, especially in adolescents – this is an injection reaction, not a reaction to the vaccine Localised discomfort, pain, redness and swelling at the injection site Mild fever Headache
Influenza	Localised pain, redness and swelling at injection site Headache Fever
MenB	Localised pain, redness and tenderness at injection site Mild to moderate fever Irritability, sleep changes, loss of appetite in young children Headache, muscle aches and nausea in older children and adults
MMR	Measles component: Fever which lasts 1–2 days; rash (not infectious) 6–12 days after immunisation Mumps component: Parotid and/or submaxillary swelling 10–14 days after immunisation Rubella component: Mild rash, fever, lymphadenopathy, joint pain 1–3 weeks after immunisation
Pneumococcal	Localised pain, redness and swelling at injection site Mild fever Irritability, sleep changes Loss of appetite
Rotavirus	Diarrhoea and or vomiting may occur after the first dose Mild abdominal pain
Varicella	Localised pain, redness and swelling at injection site Mild fever Mild rash, possibly at the injection site (2–5 lesions, appearing 5–26 days after immunisation)

## 2.3.2 Recommendations for fever and pain management

The use of paracetamol (or ibuprofen) around the time of immunisation in anticipation of immunisation-related fever or localised pain occurring is only recommended routinely for infants and children aged under 2 years receiving MenB (Bexsero) vaccine. In this case, up to three doses of paracetamol (or ibuprofen) can be given prophylactically to reduce fever (see section 13.5.1). For immunisation events that do not include administration of MenB or for children over the age of two years receiving MenB, the use of paracetamol (or ibuprofen) around the time of immunisation in anticipation of immunisation-related fever or localised pain occurring is not generally recommended. However, use of these medicines is recommended if the child is distressed due to discomfort following immunisation.

Health care providers are encouraged to discuss with parents the possible immunisation responses and non-pharmaceutical management of fever or pain, as well as the role of medicines.

## Fever

General fever-relieving measures include:

- giving extra fluids to drink (eg, more breastfeeds or water)
- reducing clothing if the baby is hot.

While a high fever alone does not need treatment, analgesics (paracetamol or ibuprofen) may be used for distress or pain in a febrile child.

## Pain management and soothing measures

For breastfeeding infants, breastfeeding before, during and after the injection can provide comfort and pain relief.<sup>3, 14</sup>

Give the rotavirus vaccine 1–2 minutes before other immunisations; rotavirus vaccines contain sucrose that has been shown to reduce pain.<sup>3, 14</sup> The infant can then be breastfed (where possible) or held comfortably while the other immunisations are given.

For infants aged under 6 months, the 5 Ss (swaddling, side/stomach position, shushing, swinging and sucking) have been found to be effective for soothing and reducing pain after immunisations.<sup>9</sup>

Using age-appropriate distraction has been shown to reduce pain and distress.<sup>3, 14</sup> Examples include showing an interesting or musical toy to an infant, or encouraging an older child to blow using a windmill toy or bubbles. Electronic games/phone games can be useful for older children and teenagers. Do not rub the injection site after the injection, as it increases the risk of vaccine reactogenicity.

For infants and children, the use of a topical anaesthetic cream or patch has been found to be effective for immunisation pain management.<sup>3, 14</sup> Parents/guardians and those administering the vaccine should check the manufacturers' recommendations before using topical anaesthetics. The correct dose for infants needs to be followed particularly carefully due to risk of methaemoglobinaemia. Topical anaesthetics may have a role in managing immunisation pain and anxiety, particularly for children who have had previous multiple medical interventions or needle phobias.

Following immunisation, if an infant or child is distressed by pain or swelling at the injection site, placing a cold, wet cloth on the area may help relieve the discomfort. Antipyretic analgesics (paracetamol or ibuprofen) may be used if the above measure does not relieve the child's distress.



## 2.3.3 Anaphylaxis and emergency management

All vaccinators must be able to distinguish anaphylaxis from fainting, anxiety, immunisation stress-related responses (ISRR), breath-holding spells and seizures.

Anaphylaxis is a very rare,<sup>10</sup> unexpected and potentially fatal allergic reaction. It develops over several minutes and usually involves multiple body systems. Unconsciousness is rarely the sole manifestation and only occurs as a late event in severe cases. A strong central pulse (eg, carotid) is maintained during a faint (vasovagal syncope), but not in anaphylaxis.

In general, the more severe the reaction, the more rapid the onset. Most life-threatening adverse events begin within 10 minutes of vaccination. The intensity usually peaks at around one hour after onset. Symptoms limited to only one system can occur, leading to delay in diagnosis. Biphasic reactions, where symptoms recur 8 to 12 hours after onset of the original attack, and prolonged attacks lasting up to 48 hours have been described. All patients with anaphylaxis should be hospitalised.

### Signs of anaphylaxis

Anaphylaxis is a severe adverse event of rapid onset, characterised by circulatory collapse. In its less severe (and more common) form, the early signs are generalised erythema and urticaria with upper and/or lower respiratory tract obstruction. In more severe cases, limpness, pallor, loss of consciousness and hypotension become evident, in addition to the early signs. Vaccinators should be able to recognise all the signs and symptoms of anaphylaxis given in Table 2.10.

**Table 2.10: Signs and symptoms of anaphylaxis**

	Signs and symptoms	Severity
Early warning signs (usually within a few minutes)	Dizziness, perineal burning, warmth, pruritus, flushing, urticaria, nasal congestion, sneezing, lacrimation, angioedema	Mild to moderate
	Angioedema, hoarseness (laryngeal oedema), dyspnoea, abdominal pain, vomiting, substernal pressure	Moderate to severe
Life-threatening symptoms (usually from soon after the injection to within 20 minutes after)	Bronchospasm, stridor, collapse, hypotension, dysrhythmias	Severe

There is no place for conservative management of anaphylaxis. Early administration of adrenaline is essential (for more details, see Table 2.12).

Misdiagnosis of faints and other common causes of collapse as anaphylaxis may lead to inappropriate use of adrenaline. Misdiagnosis as a faint could also lead to a delay in the administration of adrenaline.

Vaccinators should therefore be able to distinguish anaphylaxis from fainting (vasovagal syncope), anxiety and breath-holding spells (see Table 2.11). Infants and babies rarely faint. Sudden loss of consciousness, limpness, pallor and vomiting (signs of severe anaphylaxis in children) should be presumed to be an anaphylactic reaction.

In adults and older children, the most common adverse event is a syncopal episode (fainting), either immediately or soon after vaccination. During fainting the individual suddenly becomes pale, loses consciousness and if sitting or standing will slump to the ground. Recovery of consciousness occurs within a minute or two. Fainting is sometimes accompanied by brief clonic seizure activity, but this generally requires no specific treatment or investigation if it is a single isolated event.

## Immunisation stress-related response

Immunisation stress-related responses (ISRR) is a term used to cover a spectrum of responses to stress generated by immunisations.<sup>11</sup> These responses vary from fainting and hyperventilation through to dissociative neurological symptoms, which include non-epileptic seizures. They usually occur in individuals but have also been identified in clusters; this is often referred to as mass psychogenic illness. These stress responses are complex and involve both physiological and psychological factors. For more information see the WHO manual for health professionals, available from [www.who.int/publications/i/item/9789241515948](http://www.who.int/publications/i/item/9789241515948).

**Table 2.11: Distinguishing anaphylaxis from a faint (vasovagal reaction)**

	Faint	Anaphylaxis
<b>Onset</b>	Usually before, at the time, or soon after the injection	Soon after the injection, but there may be a delay of up to 30 minutes
<b>System</b>		
Skin	Pale, sweaty, cold and clammy	Red, raised and itchy rash; swollen eyes and face; generalised rash
Respiratory	Normal to deep breaths	Noisy breathing due to airways obstruction (wheeze or stridor); respiratory arrest
Cardiovascular	Bradycardia; transient hypotension	Tachycardia; hypotension; dysrhythmias; circulatory arrest
Gastrointestinal	Nausea/vomiting	Abdominal cramps
Neurological	Transient loss of consciousness; good response once supine/flat	Loss of consciousness; little response once supine/flat

## Distinguishing a hypotonic-hyporesponsive episode from anaphylaxis

A hypotonic-hyporesponsive episode is a shock-like state defined by the sudden onset of limpness (muscle hypotonia) and decreased responsiveness, with pallor or cyanosis in infants and children aged under 2 years after immunisation.

A hypotonic-hyporesponsive episode can occur from 1 hour to 48 hours after immunisation, typically lasts less than 30 minutes, and resolves spontaneously.<sup>12</sup>

A hypotonic-hyporesponsive episode is a recognised serious reaction to immunisation and should be reported to CARM (see section 1.6.3).

## Avoidance of anaphylaxis

Before immunisation:

- ensure there are no known contraindications to immunisation
- if in doubt about administering the vaccine, consult the individual's GP or a paediatrician.

Individuals should remain under observation for 20 minutes following vaccination in case they experience an immediate adverse event requiring treatment. This observation period may vary for some vaccines and age groups.

## Emergency equipment

Vaccinators, providers and quality managers are responsible for:

- ensuring emergency procedures are known by all staff
- practising emergency procedures regularly
- having an emergency kit (see Table 2.12) and adrenaline in every room where vaccinations/medications are given
- checking emergency kits regularly
- not giving vaccines when working alone.

Remember, events happen without warning. Appropriate emergency equipment must be immediately at hand whenever immunisations are given, and all vaccinators must be familiar with the practical steps necessary to save lives following an anaphylactic reaction (see Table 2.12 and Table 2.13).

**Table 2.12: Emergency equipment**

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**An emergency kit should contain:**

- adrenaline\* 1:1,000 (at least 3 ampoules) and dosage chart
  - syringes: 1.0 mL (a minimum of 3; tuberculin not insulin, as the insulin needle is too short for IM injection)
  - needles: a range of needle lengths and gauges, including 23 or 25 G × 25 mm, 22 G × 38 mm
- Auto-injectors for self-administration of adrenaline should not be used as a substitute for a proper anaphylaxis pack. However, if an adrenaline auto-injector is the only available adrenaline preparation when treating anaphylaxis, health care providers should use it.
- 

**Other emergency equipment required**

It is also necessary to have on hand:

- adult and paediatric bag valve mask resuscitator (eg, Ambu bag)
  - access to a telephone.
- 

\* The expiry date of the adrenaline and other medicines should be written on the outside of the emergency kit, and the kit should be checked every 4 weeks. Adrenaline is heat and light sensitive and should be stored appropriately. Adrenaline that has a brown tinge must be discarded.

The emergency kit may need to have additional equipment for non-clinical settings (see A3.6).

Hydrocortisone injection is used only under the direction of a medical practitioner (see the Practitioner's Supply Order, list available at [pharmac.govt.nz/pharmaceutical-schedule/community-section-b/practitioners-supply-order-pso-previously-the-mppo-list/](https://www.pharmac.govt.nz/pharmaceutical-schedule/community-section-b/practitioners-supply-order-pso-previously-the-mppo-list/)).

## Emergency management

An IM injection of 1:1,000 adrenaline is the mainstay of the treatment of anaphylaxis, and adrenaline should be universally available when vaccinating. A tuberculin syringe should be used to ensure the accuracy of measurement when drawing up small doses.

In an emergency, there is no absolute contraindication to the use of adrenaline. It is, however, a very potent agent, and if used when anaphylaxis has not occurred or in excessive doses, adrenaline can cause dysrhythmias, severe hypertension and left ventricular failure. Tissue necrosis can occur if the same injection site is used repeatedly.

Intravenous adrenaline should only be used, with extreme caution, by medical staff. It is not appropriate as the first line of treatment of anaphylaxis.

**Table 2.13: Initial anaphylaxis response/management**

**CALL FOR HELP – send for professional assistance (ambulance, doctor).  
Never leave the individual alone.**

**ASSESS FOR ANAPHYLAXIS** (see Table 2.10 for full details)

**Airway and breathing**

Noisy breathing due to airways obstruction; or respiratory arrest

**Circulation/shock**

Tachycardia; hypotension; dysrhythmias; circulatory arrest

**Skin changes**

Red, raised and itchy rash; swollen eyes and face; generalised rash

**If cardiac arrest** – commence age-appropriate CPR and life support measures

**LAY THE PATIENT DOWN** (do not allow them to stand)

If they have breathing difficulties, elevate the head and chest.

**ADMINISTER ADRENALINE** by deep IM injection into outer thigh

Adrenaline dosage for 1:1,000 formulation is 0.01 mL/kg up to a maximum of 0.5 mL.

For those under 10 kg or if weight is not known, use the following guidelines:

Age	Dose
under 2 years	0.1 mL
2–4 years	0.2 mL
5–11 years	0.3 mL
12 years and over	0.5 mL
Adult	0.5 mL

You can expect to see some response to the adrenaline within 1–2 minutes. If necessary, adrenaline can be repeated at 5–15-minute intervals, while waiting for assistance.

**ADMINISTER OXYGEN**, if available, at high flow rates when there is respiratory distress, stridor or wheeze.

**IF HYPOTENSIVE, ELEVATE LEGS.**

**RECORD VITAL SIGNS** every 5–10 minutes. All observations and interventions need to be clearly documented in medical notes and should accompany the individual to hospital.

**ADMIT TO HOSPITAL** – all cases of anaphylaxis should be admitted to hospital for observation. Rebound anaphylaxis can occur 12–24 hours after the initial episode.

Note: IV adrenaline should only be used, with extreme caution, by medical staff trained in its use or in liaison with an emergency specialist

In the unlikely event of a cardiac or respiratory arrest following anaphylaxis, assess respiration without putting your face close to the patient’s face, don PPE as soon as it is available and ventilate via a bag valve mask.

## Ongoing management in hospital or by a medical practitioner

Individuals who experience vaccine-related anaphylaxis should be admitted to hospital. If the individual is in an unstable or deteriorating condition, and is not being transported by ambulance, they must be accompanied by the attending health professional so that treatment can be continued during transfer.

Hydrocortisone may be used as adjunctive medication. Nebulised salbutamol is helpful for bronchospasm. For further information, refer to the product data sheet.

Additional drugs that may be administered under the direction of a medical practitioner include:

- nebulised adrenaline: for laryngeal oedema
- bronchodilators: salbutamol 5 mg nebulised, to help reverse bronchospasm
- corticosteroids: prednisone 2 mg/kg (up to 40 mg) orally, or hydrocortisone 4 mg/kg IV, to help resolve tissue swelling (prednisolone syrup may be more appropriate for young children and infants).

Observation for a period of up to 24 hours after stabilisation of the individual's condition is recommended due to the risk of late deterioration from delayed and biphasic reactions.

All anaphylaxis reactions should be reported to CARM (see section 1.6.3).

## 2.3.4 Documentation and insurance

Accurate documentation, including information on the Aotearoa Immunisation Register (AIR), COVID-19 immunisation register (CIR), School-Based Vaccination System (SBVS) and practice management system (PMS), is essential. If the vaccinator has not kept accurate clinical records, it is difficult to prove what action/care was or was not taken/delivered if the patient notes are subject to legal scrutiny.

In addition to the information recorded on the AIR (see section 2.3.5), CIR, SBVS or PMS, information that should be collected in the patient's clinical notes includes:

- confirmation that informed consent was given
- confirmation that the individual was observed for the recommended time and no adverse events occurred during the observation period (if an adverse event does occur, it is essential to document the action and treatment given and inform CARM – see section 1.6.3).

The vaccinator should also complete the relevant sections in the *Well Child Tamariki Ora My Health Book* and, where applicable, the child's immunisation certificate (see Appendix 5), the Health New Zealand payment claim form (where applicable). If required, a manual vaccination recording form can be completed for entering into AIR as soon as is practical. See [www.tewhatauora.govt.nz/our-health-system/digital-health/the-aotearoa-immunisation-register-air/key/#forms](http://www.tewhatauora.govt.nz/our-health-system/digital-health/the-aotearoa-immunisation-register-air/key/#forms)

### Indemnity insurance

All vaccinators should carry indemnity insurance. Most employers have indemnity cover, but vaccinators do not have an automatic right to claim under that cover. Indemnity insurance should cover vaccinators/health professionals for disciplinary proceedings, coroners' inquiries, and claims of negligence or error that may lead to injury, death or damage.

## 2.3.5 The Aotearoa Immunisation Register

The Aotearoa Immunisation Register (AIR) is our new national register for vaccination activity that replaced both the National Immunisation Register (NIR), and the Covid Immunisation Register (CIR) in December 2023. The AIR:

- provides an accurate record of immunisation coverage rates both regionally and nationally – this information assists with programme planning to improve coverage rates and identify areas with lower immunisation rates
- collects information about the Schedule, and some targeted programmes (eg, Tdap during pregnancy, BCG vaccine)
- collects information about influenza immunisations and high-risk adolescent and adult immunisations
- enables health professionals to efficiently identify which vaccines an individual has received (especially if they have moved areas or changed health care providers) and any that are due or may have been missed
- enables individuals to have an accurate, up-to-date record of their immunisation history.

Individuals can choose to restrict access to their information in the AIR. This means they do not wish to share their information across providers, and so their full immunisation history will not be viewable via the AIR.

For more information on sign-up, programme updates and restricted access, please refer to the Aotearoa Immunisation Register website ([www.tewhatauora.govt.nz/our-health-system/digital-health/the-aotearoa-immunisation-register-air](http://www.tewhatauora.govt.nz/our-health-system/digital-health/the-aotearoa-immunisation-register-air)).

## References

1. Health and Disability Commissioner. *Code of Health and Disability Services Consumers' Rights* [updated July 2012]; URL: <https://www.hdc.org.nz/your-rights/the-code-and-your-rights/>. (accessed 8 April 2024)
2. Lee J, Robinson JL, Spady DW. Frequency of apnea, bradycardia, and desaturations following first diphtheria-tetanus-pertussis-inactivated polio-*Haemophilus influenzae* type B immunization in hospitalized preterm infants. *BMC Pediatrics*, 2006. 6(6): p. 20.
3. World Health Organization. 2015. *Report to SAGE on Reducing Pain and Distress at the Time of Vaccination* (ed.). URL: [https://www.who.int/immunization/sage/meetings/2015/april/1\\_SAGE\\_latest\\_pain\\_guidelines\\_March\\_24\\_Final.pdf](https://www.who.int/immunization/sage/meetings/2015/april/1_SAGE_latest_pain_guidelines_March_24_Final.pdf) (accessed 8 May 2020)
4. Poland GA, Borrud A, Jacobson RM, et al. Determination of deltoid fat pad thickness. Implications for needle length in adult immunization. *JAMA*, 1997. 277(21): p. 1709-11.
5. Koster MP, Stellato N, Kohn N, Rubin LG. Needle length for immunization of early adolescents as determined by ultrasound. *Pediatrics*, 2009. 124(2): p. 667-72.



6. Knuf M, Zepp F, Meyer CU, et al. Safety, immunogenicity and immediate pain of intramuscular versus subcutaneous administration of a measles-mumps-rubella-varicella vaccine to children aged 11-21 months. *European Journal of Pediatrics*, 2010. 169(8): p. 925-33.
7. Cook IF. An evidence based protocol for the prevention of upper arm injury related to vaccine administration (UAIRVA). *Hum Vaccin*, 2011. 7(8): p. 845-8.
8. Centers for Disease Control and Prevention. 2015. Vaccine Administration. in *Epidemiology and Prevention of Vaccine-Preventable Diseases (The Pink Book)* Hamborsky J, Kroger A, Wolfe S (eds). Washington DC. URL: <https://www.cdc.gov/vaccines/pubs/pinkbook/vac-admin.html>. (accessed 3 July 2020)
9. Harrington JW, Logan S, Harwell C, et al. Effective analgesia using physical interventions for infant immunizations. *Pediatrics*, 2012. 129(5): p. 815-22.
10. Bohlke K, Davis RL, Marcy SM, et al. Risk of anaphylaxis after vaccination of children and adolescents. *Pediatrics*, 2003. 112(4): p. 815-20.
11. World Health Organization. 2019. *Immunization Stress-related Response. A manual for program managers and health professionals to prevent, identify and respond to stress-related responses following immunization.* (ed.), Geneva: World Health Organization. URL: <https://www.who.int/publications-detail/978-92-4-151594-8> (accessed 07 May 2020)
12. Australian Technical Advisory Group on Immunisation (ATAGI). 2018. After vaccination. in *Australian Immunisation Handbook*. Canberra. URL: <https://immunisationhandbook.health.gov.au>. (accessed 3 July 2020)



# 3 Vaccination questions and addressing concerns

## 3.1 Some commonly asked questions

### 3.1.1 Vaccine scheduling

#### Which vaccines can be administered at the same visit?

There are no known contraindications to administering registered vaccines at the same visit, provided they are administered in separate syringes at separate sites. If two or more parenterally or intranasally administered *live* vaccines are not given at the same visit, then a minimum interval of four weeks is recommended. The rationale is based on limited data where VV has been given within four weeks of measles-containing vaccine and breakthrough varicella disease (chickenpox) has occurred. Any time interval is acceptable between administering live oral vaccines (eg, rotavirus) and live parenteral vaccines (BCG), live and inactive vaccines, or two inactive vaccines.

#### What steps are required if the Schedule is interrupted or varied?

Generally, there is no need to repeat prior doses; simply continue the Schedule as if no interruption has occurred (see Appendix 2). Special circumstances where the above does not apply are as follows:

- HepB given at birth to babies born to HBsAg-positive mothers – this dose does not count as part of a catch-up
- the two-dose course of rotavirus vaccine (RV1; Rotarix) should be started before age 15 weeks (ie, the latest is 14 weeks and 6 days) and completed by age 25 weeks (ie, the latest is 24 weeks and 6 days); if an infant reaches age 25 weeks without receiving the second dose, the first dose already given may offer them some protection against disease

- MMR given prior to age 12 months – infants who receive MMR prior to age 11 months still require two further MMR doses beyond age 12 months (scheduled at ages 12 months and 15 months)
- conjugate vaccine schedule requirements, which are age dependent (eg, children over 12 months of age do not require a full primary course of Hib-PRP or PCV vaccine, but do require one or two doses in the second year of life; see Appendix 2)
- when reconciling overseas schedules and the New Zealand Schedule – immigrant children are eligible for all scheduled vaccines including those for special groups (if applicable). Those who have commenced additional vaccine courses according to routine overseas schedules (eg. MenACWY and HepA) are not funded to complete these vaccine courses once in New Zealand. However, many of these vaccines are available for private purchase if the parent or guardian wishes to complete their child's course.

Remember that children who miss one vaccine dose may do so again, so optimising a catch-up schedule is important.

### How should the rest of the Schedule be handled when an adverse event has occurred following immunisation?

Proceeding with the Schedule after an AEFI depends on the nature of the event and the likelihood that the vaccine caused it. Most prior adverse events are not contraindications to receiving further immunisations. The only absolute contraindication to receiving a vaccine is anaphylaxis to a prior dose or an ingredient in the vaccine. However, immunocompromise can be a contraindication to receiving live vaccines (see section 4.3).

Adverse events should be reported to CARM ([nzphvc.otago.ac.nz/reporting](https://nzphvc.otago.ac.nz/reporting)). See section 1.6.3 'AEFI reporting process – notifying CARM'.

Consult the AEFI section in each of the *Handbook* chapters, and seek specialist advice (eg, from the local medical officer of health, Health New Zealand or IMAC). Other vaccines not related to the AEFI can usually be administered as per the Schedule.

## 3.1.2 Babies and children

### What if a baby had a difficult birth or was premature?

Preterm and/or low birthweight infants should receive vaccination as per the Schedule (ie, at the usual chronological age, with the usual vaccine dosage and interval), including rotavirus vaccination. These babies may be at higher risk of some of these diseases, so vaccinating them on time is particularly important. Infants with serious congenital conditions should generally receive Schedule vaccines at the usual chronological age. However, if the infant is still in hospital or has recently been discharged, please seek the advice of the treating specialist (see also section 4.2.2).

Rotavirus vaccine should be given on time to hospitalised infants, including those in neonatal units. When standard infection control precautions are maintained, the risk of rotavirus vaccine virus transmission will be minimal.<sup>1,2,3</sup> (See also sections 4.2.4, 4.2.5, 4.3, 4.4, 4.5 and chapter 20.)

## What special vaccines are offered to newborn babies?

Babies born to HBsAg-positive mothers should receive:

- 100–110 IU hepatitis B immunoglobulin (HBIG) neonatal, at or as close as possible to birth
- a birth dose of HepB (Engerix-B, 20 µg or paediatric formulation, Engerix-B 10 µg, if available), which should be given at or as close as possible to birth (preferably within 12 hours).

If HBIG and/or HepB is inadvertently omitted, administer as soon as the omission is recognised. HBIG can be administered up to seven days post-delivery. If there is a delay for longer than seven days, seek specialist advice. These babies should then continue as per the Schedule at ages 6 weeks, 3 months and 5 months. Serological testing is required at 9 months of age (see section 9.5.2).

A baby at higher risk of TB is offered a BCG immunisation soon after birth (see section 23.5 for neonatal BCG eligibility and the timing of neonatal BCG). The lead maternity carer will discuss the need for the vaccine with the mother prior to her baby's birth and vaccination will be conducted at designated BCG clinics within each district.

## What are the special requirements of immigrant children?

Immigrant children should be immunised according to the New Zealand Schedule with *due account taken of documented prior vaccine administration* and the eligibility criteria defined in the *Health and Disability Services Eligibility Direction 2011*, available on the Health New Zealand | Te Whatu Ora website at [www.tewhatauora.govt.nz/our-health-system/eligibility-for-publicly-funded-health-services](http://www.tewhatauora.govt.nz/our-health-system/eligibility-for-publicly-funded-health-services) (see also section 4.7).

All children aged under 18 years are eligible to receive Schedule vaccines and Well Child Tamariki Ora services regardless of their immigration and citizenship status, and providers can claim the immunisation benefit for administering the vaccines.

If a refugee or immigrant has no valid documentation of vaccination, an age-appropriate catch-up programme is recommended. Only clearly documented doses should be considered as given. If there is no documented vaccination history, plan the catch-up schedule assuming the vaccines have not been given (see Appendix 2). The immunisation status of all immigrant children should be checked when they register with a primary health care provider.

## Is it possible to boost a child's immune system by other means?

Eating a healthy diet, getting adequate sleep and exercise, having a smoke-free environment and minimising high levels of stress will help keep the child's immune

system healthy. However, none of the above confers the disease-specific immunity that vaccination provides (see also section 3.2.4). All children get infections (eg, common colds); this does not mean the immune system is not working.

### 3.1.3 Allergies and illnesses

#### What if the individual is unwell on the day of immunisation?

Minor illness or being in the recovery phase of an illness is not a reason to postpone immunisation. Individuals with a significant acute illness and a temperature  $>38^{\circ}\text{C}$  should have immunisation postponed until they are better. This is not because they are at particular risk of vaccine reactions, but because complications of the acute illness may be misinterpreted as a complication of the immunisation, or an AEFI may complicate the clinical picture of the acute illness. (See section 2.1.4 'Contraindications' and the contraindications sections in the disease chapters.) If immunisation is postponed, it is important to ensure the patient is placed on the recall for the immunisation later.

#### What if the individual is due to have an operation (elective surgery)?

There is no evidence that anaesthetic impairs the immune response to a vaccine or increases the risk of AEFI.

Vaccination with inactive vaccines is preferably avoided for 48 hours prior to an anaesthetic in case post-vaccination symptoms such as fever interfere with preparation for surgery; similarly, live vaccines may induce fever 6–12 days after vaccination. There is no reason to delay surgery following vaccination with a live vaccine if the individual is well at the time of immediate pre-operative assessment. There is no reason to delay vaccination after surgery once the individual is well and has recovered from the procedure. See the Association of Paediatric Anaesthetists of Great Britain and Ireland Immunisation guideline ([apagbi.org.uk/guidelines](http://apagbi.org.uk/guidelines)). Ideally, individuals scheduled for splenectomy should be immunised at least two weeks before the operation. Pneumococcal, meningococcal, Hib, influenza and varicella vaccines are recommended for these individuals pre- or post-splenectomy (see section 4.3.11 and the relevant disease chapters). Note: If the surgery is an emergency, then the immunisation programme should commence seven days post-splenectomy.

The use of blood products during major surgery can interfere with the response to live attenuated virus vaccines. Live virus vaccines should be given at least two weeks before, or deferred for up to 11 months after, doses of human normal immunoglobulin or other blood products.<sup>1</sup> The interval will be determined by the blood product and dose received (see Table A6.1).

## Can immunisations be given during an operation?

When appropriate, opportunistic vaccination can be administered while a person is under anaesthesia.<sup>2</sup>

## What if the individual has a chronic disease?

Individuals with chronic diseases should be immunised in the normal way, especially as they may be more at risk from the severe effects of vaccine-preventable diseases. However, if the illness or its treatment results in impaired immunity, immunisation with live vaccines should be considered carefully (see section 4.3), and the patient's GP, paediatrician or other specialist should be consulted before immunisation.

## What if the individual is allergic?

Only anaphylaxis to a prior dose of vaccine, or to an ingredient in the vaccine, is considered an absolute contraindication. See the contraindications and precautions section in each disease chapter. Children with asthma, eczema, hay fever and other allergies should be immunised in the usual way. Studies have shown that immunised children have slightly lower rates of atopic diseases.<sup>6,7</sup>

## Can an individual be immunised if they are known to develop a rash with antibiotics?

Individuals can be immunised if they are known to develop a rash with antibiotics. Only anaphylaxis to a prior dose of vaccine, or to an ingredient in the vaccine, is considered an absolute contraindication to vaccination. A rash alone is not anaphylaxis.

## Can all individuals receive all the vaccines?

An individual cannot receive a vaccine if they have had anaphylaxis to a prior dose of a vaccine or to an ingredient in the vaccine. They may have an underlying condition that is a contraindication to some vaccines; for example, those with illnesses or treatments that cause immunocompromise may be unable to receive live attenuated vaccines (see chapter 4 for special groups, chapters 12, 14 and 21 for MMR and chapter 24 for varicella).

## What if a child has had seizures?

A diagnosed neurological condition is not a contraindication to any vaccine on the Schedule. A history of well-controlled seizures in the vaccine recipient or a family history of seizures (febrile or afebrile) or other neurologic disorder is not a contraindication to vaccination against pertussis.<sup>3</sup>

Vaccination for children with an unstable neurological disorder (eg, poorly controlled epilepsy or deteriorating neurological state) has previously been considered a precaution for pertussis vaccination, but as these children may be high risk of severe

pertussis complications, vaccination is recommended. Individual cases should be discussed with the specialist.<sup>3</sup>

A febrile reaction may occur after any vaccine and result in a febrile seizure in a susceptible child. Vaccine-related febrile seizures are rare, although the risk is higher following administration of certain vaccines, such as influenza vaccine (section 11.7), MMR (section 12.7) and meningococcal B vaccine (MenB, Bexsero; see section 13.7.1). These seizures, although frightening for a parent, are almost always benign with no associated sequelae.

### 3.1.4 Parents, guardians and contacts

#### What if the child's mother or guardian is pregnant or breastfeeding?

These are not contraindications to giving any of the Schedule vaccines to a child, including live vaccines, such as MMR. In addition, consideration should be given to the risks for the mother or guardian and baby from diseases such as pertussis, which can be life-threatening in infants.

Pregnancy provides an important opportunity to ensure the infant's siblings have received age-appropriate immunisation.

Pertussis (as Tdap) and influenza vaccines are recommended and funded for pregnant women (see section 4.1).

#### Are the viruses in live vaccines, such as MMR and varicella, transmissible?

These are highly attenuated (weakened) viruses designed specifically to induce an immune response without causing disease. There have been no recorded cases of measles, mumps or rubella disease in individuals who were in contact with a vaccine recipient. Vaccine-strain varicella transmission to contacts is rare (documented in only 9 immunised people, resulting in 11 secondary cases), and the documented risk of transmission exists only if the immunised person develops a rash<sup>4</sup> (see chapters 12, 14 and 21 for MMR and chapter 24 for varicella).

## 3.2 Addressing myths and concerns about immunisation

Myths about immunisation have existed since the first use of smallpox vaccine over 200 years ago and have resulted in loss of confidence in immunisation programmes. Misconceptions about vaccines contribute to vaccine hesitancy, which is an issue of

global concern. This section provides information to assist providers with addressing concerns about immunisation.

### 3.2.1 Background

Concerns about immunisation should be taken seriously and responded to appropriately, providing as much information as possible. Individuals have the right to make informed decisions for themselves and those in their care, and to accept responsibility for their decisions. It is important to respect this right.

Many individuals and groups actively campaign against immunisation in New Zealand and globally. Their reasons for doing so may include personal experience, such as an adverse event they have attributed to immunisation, philosophical beliefs, conspiratorial beliefs or dissatisfaction with inadequate or superficial responses from health professionals or other authorities, who can seem at times to be dismissive of people's concerns. It is important for all health professionals to be able to provide accurate information about the benefits and risks of immunisation and to respond with as much information as possible to parent/guardian concerns or refer people appropriately.

It is not always possible to change people's position by way of scientific argument or presentation of evidence. Anti-immunisation arguments are almost exclusively based on fallacies of fact or logic, or on historical information that is no longer applicable in the current context. Often these arguments can be challenging for the health professional, particularly if the professional is unfamiliar with the argument and when they are complicated by logical flaws.

In any discussion, it may help to acknowledge that science does not always have all the answers, but that it provides a tool with which to answer questions and evaluate the evidence. It is important to point out that an event that follows immunisation is not necessarily caused by the immunisation. Finally, it is always helpful to inform parents/guardians about additional sources of reliable information (see section 2.1.2 on informed consent and section 1.6 on the safety monitoring of vaccines in New Zealand).

### 3.2.2 Understanding anti-immunisation

People tend to take on board information that supports their belief system and to ignore information that does not. The internet makes it very easy to access material that is appealing. Most people usually make logical decisions based on their perception of risk. Therefore, when a person has the perception that the risk of disease is real and that vaccines are reasonably safe and work, they are more likely to vaccinate. People are unlikely to vaccinate if they perceive that there is little risk of disease and that vaccines are not safe and do not work.<sup>5</sup>



### 3.2.3 Addressing concerns

If a parent is concerned about immunising their child, determining their concerns and addressing them can be helpful. Most often these concerns are around vaccine safety. As a health professional, you should challenge poor information, in a respectful way.

There are steps you can take when addressing a parent's or an individual's concerns (as detailed on the Canadian Paediatric Society website at [www.cps.ca/documents/position/working-with-vaccine-hesitant-parents](http://www.cps.ca/documents/position/working-with-vaccine-hesitant-parents)).<sup>6</sup> These include the following:

1. Understand the key role that sound advice from a health professional can play in parental decision making.
2. Use presumptive and motivational interviewing techniques to understand specific vaccine concerns.
3. Use clear and simple language to present evidence of disease risks and vaccine benefits, fairly and accurately.
4. Address injection pain head on.
5. Explain that community (herd) immunity does not guarantee personal protection.

For further information to help to address concerns, see also resources on the IMAC website ([immune.org.nz](http://immune.org.nz)), and other websites, such as the Centers for Disease Control and Prevention (CDC), the Immunization Action Coalition, Sharing Knowledge about Immunisation (SKAI) and the National Centre for Immunisation Research and Surveillance (see Appendix 8).

### 3.2.4 Debunking a myth

Debunking myths can be very challenging and can also backfire. When you are addressing a myth, there are three important points to remember.<sup>7</sup>

#### 1. Try not to repeat the myth. Focus on the core facts.

This is because people cannot remember if what they hear was a myth or a fact later. Debunking can serve to strengthen the myth in people's minds as either familiar or a threat to their world view. Begin with the core facts; if it is easy to do in a few clear words, state what is true first.

#### 2. Precede a myth with a warning.

Let them know that 'this is untrue' because you often cannot avoid mentioning the myth. Warn beforehand that a myth is coming and mention it once only directly prior to the correction.



### 3. Explain the fallacy – include an alternative explanation that accounts for how the myth misleads.

Explain why the misinformation is wrong. Do not leave a void but rather replace the myth with accurate information. You can highlight the problems with cherry picking, conspiracy theories and fake experts. If you have them, graphics can be extremely helpful, such as pictures of vaccine-preventable diseases or even a graph showing the impact of vaccination – if you feel it is appropriate.

### 4. State the core facts again.

Restate the fact again so that the core fact is the last thing the person processes.

## Facts and myths about immunisation

**Core fact:** Measles and rubella have been eliminated in some countries. The WHO has set targets for global eradication.

**Myth:** MMR causes autism.

**Explanation:** There is no evidence that the MMR causes autism.<sup>8,9</sup>

In 1998 a British physician announced he had found an association between the receipt of MMR and the development of a new disorder that included autism in a study of 12 children. No subsequent studies following his study have been able to reproduce his results.

In 2004 *The Lancet* retracted the original 1998 study from the scientific literature on the grounds that it was the product of dishonest and irresponsible research and the British authorities revoked the doctor's licence to practise medicine.<sup>10</sup> In 2008 a press investigation revealed that the doctor had falsified patient data and relied on laboratory reports that he had been warned were incorrect. Multiple studies have exonerated MMR vaccination.

**Core fact:** The incidence of allergic diseases has been increasing. It is thought that lack of exposure to microbes may play a role.

**Myth:** Vaccines cause allergic diseases.

**Explanation:** Extensive research shows that, if anything, vaccines may have a protective effect against allergic disease.

Many studies have explored this issue. A few have shown a positive association, but the majority show no association or a negative association. The international scientific

community generally accepts that vaccines do not lead to allergies and in fact have a small protective effect against the development of allergy.<sup>6, 11, 12</sup>

The 2012 Institute of Medicine review of adverse events rejected any causal relationship between inactivated influenza vaccine and asthma exacerbation or reactive airway disease episodes in children and adults.<sup>9</sup>

**Core fact:** On-time vaccination is associated with a reduced risk of hospitalisation for diseases such as pertussis and pneumococcal disease in children under 1 year of age.

**Myth:** Vaccines cause cot death.

**Explanation:** Vaccines may reduce the risk for cot death.

Sudden unexpected death in infancy (SUDI), also known as cot death, usually occurs in children aged under 12 months and is most common around age 3 months, when many immunisations are given. SUDI may occur by chance within a day or so of immunisation.<sup>13</sup> There is no evidence that vaccination causes SUDI. Despite solid evidence against a link, the claims continue to be made.

Many studies have conclusively shown that SUDI is not caused by immunisation.<sup>13</sup> Some studies, including the New Zealand Cot Death Study, found a lower rate of SUDI in immunised children.<sup>14</sup> This is consistent with a Scandinavian study, which found that some cases of SUDI were probably caused by undiagnosed pertussis.<sup>15</sup> A large case-control study showed no increased risk of SUDI associated with immunisation,<sup>16</sup> and a meta-analysis of nine case-control studies further suggested that immunisation is protective against SUDI.<sup>17</sup> Consistent findings from several studies using a range of methods invalidate claims that associate vaccination with SUDI or cot death.<sup>18</sup>

**Core fact:** At birth, an infant is exposed to thousands of microbes.

**Myth:** Vaccines 'overload' or 'overwhelm' the infant immune system.

**Explanation:** It is estimated that the infant immune system could respond to over 10,000 vaccines all at once.

There is no evidence of immune system 'overload', either theoretical or actual. The immune system can deal with an extraordinarily large number of different antigens at any one time.

Every day we all encounter viruses, bacteria and other agents to which the immune system responds. Any demands placed on the immune system by vaccines are minuscule compared to its ability to respond.

Vaccines have very few antigens in them. The number of immunogenic proteins and polysaccharides in modern vaccines has decreased dramatically compared with early vaccines because of advances in vaccine technology. For example, early whole-cell pertussis vaccines contained around 3,000 immunogenic proteins, compared with two to five in the modern acellular pertussis vaccines. In spite of an increase in the number of vaccines on the Schedule, an infant now receives far fewer immunogenic proteins and polysaccharides than with earlier vaccines.<sup>19</sup> There are considerably more antigens in the organisms that cause disease than in the vaccines.

**Explanation:** Delaying immunisation for fear that an infant is too young leaves the infant vulnerable to disease, particularly pertussis and pneumococcal diseases. Infants delayed for their pertussis vaccinations are 4–6 times more likely to be hospitalised with the disease.<sup>20</sup> On-time vaccination is important.

**Core fact:** Vaccines induce immunity through natural processes.

**Myth:** It is better to get 'natural immunity' than get vaccinated.

**Explanation:** There is no evidence that experiencing vaccine-preventable diseases has any benefit on health; on the contrary, these diseases are serious and sometimes fatal. Vaccinated people have fewer diseases than unvaccinated people. Some vaccines induce better protection than that resulting from natural disease. Examples are tetanus, HepB and HPV, and protein conjugate polysaccharide vaccines administered to children aged under 2 years (Hib-PRP and PCV).

**Core fact:** The scientific evidence shows there is no association between HPV vaccines and autoimmune conditions.

**Myth:** HPV vaccines cause autoimmune conditions.

**Explanation:** Several large cohort studies have been conducted to investigate the link between HPV vaccine and autoimmune conditions.<sup>21-25</sup> No association has been found in these studies.

**Core fact:** The quadrivalent human papillomavirus vaccine has reduced cervical disease in countries using the vaccine, and Australia has almost eliminated genital warts.

**Myth:** HPV vaccines cause postural orthostatic tachycardia syndrome (POTS), complex regional pain syndrome (CRPS) and chronic fatigue syndrome (CFS).

**Explanation:** There is no scientific evidence that links POTS, CRPS or CFS with HPV vaccination.

POTS is a condition in which tachycardia occurs when a patient moves from a supine position to upright. The condition is associated with a collection of other symptoms, which include palpitations, light-headedness, weakness, blurred vision, headache, extreme fatigue, nausea, syncope and sleep disturbance. Up to 50 percent of people with POTS have an antecedent viral illness and 25 percent have a family history of similar complaints. There is an overlap between POTS and CFS.<sup>26</sup>

CRPS describes a variety of disorders characterised by pain that is disproportional to the inciting event. In children and adolescents, it often presents as a painful mottled swollen limb with allodynia and hyperalgesia. Girls are six times more likely to be affected than boys and the peak age of onset is at age 12–13 years. Often minor trauma is the inciting event, but around one-third of people with CRPS are unable to recall an inciting injury or trauma.<sup>27</sup>

CFS is a disorder characterised by extreme fatigue that cannot be explained by an underlying medical condition. The causes are unknown, but it has been linked to infection with Epstein–Barr virus and human herpesvirus 6.

Cases of these disorders have been reported in association with HPV vaccination, particularly in the media, and social media. The variable time between vaccination and onset of symptoms, lack of consistent symptoms and a reporting rate that remains below the expected rate for these syndromes all point to HPV vaccine not being the cause of these conditions.<sup>28</sup>

Post-marketing surveillance systems globally continue to monitor the safety of HPV vaccination programmes.<sup>29–31</sup> The WHO’s Global Advisory Committee on Vaccine Safety has systematically reviewed HPV vaccine safety and has not found any safety issue that would alter its recommendations for use.<sup>32</sup> The main challenge with HPV vaccine is communicating its excellent safety profile.<sup>33</sup>

**Core fact:** Everything is made of chemicals and any chemical can be toxic, even water.

**Myth:** Vaccines contain toxic chemicals, viruses and cells.

**Explanation:** Vaccine ingredients are not toxic in the amounts present in a vaccine. It is the dose that differentiates a poison from a harmless substance, essential substance or a medicine.

Most of the ingredients in vaccines are present already in our bodies and we consume them in some way every day. For example, aluminium is the most common metallic element on earth, and the body makes and uses formaldehyde for synthesising deoxyribonucleic acid (DNA).

- There is approximately 60 times more formaldehyde in a pear than a vaccine.
- Polysorbate 80 is used in many foods, including ice cream.
- Vaccines do not contain extraneous cells or viruses.

- Aluminium compounds administered via vaccination do not contribute significantly to the general aluminium exposure and do not raise human serum aluminium levels.<sup>34</sup> Based on 80 years of experience, the use of aluminium adjuvants in vaccines has proven to be extremely safe and effective.<sup>35, 36</sup>

For more information on vaccine ingredients, see the IMAC website at [www.immune.org.nz/resources/factsheets](http://www.immune.org.nz/resources/factsheets).

**Core fact:** With the exception of safe water, no other intervention, not even antibiotics, has had such a major effect on mortality reduction and population growth. – S Plotkin<sup>37</sup>

**Myth:** Vaccination has played little role in controlling disease.

**Explanation:** Vaccine programmes have controlled or eliminated polio, tetanus, diphtheria, pertussis, *Haemophilus influenzae* type b, hepatitis B, pneumococcal disease, meningococcal disease, rotavirus, human papillomavirus, varicella, hepatitis, yellow fever, measles, mumps, rubella and others, in populations where vaccines have been used.

Improvements in living conditions and medical care have reduced the chances of dying from infectious disease, but without immunisation most people will still acquire vaccine-preventable infections. For example, measles, which spreads through the air, is largely unaffected by improvements in living conditions other than reduced overcrowding. Indigenous cases of measles, mumps and rubella were eliminated from Finland over a 12-year period using a two-dose MMR vaccination schedule given between 14 and 16 months and at age 6 years.<sup>38</sup> In September 2016, the Region of the Americas was the first WHO region to be declared free of measles and rubella. Endemic measles and rubella were declared eliminated in New Zealand in 2017.

**Core fact:** No vaccine is 100 percent effective and some immunised children will get the disease.

**Myth:** Vaccines do not work, as most cases of disease are in immunised children.

**Explanation:** As immunisation coverage increases, the proportion of cases that occur in children who have been immunised compared with those who are unimmunised increases. There is a mathematical relationship between vaccine effectiveness, immunisation coverage and the proportion of cases that are immunised.

To see this clearly, imagine a group of 100 children. If 90 percent of children are given a vaccine with 90 percent efficacy, then:

- 81 of the 100 children will be immune
- 10 children will be susceptible because of not having the vaccine, and another 9 because of vaccine failure.

This means that in the situation of exposure to the infection in a community, we expect that nearly half the cases of disease will be in immunised children, even though only 10 percent of immunised children were susceptible.

Of course, if all 100 children had been vaccinated only 10 would be susceptible to disease. As vaccine uptake rises, the proportion of cases of disease that occur in vaccinated people increases dramatically, but the absolute number of cases of disease falls to very low levels. Failing to provide the denominators (how many vaccinated and how many unvaccinated) can lead to misunderstanding.

For pertussis, where the protection following immunisation lasts only four to six years, immunised children can be infected but the resultant illness is usually milder, with fewer serious consequences and at an older age than if they had not received vaccine. The disease is most severe in infants, but adolescents and adults contribute to the carriage and spread of the disease (see sections 16.2 and 16.3).

For further details on the effectiveness of vaccines, see the IMAC website ([immune.org.nz/vaccines/effectiveness-and-safety](http://immune.org.nz/vaccines/effectiveness-and-safety)).

### 3.3 Addressing immunisation issues in a constantly changing environment

In recent years, the internet has exploded with a variety of forums that disseminate anti-immunisation material effectively. It is no longer practical to prepare official rebuttals to each new article. Fortunately, the internet also facilitates the rapid communication of scientific commentary on new misinformation as they appear. There are several scientists who regularly address immunisation myths in the form of regular blogs. In addition, some organisations provide position statements and discussion forums. While the format is often colloquial, the writers are respected scientists who volunteer commentary against the abuse of science and evidence-based medicine.

## References

1. Freedman M, Kroger A. 2023. General immunization practices. in *Plotkin's Vaccines: Eighth edition*, Orenstein W (eds). Philadelphia, US. p. 113-144.e6. (accessed 25 May 2023)
2. Siebert JN, Posfay-Barbe KM, Habre W, Siegrist CA. Influence of anesthesia on immune responses and its effect on vaccination in children: review of evidence. *Paediatric Anaesthesia*, 2007. 17(5): p. 410-20.
3. Liang JL, Tiwari T, Moro P, et al. Prevention of pertussis, tetanus, and diphtheria with vaccines in the United States: recommendations of the Advisory Committee on



- Immunization Practices (ACIP). *MMWR: Recommendations and Reports*, 2018. 67(2): p. 1-44.
4. American Academy of Pediatrics. 2018. Varicella-zoster infections. in *Red Book: 2018 Report of the Committee on Infectious Diseases*, Committee on Infectious Diseases, Kimberlin D, Brady M, et al. (eds). URL: <https://redbook.solutions.aap.org/redbook.aspx>. (accessed 3 July 2020)
  5. Hilton S, Petticrew M, Hunt K. 'Combined vaccines are like a sudden onslaught to the body's immune system': parental concerns about vaccine 'overload' and 'immune-vulnerability'. *Vaccine*, 2006. 24(20): p. 4321-7.
  6. MacDonald NE, Desai S, Gerstein B. Working with vaccine-hesitant parents: An update. *Paediatrics & Child Health*, 2018. 23(8): p. 561-562.
  7. Lewandowsky S, Cook J, Ecker UKH, et al. 2020. *The Debunking Handbook 2020* (ed.). URL: <https://skepticalscience.com/docs/DebunkingHandbook2020.pdf> (accessed 23 September 2021)
  8. Demicheli V, Rivetti A, Debalini MG, Di Pietrantonj C. Vaccines for measles, mumps and rubella in children. *Cochrane Database Syst Rev*, 2012(2): p. CD004407.
  9. Institute of Medicine: Committee to Review Adverse Effects of Vaccines. 2012. *Adverse effects of vaccines: Evidence and causality* (ed.), Washington, DC: The National Academies Press. URL: <https://www.nap.edu/catalog/13164/adverse-effects-of-vaccines-evidence-and-causality> (accessed January 2020)
  10. Immunization Action Coalition. 2019. MMR vaccine does not cause autism: Examine the evidence! , <https://www.immunize.org/catg.d/p4026.pdf> (accessed 20 May 2020)
  11. Offit PA, Hackett CJ. Addressing parents' concerns: do vaccines cause allergic or autoimmune diseases? *Pediatrics*, 2003. 111(3): p. 653-9.
  12. Gruber C, Warner J, Hill D, et al. Early atopic disease and early childhood immunization--is there a link? *Allergy*, 2008. 63(11): p. 1464-72.
  13. Brotherton JM, Hull BP, Hayen A, et al. Probability of coincident vaccination in the 24 or 48 hours preceding sudden infant death syndrome death in Australia. *Pediatrics*, 2005. 115(6): p. e643-6.
  14. Mitchell EA, Stewart AW, Clements M. Immunisation and the sudden infant death syndrome. New Zealand Cot Death Study Group. *Archives of Disease in Childhood*, 1995. 73(6): p. 498-501.
  15. Lindgren C, Milerad J, Lagercrantz H. Sudden infant death and prevalence of whooping cough in the Swedish and Norwegian communities. *European Journal of Pediatrics*, 1997. 156(5): p. 405-9.
  16. Vennemann MM, Butterfass-Bahloul T, Jorch G, et al. Sudden infant death syndrome: no increased risk after immunisation. *Vaccine*, 2007. 25(2): p. 336-40.
  17. Vennemann MM, Höffgen M, Bajanowski T, et al. Do immunisations reduce the risk for SIDS? A meta-analysis. *Vaccine*, 2007. 25(26): p. 4875-9.
  18. Medsafe. 2016. Sudden unexpected death in infants (SUDI): no causal link to vaccination. *Prescriber Update*. 37(4): p. 56-7  
<https://www.medsafe.govt.nz/profs/PUArticles/PDF/Prescriber%20Update%20December%202016.pdf> (accessed 10 May 2022)
  19. Offit PA, Quarles J, Gerber MA, et al. Addressing parents' concerns: do multiple vaccines overwhelm or weaken the infant's immune system? *Pediatrics*, 2002. 109(1): p. 124-9.
  20. Grant CC, Roberts M, Scragg R, et al. Delayed immunisation and risk of pertussis in infants: unmatched case-control study. *BMJ*, 2003. 326(7394): p. 852-3.
  21. Arnheim-Dahlstrom L, Pasternak B, Svanstrom H, et al. Autoimmune, neurological, and venous thromboembolic adverse events after immunisation of adolescent girls with quadrivalent human papillomavirus vaccine in Denmark and Sweden: cohort study. *BMJ*, 2013. 347: p. f5906.



22. Chao C, Klein NP, Velicer CM, et al. Surveillance of autoimmune conditions following routine use of quadrivalent human papillomavirus vaccine. *Journal of Internal Medicine*, 2012. 271(2): p. 193-203.
23. Grimaldi-Bensouda L, Guillemot D, Godeau B, et al. Autoimmune disorders and quadrivalent human papillomavirus vaccination of young female subjects. *Journal of Internal Medicine*, 2014. 275(4): p. 398-408.
24. Langer-Gould A, Qian L, Tartof SY, et al. Vaccines and the risk of multiple sclerosis and other central nervous system demyelinating diseases. *JAMA Neurol*, 2014. 71(12): p. 1506-13.
25. Scheller NM, Svanstrom H, Pasternak B, et al. Quadrivalent HPV vaccination and risk of multiple sclerosis and other demyelinating diseases of the central nervous system. *JAMA*, 2015. 313(1): p. 54-61.
26. Benarroch EE. Postural tachycardia syndrome: a heterogeneous and multifactorial disorder. *Mayo Clinic Proceedings*, 2012. 87(12): p. 1214-25.
27. Borucki AN, Greco CD. An update on complex regional pain syndromes in children and adolescents. *Current Opinion in Pediatrics*, 2015. 27(4): p. 448-52.
28. European Medicines Agency. 2015 *Pharmacovigilance Risk Assessment Committee (PRAC): Assessment Report: Human papillomavirus (HPV) vaccines (EMA/762033/2015)*. URL: [https://www.ema.europa.eu/en/documents/referral/hpv-vaccines-article-20-procedure-assessment-report\\_en.pdf](https://www.ema.europa.eu/en/documents/referral/hpv-vaccines-article-20-procedure-assessment-report_en.pdf). (accessed 10 May 2022)
29. Nguyen M, Ball R, Midthun K, Lieu TA. The Food and Drug Administration's Post-Licensure Rapid Immunization Safety Monitoring program: strengthening the federal vaccine safety enterprise. *Pharmacoepidemiology and Drug Safety*, 2012. 21 Suppl 1(Suppl 1): p. 291-7.
30. Kliewer EV, Demers AA, Brisson M, et al. The Manitoba human papillomavirus vaccine surveillance and evaluation system. *Health Reports*, 2010. 21(2): p. 37-42.
31. Gold MS, McIntyre P. Human papillomavirus vaccine safety in Australia: experience to date and issues for surveillance. *Sex Health*, 2010. 7(3): p. 320-4.
32. World Health Organization. Safety update of HPV vaccines: Meeting of the Global Advisory Committee on Vaccine Safety, 7–8 June 2017. *Weekly Epidemiological Record* 2017. 28(92): p. 393-404.
33. World Health Organization. Meeting of the Strategic Advisory Group of Experts on Immunization, April 2016 – conclusions and recommendations. *Weekly Epidemiological Record* 2016. 91(21): p. 266–84.
34. Karwowski MP, Stamoulis C, Wenren LM, et al. Blood and Hair Aluminum Levels, Vaccine History, and Early Infant Development: A Cross-Sectional Study. *Academic Pediatrics*, 2018. 18(2): p. 161-165.
35. Lindblad EB. Aluminium adjuvants--in retrospect and prospect. *Vaccine*, 2004. 22(27-28): p. 3658-68.
36. Global Advisory Committee on Vaccine Safety. 2008 *Statement from the Global Advisory Committee on Vaccine Safety on aluminium-containing vaccines*. WHO; 2008; URL: [https://www.who.int/vaccine\\_safety/committee/topics/aluminium/statement\\_112002/en/](https://www.who.int/vaccine_safety/committee/topics/aluminium/statement_112002/en/). (accessed 25 May 2020)
37. Plotkin S, Orenstein W, Offit P, Edwards KE, *Plotkin's Vaccines (7th edition)*. 2018, Philadelphia, US: Elsevier.
38. Peltola H, Heinonen OP, Valle M, et al. The elimination of indigenous measles, mumps, and rubella from Finland by a 12-year, two-dose vaccination program. *New England Journal of Medicine*, 1994. 331(21): p. 1397-402.

# 4 Immunisation of special groups

This chapter discusses the special immunisation requirements of individuals at risk of vaccine-preventable diseases due to certain conditions or underlying disease, or through their occupation or other risk factors. The topics covered are:

- pregnancy and lactation (section 4.1)
- infants with special immunisation considerations from birth (section 4.2)
- immunocompromised individuals (section 4.3)
- chronic kidney disease (section 4.4)
- chronic liver disease (section 4.5)
- other special groups (section 4.6)
- immigrants and refugees (section 4.7)
- occupation-related vaccinations (section 4.8)
- travel (section 4.9).

Note: Vaccinators are advised to check the Pharmaceutical Schedule and any online updates (available at [pharmac.govt.nz/](http://pharmac.govt.nz/)) for changes to funding decisions for special groups.

## 4.1 Pregnancy and lactation

### 4.1.1 Women planning pregnancy

Women and other potential birthing parents who are planning pregnancy should know whether they are immune to measles, rubella and varicella (see sections 12.8.3, 21.5.3 and 24.5.4).

#### Measles, mumps and rubella vaccine

Two doses of MMR are recommended and funded for eligible women who do not have documented evidence of immunity to measles, mumps and rubella (see section 12.8.3 for evidence). Pregnancy should be avoided for four weeks after vaccination (see section 21.6.1).

## Varicella vaccine

Two doses of VV are recommended but not funded for adults who are susceptible to varicella (see section 24.5). VV should not be given to those who are pregnant, and pregnancy should be avoided for four weeks after vaccination (see section 24.5.4).

### 4.1.2 During pregnancy

There are no safety concerns around giving non-live vaccines in pregnancy, including subunit vaccines and COVID-19 mRNA vaccine.<sup>1, 2</sup> Live vaccines should not be administered to a pregnant woman because of the theoretical possibility of fetal harm. Seek specialist advice in circumstances where the risk of exposure to an infection outweighs any potential risk of the fetus from immunisation.

Although MMR should not be given when pregnant, in follow-up studies of women who inadvertently received MMR during pregnancy, there was no evidence that MMR is teratogenic or harmful to the mother, her fetus or her newborn.<sup>3</sup> Inadvertent immunisation with a rubella-containing vaccine in early pregnancy is no longer considered an indication for termination of pregnancy.<sup>3</sup> See the relevant disease chapters, particularly measles (section 12.8.2), rubella (section 21.8.2) and varicella (section 24.8.6), for recommendations on managing exposure to diseases during pregnancy.

## COVID-19 vaccine

Women and other people who are pregnant are encouraged to be routinely vaccinated with mRNA-CV at any stage of pregnancy (see sections 5.2.2 and 5.5.5) and to discuss questions or concerns with their health professional. People who are trying to become pregnant do not need to avoid pregnancy after receiving mRNA-CV.

## Influenza vaccine

The quadrivalent influenza vaccine is recommended and funded for pregnant women and should be offered at any stage of pregnancy, as soon as the annual influenza vaccine becomes available (see section 11.5). Both the pregnant woman and the fetus are at increased risk of influenza complications;<sup>4, 5</sup> influenza vaccination is therefore recommended during pregnancy to reduce this risk.<sup>6</sup> When pregnancy spans two influenza seasons, two vaccinations (one from each season) are recommended to protect against all the predicted strains.

Maternal influenza vaccination also offers protection to the neonate through maternal antibody transfer.<sup>3, 4</sup> Influenza vaccines are not registered for infants aged under 6 months; therefore vaccination during pregnancy helps protect newborns and infants who are too young to be vaccinated.<sup>4, 5</sup> Maternal influenza vaccination is significantly associated with reduced risk of influenza virus infection<sup>5</sup> and hospitalisation for an influenza-like illness in infants up to 6 months of age.<sup>5, 7</sup>

There is no evidence that influenza vaccine prepared from a virus subunit causes harm to the fetus or neonate.<sup>8-10</sup>

## Pertussis vaccine (Tdap)

Pertussis is a severe infection in infants too young to have been fully immunised. The tetanus, diphtheria and pertussis vaccine (Tdap) is recommended and funded to be given from 16 weeks' gestation in every pregnancy, preferably in the second trimester, to protect both the mother and her infant from pertussis (see section 16.5).<sup>11-13</sup> Postpartum maternal Tdap vaccination can reduce the risk of a mother infecting her baby but does not have the added benefit of providing passive antibodies.

See section 16.5 for information about maternal pertussis vaccine effectiveness and safety.

## Household members and other close contacts

Confirmation of pregnancy should act as a trigger to review the pertussis vaccination status of all the pregnant woman's close contacts. This includes making sure siblings have received the usual Schedule vaccines and offering Tdap to adults, although this is only currently funded for certain special groups.

### 4.1.3 Breastfeeding and post-partum

All vaccines on the National Immunisation Schedule and those recommended for special groups are safe for breastfeeding women and other lactating people.

## Measles, mumps and rubella vaccine

Up to two doses of MMR are recommended and funded **after delivery** for eligible women who do not have documented evidence of immunity to measles, mumps and rubella. Breastfeeding is not a contraindication to MMR (see section 12.8.3).

## Pertussis vaccine (Tdap)

A singled dose of Tdap is funded for parents or primary caregivers of infants admitted to a neonatal intensive care unit or special care baby unit for more than three days and whose mothers had not received Tdap at least 14 days prior to birth.

A single dose of Tdap is also recommended but not funded for all new mothers who did not receive a Tdap vaccination during pregnancy.

## Varicella vaccine

VV is recommended but not funded for all susceptible adults. Pregnant women who are non-immune can be offered VV **after delivery**.

If the mother is susceptible to varicella, VV for the mother is recommended and funded after delivery if the baby or other household members are immunocompromised (see section 24.5).

## 4.2 Infants with special immunisation considerations from birth

Further details are given in section 4.3 for infants born with primary immunodeficiency (section 4.3.2), including Down syndrome; secondary immunodeficiency (section 4.3.3); functional asplenia (section 4.3.11); and HIV (section 4.3.12).

### 4.2.1 Infants born to mothers with positive or unknown hepatitis B (HBsAg) status

Infants born to mothers who are known to be HBsAg-positive require hepatitis B vaccine (HepB) plus hepatitis B immunoglobulin (HBIG) to be given at or as soon as possible after birth; to continue vaccination as per the Schedule at 6 weeks, 3 and 5 months; and to undergo serological testing for hepatitis B antigen and antibodies (HBsAg and anti-HBs) at 9 months of age.

Infants of mothers whose HBsAg status is unknown at the time of delivery require HepB at birth while waiting for the results of urgent HBsAg testing on the mother (see section 9.5.2). If mother is found to be HBsAg positive, HBIG will also be required.

### 4.2.2 Preterm and/or low birthweight infants

Vaccination as per the Schedule (ie, at the usual chronological age, with the usual vaccine dosage and interval) is recommended for preterm and/or low birthweight infants. There is a potential risk of apnoea in preterm infants with respiratory immaturity. Apnoea monitoring should be considered after the first vaccination event.<sup>12</sup> For infants who experience apnoea after their first vaccination event, apnoea monitoring should be considered for 48–72 hours after subsequent vaccination events, but avoiding or delaying vaccination is not recommended.<sup>14</sup>

#### Hepatitis B vaccine

All preterm and low birthweight infants born to HBsAg-positive mothers should be managed the same way as term infants and receive HepB and HBIG to be given at or as

soon as possible after birth (see section 9.5.2). These infants should continue vaccination as per the usual Schedule, starting at age 6 weeks.

## Rotavirus vaccine

If an infant is in hospital at 6 weeks old, the Schedule vaccines, including rotavirus vaccine, should be given in hospital. Standard infection control precautions should be maintained. Administration of rotavirus vaccine to medically stable, hospitalised infants at 6 weeks of age has been shown to be well-tolerated. No increase in nosocomial rotavirus transmission has been observed within neonatal intensive care units.<sup>15-17</sup>

Rotavirus vaccine can be given to preterm infants who are receiving corticosteroids. For immunocompromised infants or mothers, also see section 4.3.2 and section 4.2.5.

## Pneumococcal vaccines

Infants born before 28 weeks' gestation are eligible for pneumococcal vaccination as part of an extended immunisation programme for high-risk groups (see section 17.5.2), ie, a three-dose primary series of PCV13 (Prevenar 13) given at ages 6 weeks, 3 months, 5 months with a booster at age 12 months; some may benefit from 23PPV beyond age 2 years, if they still have lung disease.

Infants born at 28 weeks' gestation or later, who do not have a condition eligible for extended pneumococcal immunisation, should receive PCV13 as per the Schedule at ages 6 weeks, 5 months and 12 months.

## Influenza vaccine

Preterm and/or low birth weight infants with an eligible condition are recommended to receive an annual funded influenza vaccination from 6 months of age (see Table 11.2).

Influenza vaccination is recommended for close contacts of preterm infants, including children from age 6 months (for funding eligibility see Table 11.2).

## Pertussis vaccine (Tdap)

It is essential that siblings of preterm infants are up to date with Schedule vaccinations, to reduce the risk of pertussis transmission to the infant (see section 16.5). Adolescents should have received Tdap in year 7 or at age 11 years as part of the Schedule.

Pertussis-containing vaccine is funded for primary and catch-up vaccination of all children aged under 18 years (see Appendix 2 for catch-up schedules).

A single dose of Tdap is recommended and funded for parents or primary caregivers of infants admitted to a neonatal intensive care unit or special care baby unit for more than three days and whose mother did not receive maternal Tdap vaccination at least 14 days before the baby's birth.

Regardless of maternal vaccination history, it is recommended that all caregivers of infants born at less than 32 weeks' gestation receive a single dose of Tdap (not

funded). This is because by 28–32 weeks' gestation the level of transplacental maternal antibodies in the infant is only half of the maternal circulating level, compared with higher than maternal levels by term.<sup>11, 18, 19</sup>

### 4.2.3 Infants with congenital heart disease

Congenital heart disease (CHD) may occur alone (eg, a single ventricle defect or shunt dependent lesion), or with other congenital defects (eg, immunodeficiency, endocrine dysfunction and facial abnormalities in DiGeorge syndrome or asplenia in heterotaxy syndrome).

#### Vaccination of infants with congenital heart disease

Infants with CHD and who are immunocompetent can receive vaccination as per the Schedule including rotavirus and varicella vaccines. For infants with CHD who were also born preterm or with a low birthweight, see also section 4.2.2.

Infants with a complex single ventricle defect or shunt dependent lesion who have undergone the Norwood procedure may have an increased risk of systemic decompensation. There is limited evidence linking the onset of decompensation to vaccination. As a precautionary measure, these infants may require hospital admission for observation or close parental monitoring at home for 48–72 hours after vaccination events. Discuss monitoring requirements with the infant's specialist prior to vaccination.<sup>20</sup>

Timing of vaccination may be affected when cardiac surgery is scheduled to avoid adding extra stress on these infants during this time. Vaccines should be administered at least one week before planned cardiac surgery. After cardiac surgery, administration of subunit vaccines should be delayed by 4–6 weeks for those at risk of systemic decompensation (eg, after a Norwood procedure).

For further information see Starship guidelines available from [www.starship.org.nz/guidelines/immunisations-and-cardiac-infants/](http://www.starship.org.nz/guidelines/immunisations-and-cardiac-infants/)

#### Live vaccines after blood product administration

If an infant has received blood products (eg, bypass or blood transfusion during surgery), delay administration of live vaccine is until seven months post-surgery.<sup>20</sup> This does not apply to administration of rotavirus vaccine.

This standdown period can be shortened to 3 months (as per UK guidelines), especially if measles is circulating in the community. See Table A6.1 in Appendix 6 for suggested intervals between administration of blood products and MMR or VV. MMR and VV will not cause harm if given earlier than the intervals indicated in Table A6.1, but the immune response could be suboptimal, leaving a patient at risk for the relevant disease(s). In an outbreak situation (e.g. measles) immunisation may be given at any time as the benefit could outweigh the potential impaired response.



If no blood products have been given, the usual 4–6 weeks post-operative interval is recommended for those at risk of systemic decompensation, as above.

Some cardiac defects can be associated with immune deficiency, eg Di George syndrome. Most such patients can safely be given live viral vaccines when due – after assessment of immune function (see section 4.3.2). Seek specialist advice.

### Pneumococcal vaccine

Children who have cardiac disease with cyanosis or failure, chronic pulmonary disease, Down syndrome, functional asplenia, immunodeficiency, or renal failure are eligible for extended pneumococcal immunisations as high-risk groups (see section 17.5.2).

### Influenza vaccine

Infants and children with CHD, with or without cyanosis or failure, and children on long-term aspirin are eligible to receive funded annual influenza vaccination from 6 months of age (see Table 11.2).

Influenza vaccination is recommended (but not funded) for close contacts of infants and children with CHD, including children (see section 11.5.4).

### Pertussis vaccination

It is essential that siblings and other close household members of infants with CHD are up to date with Schedule vaccinations, to reduce the risk of pertussis transmission to the infant (see section 16.5). Ensure catch-up vaccination of all children aged under 18 years (see Appendix 2 for catch-up schedules).

### Varicella vaccine

Children on long-term aspirin can receive varicella vaccination as per the Schedule. There has been no reported association between varicella vaccination and the onset of Reye's syndrome in children on long-term aspirin to prevent thrombosis. The use of aspirin during natural chickenpox infection has been associated with Reye's syndrome.<sup>20</sup>

## 4.2.4 Infants with immunocompromise, including primary immunodeficiencies from birth

Seek guidance on immunisation of infants with severe primary immunodeficiencies (see section 4.3.2). Often these infants are unable to mount adequate responses to vaccines. Note: Rotavirus vaccine is contraindicated in any infant with possible severe combined immune deficiencies (SCID) due to the risk of chronic diarrhoea and prolonged viral shedding.<sup>21, 22</sup>

Some infants with congenital liver or kidney conditions are likely to need transplantation. An accelerated immunisation schedule for these infants is provided in Table 4.4. Extra immunisations may be warranted for other chronic kidney and chronic

liver conditions (see sections 4.4 and 4.5). Infants with biliary atresia may have polysplenia (functional hyposplenia; see section 4.3.11).

Infants of mothers who have received immunomodulatory biologic agents (also known as biologic response modifiers) during pregnancy also may have a reduced response to the primary series vaccinations (section 4.2.5).

## 4.2.5 Infants of mothers who received immunomodulatory biologic agents during pregnancy

For infants aged under 12 months, please discuss immunomodulatory therapies taken during pregnancy with their mother or specialist, or contact IMAC (on 0800 IMMUNE / 0800 466 863) before administration of rotavirus, BCG, MMR or VV vaccines.

In recent years there has been rapid development of targeted immunomodulatory biologic agents (also known as biologic response modifiers; BRM), and an increasing number of pregnant women are receiving such therapies. Common examples include adalimumab, infliximab and rituximab. Studies of the effects of these agents on the infant's immune system and ability to respond to vaccination are limited.<sup>23</sup>

Multiple factors influence the potential for these agents to be detected and/or cause immunosuppression in an infant for months after they are born. These include, the agent or combination of agents used, gestational age(s) when administered, ability of the agent(s) and/or their metabolites to cross the placenta, and time between administration of the last antenatal dose and the chronological age of the infant.<sup>24</sup>

A study analysing a US vaccine safety database is encouraging regarding the safety of rotavirus vaccine in the first year of life, and measles-containing vaccine in the first two years of life, in infants exposed in utero to immunomodulatory biologic agents, with no increased rates of adverse events.<sup>25</sup> The commonest agents represented were anakinra, adalimumab, infliximab and etanercept, but other agents were only used in a few women so the safety of these remains unknown.

### Rotavirus vaccine

Although there is limited data on rotavirus vaccine safety when given to infants born to mothers receiving immunomodulatory therapy during pregnancy,<sup>20, 23, 26</sup> in most cases it is considered to be safe, since the immune response to rotavirus vaccine is secretory in the intestinal wall, and not parenteral.

For anti-TNF biologic agents given in utero (eg, infliximab, adalimumab, ustekinumab, certolizumab, etanercept and vedolizumab), there is no evidence of safety concerns.<sup>26</sup>

<sup>27</sup> Infants exposed to tacrolimus in utero (a commonly used non-biologic

immunomodulatory agent) are also able to receive rotavirus vaccine. Caution is still recommended for some immunomodulatory agents and the decision to administer rotavirus vaccine to infants born to mothers who received other immunomodulatory biologic agents, particularly those that are not anti-TNF agents (eg rituximab), during pregnancy should be determined case by case.

The level of circulating wild-type rotavirus is beginning to increase in New Zealand for the first time since the vaccine was introduced in 2015. This is associated with lower RV coverage in the post-COVID-19 pandemic era. Previously, with very low rotavirus levels the risk of gastroenteritis following rotavirus vaccination in infants may have been greater than the risk of acquiring the disease. But with increasing disease in the community, the risk of wild-type gastroenteritis outweighs the potential for vaccine-virus induced illness.

If an infant turns 15 weeks of age before the first rotavirus vaccine dose can be administered, they will not be able to receive any rotavirus vaccine doses.

### BCG vaccine

Infants born to mothers who received immunomodulatory biologic agents during pregnancy must not be vaccinated with a BCG vaccine without specialist consultation (see box above).

### Measles, mumps and rubella, and varicella vaccines.

Infants aged under 12 months born to mothers who received immunomodulatory biologic agents during pregnancy should not be vaccinated with MMR or VV unless specialist consultation has been sought. Normally, it is only recommended to give MMR and VV before age 12 months if there is an increased risk of exposure, such as during an outbreak or following close contact with a case (see sections 12.5.1, 12.8 and 24.8.3) or if an infant is on an accelerated vaccination schedule prior to solid organ transplantation (see section 4.3.10).

## 4.3 Immunocompromised individuals

This section discusses immunisation recommendations for certain groups with immunocompromise.

- Vaccination of close contacts of immunocompromised individuals (section 4.3.1)
- Primary immunodeficiency (section 4.3.2)
- Secondary (acquired) immunodeficiency (section 4.3.3)
- Individuals receiving corticosteroids (section 4.3.4)
- Individuals receiving non-corticosteroid immunomodulatory agents (section 4.3.5)
- Vaccination prior to planned immunosuppression (section 4.3.6)

- (Re)vaccination following immunosuppression (section 4.3.7)
- Oncology including Immune checkpoint inhibitors (immunostimulant) therapy (section 4.3.8)
- Haematopoietic stem cell transplantation (section 4.3.9)
- Solid organ transplantation (section 4.3.10)
- Functional asplenia, hyposplenia and pre-/post-splenectomy (section 4.3.11)
- HIV infection (section 4.3.12)

The nature and degree of immunocompromise determines an individual's immune response and which vaccines are recommended and can be safely administered. Individuals who are immunodeficient or immunosuppressed due to a disease and/or treatment may have an increased risk from infectious diseases. These individuals should be vaccinated as a matter of priority, however, it should be recognised that they have a suboptimal response.

Children aged under 18 years, and adults aged 18 years or older who are eligible to receive publicly funded health and disability services in New Zealand, are eligible to receive the usual Schedule vaccines and additional funded vaccines when they meet the eligibility criteria for special groups.

Vaccinators are advised to regularly check the Pharmaceutical Schedule and any online updates ([pharmac.govt.nz/](http://pharmac.govt.nz/)) for changes to funding decisions for special groups.

It is important to ensure that the household members of these individuals are immune to vaccine-preventable diseases whenever possible.

The following definitions are used in this *Handbook*:

- **Immunocompetent** – a broad term referring to normal immune system function.
- **Immunocompromise** – a broad term referring to altered immune system function. The individual's ability to mount an immune response may be reduced or increased because of a disease, treatment or genetic disorder.
- **Immunomodulation** – changes in immune system function in response to medication, cancer chemotherapy or immunotherapy treatments.
- **Immunostimulant** – a substance able to stimulate or increase an immune response.
- **Immunosuppression** – a reduced ability to mount an immune response caused by medication, cancer chemotherapy or immunotherapy treatment.
- **Immunodeficiency** – a reduced ability to mount an immune response and fight off infection. Immunodeficiency conditions are classified as primary and secondary, dependent on the cause.

## 4.3.1 Vaccination of close contacts of immunocompromised individuals

Immunocompetent siblings, household members and other close contacts of immunocompromised individuals are recommended to receive all the Schedule vaccines at the recommended ages.

All Schedule vaccines can be given to close contacts of immunocompromised individuals. It is important to ensure that close contacts are immune for the added protection of the immunocompromised individual.

### Rotavirus vaccine

Rotavirus vaccine can be given to infants who are in close contact with an immunocompromised individual. The evidence shows that transmission of the rotavirus vaccine virus to contacts is low, and no cases were symptomatic.<sup>15-17</sup>

### Measles, mumps and rubella vaccine

MMR can be given to children and eligible adults who are in close contact with an immunocompromised individual. MMR vaccine viruses are considered non-transmissible; there is no evidence of the current MMR vaccine viruses being transmitted from vaccine recipient to a close contact.<sup>28, 29</sup> See section 12.5 for information about eligibility and the recommended MMR vaccination schedule.

### Varicella vaccine

Age-appropriate varicella (VV) vaccine can be given to close contacts of an immunocompromised individual. Transfer of vaccine virus to an immunocompromised person is rare and only possible if the vaccinated person develops a varicella-like rash. In this situation, the rash should be covered and close contact with the person who is immunocompromised avoided for the duration of the rash.<sup>30</sup> (See section 24.5 for eligibility.)

### Influenza vaccine

Annual influenza vaccination is recommended for all children aged 6 months or older and adults, particularly those who are close contacts of an immunocompromised individual. See chapter 11 for funded vaccine eligibility.

### COVID-19 vaccine

For greater protection of high-risk individuals, close contacts are recommended to be up to date with COVID-19 immunisation as per current guidance (see Table 5.2).

## BCG vaccine

If indicated by the usual BCG eligibility criteria (see section 23.5.2), it is safe to give BCG vaccine to infants of immunocompromised household members.

### 4.3.2 Primary immunodeficiency

Primary immunodeficiencies that present in childhood are usually caused by an inherited genetic disorder. They can result in defects in antibody production (B-lymphocyte disorders), defects in the development of cell-mediated immunity (T-lymphocyte disorders), combination defects (disorders or syndromes affecting B- and T-lymphocytes) and defects of complement and phagocytic function.<sup>31</sup>

Children with Down syndrome (trisomy 21) are at increased risk from respiratory and severe infections due to multiple immune deficits in both the innate and adaptive immune systems, as well as anatomical structural differences,<sup>32, 33</sup> and could be considered as primary immune deficiency. Note that live vaccines **are not contraindicated** for children with Down syndrome, unless an underlying comorbidity that results in severe immunocompromise is also present.

#### Vaccines used to test for a primary immunodeficiency

Hib-PRP, 23PPV, PCV13 and Tdap vaccines may be used in testing for a primary immunodeficiency, on the recommendation of an internal medicine physician or paediatrician. Hib-PRP, PCV13 and Tdap vaccines are funded for primary immunodeficiency testing in children aged under 18 years and eligible adults.

#### Vaccines for individuals with a primary immunodeficiency

##### Live vaccines – caution

Diagnosis of primary immunodeficiency is often not made before children start their Schedule vaccinations. For infants who have the potential to be immunodeficient (eg, have a familial history of inherited immunodeficiency) administration of live vaccines such as BCG (see section 23.6.2), rotavirus vaccine, MMR, and/or varicella vaccines may be contraindicated or need to be deferred until specialist consultation is sought.

Live vaccines are contraindicated for all individuals with T lymphocyte-mediated immunodeficiency, a combined B- and T-lymphocyte deficiency or interferon alpha receptor (IFNAR) deficiencies and signalling pathway defects.<sup>34</sup> Many of these individuals will be on immunoglobulin replacement therapy, which provides passive protection against most vaccine-preventable infections.

## COVID-19 vaccine

### *Young children aged 6 months to 4 years, inclusive*

Children aged 6 months to 4 years with primary immunodeficiency are recommended to receive three doses of mRNA-CV (3 µg). First and second doses are given three weeks apart and dose three is given at least eight weeks after the second dose. An additional dose of mRNA-CV (3 µg) can be given six months after the primary course. This spacing can be reduced to at least three months, on a case-by-case basis, where there is a clinical need.

### *Individuals aged 5 years and over*

Certain individuals from 5 years of age with a primary immunodeficiency are eligible for three primary doses of mRNA-CV (10 µg or 30 µg, as age appropriate) (see section 5.5.2 for details); each dose is given eight weeks apart.

Regardless of any previous doses received after completion of the primary course, an additional dose of mRNA-CV (10 µg or 30 µg, as age appropriate) is recommended for all individuals aged 5 years and over with primary immunodeficiency, particularly for those eligible for three primary doses, to be given six months after a previous dose. This spacing can be reduced to at least three months, on a case-by-case basis, where there is a clinical need (see section 5.5.3).

If a significant adverse reaction to mRNA-CV has occurred, it is recommended to seek advice from IMAC to determine whether further doses are contraindicated.

## Influenza vaccine

Influenza vaccine is funded for all individuals with primary immunodeficiency, including Down syndrome, aged 6 months or older. Regardless of their age, all immunodeficient individuals who receive influenza vaccine for the first time are recommended to receive two vaccine doses at least four weeks apart (second dose unfunded), and one funded dose annually after that. A second dose is funded for children aged 6 months to under 9 years when influenza vaccine is being used for the first time.

## Pneumococcal vaccines

Pneumococcal vaccines are funded for individuals diagnosed with a primary immunodeficiency.

### *Infants and children aged under 5 years*

Children in this age group with a diagnosed primary immunodeficiency or Down syndrome are eligible to receive extended pneumococcal immunisation for high-risk groups (see section 17.5.2).

PCV13 is given as a three-dose primary course plus booster, administer a 3-month dose in addition to the usual Schedule (ie, at ages 6 weeks, 3 months, 5 months and 12 months; see sections 17.5.2 and 17.5.3) followed by age-appropriate 23PPV vaccinations.



### *Children aged 5 years or older and adults*

Children aged 5 years or older and adults with a diagnosed primary immunodeficiency or inherited complement deficiency are eligible to receive one PCV13 followed by age-appropriate 23PPV vaccinations (see section 17.5.2).

### *Children with Down syndrome aged 5 years to under 18 years*

Children in this age group who **have** received at least two doses of PCV10 and have Down syndrome are recommended and funded to receive one PCV13 followed by up to two doses of 23PPV (see section 17.5.2).

Children in this age group who **have not** received at least two doses of PCV10 and have Down syndrome are recommended and funded to receive up to two doses of 23PPV (see section 17.5.2).

## Meningococcal vaccines

Meningococcal vaccines are recommended and funded for individuals with an inherited complement deficiency.

The current funded meningococcal vaccines are recombinant group B vaccine (MenB, Bexsero), quadrivalent group ACWY meningococcal conjugate vaccines (MenACWY, Nimenrix and MenQuadfi).

### *Meningococcal ACWY conjugate vaccines*

#### *Infants aged under 12 months*

Infants aged under 12 months who have an inherited complement deficiency are recommended and funded to receive two doses of MenACWY (Nimenrix) given a minimum of eight weeks apart (see section 13.5). This includes infants who received MenC (NeisVac-C) prior to 1 July 2024 (ie. with no protection against groups A, W and Y).

#### *Children aged 12–23 months*

Children aged 12–23 months who are diagnosed with an inherited complement deficiency are recommended and funded to receive two doses of MenACWY (MenQuadfi) given at 8–12 weeks apart (see note below). This includes infants who received NeisVac-C prior to 1 July 2024 (ie, with no protection against groups A, W and Y). A booster dose is recommended after three years then five yearly.

Note: A second primary dose of MenQuadfi for those aged 12 months and over is off-label and requires a prescription from an authorised prescriber under section 25 of the Medicines Act.

Infants who previously received any MenACWY vaccine can complete their immunisation course with MenQuadfi. Infants who have received two previous doses of Nimenrix when aged under 12 months, can have one dose of MenQuadfi from age 12 months, given at least 6 months after the second dose.

#### *Children aged 2 years to under 7 years*

Children aged 2 years to under 7 years who are diagnosed with an inherited complement deficiency are recommended and funded to receive two doses of MenACWY given 8–12 weeks apart (a prescription is required for a second primary dose, see note above). Give a booster dose after three years, if still aged under 7 years, then five yearly.

#### *Children aged 7 years or older and adults*

Children aged 7 years or older and adults who are diagnosed with an inherited complement deficiency are recommended and funded to receive two doses of MenACWY at least eight weeks apart (a prescription is required for a second primary dose, see note above). A booster dose is recommended to be given every five years.

#### *Group B meningococcal recombinant vaccine*

Vaccination with MenB (Bexsero), to protect against disease caused by the meningococcal group B, is recommended and funded for infants, children and adults **with an inherited complement deficiency** and an increased risk of meningococcal disease.

MenB is funded routinely as part of the Schedule for all infants, given at either ages 3 months, 5 months and 12 months, or an alternate schedule (involving additional visits) at ages 8 weeks and 4 months plus booster at 12 months. Catch-up is available for children aged 13 months to under 5 years until 31 August 2025 (see Section 13.5 for details).

#### *Infants aged under 12 months*

Infants aged 8 weeks to <12 months who are diagnosed with an inherited complement deficiency are recommended and funded to receive two doses of MenB at least eight weeks apart, followed by a booster dose given at least six months after the second dose, from age 12 months. For those aged younger than 8 weeks, to align with the routine schedule visit, MenB can be given at ages 6 weeks and 3 months; this is off-label use and requires a prescription. No prescription is required if given as per the alternative schedule at ages 8 weeks and 4 months.

#### *Children aged 12 to 23 months*

Children aged from 12 months to 23 months who are diagnosed with an inherited complement deficiency are recommended and funded to receive two doses of MenB at least eight weeks apart, followed by a booster dose given 12–23 months after the second dose. The spacing between doses one and two can be reduced to six weeks if indicated, with a prescription.

#### *Children from age 2 years and adults*

Children aged from 2 years and adults who are diagnosed with an inherited complement deficiency are recommended and funded to receive two doses of MenB at least eight weeks apart. This can be reduced to four weeks if clinically required.

Booster doses of MenB are funded five yearly after the age of 12 months for patients with inherited complement deficiency.

Note: MenB elicits a robust immune response, and sometimes high fevers in infants. Routine use of paracetamol (or ibuprofen) with every dose of MenB in children aged under 2 years, whether given alone or with other vaccines, is recommended to reduce the risk of high fever and injection-site pain (see section 13.5.1)

### Herpes zoster vaccine

Individuals aged 18 years and over, including those aged 66 years and over, with primary immunodeficiency are recommended and funded two doses of recombinant zoster vaccine (rZV, Shingrix), given two to six months apart. See section 25.5.1.

## Vaccination advice, by primary immunodeficiency

Below is a summary of the vaccination recommendations for individuals with a primary immunodeficiency.<sup>35</sup> (See also Table A6.1 in Appendix 6.)

Live vaccines are contraindicated for all individuals with T lymphocyte-mediated immunodeficiency, a combined B- and T-lymphocyte deficiency or interferon receptor (IFNAR) deficiencies.<sup>34</sup> Many of these individuals will be on immunoglobulin replacement therapy, which provides passive protection against most vaccine-preventable infections.

### B lymphocyte deficiencies (humoral)

#### *X-linked agammaglobulinaemia and common variable immune deficiency*

- BCG vaccine is contraindicated.
- Only administer live-virus vaccines (rotavirus, MMR, VV) after discussion with the individual's specialist.
- The efficacy of any vaccine that is dependent on a humoral response, such as 23PPV, is doubtful.
- During IVIG therapy, only influenza vaccination is recommended.

#### *Selective IgA deficiency, IgG subclass deficiency and hypogammaglobulinaemia*

- BCG vaccine may be contraindicated.
- Live-virus vaccines (rotavirus, MMR, VV) can be administered.
- All vaccines are probably effective.
- Influenza vaccine is recommended.

### Combined lymphocyte deficiencies (T and B cell)

#### *Complete defects (eg, SCID or athymia)*

- All live vaccines are contraindicated.

- All other vaccines are likely to be ineffective prior to immune reconstitution, and passive protection must be optimised.

*Partial defects (eg, most patients with DiGeorge syndrome, Wiskott Aldrich syndrome, ataxia telangiectasia)*

- Provision of selected live vaccines is dependent on specialist advice after assessment of degree of immune compromise.
- Hib, pneumococcal (PCV13 and 23PPV), and meningococcal vaccines are recommended, except when the individual receives IVIG therapy. Meningococcal vaccines are not funded for these indications.
- Non-live vaccines should be provided as per the usual Schedule, except when the individual receives IVIG therapy.
- Influenza vaccination is recommended, including individuals who receive IVIG therapy.

### Complement deficiencies

*Deficiency of C1–9, mannose-binding lectin, properdin, factor B*

- There are no specific contraindications or precautions.
- The usual Schedule vaccines are probably effective.
- Influenza, Hib, pneumococcal (PCV13 and 23PPV) and meningococcal vaccines are recommended and funded.

### Phagocytic function deficiencies

*Chronic granulomatous disease and cyclic neutropenia*

- BCG and live-bacteria vaccines are contraindicated.
- Live-virus vaccines (rotavirus, MMR, VV) can be administered.
- The usual Schedule vaccines are probably effective.
- Influenza vaccine is recommended.

*Leukocyte adhesion defect, myeloperoxidase deficiency*

- All live vaccines are contraindicated.
- Influenza, Hib, pneumococcal (PCV13 and 23PPV) and meningococcal vaccines are recommended. Meningococcal vaccines are not funded for these indications.

### Interferon alpha receptor deficiencies

IFNAR deficiencies can increase the risk of severe reaction to some live viral vaccines. Other childhood vaccines, including oral RV and mRNA-CV, are safely received. IFNAR deficiencies are extremely rare immune disorder that can result in a defective response to certain viruses.<sup>36, 37</sup> These disorders require genetic testing to be diagnosed and cannot be prevented. IFNAR1 deficiency was only discovered in 2019. This genetic condition increases the risk of serious illness when the individual is exposed to certain respiratory viruses, including COVID-19, influenza and RSV,<sup>38-40</sup> and some live vaccines such as measles, mumps and yellow fever.<sup>41</sup>

### 4.3.3 Secondary (acquired) immunodeficiency

Secondary immunodeficiencies are acquired. They occur in individuals with HIV, individuals with malignant neoplasms, solid-organ transplant recipients, and in individuals receiving cancer chemotherapy or other immunotherapies.<sup>35</sup>

The ability of individuals with a secondary immunodeficiency to develop an adequate immunological response depends on the disease and/or the type and intensity of immunosuppressive therapy. After immunosuppressive therapy is discontinued, immune recovery can take weeks to years. Ideally, vaccination should be conducted prior to any planned immunosuppression.

#### Vaccines for individuals with acquired immunodeficiency

In diseases such as HIV or chronic renal failure, where immune impairment is likely to be progressive, ensuring the individual is up to date with Schedule and additional funded vaccines earlier in their disease and when at optimal disease control may result in better antibody responses.

Before commencing a therapy that would be expected to cause significant immunosuppression, a full vaccination history should be obtained. Then, if circumstances permit, such as prior to commencing immunosuppressive therapy for rheumatological disease or prior to solid organ transplant, vaccination should be completed following the usual Schedule (including HPV vaccine from age 9 years). Administration of additional funded vaccines (eg, varicella for children, zoster for certain adults, meningococcal or pneumococcal vaccines) may be appropriate. However, when immediate commencement of therapy is clinically indicated, it is not recommended to delay therapy to allow for vaccination.

#### Live vaccines – caution

Live vaccines (BCG, rotavirus, MMR and VV) are contraindicated for individuals who are immunosuppressed because of the risk of disseminated vaccine disease.

Individuals who are not considered to be significantly immunodeficient or immunosuppressed can receive live vaccines. For individuals who are due to commence elective immunosuppressive therapy, live vaccines (MMR and VV) should be administered at least four weeks prior to commencement of therapy. Live vaccines should also be administered at least four weeks before a predicted transplant.

On a case-by-case basis with appropriate follow-up in place, a specialist may recommend that VV is administered less than four weeks before a predicted transplant or to a post-transplantation paediatric patient.<sup>42</sup> With specialist input MMR may also be considered in clinically well patients at least one year after solid organ transplantation on low level immunosuppression.<sup>43</sup>

See sections 12.5 and 24.5 for information about the recommended MMR and VV vaccination schedules and eligibility criteria.

## COVID-19 vaccine

### *Young children aged 6 months to 4 years, inclusive*

Children aged 6 months to 4 years with a secondary (acquired) immunodeficiency are recommended to receive three doses of mRNA-CV (3 µg). First and second doses are given three weeks apart and dose three is given at least eight weeks after the second dose. An additional dose of mRNA-CV (3 µg) can be given six months after the primary course. This spacing can be reduced to at least three months, on a case-by-case basis, where there is a clinical need.

### *Individuals aged 5 years and over*

Certain individuals from 5 years of age with a secondary (acquired) immunodeficiency are eligible for three primary doses of mRNA-CV (10 µg or 30 µg, as age appropriate) (see section 5.5.2 for details); each dose is given 8 weeks apart.

Regardless of any doses received after completion of the primary course, an additional dose of mRNA-CV (10 µg or 30 µg, as age appropriate) is recommended for individuals aged 5 years and over with a secondary (acquired) immunodeficiency, and particularly those eligible for three primary doses, to be given six months after the previous dose. This spacing can be reduced to at least three months, on a case-by-case basis, where there is a clinical need (see section 5.5.3).

If a significant adverse reaction to mRNA-CV has occurred, it is recommended to seek advice from IMAC to determine whether further doses are contraindicated.

## Influenza vaccine

Influenza vaccine is funded for all individuals with immunodeficiency or immunosuppressed aged 6 months or older. Regardless of their age, all immunocompromised individuals who receive influenza vaccine for the first time are recommended to receive two vaccine doses at least four weeks apart (second dose unfunded), and one funded dose annually after that. A second dose is funded for children aged 6 months to under 9 years when influenza vaccine is being used for the first time.

## *Haemophilus influenzae type b (Hib-PRP) vaccines*

### *Infants and children aged under 5 years*

Vaccination against Hib disease for infants and children aged under 5 years is included in the usual Schedule. DTaP-IPV-HepB/Hib vaccine is recommended at 6 weeks, 3 months and 5 months of age followed by a booster dose of Hib-PRP vaccine at age 15 months.

### *Children aged 5 years or older and adults*

Children aged 5 years or older and adults who have functional asplenia, or are pre-/post-solid organ transplantation, pre-/post-splenectomy, post-chemotherapy, receiving immunosuppressive therapy for longer than 28 days, or on renal dialysis, are recommended and funded to receive one dose of monovalent Hib-PRP vaccine.



A three-dose series of Hib-PRP-containing vaccine is recommended for children and adults who are post-haematopoietic stem cell transplantation (see section 4.3.9).

## Pneumococcal vaccines

### *Infants and children aged under 5 years*

Children in this age group who have functional asplenia, HIV, nephrotic syndrome or renal failure, or are pre-/post-solid organ transplantation, pre-/post-splenectomy, post-haematopoietic stem cell transplantation, or have been receiving high-dose corticosteroid therapy for more than two weeks, other immunosuppressive therapy for longer than 28 days, or radiotherapy are recommended and funded to receive additional pneumococcal vaccinations as part of an extended immunisation programme for special groups (see section 17.5.2).

PCV13 is given as a three-dose primary series plus booster, administer a 3-month dose in addition to the usual Schedule (ie, at ages 6 weeks, 3 months, 5 months and 12 months; see sections 17.5.2 and 17.5.3) once the eligible condition has been identified followed by age-appropriate 23PPV vaccinations. For children aged 12 months to under 5 years who have not received PCV13, see Table 17.3.

### *Children aged 5 years to under 18 years*

Children in this age group who have a condition listed in the *Infants and children aged under 5 years* section above are recommended and funded to receive one PCV13 followed by up to two doses of 23PPV (see section 17.5.2).

### *Children aged 5 years or older and adults*

Children in this age group and adults who have an acquired complement deficiency, functional asplenia or HIV, or are pre-/post-solid organ transplantation, pre-/post-splenectomy, post-chemotherapy, post-haematopoietic stem cell transplantation, or on renal dialysis, are recommended and funded to receive one PCV13 followed by age-appropriate 23PPV vaccinations (see section 17.5.2).

It is recommended that individuals in this age group who will be or have been receiving high-dose corticosteroid therapy for more than two weeks or other immunosuppressive therapy for longer than 28 days receive pneumococcal vaccination (this is not funded).

## Meningococcal vaccines

Infants, children and adults with acquired complement deficiency, functional asplenia, HIV, or are pre-/post-splenectomy, or are pre-/post-solid organ transplantation, are post-haematopoietic stem cell transplantation, or pre and post immunosuppression for longer than 28 days are recommended and funded meningococcal vaccination.

The current funded meningococcal vaccines are recombinant group B vaccine (MenB, Bexsero), quadrivalent group ACWY meningococcal conjugate vaccines (MenACWY, Nimenrix and MenQuadfi).



## *Meningococcal conjugate vaccines*

### *Infants aged under 12 months*

Infants aged 6 weeks to under 12 months who have an acquired complement deficiency, functional asplenia or HIV, or are pre-/post-splenectomy, pre-/post-solid organ transplantation, or post-haematopoietic stem cell transplantation, or pre/post immunosuppressive therapy for longer than 28 days are recommended and funded to receive two doses of MenACWY (Nimenrix) given a minimum of eight weeks apart. From age 12 months, give a dose of MenQuadfi at least six months after the second dose, then a booster dose after three years and five-yearly.

### *Children aged 12–23 months*

Children in this age group who have an acquired complement deficiency, functional asplenia or HIV, or are pre-/post-splenectomy or pre-/post-solid organ transplantation, are recommended and funded to receive two doses of MenACWY (MenQuadfi) given at 8–12 weeks apart (see note below).

Note: A second primary dose of MenQuadfi, for those aged 12 months and over, is off-label and requires a prescription from an authorised prescriber under section 25 of the Medicines Act.

A booster dose is recommended and funded after three years, if still aged under 7 years, then five yearly for those with acquired complement deficiency, functional or anatomical asplenia, HIV, or are pre-/post-splenectomy, or are pre-/post-solid organ transplantation.

Children in this age group who are post-haematopoietic stem cell transplantation or will be or have been receiving immunosuppressive therapy for longer than 28 days are recommended and funded to receive two doses of MenACWY give 8-12 weeks apart (see note). Booster doses of MenACWY after three years and then five-yearly are recommended (although not funded) if immunosuppression is long-term.

### *Children aged 2 years to under 7 years*

Children in this age group who have an acquired complement deficiency, functional asplenia, HIV, or are pre-/post-splenectomy or pre-/post-solid organ transplantation, are recommended and funded to receive two doses of MenACWY given 8-12 weeks apart (a prescription is required for a second primary dose, see note above). Give a booster dose after three years, if still aged under 7 years, then five-yearly.

Children in this age group who are post-haematopoietic stem cell transplantation or receiving immunosuppressive therapy for longer than 28 days are recommended and funded to receive two doses of MenACWY given 8–12 weeks apart. If immunosuppression is long-term, booster doses of MenACWY after three years, if still aged under 7 years, and then five-yearly are recommended (although not funded).

#### *Children aged 7 years or older and adults*

Children in this age group and adults who have an acquired complement deficiency, functional asplenia, HIV, or are pre-/post-splenectomy or pre-/post-solid organ transplantation, are recommended and funded to receive two doses of MenACWY at least eight weeks apart (a prescription is required for a second primary dose, see note above). A booster dose is recommended to be given every five years.

Children in this age group and adults who are post-haematopoietic stem cell transplantation or will be or have been receiving immunosuppressive therapy for longer than 28 days are recommended and funded to receive two doses of MenACWY at least eight weeks apart. If immunosuppression is long-term, a booster dose of MenACWY is recommended (but not funded) every five years.

#### *Group B meningococcal vaccine*

Vaccination with MenB (Bexsero), to protect against disease caused by the meningococcal group B, is recommended and funded for infants, children and adults who have an acquired complement deficiency, functional asplenia or HIV, or are pre- and post-splenectomy or pre- or post-solid organ transplantation, or post-haematopoietic stem cell transplantation, or prior to planned and following immunosuppressive therapy for longer than 28 days.

MenB is funded as part of the Schedule for all infants, given at either ages 3 months, 5 months and 12 months, or an alternate schedule (involving additional visits) at ages 8 weeks and 4 months plus booster at 12 months, and a catch-up is available for children aged 13 months to under 5 years until 31 August 2025 (see Section 13.5 for details).

#### *Infants aged under 12 months*

Infants aged 8 weeks to <12 months who have an acquired immunodeficiency, as listed above, are recommended and funded to receive two doses of MenB at least eight weeks apart, followed by a booster dose at least six months after the second dose, from 12 months of age. For those aged younger than 8 weeks, to align with the routine schedule visit, MenB can be given at ages 6 weeks and 3 months. This is off-label use and requires a prescription from an authorised prescriber. No prescription is required if given as per the alternative schedule at ages 8 weeks and 4 months.

#### *Children from age 12 to 23 months*

Children aged from 12 months to 23 months who are diagnosed with an acquired immunodeficiency are recommended and funded to receive two doses of MenB at least eight weeks apart, followed by a booster dose given 12–23 months after the second dose. The spacing between doses one and two can be reduced to six weeks if indicated, with a prescription.

#### *Children from age 2 years and adults*

Children aged from 2 years and adults who are diagnosed with an acquired immunodeficiency are recommended and funded to receive two doses of MenB at least eight weeks apart. This can be reduced to four weeks apart, if clinically necessary.

Booster doses are funded five yearly as required after the age of 12 months for patients pre- and post-splenectomy, with functional or anatomical asplenia, HIV, acquired complement deficiency or pre- or post-solid organ transplant.

Note: MenB elicits a robust immune response, and sometimes high fevers in infants. Routine use of paracetamol (or ibuprofen) with every dose of MenB in children aged under 2 years, whether given alone or with other vaccines, is recommended to reduce the risk of high fever and injection-site pain (see section 13.4.4).

### Herpes zoster vaccine

Individuals from age 18 years, including those aged 66 years and over, with secondary (acquired) immunodeficiency are recommended two doses of recombinant zoster vaccine (rZV, Shingrix), given two to six months apart. Funded vaccine is limited to individuals with certain acquired immunodeficiencies and named conditions requiring immunosuppressive therapies. See section 25.5.1.

## 4.3.4 Individuals receiving corticosteroids

Corticosteroids reduce inflammation and generally suppress the immune system. The minimum amount of corticosteroid administration sufficient to cause immunosuppression is not well defined, and is dependent on the treatment used, dose, route of administration and duration. A daily dosage equivalent to 2 mg/kg oral prednisone or greater, or a total daily dosage of 20 mg or greater, particularly when given for 14 days or more, is considered sufficient to raise concern about the safety of live vaccines. Individuals receiving fludrocortisone or long-term dexamethasone should not receive live vaccines during treatment and for three months after discontinuation.

A single dose of dexamethasone for management of an acute respiratory illness in children is not associated with a decrease in endogenous corticosteroid levels<sup>44</sup> or immunosuppression. No minimum interval is required between administration of a single dose of dexamethasone and a live vaccine, as long the individual is not acutely unwell.

Rotavirus vaccine can be given to preterm infants born who are receiving corticosteroids.

Live vaccines *can be* administered to individuals who:

- are using topical corticosteroid therapy, including on the skin or respiratory tract (by aerosol), or receiving local intra-articular, bursal or tendon corticosteroid injections because such therapies do not usually result in immunosuppression
- are receiving maintenance physiological doses of corticosteroids
- are receiving oral budesonide or fluticasone to treat an inflammatory bowel condition
- received a single dose of dexamethasone for management of an acute respiratory illness

- are receiving low to moderate doses of systemic steroids given daily or on alternate days
- are receiving high-dose corticosteroids for fewer than 14 days.

Live vaccines *should not* be administered to individuals:

- receiving high dose corticosteroids daily or on alternate days for more than 14 days
- receiving long-term dexamethasone or hydrocortisone that is not for physiological maintenance or fludrocortisone
- who have a disease process that causes immunosuppression, except in special circumstances after discussion with the individual's specialist.

See Table 4.1 for guidelines according to each corticosteroid agent.

**Table 4.1: Guidelines for live vaccine administration for individuals receiving corticosteroid agents**

Corticosteroid agent	Dose regime	Administration of live vaccines	
Topical or local corticosteroid doses	Any agent, any dose <ul style="list-style-type: none"> <li>• applied to the skin</li> <li>• inhaled</li> <li>• injected locally into a joint, bursa or tendon</li> </ul>	Any time before, during or after treatment	
Budesonide	Oral or inhaled, any dose	Any time before, during or after treatment	
Dexamethasone	Single dose for an acute respiratory illness	Any time before or after dose	
	Physiological maintenance doses	Any time before, during or after treatment	
	Long-term treatment not for physiological maintenance	Delay for 3 months after discontinuation	
Fludrocortisone	Any dose	Delay for 3 months after discontinuation	
Fluticasone	Oral or inhaled, any dose	Any time before, during or after treatment	
Hydrocortisone	Physiological maintenance doses	Any time before, during or after dose	
	Long-term treatment not for physiological maintenance	Delay for 3 months after discontinuation	
Prednisone / Prednisolone <sup>45</sup>	<i>Infants and children &lt; 10kg</i>	<i>Children and adults ≥ 10kg</i>	
	<2mg/kg per day, any duration	<20mg per day, any duration	Any time before, during or after treatment
	≥2mg/kg per day for <14 days	≥20mg per day for <14 days	Immediately on discontinuation
	≥2mg/kg per day for ≥14 days	≥20 mg per day for ≥14 days	Delay for 1 month after discontinuation

Note: The guidelines in this table are intended to ensure safety of administration of the live vaccines to individuals receiving corticosteroids; optimal vaccine immunogenicity may not be achieved.

## COVID-19 vaccine

### *Young children aged 6 months to 4 years, inclusive*

Children aged 6 months to 4 years receiving high-dose corticosteroids agents (see section 5.5.2 for details) are recommended to receive three doses of mRNA-CV (3 µg). First and second doses are given three weeks apart and dose three is given at least eight weeks after the second dose. An additional dose of mRNA-CV (3 µg) can be given six months after the primary course. This spacing can be reduced to at least three months, on a case-by-case basis, where there is a clinical need.

### *Individuals aged 5 years and over*

Certain individuals from 5 years of age receiving corticosteroids agents are eligible for three primary doses of mRNA-CV (10 µg or 30 µg, as age appropriate) (see section 5.5.2 for details); each dose is given eight weeks apart.

Regardless of any previous doses received after completion of the primary course, an additional dose of mRNA-CV (10 µg or 30µg, as age appropriate) is recommended for all individuals aged 5 years and over receiving corticosteroid agents, and particularly those eligible for three primary doses, to be given six months after a previous dose. This spacing can be reduced to at least three months, on a case-by-case basis, where there is a clinical need (see section 5.5.3).

If a significant adverse reaction to mRNA-CV has occurred, it is recommended to seek advice from IMAC to determine whether further doses are contraindicated.

## 4.3.5 Individuals receiving non-corticosteroid immunomodulatory agents

### Non-biologic agents

Hydroxychloroquine, mesalazine/5-ASA, olsalazine and sulfasalazine act on the immune system and reduce the inflammatory responses associated with immune-mediated inflammatory disease (IMID, also known as autoimmune diseases) but do not cause immunosuppression.<sup>46</sup>

Azathioprine, 6-mercaptopurine, methotrexate, cyclophosphamide, cyclosporine, leflunomide, mycophenolate mofetil and tacrolimus suppress immune system function to varying degrees, dependent on the agent and intensity of therapy, to reduce symptoms and tissue damage associated with IMID or prevent rejection of a transplanted organ.<sup>46</sup>

See Table 4.2 for guidelines for administration of live vaccines according to each non-biologic agent.

## Biologic agents

Immunotherapeutic treatment of disease has increased rapidly over recent years. The treatment relies on administration of biologic agents that selectively target components of the immune system (eg, antibodies, cytokines and proteins) to alter an individual's immune response to treat disease.<sup>46</sup>

In IMID, such as rheumatoid arthritis and inflammatory bowel disease, biologic agents target a specific part of the individual's immune response against 'self' to stop the immune response creating inflammation and damage.<sup>46</sup> However, they also affect the immune response against genuine antigens and cause immunosuppression. Use of a combination of therapies may have a cumulative effect that increases the level of immunosuppression in an individual.

In atopic conditions and inflammation such as chronic spontaneous urticaria and allergic asthma, biologic agents inhibit the activation of allergen specific IgE antibodies and mast cells or decrease the number of eosinophils that contribute to allergy related inflammation.<sup>46</sup> These treatments do not cause immunosuppression.

Other biologic agents stimulate an individual's immune response by blocking immune checkpoints on healthy cells and cancer cells to increase their anti-tumour response, see Oncology, section 4.3.8.

Live vaccines *can be* administered to individuals:

- receiving hydroxychloroquine, mesalazine/5-ASA, olsalazine and sulfasalazine
- with low-level immunosuppression regimens of azathioprine, 6mercaptopurine or methotrexate
- receiving intra-ocular biologic therapy because such therapy does not usually result in immunosuppression
- taking omalizumab or mepolizumab to manage allergic conditions such as chronic spontaneous urticaria and allergic asthma.

Live vaccines *should not* be administered to individuals:

- with high-level immunosuppression regimens of azathioprine, 6mercaptopurine or methotrexate
- receiving treatment with any dose of cyclophosphamide, cyclosporine, leflunomide, mycophenolate mofetil, or tacrolimus
- receiving treatment with monoclonal antibody inhibitors, TNF inhibitors and kinase inhibitors, and immune checkpoint inhibitors (see Oncology, section 4.3.8).
- Infants aged under 12 months born to mothers who received immunomodulatory biologic agents in pregnancy may also be temporarily immunocompromised (see section 4.2.5).

For infants aged under 12 months, please discuss immunomodulatory therapies taken during pregnancy with their mother or specialist, or contact IMAC (on 0800 IMMUNE / 0800 466 863) before administration of rotavirus, BCG, MMR or VV vaccines.

See Table 4.2 for guidelines for administration of live vaccines according to each biologic agent.

**Table 4.2: Guidelines for live vaccine administration for individuals receiving non-corticosteroid agents**

	Dose regime	Administration of live vaccines	Dose regime	Administration of live vaccines
<b>Non-biologic agent</b>				
Hydroxychloroquine Mesalazine/5-ASA Olsalazine Sulfasalazine	Any dose	Any time before, during or after treatment		
Azathioprine 6-mercaptopurine	≤3 mg/kg per day ≤1.5 mg/kg per day	Any time before, during or after treatment	>3mg/kg per day >1.5mg/kg per day	Delay for 3 months after discontinuation
Methotrexate	≤0.4 mg/kg per week		>0.4mg/kg per week	
Cyclophosphamide Cyclosporine Mycophenolate mofetil Tacrolimus			Any dose	Delay for 3 months after discontinuation
Leflunomide Teriflunomide			Any dose	Delay for 6 months after discontinuation
Axitinib Imatinib Ruxolitinib Tofacitinib			Any dose	Delay for 12 months after discontinuation
<b>Biologic agent</b>				
Locally injected biologic dose	Any agent, any dose Intra-ocular injection	Any time before, during or after dose		
Omalizumab Mepolizumab	Any dose	Any time before, during or after dose		
Fingolimod Natalizumab			Any dose	Delay for 3 months after discontinuation

*Continued overleaf*



Dose regime	Administration of live vaccines	Dose regime	Administration of live vaccines
Atezolizumab Ipilimumab Nivolumab Pembrolizumab Sirolimus		Any dose	Delay for 6 months after discontinuation
			<i>Continued overleaf</i>
Abatacept Adalimumab Anakinra Etanercept Infliximab Rituximab Tocilizumab Trastuzumab		Any dose	Delay for 12 months after discontinuation
Ocrelizumab		Any dose	Delay for 3 years after discontinuation

For children aged under 18 years, see the Starship Clinical Guidelines *Immunosuppression and Immunisation in Rheumatology* (available at [www.starship.org.nz/guidelines/immunosuppression-infection-and-immunisation-in-rheumatology](http://www.starship.org.nz/guidelines/immunosuppression-infection-and-immunisation-in-rheumatology)).

For adults, see the IMAC factsheet *Immunisation for adults requiring immunosuppressive disease-modifying therapy*. For other adults who have received chemotherapy, see also the IMAC factsheet *Immunisation for adults post chemotherapy who are not taking immunosuppressive disease-modifying drugs* (both available at <https://www.immune.org.nz/resources/factsheets>)

## COVID-19 vaccine

### *Young children aged 6 months to 4 years, inclusive*

Children aged 6 months to 4 years receiving certain biologic and non-biologic immunosuppressive agents (see section 5.5.2 for details) are recommended to receive three doses of mRNA-CV (3 µg). First and second doses are given three weeks apart and dose three is given at least eight weeks after the second dose. An additional dose of mRNA-CV (3 µg) can be given six months after the primary course. This spacing can be reduced to at least three months, on a case-by-case basis, where there is a clinical need.

### *Individuals aged 5 years and over*

Individuals from 5 years of age receiving certain biologic and non-biologic immunosuppressive agents are eligible for three primary doses of mRNA-CV (10 µg or 30 µg, as age appropriate) (see section 5.5.2 for details); each dose is given eight weeks apart.

Regardless of any previous doses received after completion of the primary course, an additional dose of mRNA-CV (10 µg or 30µg, as age appropriate) is recommended for all individuals aged 5 years and over receiving immunosuppressive agents, and in particular those eligible for three primary doses, to be given six months after a previous dose. This spacing can be reduced to at least three months, on a case-by-case basis, where there is a clinical need (see section 5.5.3).

If a significant adverse reaction to mRNA-CV has occurred, it is recommended to seek advice from IMAC to determine whether further doses are contraindicated.

### Herpes zoster vaccine

Individuals from age 18 years, including those aged 66 years and over, receiving immunosuppressive therapy are recommended two doses of recombinant zoster vaccine (rZV, Shingrix), given two to six months apart. This vaccine is only funded for individuals with certain rheumatological immune-mediated inflammatory diseases receiving disease-modifying immunotherapies (formerly known as DMARDs). See section 25.5.1.

## 4.3.6 Vaccination prior to planned immunosuppression

A variety of immune-mediated inflammatory diseases (IMID), across many subspecialties (eg, rheumatology, dermatology, gastroenterology etc), require treatment escalation to immunosuppressive therapy over a variable time course. Routine and additional vaccinations should be given prior to any planned immunosuppression, where clinically possible.

- Complete all age-appropriate vaccinations according to the Schedule; previous doses do not need to be repeated prior to immunosuppression.
- Live viral vaccines are recommended to be administered prior to planned immunosuppression, if time permits, as they cannot be given once immunosuppression has commenced. Clinically indicated immunosuppression should not be delayed in order to give live vaccines.
- Whilst non-live vaccines can also be given safely when receiving immunosuppression, the immune response is likely to be reduced. If immunosuppression is short-lasting, administration of non-live vaccines (eg, completion of meningococcal vaccines) can be given once immunosuppression has been reduced or stopped.
- The required interval before resuming live vaccination varies with the agents given – see Table 4.1 and Table 4.2, and seek specialist advice.

For additional and accelerated recommendations for the immunisation of infants and children diagnosed with conditions requiring immunosuppression for 28 days or longer, see Table 4.3.

For infants aged under 12 months of age, seek specialist advice.  
 For additional recommendations for the immunisation of adults see IMAC factsheet *Immunisation for adults requiring immunosuppressive disease modifying therapy* (available at [www.immune.org.nz/resources/factsheets](http://www.immune.org.nz/resources/factsheets)).

**Table 4.3: Additional vaccine recommendations for children (12 months to 18 years) when diagnosed with a condition requiring immunosuppression for 28 days or longer, or having completed immunosuppression**

Refer to the Pharmaceutical Schedule ([pharmac.govt.nz/](http://pharmac.govt.nz/)) for any changes to funding decisions. Children should receive the usual Schedule vaccines, including rotavirus vaccine for infants prior to planned immunosuppression.

Relevant age	Vaccine (trade name)	Recommended vaccination schedule
Ages 12 months to 18 years when diagnosed with a condition requiring immunosuppression	PCV13	<ul style="list-style-type: none"> <li>Children aged 12–59 months, who have not yet received any PCV13               <ul style="list-style-type: none"> <li>– give 2 doses of PCV13 at least 8 weeks apart <sup>a</sup></li> </ul> </li> <li>Children aged 5 years to under 18 years:               <ul style="list-style-type: none"> <li>– give 1 dose of PCV13 even if fully vaccinated <sup>a</sup></li> </ul> </li> </ul>
	23PPV (Pneumovax 23)	Following completion of the PCV schedule, give 1 dose at least 8 weeks after the last PCV13 dose, from age 2 years. <sup>b</sup> Revaccinate once after 5 years.
	MenACWY (MenQuadfi) <sup>b</sup>	<ul style="list-style-type: none"> <li>If aged 12 months to under 7 years at diagnosis, give 2 doses <sup>b</sup> of MenACWY 8–12 weeks apart. A booster dose is recommended after 3 years, while still under the age of 7 years, then 5-yearly</li> <li>If aged 7 years or older give 2 doses <sup>b</sup> of MenACWY 8 weeks apart followed by a booster dose 5-yearly</li> </ul>
	MenB (Bexsero) <sup>c</sup>	<ul style="list-style-type: none"> <li>For children aged from 12 to 23 months, who have not yet received any MenB, give 2 doses 8 weeks apart. Give a booster dose 12–23 months after second dose.</li> <li>From age 2 years, give 2 doses 8 weeks apart (or reduced to 4 weeks apart, if clinically necessary).</li> <li>Give booster doses 5-yearly <sup>d</sup></li> </ul>
	Hib-PRP (Act-HIB)	<ul style="list-style-type: none"> <li>If child is aged 12–15 months, give 1 dose at age 15 months as per the Schedule</li> <li>If aged 16 months to under 5 years and has not received a single Hib-PRP dose after age 12 months, give 1 dose</li> <li>If aged 5 years or older, give 1 dose, unless fully vaccinated</li> </ul>
	Influenza (age-appropriate vaccine) <sup>e</sup>	Give annually <ul style="list-style-type: none"> <li>In previously unvaccinated children age &lt;9 years, give 2 doses 4 weeks apart, then 1 dose in each subsequent year</li> </ul>
	MMR	<ul style="list-style-type: none"> <li>2 doses given 4 weeks apart, if time permits, to be given at least 4 weeks prior to planned immunosuppression <sup>f</sup></li> </ul>

*Continued overleaf*

Relevant age	Vaccine (trade name)	Recommended vaccination schedule
	Varicella (Varilrix)	<ul style="list-style-type: none"> <li>2 doses given 4 weeks <sup>f</sup> apart, if time permits, and to be given at least 4 weeks prior to planned immunosuppression <sup>g</sup></li> </ul>
	COVID-19 (mRNA-CV)	<ul style="list-style-type: none"> <li>Ensure individual is up to date with age-appropriate vaccine and schedule, see Table 5.3</li> </ul>

- If 23PPV has already been given (prior to any doses of PCV13) to children aged under 18 years, wait at least 8 weeks before administering PCV13 (note – this differs from a 1-year gap recommended in adults).
- A prescription is required for a second primary dose of MenQuadfi for those aged 12 months and over.
- It is recommended to administer prophylactic paracetamol (or ibuprofen) to reduce fever in children age under 2 years (see section 13.7.1).
- Although, the need for a booster dose after this vaccination schedule has not been established, it is recommended and funded for certain special groups.
- Check [immune.org.nz](http://immune.org.nz) for most recent influenza vaccine brands and appropriate age ranges.
- Live viral vaccines are recommended to be administered prior to planned immunosuppression. Clinically indicated immunosuppression should not be delayed in order to give live vaccines.
- Accelerated timing for VV differs from Table 24.1. For vaccination **after** immunosuppression, standard interval of 6 weeks would apply.

### 4.3.7 (Re)vaccination following immunosuppression

All vaccines on the Schedule are funded for vaccination or re-vaccination of individuals following immunosuppression. Note that the period of immunosuppression due to steroid or other immunosuppressive therapy must be longer than 28 days. The timing and number of doses should be discussed with the individual's specialist. Ideally, vaccination should be conducted prior to any planned immunosuppression. See also the relevant disease chapters.

### 4.3.8 Oncology

This section provides general guidelines for vaccination during and after cancer treatment. Specific vaccination questions should be discussed with an expert paediatrician, infectious diseases physician or oncologist.

Note: The exception to these guidelines is individuals being treated with immune checkpoint inhibitors for whom vaccination may be contraindicated (see below).

## Vaccination during cancer chemotherapy

While administration of inactivated and subunit (non-live) vaccines is safe for individuals undergoing cancer chemotherapy, their response and subsequent protection may be reduced compared with healthy individuals.

Influenza vaccination is recommended for children age 6 months and over and adults prior to planned or when undergoing cancer chemotherapy as soon as the vaccine becomes available; there is no need to wait until three months after the individual's last treatment.<sup>47, 48</sup> Influenza vaccination can be administered at any time during a cancer chemotherapy cycle.<sup>49</sup>

In both children and adults, administration of two influenza vaccine doses a minimum of four weeks apart could improve the immune response to vaccination.<sup>50</sup>

Administration of live vaccines during cancer chemotherapy is absolutely contraindicated because of the risk of disseminated vaccine disease. For recommendations regarding vaccination of close contacts of immunocompromised individuals, see section 4.3.1.

## Vaccination after cancer chemotherapy

In general, booster dose(s) of a diphtheria/tetanus/pertussis-containing vaccine, and hepatitis B, polio (IPV) and pneumococcal vaccines (PCV13 followed by 23PPV) should be given, from not less than three months after cancer chemotherapy has ended (when the lymphocyte count is  $>1.0 \times 10^9/L$ ).

In general, administration of age-appropriate live vaccines should be delayed for at least six months after cancer chemotherapy. This interval may need to be extended according to:

- the intensity and type of therapy
- receipt of blood products or immunoglobulin (for MMR and VV, see Table A6.1 in Appendix 6)
- underlying disease.

MMR vaccination is not required post-chemotherapy for adults born prior to 1969 or who have documented evidence of measles, mumps and rubella immunity (see section 12.8.3). Adults born in 1969 or later who do not have documented evidence of immunity to measles, mumps and rubella should receive up to two documented doses of MMR, as per the usual adult catch-up Schedule, at least six months post-chemotherapy and when their lymphocyte count is  $>1.0 \times 10^9/L$ .

For children aged under 18 years, see the Starship Clinical Guideline *Immunisation of children during and after cancer therapy* for age-appropriate schedules and worksheets (available at [www.starship.org.nz/guidelines/immunisation-of-children-during-and-after-cancer-therapy](http://www.starship.org.nz/guidelines/immunisation-of-children-during-and-after-cancer-therapy)).

For adults, see the IMAC factsheet *Immunisation for adults requiring immunosuppressive disease-modifying therapy*. For other adults who have received

chemotherapy, see also the IMAC factsheet *Immunisation for adults post chemotherapy who are not taking immunosuppressive disease-modifying drugs* (both available at <https://www.immune.org.nz/resources/factsheets>)

### Herpes zoster vaccine

Individuals from age 18 years, including those aged 66 years and over, who are potentially immunocompromised post-chemotherapy or other cancer treatments are recommended two doses of recombinant zoster vaccine (rZV, Shingrix), given two to six months apart. Funded vaccine is limited to individuals who are immunocompromised following a haematological malignancy diagnosis, or post-haematopoietic stem cell transplantation and post-cellular therapy (eg CAR T-cell therapy). See section 25.5.1.

### Vaccination and radiotherapy

Individuals who are only receiving localised radiotherapy to treat a tumour or lesion can be vaccinated with subunit vaccines and live vaccines at any time prior to, during, or after radiotherapy.<sup>51</sup>

### Immune checkpoint inhibitor (immunostimulant) therapy

A person who is currently receiving any of the four immune checkpoint inhibitor medications currently available in New Zealand – namely, nivolumab (Opdivo), pembrolizumab (Keytruda), atezolizumab (Tecentriq) and ipilimumab (Yervoy) – or has received these in the previous six months can receive any non-live vaccine, including influenza and mRNA-CV, without consulting their specialist prior to vaccination. The administration of live vaccines (MMR and VV) is contraindicated.

## 4.3.9 Haematopoietic stem cell transplantation

Haematopoietic stem cell transplantation (HSCT) is used to treat haematological disease, such as acute leukaemia, and some immunodeficiency syndromes, such as severe combined immunodeficiency. Transplant recipients undergo a conditioning regime to destroy their immune system and underlying disease then receive an infusion of cells to reconstitute a new immune system. The transplanted cells may be collected from bone marrow, umbilical cord blood, or peripheral blood. They may be donated by another person (called an allogeneic transplant), or may be the recipient's own cells that have been processed to ensure they are disease free (called an autologous transplant).<sup>52</sup>

After HSCT, it takes months to years for the recipient's new immune system to reconstitute and become functional. However, the age of the recipient, underlying disease, conditioning regime, type of transplantation and complications such as graft versus host disease (GVHD) can affect and prolong recovery time.<sup>52, 53</sup>

## Vaccination of individuals post-HSCT

Initially, the recipient may have temporary measurable donor-derived protection against some diseases, but their reconstituted immune system will need full (re)vaccination to provide long-term protection against vaccine-preventable diseases. Administration of subunit vaccines, such as PCV13, may be recommended as early as three months post-HSCT. Annual influenza vaccination may be recommended from six months post-HSCT. It is generally recommended to commence immunisation with live viral vaccines no less than 24 months post-HSCT and in the absence of GVHD and immunosuppressive therapy.<sup>53, 54</sup>

For children aged under 18 years, see the Starship Clinical Guideline *Immunisation of children during and after cancer therapy* for age-appropriate schedules and worksheets (available at [www.starship.org.nz/guidelines/immunisation-of-children-during-and-after-cancer-therapy](http://www.starship.org.nz/guidelines/immunisation-of-children-during-and-after-cancer-therapy)).

For adults, see the vaccination protocol provided by the person's New Zealand-based haematology clinic or the IMAC factsheet *Immunisation for adults post-haematopoietic stem cell transplantation (HSCT)* (available at [www.immune.org.nz/resources/factsheets](http://www.immune.org.nz/resources/factsheets)).

For recommendations regarding vaccination of close contacts of immunocompromised individuals, see section 4.3.1.

### COVID-19 vaccine

#### *Young children aged 6 months to 4 years, inclusive*

Children aged 6 months to 4 years who received HSCT in the past 24 months are recommended to receive three doses of mRNA-CV (3 µg) (maroon cap). First and second doses are given three weeks apart and dose three is given at least eight weeks after the second dose. An additional dose of mRNA-CV (3 µg) can be given six months after the primary course. This spacing can be reduced to at least three months, on a case-by-case basis, where there is a clinical need.

Individuals aged from 6 months who have received HSCT since receiving their first COVID-19 vaccination course can be revaccinated with primary course and additional dose, as age appropriate.

#### *Individuals aged 5 years and over*

Individuals aged from 5 years who have received HSCT in the previous 24 months or with ongoing immunosuppression or graft-versus-host disease for more than 24 months (see section 5.5.2 for details) are eligible for three primary doses of mRNA-CV (10 µg or 30 µg, as age appropriate); each dose is given eight weeks apart..

Individuals aged from 5 years who have received HSCT since receiving their first COVID-19 vaccination course can be revaccinated with primary course and additional dose, as age appropriate.

Regardless of any previous doses received after completion of the primary course, an additional dose of mRNA-CV (10 µg or 30µg, as age appropriate) is recommended for all individuals aged 5 years and over for recipients of HSCT, and particularly those



eligible for three primary doses, to be given six months after the previous dose. This spacing can be reduced to at least three months, on a case-by-case basis, where there is a clinical need (see section 5.5.3).

If a significant adverse reaction to mRNA-CV has occurred, it is recommended to seek advice from IMAC to determine whether further doses are contraindicated.

### *Haemophilus influenzae* type b (Hib-PRP) vaccines

#### *Infants and children aged under 5 years*

Vaccination against Hib disease for infants and children aged under 5 years is included in the usual Schedule. DTaP-IPV-HepB/Hib vaccine is recommended at 6 weeks, 3 months and 5 months of age followed by a booster dose of Hib-PRP vaccine at age 15 months.

#### *Children and adults post-haematopoietic stem cell transplantation*

A three-dose series of Hib-PRP is recommended for children and adults who are post-haematopoietic stem cell transplantation. Children aged under 18 years who are revaccinated using DTaP-IPV-HepB/Hib will receive three doses of Hib-PRP-containing vaccine (funded). For children aged 10 years and over, this is an off-label use of this vaccine which requires a prescription from an authorised prescriber or the patient's specialist.

For adults who receive monovalent Hib-PRP, one dose is funded, and the immunisation benefit can be claimed for vaccine administration. Doses two and three are not funded. Hib-PRP can only be ordered from ProPharma and an immunisation benefit cannot be claimed for vaccine administration.

### Herpes zoster vaccine

Individuals from age 18 years, including those aged 66 years and over, post HSCT are recommended and funded two doses of recombinant zoster vaccine (rZV, Shingrix), given two to six months apart. See section 25.5.1.

## 4.3.10 Solid organ transplantation

### Vaccination of individuals pre-/post solid organ transplantation

In addition to the usual Schedule vaccines, individuals who are pre-/post-solid organ transplantation are eligible to receive additional funded vaccines. Ideally, vaccination should be conducted prior to any planned immunosuppression.<sup>55</sup> An accelerated immunisation schedule is provided for infants with congenital biliary or renal conditions requiring transplant (see Table 4.4).

Additional funded vaccines may include hepatitis A vaccine; hepatitis B vaccine if the person was not previously vaccinated or does not have evidence of immunity (see section 9.5.4); *Haemophilus influenzae* type b (Hib-PRP), influenza, pneumococcal, meningococcal and varicella vaccines.

It is recommended to follow an accelerated schedule of vaccinations for infants and children likely to be listed for solid organ transplantation, see Table 4.4 for infant recommendations.

For pre-/post-solid organ transplantation advice for adult immunisation, see the IMAC factsheet *Immunisation for adults pre-/post-solid organ transplantation (excluding kidney transplantation)* or *Immunisation for adults pre-dialysis, on dialysis or pre-/post-kidney transplant* (both available at [www.immune.org.nz/resources/factsheets](http://www.immune.org.nz/resources/factsheets)).

For recommendations regarding vaccination of close contacts of immunocompromised individuals, see section 4.3.1.

### Live vaccines – caution

Live vaccines should also be administered at least four weeks before a predicted transplant. Administration of live vaccines (MMR and VV) is generally contraindicated post-transplantation due to immunosuppression. However, on a case-by-case basis with appropriate follow-up in place, a specialist may recommend that VV is administered less than four weeks before a predicted transplant or to a post-transplantation paediatric patient.<sup>42</sup> With specialist input MMR may also be considered in clinically well patients at least 1 year after solid organ transplantation on low level immunosuppression.

See *Vaccines for individuals with acquired immunodeficiency* in section 4.3.3 for precautions and contraindications for the administration of live vaccines (MMR and VV), eligibility and recommendations for influenza, Hib, pneumococcal and meningococcal vaccines, and recommendations when an individual who is immunosuppressed/post-solid organ transplantation is a contact of a measles or chickenpox case.

**Table 4.4: Accelerated vaccination schedule with additional vaccine recommendations for infants likely to require liver or kidney transplantation**

**Funded vaccines are in shaded rows.** Refer to the Pharmaceutical Schedule ([pharmac.govt.nz/](http://pharmac.govt.nz/)) for any changes to funding decisions.

Age	Vaccination	Comments
<b>Do not start earlier than age 6 weeks.</b>		
6 weeks	RV1 (Rotarix) PCV13 <sup>a</sup> (Prevenar 13) DTaP-IPV-HepB/Hib (Infanrix-hexa)	It is preferable to not give RV1 within 4 weeks of predicted transplant
2 months	MenB (Bexsero) <sup>b</sup> MenACWY (Nimenrix)	
3 months	RV1 PCV13 (Prevenar 13) DTaP-IPV-HepB/Hib (Infanrix-hexa)	It is preferable to not give RV1 within 4 weeks of predicted transplant
4 months	MenB (Bexsero) <sup>b</sup> MenACWY (Nimenrix)	
5 months	PCV13 (Prevenar 13) DTaP-IPV-HepB/Hib (Infanrix-hexa)	
6 months	Influenza (junior formulation) <sup>c</sup>	Give two doses 4 weeks apart in the first year receiving influenza vaccine, and one dose in subsequent years Give annually
	MMR (Priorix) <sup>d</sup>	MMR should not be given less than 4 weeks before the predicted transplant
	HepA (Havrix Junior)	Liver transplant only
	Check anti-HBs serology	If anti-HBs is negative, give a further three doses of monovalent HepB vaccine (Engerix-B 20 µg) 4 weeks apart
From 6 months	COVID-19 (mRNA-CV (3 µg))	Give two doses 3 weeks apart then a third dose 8 weeks (minimum 4 weeks) later An additional dose can be given 6 months after the previous dose.
9 months	Varicella (Varilrix) <sup>d</sup>	In general, VV should not be given less than 4 weeks before the predicted transplant but may be given closer at the discretion of the specialist

*Continued overleaf*

12 months	PCV13 (Prevenar 13) <sup>a</sup>	
	MMR <sup>d</sup>	MMR should not be given less than 4 weeks before the predicted transplant
	Varicella (Varilrix)	In general, VV should not be given less than 4 weeks before the predicted transplant but may be given closer at the discretion of the specialist
	MenB (Bexsero) <sup>b</sup>	At least 6 months after second dose, give 1 dose to those who received two primary doses in infancy, followed by booster dose 5-yearly  If previously unvaccinated, give 2 doses 8 weeks apart, then a booster 12–23 months after dose two followed by booster doses given 5-yearly
	MenACWY (MenQuadfi)	Give one dose <sup>e</sup> Give booster doses after 3 years, then 5 yearly
13 months	DTaP-IPV-HepB/Hib (Infanrix-Hexa)	
	MMR (Priorix)	MMR should not be given less than 4 weeks before the predicted transplant
	HepA (Havrix Junior)	
14 months	MenACWY (MenQuadfi) <sup>e</sup>	Give a second dose <sup>e</sup> , at least 8 weeks after first, if have not already receive 2 MenACWY doses (including to those who received MenC prior to 1 July 2024).
2 years	23PPV (Pneumovax 23)	Give one dose Revaccinate once after 5 years
4 years	DTaP-IPV (Infanrix-IPV)	
From age 9 years	HPV9 (Gardasil 9)	Give 3 doses at 0, 2 and 6 months
11 years	Tdap (Boostrix)	
6 months post- transplant	HepB (Engerix-B), plus anti-HBs serology before and 4 weeks after the initial HepB series	Give 3 doses of monovalent HepB vaccine (Engerix-B 20 ug) If there is an inadequate immune response to the initial 3-dose HepB series, give a further 3 doses
	23PPV (Pneumovax 23)	If child is at least 24 months old and dose not given pre-transplant Revaccinate once after 5 years
	Influenza (age-appropriate vaccine) <sup>c</sup>	For infants and children aged 6 months to under 9 years, give 2 doses 4 weeks apart in the first year of receiving the influenza vaccine, and 1 dose in subsequent years Give annually
12 months post- transplant	Resume the usual Schedule, except live vaccines	Live vaccines <sup>d,f</sup> are generally contraindicated post-transplantation

*Continued overleaf*

Household members of transplant recipients	National Immunisation Schedule vaccines	Immune-competent siblings and other household members may receive all the Schedule vaccines and should be fully vaccinated for their age.
	COVID-19	All household members should receive age-appropriate vaccination according to the recommended schedule (see Table 5.2).
	Influenza (with age-appropriate vaccine) <sup>c</sup>	Recommended annually for all household members and close contacts
	Varicella	Two doses of VV are funded for susceptible household members of transplant recipients.

- A three-dose primary series plus a booster dose of PCV13, administered at 6 weeks, 3 months, 5 months, and 12 months, provides an additional dose at age 3 months to the usual Schedule.
- Recommended to administer prophylactic paracetamol (or ibuprofen) to reduce fever in children age under 2 years (section 13.7.1).
- Check [immune.org.nz](https://www.immune.org.nz) website for most recent updates on funded influenza vaccine and appropriate age ranges.
- MMR and VV can be given on the same day; if not, seek 4 weeks of separation between them.
- If a child at age 14 months has **not** already received two or more MenACWY doses (eg if given MenC prior to 1 July 2024), give a second dose of MenACWY, at least 8 weeks after first. A prescription is required for a second primary dose of MenQuadfi for those aged 12 months and over.
- On a case-by-case basis, a specialist may recommend that VV is administered to their post-transplantation paediatric patient.

## COVID-19 vaccine

### *Young children aged 6 months to 4 years, inclusive*

Children aged 6 months to 4 years receiving or having received immunosuppressive therapy following a solid organ transplant are recommended to receive three doses of mRNA-CV (3 µg). First and second doses are given three weeks apart and dose three is given at least eight weeks after the second dose. An additional dose of mRNA-CV (3 µg) can be given six months after the primary course. This spacing can be reduced to at least three months, on a case-by-case basis, where there is a clinical need.

### *Individuals aged 5 years and over*

Individuals aged from 5 years receiving or having received immunosuppressive therapy following a solid organ transplant are eligible for three primary doses of mRNA-CV (10 µg or 30 µg, as age appropriate) (see section 5.5.2 for details); each dose is given eight weeks apart

Regardless of any previous doses received after completion of the primary course, an additional dose of mRNA-CV (10 µg or 30 µg, as age appropriate) is recommended for all individuals aged 5 years and over following a solid organ transplant, and in particular, those eligible for a third primary dose, to be given six months after a previous dose. This spacing can be reduced to at least three months, on a case-by-case basis, where there is a clinical need (see section 5.5.3).

Based on clinical discretion, if all scheduled doses have been completed prior to commencement of chemotherapy or solid organ transplant, a single further dose of mRNA-CV can be given from the age of 5 years.

If a significant adverse reaction to mRNA-CV has occurred, it is recommended to seek advice from IMAC to determine whether further doses are contraindicated.

### Herpes zoster

Individuals from age 18 years, including those aged 66 years and over, pre or post solid organ transplant are recommended and funded two doses of recombinant zoster vaccine (rZV, Shingrix), given two to six months apart. See section 25.5.1.

### Measles or chickenpox exposure post-transplantation

Specialist advice should be sought if an individual who is immunosuppressed is a suspected or confirmed contact of a measles or chickenpox case. Post-transplantation, the use of passive immunisation with IG after exposure to measles or chickenpox should be based on the documentation of negative antibody titres, or where immune status is unknown. See *Human normal immunoglobulin prophylaxis for contacts* and *Prophylaxis with intravenous immunoglobulin* in section 12.8.2 and *Post-exposure prophylaxis with zoster immunoglobulin* in section 24.8.2.

## 4.3.11 Functional asplenia, hyposplenia and pre-/post-splenectomy

The spleen has an important role in initiating the immune response to encapsulated bacteria, including *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type b (Hib), and removing them from the circulatory system.

There are three main reasons why an individual may not have a fully functioning spleen:

- congenital disorders (eg, asplenia, hyposplenia or polysplenia associated with a congenital syndrome)
- disease (eg, Coeliac disease, acute leukaemia)
- surgical removal (eg, trauma, autoimmune haemolytic anaemia).

Individuals with reduced spleen function or an absent spleen are at increased risk of overwhelming infection by encapsulated bacteria.<sup>56</sup> This is a medical emergency and carries a high mortality rate. The risk of overwhelming infection after splenectomy is more than 50 times higher than the risk in the general population. Opinion is divided on whether this level of risk is life-long or decreases over time after the splenectomy.

### Vaccination of individuals with asplenia or hyposplenia or pre-/post-splenectomy

No vaccines are contraindicated for individuals with functional or anatomical asplenia (pre-/post-splenectomy), and they are eligible for additional funded influenza, Hib, pneumococcal and meningococcal vaccines. Providers should also ensure that they are up to date with Schedule vaccines, including Tdap and MMR.

When a splenectomy is planned, individuals should ideally complete the vaccinations they require up to two weeks prior to their surgery. If this is not possible, preferably administer vaccines until 14 days before the splenectomy and continue from seven days after the splenectomy, or prior to discharge from hospital, if sooner. When the splenectomy is unexpected, for example due to trauma, commence vaccination from seven days after surgery or prior to discharge from hospital. In all cases a vaccination plan must be formulated and communicated to the GP for completion (see Table 4.5).

Individuals with reduced spleen function (eg, because of disease or partial splenectomy), are recommended (but not funded) to receive pneumococcal and meningococcal vaccines and annual influenza vaccination.

See *Vaccines for individuals with acquired immunodeficiency* in section 4.3.3 for eligibility and recommendations for influenza, Hib, pneumococcal and meningococcal vaccines.

Table 4.5 summarises the additional vaccine recommendations and schedules for infants and children aged under 18 years with functional or anatomical asplenia. The funded vaccines are shown in shaded rows.

For adults, see the IMAC factsheet *Immunisation for adults pre-/post-splenectomy or with functional asplenia* (available at [www.immune.org.nz/resources/factsheets](http://www.immune.org.nz/resources/factsheets)).



**Table 4.5: Additional vaccine recommendations for infants and children aged under 18 years with functional or anatomical asplenia**

Funded vaccines are in the shaded rows.

Refer to the Pharmaceutical Schedule ([pharmac.govt.nz/](http://pharmac.govt.nz/)) for any changes to funding decisions.

Relevant age	Vaccine (trade name)	Recommended vaccination schedule
Under 12 months when diagnosed with functional asplenia or pre- or post-splenectomy <sup>a</sup>	PCV13 (Prevenar 13) <sup>b</sup>	Give PCV13 <sup>b</sup> at ages 6 weeks, and 3, 5 and 12–15 months or an age-appropriate catch-up schedule: <ul style="list-style-type: none"> <li>• <b>If aged under 7 months</b>, give PCV13 <sup>b</sup> at ages 6 weeks, 3 months, 5 months and 12 months</li> <li>• For those who <b>have not been immunised</b> age 7–11 months: give 2 doses of PCV13 (8 weeks apart) and a further dose at least 8 weeks later, from age 12 months</li> <li>• For children aged 7–11 months <b>who have completed</b> a 2-dose primary course with PCV10, give 1 dose of PCV13 as soon as possible and another dose (of PCV13) at least 8 weeks later, from age 12 months</li> </ul>
	23PPV (Pneumovax 23)	Following completion of the PCV schedule, give 1 dose at least 8 weeks after the last PCV13 dose, from age 2 years <ul style="list-style-type: none"> <li>• Revaccinate once after 5 years</li> </ul>
	MenACWY (Nimenrix)	<ul style="list-style-type: none"> <li>• If aged under 12 months, give 2 doses of MenACWY 8 weeks apart.</li> <li>• Give a booster dose of MenACWY (MenQuadfi), at least 6 months later, from age 12 months</li> </ul>
	MenB (Bexsero) <sup>c</sup>	<ul style="list-style-type: none"> <li>• Give one dose at age 8 weeks <sup>d</sup>, 4 months and 12 months</li> <li>• Or give two doses at least 8 weeks <sup>e</sup> apart and a booster dose at least 6 months later, from age 12 months</li> <li>• Give a booster dose 5-yearly.</li> </ul>
	Influenza <sup>f</sup>	Annual vaccination from age 6 months. <ul style="list-style-type: none"> <li>• In the first year, give 2 doses 4 weeks apart, then 1 dose in each subsequent year</li> </ul>
	COVID-19 (Comirnaty 3 µg)	From age 6 months, give two doses 3 weeks apart and a third dose 8 weeks later. An additional dose can be offered 6 months after the previous dose.

*Continued overleaf*

Relevant age	Vaccine (trade name)	Recommended vaccination schedule
Aged 12 months to under 18 years when diagnosed with functional asplenia or pre- or post-splenectomy <sup>a</sup>	PCV13 (Prevenar 13)	<ul style="list-style-type: none"> <li>Children aged 12–59 months, who have not yet received a primary course of PCV13: <ul style="list-style-type: none"> <li>– give 2 doses of PCV13 at least 8 weeks apart</li> </ul> </li> <li>Children aged 5 years to under 18 years: <ul style="list-style-type: none"> <li>– give 1 dose of PCV13 even if fully vaccinated <sup>g</sup></li> </ul> </li> </ul>
	23PPV (Pneumovax 23)	Following completion of the PCV schedule, give 1 dose at least 8 weeks after the last PCV13 dose, from age 2 years. Revaccinate once after 5 years.
	MenACWY (MenQuadfi)	<ul style="list-style-type: none"> <li>If aged 12 months to under 7 years at diagnosis <sup>h,j</sup>, give 2 doses of MenACWY 8–12 weeks apart.</li> <li>Give a booster dose after 3 years, if still aged under 7 years, then 5-yearly <sup>j</sup></li> <li>If aged 7 years or older give 2 doses <sup>i</sup> of MenACWY 8 weeks apart followed by a booster dose 5-yearly. <sup>j</sup></li> </ul>
	MenB (Bexsero) <sup>c</sup>	<ul style="list-style-type: none"> <li>From age 12 to 23 months, give 2 doses 8 weeks <sup>e</sup> apart followed by a booster given 12–23 months after second dose.</li> <li>From age 2 years, give 2 doses 8 weeks apart. <sup>e</sup></li> <li>Give booster doses 5-yearly <sup>j</sup></li> </ul>
	Hib-PRP (Act-HIB)	<ul style="list-style-type: none"> <li>If child is aged 12–15 months, give 1 dose at age 15 months as per the Schedule</li> <li>If aged 16 months to under 5 years and has not received a single Hib-PRP dose after age 12 months, give 1 dose</li> <li>If aged 5 years or older, give 1 dose, unless fully vaccinated</li> </ul>
	Influenza (age appropriate vaccine) <sup>f</sup>	<p>Give annually</p> <ul style="list-style-type: none"> <li>In previously unvaccinated children age &lt;9 years, give 2 doses 4 weeks apart, then 1 dose in each subsequent year</li> </ul>
COVID-19 (mRNA-CV)	Ensure individual is up to date with age-appropriate vaccine and schedule, see Table 5.3	

- Where possible, the vaccines should be administered at least 14 days before elective splenectomy and continue from 7 days after the splenectomy. For emergency splenectomy, the vaccines should be administered from 7 days post-operatively or prior to discharge from hospital.
- A three-dose primary series plus a booster dose of PCV13, administered at 6 weeks, 3 months, 5 months, and 12 months, provides an additional dose at age 3 months to the usual Schedule.
- It is recommended to administer prophylactic paracetamol (or ibuprofen) to reduce fever in children age under 2 years (see section 13.7.1).
- For children at high risk of meningococcal disease aged younger than 2 months, to align with the routine schedule visit MenB is recommended to be given at ages 6 weeks and 3 months. This is off-label use and requires a prescription and written consent. No prescription is required if given as per the alternative schedule at ages 8 weeks and 4 months.
- For infants aged 8 weeks – under 24 months, the spacing between MenB dose 1 and 2 can be reduced to 6 weeks if indicated, with a prescription. For those aged over 24 months, spacing can be reduced to four weeks (no prescription required).
- Check [immune.org.nz](http://immune.org.nz) for most recent influenza vaccine brands and appropriate age ranges.
- If 23PPV has already been given (prior to any doses of PCV13) to children aged under 18 years, wait at least 8 weeks before administering PCV13 (note – this differs from a 1-year gap recommended in adults).

- h. If child was aged under 12 months at time of diagnosis, and received two doses of MenC prior to 1 July 2024, administer two doses of MenACWY 8 weeks apart (see footnote i).
- i. A prescription is required for a second primary dose of MenQuadfi for those aged 12 months and over.
- j. Although the need for a booster dose after this vaccination schedule has not been established, it is recommended and funded for certain special groups.

### 4.3.12 HIV infection

Human immunodeficiency virus (HIV) infects CD4+ T cells leading to a progressive decline in CD4 cell count, increasing immunodeficiency and vulnerability to infection, and suboptimal responses to vaccines.

The efficacy of any vaccine may be reduced in HIV-positive individuals, and antibody levels within these individuals may wane faster than in individuals who are HIV-negative. Although antiretroviral therapy may improve immune responses, it is unlikely these individuals will achieve the levels of antibodies seen in individuals who are HIV-negative. Serological testing and the need for additional doses (eg, HepB: see section 9.5.7 and Table 9.6) should be discussed with the individual's specialist.

#### Vaccination of individuals with HIV infection

In addition to the usual Schedule vaccines, individuals who are HIV-positive to receive additional funded vaccines including Hib, pneumococcal, and meningococcal vaccines. Individuals who are HIV-positive are also eligible to receive funded influenza vaccination.

#### Live vaccines – caution

It is recommended that infants who are HIV-positive receive rotavirus vaccine as per the Schedule. Administration of BCG vaccination is contraindicated for all HIV-positive individuals regardless of their CD4+ percentage/count.<sup>57</sup>

MMR and VV may be administered as per the Schedule to:

- children aged 1–13 years who have a recent CD4+ lymphocyte percentage of  $\geq 15$  percent
- children aged 14 years to under 18 years who have a recent CD4+ count of  $\geq 200$  cells/ml
- MMR and VV can be administered as per the Schedule to adults aged 18 years or older who have a recent CD4+ lymphocyte count of  $\geq 200$  cells/mm<sup>3</sup>.<sup>49</sup>

See *Vaccines for individuals with acquired immunodeficiency* in section 4.3.3 for eligibility and recommendations for influenza, Hib, pneumococcal and meningococcal vaccines.

Table 4.6 (for children aged under 5 years when diagnosed) and Table 4.7 (for children aged 5 to under 18 years) summarise additional vaccine recommendations and schedules for HIV-positive children. The funded vaccines are shown in shade rows.

For adults, see the IMAC factsheet *Immunisation for adults with HIV infection* (available at [www.immune.org.nz/resources/factsheets](http://www.immune.org.nz/resources/factsheets)).

**Table 4.6: Additional vaccine recommendations for children aged under 5 years when diagnosed with HIV**

Note: HIV-positive children should receive the usual Schedule vaccines, including rotavirus vaccine for infants; BCG should not be given; MMR and VV may be administered as per the recommendations below. **Funded vaccines are in shaded rows.** Refer to the Pharmaceutical Schedule ([pharmac.govt.nz/](http://pharmac.govt.nz/)) for any changes to funding decisions.

Relevant age	Vaccine (trade name)	Recommended vaccine schedule
Infants aged under 12 months when diagnosed	PCV13 (Prevenar 13) <sup>a</sup>	Give PCV13 <sup>a</sup> at ages 6 weeks and 3, 5 and 12–15 months or an age-appropriate catch-up schedule: <ul style="list-style-type: none"> <li>• <b>If aged under 7 months</b>, give PCV13<sup>a</sup> at ages 6 weeks, 3 months, 5 months and 12 months</li> <li>• For those <b>who have not been immunised</b> age 7–11 months: give two doses of PCV13 (8 weeks apart) and a further dose at least 8 weeks later, from age 12 months</li> <li>• For children aged 7–11 months <b>who have completed</b> a 2-dose primary course with PCV10, give 1 dose of PCV13 as soon as possible and another dose (of PCV13) at least 8 weeks later, from age 12 months</li> </ul>
	23PPV (Pneumovax 23)	Following completion of the PCV schedule, give one dose at least 8 weeks after the last PCV13 dose, from age 2 years Revaccinate once after 5 years
	MenACWY (Nimenrix)	<ul style="list-style-type: none"> <li>• If aged under 12 months, give 2 doses of MenACWY (Nimenrix) 8 weeks apart followed by MenACWY (MenQuadfi) at least 6 months after later, from age 12 months.</li> </ul> Administer one MenACWY booster dose after 3 years, then 5-yearly
	MenB (Bexsero) <sup>b</sup>	<ul style="list-style-type: none"> <li>• Give one dose at age 8 weeks<sup>c</sup>, 4 months and 12 months</li> <li>• Or give two doses at least 8 weeks<sup>d</sup> apart and a booster dose at least 6 months later, from age 12 months</li> </ul>
	Influenza (junior formulation) <sup>e</sup>	Annual vaccination from age 6 months In the first year, give 2 doses 4 weeks apart, then 1 dose in each subsequent year
	COVID-19 (mRNA-CV (3µg))	From age 6 months, give two doses 3 weeks apart and a third dose 8 weeks later. An additional dose can be offered from 6 months after the third primary dose.

*Continued overleaf*

Relevant age	Vaccine (trade name)	Recommended vaccine schedule
Children aged 12 months to under 5 years when diagnosed	PCV13 (Prevenar 13)	<ul style="list-style-type: none"> <li>Children aged 12–59 months, who have not yet received any PCV13, give 2 doses of PCV13 at least 8 weeks apart<sup>f</sup></li> <li>Children aged 5 years to under 18 years, give 1 dose of PCV13 even if fully vaccinated<sup>f</sup></li> </ul>
	23PPV (Pneumovax 23)	<p>Following completion of the PCV schedule, give 1 dose at least 8 weeks after the last PCV13 dose, from age 2 years</p> <p>Revaccinate once after 5 years</p>
	Influenza (age-appropriate vaccine) <sup>e</sup>	<p>Give annually</p> <p>In previously unvaccinated children, give 2 doses 4 weeks apart, then 1 dose in each subsequent year.</p>
	MMR <sup>g</sup> (Priorix)	<p>If CD4+ lymphocyte percentage is <math>\geq 15\%</math>:</p> <ul style="list-style-type: none"> <li>give the first MMR dose at age 12 months, followed by the 2nd dose 4 weeks later</li> </ul>
	Varicella <sup>g</sup> (Varilrix)	<p>If CD4+ lymphocyte percentage is <math>\geq 15\%</math></p> <ul style="list-style-type: none"> <li>give 2 doses (starting 4 weeks after the 2nd MMR), at least 3 months apart</li> </ul>
	MenACWY (MenQuadfi)	<p>Give 2 doses of MenACWY<sup>h,i</sup> 8 to 12 weeks apart followed by a booster dose after 3 years, if still aged under 7 years, then 5-yearly</p>
	MenB (Bexsero) <sup>b</sup>	<ul style="list-style-type: none"> <li>From age 12 to 23 months, give 2 doses 8<sup>d</sup> weeks apart followed by a booster given 12–23 months after second dose.</li> <li>From age 2 years, give 2 doses 8<sup>d</sup> weeks apart</li> <li>Give booster doses 5-yearly<sup>j</sup>.</li> </ul>
	COVID-19 (Comirnaty (3µg))	<ul style="list-style-type: none"> <li>Give two doses 3 weeks apart and a third dose 8 weeks later.</li> <li>An additional dose can be offered from 6 months after the third primary dose.</li> </ul>

- A three-dose primary series plus a booster dose of PCV13, administered at 6 weeks, 3 months, 5 months, and 12 months, provides an additional dose at age 3 months to the usual Schedule.
- For infants aged under 12 months funding for Nimenrix is potentially accessible through named patient pharmaceutical assessment (NPPA).
- Recommended to administer prophylactic paracetamol (or ibuprofen) to reduce fever in children age under 2 years (see section 13.7.1)
- For children at high risk of meningococcal disease aged younger than 2 months, to align with the routine schedule visit MenB can be given at ages 6 weeks and 3 months. This is off-label use and requires a prescription and written consent. No prescription is required if given as per the alternative schedule at ages 8 weeks and 4 months.
- For infants aged 8 weeks – under 24 months, the spacing between MenB dose 1 and 2 can be reduced to 6 weeks apart, if necessary, with a prescription. For children aged over 24 months, spacing can be reduced to four weeks apart, if necessary (no prescription required).
- Check [immune.org.nz](http://immune.org.nz) for most recent influenza vaccine brands and appropriate age ranges.
- If 23PPV has already been given (prior to any doses of PCV13) to children aged under 18 years, wait at least 8 weeks before administering PCV13 (note – this differs from a 1-year gap recommended in adults).
- Only a single live vaccine is recommended at each visit for individuals with HIV infection. A minimum interval of 4 weeks is required between live vaccine doses administered at different visits.
- A prescription is required for a second primary dose of MenQuadfi for those aged 12 months.

- j. Although the need for a booster dose after this vaccination schedule has not been established, it is recommended and funded for certain special groups.

**Table 4.7: Additional vaccine recommendations for children aged 5 to under 18 years when diagnosed with HIV**

Note: HIV-positive children should receive the usual Schedule vaccines, MMR and varicella vaccines may be administered as per the recommendations below. **Funded vaccines are in shaded rows.**

Refer to the Pharmaceutical Schedule ([pharmac.govt.nz/](http://pharmac.govt.nz/)) for any changes to funding decisions.

Vaccine (trade name)	Recommended vaccine schedule
HPV9 (Gardasil 9) <sup>a</sup>	From age 9 years, give 3 doses of HPV at 0, 2 and 6 months. <sup>a</sup>
PCV13 (Prevenar 13) <sup>b</sup>	For children who have not previously received PCV13, give 1 dose of PCV13. <sup>b</sup>
23PPV (Pneumovax 23)	Give 1 dose of 23PPV at least 8 weeks after the PCV13 dose. Revaccinate once with 23PPV, 5 years after the first 23PPV
MenACWY (MenQuadfi)	<ul style="list-style-type: none"> <li>• If aged 5 years to under 7 years give 2 doses of MenACWY 8 to 12 weeks apart followed by a booster dose after 3 years and then 5-yearly</li> <li>• If aged 7 years or older give 2 doses of MenACWY 8 to 12 weeks apart followed by a booster dose 5-yearly</li> </ul>
MenB (Bexsero)	Give 2 doses 8 <sup>c</sup> weeks apart followed by a booster <sup>d</sup> dose 5-yearly
MMR <sup>e</sup> (Priorix)	<p>If aged ≤13 years and CD4+ lymphocyte percentage is ≥15%, or if aged ≥14 years and CD4+ lymphocyte count is ≥200 cells/mm<sup>3</sup>:</p> <ul style="list-style-type: none"> <li>• give 2 doses of MMR at least 4 weeks apart</li> </ul>
Varicella <sup>e</sup> (Varilrix)	<p>If no history of varicella disease or vaccination, and</p> <ul style="list-style-type: none"> <li>• if aged ≤13 years and CD4+ lymphocyte percentage is ≥15%, or</li> <li>• if aged ≥14 years and CD4+ lymphocyte count is ≥200 cells/mm<sup>3</sup>, give 2 doses (starting 4 weeks after 2nd MMR) at least 3 months apart</li> </ul>
Influenza <sup>f</sup>	<ul style="list-style-type: none"> <li>• If aged under 9 years give 2 doses 4 weeks apart in the first year receiving influenza vaccine (both doses are funded), and 1 dose in subsequent years</li> <li>• If aged 9 years or older give 1 dose</li> <li>• Give annually</li> </ul>
COVID-19 (Comirnaty)	<ul style="list-style-type: none"> <li>• Give one dose of age-appropriate mRNA-CV (ie mRNA-CV (30 µg) from age 12 years or mRNA-CV (10 µg) for ages 5-11 years, inclusive)</li> <li>• An additional dose can be offered from 6 months after the previous dose from age 5 years.</li> </ul>

- a. HPV9 is approved for use from age 9 years.
- b. If 23PPV has already been given (prior to any doses of PCV13) to children aged under 18 years, wait at least 1 year before administering PCV13.
- c. This can be reduced to 4 weeks apart if clinically required.
- d. Although the need for a booster dose after this vaccination schedule has not been established, it is recommended and funded for certain special groups.
- e. Only a single live vaccine is recommended at each visit for individuals with HIV infection. A minimum interval of 4 weeks is required between live vaccine doses administered at different visits.
- f. Check [immune.org.nz](http://immune.org.nz) for most recent influenza vaccine brands and appropriate age ranges.

Source: Starship Child Health



## COVID-19 vaccine

### *Young children aged 6 months to 4 years, inclusive*

Children aged 6 months to 4 years with active HIV infection or AIDS (with CD4 count <200 cells per  $\mu\text{l}$ ) are recommended to receive three doses of mRNA-CV (3  $\mu\text{g}$ ). First and second doses are given three weeks apart and dose three is given at least eight weeks after the second dose. An additional dose of mRNA-CV (3  $\mu\text{g}$ ) can be given six months after the primary course. This spacing can be reduced to at least three months, on a case-by-case basis, where there is a clinical need.

### *Individuals aged 5 years and over*

Individuals aged from 5 years with active HIV infection or AIDS (with CD4 count <200 cells per  $\mu\text{l}$ ) are eligible for three primary doses of mRNA-CV (10  $\mu\text{g}$  or 30  $\mu\text{g}$ , as age appropriate) (see section 5.5.2 for details); each dose is given eight weeks apart.

Regardless of any previous doses received after completion of the primary course, an additional dose of mRNA-CV (10  $\mu\text{g}$  or 30  $\mu\text{g}$ , as age appropriate) is recommended for all individuals aged 5 years and over living with HIV infection, and in particular those eligible for three primary doses, given six months after a previous dose. This spacing can be reduced to at least three months, on a case-by-case basis, where there is a clinical need (see section 5.5.3).

If a significant adverse reaction to mRNA-CV has occurred, it is recommended to seek advice from IMAC to determine whether further doses are contraindicated.

## Herpes zoster

Individuals from age 18 years, including those aged 66 years and over, with HIV infection are recommended two doses of recombinant zoster vaccine (rZV, Shingrix), given two to six months apart. Funded vaccine is available for those with poorly controlled HIV. This includes people living with advanced or untreated HIV infection with CD4 counts less than 350/ $\mu\text{L}$  or those with a higher CD4 count not established on effective anti-retroviral therapy (i.e. with a viral load of over 500 copies/mL or 2.7  $\text{Log}_{10}$ ). See section 25.5.1

## 4.4 Chronic kidney disease

Individuals immunised during the early stages of chronic kidney disease (CKD) generally respond to vaccination. However, the immune system response to vaccination decreases with advancing kidney disease.<sup>58, 59</sup> Cases of children developing a disease for which they have serological evidence of immunity have been reported.<sup>59</sup>

Individuals with nephrotic syndrome, kidney failure or end-stage kidney disease (CKD stages 4–5) have an increased risk of peritonitis and/or sepsis caused by encapsulated bacteria, *Streptococcus pneumoniae*, *Haemophilus influenzae* type b and *Neisseria meningitidis*.<sup>58–60</sup> Individuals on haemodialysis have an increased risk of exposure to hepatitis B virus. Adults with CKD also have an increased risk of zoster.<sup>61</sup>

## Vaccination of individuals with chronic kidney disease

Individuals with CKD who are not receiving immunosuppressive therapy to manage their condition can receive vaccination as per the usual Immunisation Schedule. In addition to the usual Immunisation Schedule vaccines, individuals with CKD may be eligible to receive additional funded vaccines. These should be given as soon as the individual meets the eligibility criteria (eg, CKD stages 4–5: pre-dialysis, on dialysis, pre-kidney transplant, post-kidney transplant). There is no relationship between vaccination and deterioration of renal function or a reduction in the efficacy of dialysis.<sup>59</sup>

Additional funded vaccines may include hepatitis A, hepatitis B, *Haemophilus influenzae* type b (Hib), pneumococcal, and meningococcal vaccines. Individuals with CKD are also eligible to receive funded influenza vaccination.

See *Vaccines for individuals with acquired immunodeficiency* in section 4.3.3 for eligibility and recommendations for influenza, *Haemophilus influenzae* type b (Hib), pneumococcal and meningococcal vaccines.

For children aged under 18 years, see the Starship Clinical Guideline *Renal vaccination record for Starship paediatric CKD* (available at [www.starship.org.nz/guidelines/renal-vaccination-record-for-starship-paediatric-ckd](http://www.starship.org.nz/guidelines/renal-vaccination-record-for-starship-paediatric-ckd)).

For adults, see the IMAC factsheet *Immunisation for adults pre-dialysis, on dialysis or pre-/post-kidney transplant* (available at [www.immune.org.nz/resources/factsheets](http://www.immune.org.nz/resources/factsheets)).

### Live vaccines – caution

Administration of live vaccines (MMR and VV) are generally contraindicated for individuals who are immunosuppressed because of the risk of disseminated vaccine disease. However, individuals with CKD who are considered to have minimal immunosuppression may be able to receive VV.<sup>45</sup>

## COVID-19

### *Young children aged 6 months to 4 years, inclusive*

Children aged 6 months to 4 years receiving long term haemodialysis or peritoneal dialysis are recommended to receive three doses of mRNA-CV (3 µg). First and second doses are given three weeks apart and dose three is given at least eight weeks after the second dose. An additional dose of mRNA-CV (3 µg) can be given six months after the primary course. This spacing can be reduced to at least three months, on a case-by-case basis, where there is a clinical need.

### *Individuals aged 5 years and over*

Individuals from 5 years of age receiving long term haemodialysis or peritoneal dialysis are eligible three primary doses of mRNA-CV (10 µg or 30 µg, as age appropriate) (see section 5.5.2 for details); each dose is given eight weeks apart.

Regardless of any previous doses received after completion of the primary course, an additional dose of mRNA-CV (10 µg or 30µg, as age appropriate) is recommended for all individuals aged 5 years and over with chronic kidney disease, and particularly those eligible for three primary doses, to be given six months after the previous dose. This spacing can be reduced to at least three months, on a case-by-case basis, where there is a clinical need (see section 5.5.3).

If a significant adverse reaction to mRNA-CV has occurred, it is recommended to seek advice from IMAC to determine whether further doses are contraindicated.

### *Herpes zoster*

Individuals from age 18 years, including those aged 66 years and over, with chronic kidney disease are recommended two doses of recombinant zoster vaccine (rZV, Shingrix), given two to six months apart. This vaccine is funded for those with end-stage CKD-4 and -5. See section 25.5.1.

## **4.5 Chronic liver disease**

Chronic liver disease in infants and children may present as part of a congenital syndrome. They may have other conditions (eg, infants with biliary atresia may also have a non-functioning spleen) and eligibility for additional funded vaccines.

### **Vaccination of individuals with chronic liver disease**

Individuals with chronic liver disease who are not receiving immunosuppressive therapy to manage their condition can receive vaccination as per the usual Schedule.

In addition to the usual Schedule vaccines, infants and children with chronic liver disease are eligible to receive funded hepatitis A vaccination from 12 months of age (see section 8.5.1). However, if they are likely to require a liver transplant an accelerated vaccination schedule may be advised as per Table 4.4. The aim of the accelerated schedule is to maximise protection against vaccine-preventable diseases and to deliver live vaccines prior to transplantation and immunosuppression. Prior to transplantation, hepatitis A vaccine could be administered from as early as 7 months of age. Additional pre-transplantation funded vaccines include influenza, pneumococcal, meningococcal, and varicella vaccines (see section 4.3.3).

It is recommended that adults with chronic liver disease receive influenza vaccination annually but this is not currently funded. Adults who are likely to require a liver transplant are eligible for additional funded vaccines, including hepatitis A vaccine; hepatitis B vaccine, if the individual was not previously vaccinated or does not have

evidence of immunity; *Haemophilus influenzae* type b (Hib), influenza, pneumococcal, meningococcal and varicella vaccines (see section 4.3.10).

## COVID-19 vaccine

### *Young children aged 6 months to 4 years, inclusive*

Children aged 6 months to 4 years with a chronic liver disease are recommended to receive three doses of mRNA-CV (3 µg). First and second doses are given three weeks apart and dose three is given at least eight weeks after the second dose. An additional dose of mRNA-CV (3 µg) can be given six months after the primary course. This spacing can be reduced to at least three months, on a case-by-case basis, where there is a clinical need.

### *Individuals aged 5 years and over*

Children from 5 years of age with chronic liver disease are eligible for three primary doses of mRNA-CV (10 µg or 30 µg, as age appropriate) (see section 5.5.2 for details); each dose is given 8 weeks apart.

Regardless of any doses received after completion of the primary course, an additional dose of mRNA-CV (10 µg or 30 µg, as age appropriate) is recommended for children aged 5 years and over and adults with chronic liver disease, and particularly those eligible for three primary doses, to be given six months after the previous dose. This spacing can be reduced to at least three months, on a case-by-case basis, where there is a clinical need (see section 5.5.3).

If a significant adverse reaction to mRNA-CV has occurred, it is recommended to seek advice from IMAC to determine whether further doses are contraindicated.

## 4.6 Other special groups

It is recommended that all individuals receive vaccination as per the usual Schedule except when pre-vaccination screening identifies a contraindication for a specific vaccine (see section 2.1.4). Additional vaccines may be recommended (but are not always funded) for individuals with some conditions or in some circumstances not previously discussed in this chapter.

Table 4.8 lists other special groups and recommended additional vaccines. Funded vaccines are shown in shaded rows.

**Table 4.8: Additional vaccine recommendations for other special groups**

**Funded vaccines are in shaded rows.** See the table footnotes for more information when indicated. Vaccinators are advised to check the Pharmaceutical Schedule ([pharmac.govt.nz/](http://pharmac.govt.nz/)) for any changes to funding decisions.

Special group	Recommended vaccines
Individuals: <ul style="list-style-type: none"> <li>with cerebrospinal fluid (CSF) leak</li> <li>with chronic pulmonary disease, including asthma treated with high-dose corticosteroid therapy, and cystic fibrosis</li> <li>receiving corticosteroid therapy for more than two weeks and who are on an equivalent daily dosage of prednisone of 2 mg/kg per day or greater, or children who weigh more than 10 kg on a total daily dosage of 20 mg or greater</li> <li>with diabetes</li> <li>with intracranial shunt</li> <li>receiving radiotherapy</li> </ul>	Children, aged under 5 years <ul style="list-style-type: none"> <li>PCV13, 23PPV</li> <li>Influenza, annually</li> <li>mRNA-CV (3 µg) (excluding asthma)</li> </ul> Children aged 5 years to under 18 years, (including for those who received previous doses of a non-PCV13 vaccine (PCV10 and PCV7)) <ul style="list-style-type: none"> <li>PCV13, 23PPV</li> <li>Influenza, annually</li> <li>mRNA-CV (10 µg or 30µg, as age appropriate)</li> </ul>
<ul style="list-style-type: none"> <li>living in boarding schools, hostels, university halls of residence, or other close quarters<sup>a</sup></li> </ul>	MenACWY <sup>a</sup> MMR (if susceptible) MenB <sup>a</sup> Hepatitis B (if susceptible) VV (if susceptible) Influenza, annually
<ul style="list-style-type: none"> <li>with cochlear implants</li> </ul>	<i>Haemophilus influenzae</i> type b (Hib-PRP) Influenza, annually Pneumococcal (PCV13, 23PPV)
<ul style="list-style-type: none"> <li>living in correctional facilities<sup>a</sup></li> </ul>	MenACWY <sup>a</sup> MMR (if susceptible) MenB <sup>a</sup> Hepatitis B (if susceptible) Influenza, annually
<ul style="list-style-type: none"> <li>with error of metabolism at risk of major metabolic decompensation</li> </ul>	Influenza, annually Varicella (VV)
<ul style="list-style-type: none"> <li>with rheumatic heart disease</li> </ul>	Influenza, annually
<ul style="list-style-type: none"> <li>who are case contacts of an individual with hepatitis A</li> </ul>	Hepatitis A (if susceptible)
<ul style="list-style-type: none"> <li>with hepatitis B infection</li> </ul>	Hepatitis A (if susceptible)
<ul style="list-style-type: none"> <li>who are household or sexual contacts of an individual with hepatitis B</li> </ul>	Hepatitis B (if susceptible)
<ul style="list-style-type: none"> <li>with hepatitis C infection</li> </ul>	Hepatitis A (if susceptible) Hepatitis B (if susceptible)
<ul style="list-style-type: none"> <li>with a needle-stick injury</li> </ul>	Hepatitis B (if susceptible)

Continued overleaf

Special group	Recommended vaccines
<ul style="list-style-type: none"> <li>who have had non-consensual sexual intercourse<sup>b</sup></li> </ul>	Hepatitis B (if susceptible)
Intravenous drug users	Hepatitis A (if susceptible) Hepatitis B (if susceptible) Influenza, annually
Men who have sex with men <sup>b</sup>	HPV <sup>c</sup> Hepatitis A (if susceptible) Hepatitis B (if susceptible)
Case contacts of an individual with meningococcal disease of any group	MenACWY <sup>d</sup> MenB
Individuals who have previously had meningococcal disease of any group	MenACWY <sup>d</sup> MenB
Children at risk of exposure to tuberculosis	BCG vaccination for children aged under 5 years who: <ul style="list-style-type: none"> <li>will be living in a house or family/whānau with a person with either current TB or a history of TB</li> <li>have one or both parents or household members or carers who within the last five years lived for a period of six months or longer in countries with a TB rate <math>\geq 40</math> per 100,000</li> <li>during their first five years will be living for three months or longer in a country with a TB rate <math>\geq 40</math> per 100,000.</li> </ul> See section 23.5.2

- One dose of MenACWY and two doses of MenB are funded for individuals aged 13–25 years inclusively who are entering within the next 3 months, or who are in their first year of living in a boarding school hostel, tertiary education halls of residence, military barrack, youth justice residences or prison. This includes children who turn 13 years of age while living in boarding school hostels. MenACWY (MenQuadfi or Nimenrix) and MenB (Bexsero) are recommended but unfunded for individuals aged 13-25 years who do not meet these criteria.
- These individuals are advised to discuss their risk of exposure to mpox (monkeypox) with a sexual health clinic or see the Health New Zealand | Te Whatu Ora website at [www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/diseases-and-conditions/monkeypox](http://www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/diseases-and-conditions/monkeypox).
- Three doses are funded for those aged 26 years or under.
- As age-appropriate: give MenACWY (Nimenrix) to those aged under 12 months; give MenQuadfi to those aged 12 months and over.

## 4.7 Immigrants and refugees

Adults and children who enter New Zealand as refugees or immigrants will need an assessment of their **documented** vaccination status and an appropriate planned catch-up programme. The programme may require modification based on **documented** doses: only clearly documented doses should be considered as given. If there is no

documented vaccination history, plan the catch-up schedule assuming the vaccines have not been given, see Appendix 2 for catch-up schedules.

Immunisation schedules vary from country to country. Check all migrant and former refugee children immunisation records to ensure they are up to date with the New Zealand Schedule, in particular ensure they have received MMR as opposed to a measles-rubella vaccine only.

For assistance with planning catch-up schedules, contact your local immunisation coordinator; or call IMAC on 0800 IMMUNE/0800 466 863, or discuss with an experienced colleague.

All children aged under 18 years are eligible to receive Schedule vaccines and Well Child Tamariki Ora services regardless of their immigration and citizenship status, and providers can claim the immunisation benefit for administering the vaccines.

Adult refugees aged 18 years or older are eligible to receive Schedule vaccines, and providers can claim the immunisation benefit for administering the vaccines. Non-residents who were aged under 18 years when they commenced HPV vaccination are currently funded to complete the course, even if they are aged 18 years or older when they complete it. Other adults aged 18 years or older must meet all the applicable eligibility criteria described in the *Health and Disability Services Eligibility Direction 2011* to receive funded healthcare services, including Schedule vaccines. For more information about eligibility for publicly funded services, see the Health New Zealand | Te Whatu Ora website (<https://www.tewhatoru.govt.nz/our-health-system/eligibility-for-publicly-funded-health-services>).

See also the *Recommendations for Comprehensive Post-Arrival Health Assessment for People from Refugee-like Backgrounds (2016 edition)*, available on the Australasian Society for Infectious Diseases website ([asid.au/products/refugee-guidelines-2016](http://asid.au/products/refugee-guidelines-2016)).

## Tuberculosis

In New Zealand, BCG vaccination is recommended and funded for infants and children aged under 5 years at increased risk of tuberculosis (TB). For further details, see section 23.5.2 and the Ministry of Health *Guidelines for Tuberculosis Control in New Zealand, 2019* (available at [www.tewhatoru.govt.nz/publications/guidelines-for-tuberculosis-control-in-new-zealand-2019](http://www.tewhatoru.govt.nz/publications/guidelines-for-tuberculosis-control-in-new-zealand-2019)).

Quota refugees are screened for active TB prior to arrival in New Zealand. If they are found to have active TB, their arrival is delayed until they are treated. The requirement for active TB screening of visitors and immigrants to New Zealand varies, dependent on the country they are coming from and/or how long they intend to stay in New Zealand.<sup>62</sup> In New Zealand over 2010–2016, the highest number of new TB cases were in people born overseas followed by people living with a person born overseas. Over 2012–2016, the average time between arrival in New Zealand and a new diagnosis of TB was around five years.<sup>63</sup> See section 23.3.2 for risk factors and for countries with high incidence of TB.



Medical practitioners and laboratories are required to notify the Medical Officer of Health of suspected or confirmed cases of active TB. A person who has, or is suspected to have, active TB is entitled to the same level of funded health services as New Zealand citizens can expect.<sup>62</sup>

## Hepatitis B

If a member of a refugee or immigrant family is found to be a hepatitis B carrier, it is recommended that all the family be screened, and vaccination offered to all those who are non-immune. Even if no one in the family is a hepatitis B carrier, it is recommended that all children aged under 18 years be vaccinated against hepatitis B. See chapter 9 for more information and Appendix 2 for catch-up schedules.

## Varicella

Individuals who have grown up in the tropics are less likely to have had chickenpox in childhood and may be non-immune as adolescents and adults. Adult chickenpox can be severe, and maternal varicella occurring in the first half of pregnancy can cause the rare but devastating congenital varicella syndrome (see Table 24.4). If there is no history of chickenpox or previous varicella vaccination, VV should be offered. Funded only for those turning 11 years of age on or after 1 July 2017 and currently aged under 18 years.

## COVID-19

All individuals aged from 5 years living in New Zealand are eligible for COVID-19 vaccination (age-appropriate mRNA-CV [10 µg or 30 µg]), regardless of health and disability services eligibility. Additional doses are available from age 16 years with mRNA-CV (30 µg), see 5.5.3. See section 5.5.4 for timing of COVID-19 vaccination following prior COVID-19 infection.

# 4.8 Occupation-related vaccination

Certain occupations result in increased risk of contracting some vaccine-preventable diseases. Some infected workers, particularly health care workers and those working in early childhood education services, may transmit infections such as influenza, rubella, measles, mumps, varicella and pertussis to susceptible contacts, with the potential for serious outcomes.

Where workers are at significant occupational risk of acquiring or transmitting a vaccine-preventable disease, the employer should implement a comprehensive risk-based occupational vaccination programme, including vaccination policies, staff vaccination records, information about the relevant vaccine-preventable diseases and the management of vaccine refusal. Employers should take all reasonably practicable steps to encourage workers to be immunised as appropriate for the workplace environment and tasks. For information on what is required as evidence of immunity

against vaccine preventable diseases, see the IMAC factsheet *Occupation related immunisation* (available at [www.immune.org.nz/resources/factsheets](http://www.immune.org.nz/resources/factsheets)).

The vaccines in Table 4.9 are recommended for certain occupational groups. In addition to the vaccines listed here, all adults should be up to date with age-appropriate Schedule vaccines (see section A2.3 in Appendix 2 for catch-up vaccination advice for adults aged 18 years or older) and includes COVID-19 vaccines.

If a non-immune individual is exposed to a vaccine-preventable disease, post-exposure prophylaxis and control measures should be administered where indicated (see the relevant disease chapters and in the *Communicable Disease Control Manual*, available at <https://www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/>).

**Table 4.9: Recommended vaccines, by occupational group**

Occupation	Recommended vaccines
<p><b>Workers in health care settings</b></p> <p>Health care staff who work with patients or are working in clinical areas where patient care is being administered.</p> <p>For example, medical staff, nursing staff, lead maternity carers, radiography staff, dentists, other health professional staff and students, and allied staff in health care settings, such as cleaning and catering staff.</p>	<p>Tdap – at least every 10 years<sup>a</sup></p> <p>MMR</p> <p>Varicella</p> <p>Hepatitis B</p> <p>Influenza, annually</p> <p>COVID-19</p>
<p><b>Carers</b></p> <p>Health care assistants, long-term facility carers and nursing home staff</p>	<p>Tdap – at least every 10 years<sup>a</sup></p> <p>MMR</p> <p>Varicella</p> <p>Hepatitis B</p> <p>Influenza, annually</p> <p>COVID-19</p>
<p><b>Individuals who work with children</b></p> <p>Early childhood education services staff</p>	<p>Tdap – at least every 10 years<sup>a</sup></p> <p>IPV</p> <p>MMR</p> <p>Varicella</p> <p>Hepatitis A</p> <p>Hepatitis B</p> <p>Influenza, annually</p> <p>COVID-19</p>

*Continued overleaf*

Occupation	Recommended vaccines
Other individuals working with children, including: <ul style="list-style-type: none"> <li>• correctional staff working where infants/children live with mothers</li> <li>• school teachers (including student teachers)</li> <li>• outside school hours carers</li> <li>• child counselling services workers</li> <li>• youth services workers</li> </ul>	<p>Tdap – at least every 10 years<sup>a</sup></p> <p>IPV</p> <p>MMR</p> <p>Varicella</p> <p>Influenza, annually</p> <p>COVID-19</p>
<b>Emergency and essential service workers</b>	
Police and emergency workers	<p>Tdap – at least every 10 years<sup>a</sup></p> <p>IPV</p> <p>MMR</p> <p>Varicella</p> <p>Hepatitis B</p> <p>Influenza, annually</p> <p>COVID-19</p>
Armed forces personnel	<p>Tdap – at least every 10 years<sup>a</sup></p> <p>IPV</p> <p>MMR</p> <p>Varicella</p> <p>Hepatitis A (if deployed to high-risk countries)</p> <p>Hepatitis B</p> <p>Influenza, annually</p> <p>COVID-19</p> <p>MenB (if living in close quarters)</p> <p>MenACWY<sup>b</sup> (if living in close quarters and/or deployed to high-risk countries)</p> <p>Yellow fever, rabies, typhoid, Japanese encephalitis (as appropriate, if deployed to high-risk countries)</p>
Staff of correctional facilities	<p>Tdap – at least every 10 years<sup>a</sup></p> <p>IPV</p> <p>MMR</p> <p>Varicella</p> <p>Hepatitis B</p> <p>Influenza, annually</p> <p>COVID-19</p>
Staff of immigration/refugee centres	<p>Tdap – at least every 10 years<sup>a</sup></p> <p>IPV</p> <p>MMR</p> <p>Varicella</p> <p>Hepatitis B</p> <p>Influenza, annually</p> <p>COVID-19</p>

*Continued overleaf*

Occupation	Recommended vaccines
Border staff (eg, cleaners, security staff, custom and border officials, hotel workers, airline staff, port authorities, police, defence force staff and health professionals)	Influenza, annually MMR COVID-19
<b>Individuals who work with animals</b>	
Veterinarians, veterinary students and veterinary nurses	Tdap IPV MMR Influenza, annually
Zoo staff who work with primates, livestock, wild birds and marine mammals.	Tdap IPV MMR Hepatitis A Influenza, annually
Those working with livestock, poultry and others handling poultry, including those who may be involved in culling during an outbreak of avian influenza.	Tdap IPV MMR Influenza, annually
<b>Individuals exposed to human tissue, blood, body fluids or sewage</b>	
Laboratory staff	Tdap MMR Varicella Hepatitis A (if exposed to faeces) Hepatitis B Influenza, annually MenACWY and MenB (if regularly working with <i>Neisseria meningitidis</i> cultures) IPV (10-yearly booster doses if handling faecal samples from those coming from high-risk countries) COVID-19
Workers who perform skin penetration procedures (eg, tattooists, body-piercers)	Tdap IPV
Funeral workers, embalmers and other workers who have regular contact with human tissue, blood or body fluids and/or used needles or syringes	Hepatitis B
Sewage workers, plumbers or other workers in regular contact with untreated sewage	Tdap IPV MMR Hepatitis A Hepatitis B
Sex workers <sup>c</sup>	Tdap IPV MMR Hepatitis B HPV

- a. Tdap booster frequency can vary from 5- to 10-yearly in accordance with employer recommendations for those working with most vulnerable people, including neonatal and maternal care, infants and immunocompromised or those at increased risk from respiratory infections.
- b. One dose of MenACWY and two doses of MenB are funded for individuals aged 13–25 years inclusively who are entering within the next 3 months, or who are in their first year of living in a boarding school hostel, tertiary education halls of residence, military barracks, youth justice residences or prison.
- c. These individuals are advised to discuss their risk of exposure to mpox (monkeypox) with a sexual health clinic. See chapter 14. .

## 4.9 Travel

All travellers should be encouraged to consider vaccination requirements well in advance of overseas travel, including those who travel frequently for work or to visit family. It is recommended that they are up to date with age-appropriate Schedule vaccines (see Appendix 2 for advice on planning catch-up vaccination) and receive current information on overseas travel requirements (eg, COVID-19, typhoid, yellow fever, rabies, Japanese encephalitis vaccination).

Travellers can seek advice from a primary care practice with expertise in travel medicine or a specialist travel medicine clinic. Information is also available on the New Zealand Safe Travel ([safetravel.govt.nz](https://safetravel.govt.nz)) and WHO ([who.int/travel-advice](https://www.who.int/travel-advice)) websites.

### Students entering New Zealand for study

International visitors, especially students entering New Zealand for educational purposes to attend schools and tertiary institutions, are recommended to be immunised and to check that their immunisations are appropriate for New Zealand. The recommended immunisations for adults are given in Table 2.4 – note, these may not be funded for all students.

All children aged under 18 years are eligible to receive Schedule vaccines regardless of their immigration and citizenship status, and providers can claim the immunisation benefit for administering the vaccines.

Adults and children who enter New Zealand as students are recommended to have an assessment of their **documented** vaccination status, and if necessary, an appropriate planned catch-up programme based on their documented doses.

## References

1. Global Advisory Committee on Vaccine Safety. 2014 *Safety of immunization during pregnancy: A review of the evidence*. Geneva. URL: [https://www.who.int/vaccine\\_safety/publications/safety\\_pregnancy\\_nov2014.pdf?ua=1](https://www.who.int/vaccine_safety/publications/safety_pregnancy_nov2014.pdf?ua=1). (accessed 2021 June 11)
2. Shimabukuro TT, Kim SY, Myers TR, et al. Preliminary findings of mRNA COVID-19 vaccine safety in pregnant persons. *New England Journal of Medicine*, 2021. 384(24): p. 2273-2282.
3. Reef SE, Plotkin S. 2018. Rubella Vaccines, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
4. Omer SB, Bednarczyk R, Madhi SA, Klugman KP. Benefits to mother and child of influenza vaccination during pregnancy. *Human Vaccines & Immunotherapeutics*, 2012. 8(1): p. 130-7.
5. Sakala IG, Honda-Okubo Y, Fung J, Petrovsky N. Influenza immunization during pregnancy: Benefits for mother and infant. *Human Vaccines & Immunotherapeutics*, 2016. 12(12): p. 3065-3071.
6. Marshall H, McMillan M, Andrews RM, et al. Vaccines in pregnancy: The dual benefit for pregnant women and infants. *Human Vaccines & Immunotherapeutics*, 2016. 12(4): p. 848-56.
7. Shakib JH, Korgenski K, Presson AP, et al. Influenza in Infants Born to Women Vaccinated During Pregnancy. *Pediatrics*, 2016. 137(6): p. e20152360.
8. Global Advisory Committee on Vaccine Safety. 2014 *Safety of immunization during pregnancy: A review of the evidence*. World Health Organization; 2014 [updated 2014]; URL: [https://www.who.int/vaccine\\_safety/publications/safety\\_pregnancy\\_nov2014.pdf?ua=1](https://www.who.int/vaccine_safety/publications/safety_pregnancy_nov2014.pdf?ua=1). (accessed 2 December 2019)
9. McHugh L, Marshall HS, Perrett KP, et al. The safety of influenza and pertussis vaccination in pregnancy in a cohort of Australian mother-infant pairs, 2012-2015: The FluMum Study. *Clinical Infectious Diseases*, 2019. 68(3): p. 402-408.
10. McMillan M, Porritt K, Kralik D, et al. Influenza vaccination during pregnancy: a systematic review of fetal death, spontaneous abortion, and congenital malformation safety outcomes. *Vaccine*, 2015. 33(18): p. 2108-17.
11. Eberhardt CS, Blanchard-Rohner G, Lemaître B, et al. Pertussis antibody transfer to preterm neonates after second- versus third-trimester maternal immunization. *Clinical Infectious Diseases*, 2017. 64(8): p. 1129-1132.
12. Schulzke S, Heininger U, Lucking-Famira M, Fahrenstich H. Apnoea and bradycardia in preterm infants following immunisation with pentavalent or hexavalent vaccines. *European Journal of Pediatrics*, 2005. 164(7): p. 432-5.
13. Vaz-de-Lima LRA, Sato HK, Fernandes EG, et al. Association between the timing of maternal vaccination and newborns' anti-pertussis toxin antibody levels. *Vaccine*, 2019. 37(36): p. 5474-5480.
14. Clifford V, Crawford NW, Royle J, et al. Recurrent apnoea post immunisation: Informing re-immunisation policy. *Vaccine*, 2011. 29(34): p. 5681-5687.
15. Chiu M, Bao C, Sadarangani M. Dilemmas with rotavirus vaccine: The neonate and immunocompromised. *Pediatric Infectious Disease Journal*, 2019. 38(Suppl 6): p. S43-46.
16. Esposito S, Pagni L, Mosca F, Principi N. Rotarix® and RotaTeq® administration to preterm infants in the neonatal intensive care unit: Review of available evidence. *Vaccine*, 2018. 36(36): p. 5430-5434.

17. Sicard M, Bryant K, Muller ML, Quach C. Rotavirus vaccination in the neonatal intensive care units: where are we? A rapid review of recent evidence. *Current Opinion in Pediatrics*, 2020. 32(1): p. 167-191.
18. Eberhardt CS, Blanchard-Rohner G, Lemaitre B, et al. Maternal immunization earlier in pregnancy maximizes antibody transfer and expected infant seropositivity against pertussis. *Clinical Infectious Diseases*, 2016. 62(7): p. 829-836.
19. van den Berg JP, Westerbeek EA, van der Klis FR, et al. Transplacental transport of IgG antibodies to preterm infants: a review of the literature. *Early Human Development*, 2011. 87(2): p. 67-72.
20. Wilson E, Finucane K, Hamer M, Spinetto H. 2015 *Immunisations and cardiac infants*. Starship Child Health; 2015 [updated 2019]; URL: <https://www.starship.org.nz/guidelines/immunisations-and-cardiac-infants>. (accessed 28 April 2020)
21. Bakare N, Menschik D, Tiernan R, et al. Severe combined immunodeficiency (SCID) and rotavirus vaccination: reports to the Vaccine Adverse Events Reporting System (VAERS). *Vaccine*, 2010. 28(40): p. 6609-12.
22. Klinkenberg D, Blohm M, Hoehne M, et al. Risk of rotavirus vaccination for children with SCID. *Pediatric Infectious Disease Journal*, 2015. 34(1): p. 114-5.
23. Østensen M. Antirheumatic biologics in pregnant patients: a call for studies to address the knowledge gap. *Expert Review of Clinical Immunology*, 2018. 14(2): p. 95-97.
24. Berkhout A, Clark JE, Wen SC-H. In utero exposure to biologic disease-modifying anti-rheumatic drugs and effects to the infant: infectious complications, vaccine response, and safety of live vaccine administration. *Expert Review of Vaccines*, 2019. 18(5): p. 495-504.
25. Zerbo O, Modaresi S, Goddard K, et al. Safety of Live-Attenuated Vaccines in Children Exposed to Biologic Response Modifiers in Utero. *Pediatrics*, 2022. 150(1).
26. Fitzpatrick T, Alsager K, Sadarangani M, et al. Immunological effects and safety of live rotavirus vaccination after antenatal exposure to immunomodulatory biologic agents: a prospective cohort study from the Canadian Immunization Research Network. *Lancet Child Adolesc Health*, 2023. 7(9): p. 648-656.
27. Beaulieu DB, Ananthakrishnan AN, Martin C, et al. Use of biologic therapy by pregnant women with inflammatory bowel disease does not affect infant response to vaccines. *Clinical Gastroenterology and Hepatology*, 2018. 16(1): p. 99-105.
28. Greenwood KP, Hafiz R, Ware RS, Lambert SB. A systematic review of human-to-human transmission of measles vaccine virus. *Vaccine*, 2016. 34(23): p. 2531-6.
29. Kamboj M, Sepkowitz KA. Risk of transmission associated with live attenuated vaccines given to healthy persons caring for or residing with an immunocompromised patient. *Infection Control and Hospital Epidemiology*, 2007. 28(6): p. 702-7.
30. Marin M, Leung J, Gershon AA. Transmission of Vaccine-Strain Varicella-Zoster Virus: A Systematic Review. *Pediatrics*, 2019. 144(3): p. e20191305.
31. American Academy of Pediatrics. 2018. Immunization and other considerations in immunocompromised children. in *Red Book: 2018 report of the Committee on Infectious Diseases*, Kimberlin D, Brady M, Jackson M, and Long S (eds). Elk Grove Village, Illinois. p. 72-91. URL: <https://redbook.solutions.aap.org/redbook.aspx>. (accessed 3 July 2020)
32. Huggard D, Doherty DG, Molloy EJ. Immune Dysregulation in Children With Down Syndrome. *Front Pediatr*, 2020. 8: p. 73.
33. Ram G, Chinen J. Infections and immunodeficiency in Down syndrome. *Clinical and Experimental Immunology*, 2011. 164(1): p. 9-16.
34. Duncan CJA, Randall RE, Hambleton S. Genetic lesions of type I interferon signalling in human antiviral immunity. *Trends in Genetics*, 2021. 37(1): p. 46-58.



35. American Academy of Pediatrics. 2021. Immunization and other considerations in immunocompromised children. in *Red Book: 2021-2024 report of the Committee on Infectious Diseases (32nd Edition)*, Kimberlin D, Barnett E, Lynfield R, and Saywer M (eds). Elk Grove Village, Illinois. p. 72-86. URL: <https://redbook.solutions.aap.org/redbook.aspx>. (accessed 20 December 2022)
36. Bastard P, Hsiao K-C, Zhang Q, et al. A loss-of-function *IFNAR1* allele in Polynesia underlies severe viral diseases in homozygotes. *J. Exp. Med.*, 2022. 219(6).
37. Duncan CJA, Skouboe MK, Howarth S, et al. Life-threatening viral disease in a novel form of autosomal recessive *IFNAR2* deficiency in the Arctic. *Journal of Experimental Medicine*, 2022. 219(6).
38. Meffre E, Iwasaki A. Interferon deficiency can lead to severe COVID. *Nature*, 2020. 587(7834): p. 374-376.
39. Pairo-Castineira E, Clohisey S, Klaric L, et al. Genetic mechanisms of critical illness in COVID-19. *Nature*, 2021. 591(7848): p. 92-98.
40. Zhang Q, Bastard P, Liu Z, et al. Inborn errors of type I IFN immunity in patients with life-threatening COVID-19. *Science*, 2020. 370(6515): p. eabd4570.
41. Hernandez N, Bucciol G, Moens L, et al. Inherited *IFNAR1* deficiency in otherwise healthy patients with adverse reaction to measles and yellow fever live vaccines. *Journal of Experimental Medicine*, 2019. 216(9): p. 2057-2070.
42. Danziger-Isakov L, Posfay-Barbe KM. Optimal approach to immunization in pediatric solid organ transplantation. *Pediatric Transplantation*, 2012. 16(7): p. 680-683.
43. Suresh S, Upton J, Green M, et al. Live vaccines after pediatric solid organ transplant: Proceedings of a consensus meeting, 2018. *Pediatric Transplantation*, 2019. 23(7): p. e13571.
44. Gill N, Sirizzotti N, Johnson D, et al. Endogenous glucocorticoid response to single-dose dexamethasone for croup in children: A pharmacodynamic study. *Pediatric Emergency Care*, 2020. 36(1): p. 50-56.
45. Gedalia A, Shetty AK. Chronic steroid and immunosuppressant therapy in children. *Pediatrics in Review*, 2004. 25(12): p. 425-34.
46. Mathias CB, McAleer JP, Szollosi DE. 2020. *Pharmacology of immunotherapeutic drugs* (ed.), Cham: Springer. URL: <https://link.springer.com/book/10.1007%2F978-3-030-19922-7> (accessed 3 July 2020)
47. Doganis D, Kafasi A, Dana H, et al. Immune response to influenza vaccination in children with cancer. *Human Vaccines & Immunotherapeutics*, 2018. 14(9): p. 2310-2317.
48. Vollaard A, Schreuder I, Slok-Raijmakers L, et al. Influenza vaccination in adult patients with solid tumours treated with chemotherapy. *European Journal of Cancer*, 2017. 76: p. 134-143.
49. Keam B, Kim MK, Choi Y, et al. Optimal timing of influenza vaccination during 3-week cytotoxic chemotherapy cycles. *Cancer*, 2017. 123(5): p. 841-848.
50. Pollyea DA, Brown JM, Horning SJ. Utility of influenza vaccination for oncology patients. *Journal of Clinical Oncology*, 2010. 28(14): p. 2481-90.
51. Belka C, Ottinger H, Kreuzfelder E, et al. Impact of localized radiotherapy on blood immune cells counts and function in humans. *Radiotherapy and Oncology*, 1999. 50(2): p. 199-204.
52. Conrad A, Alcazer V, Valour F, Ader F. Vaccination post-allogeneic hematopoietic stem cell transplantation: What is feasible? *Expert Review of Vaccines*, 2018. 17(4): p. 299-309.
53. Cordonnier C, Einarsdottir S, Cesaro S, et al. Vaccination of haemopoietic stem cell transplant recipients: guidelines of the 2017 European Conference on Infections in Leukaemia (ECIL 7). *The Lancet Infectious Diseases*, 2019. 19(6): p. e200-212.

54. Chong PP ,Avery RK. A comprehensive review of immunization practices in solid organ transplant and hematopoietic stem cell transplant recipients. *Clinical Therapeutics*, 2017. 39(8): p. 1581-1598.
55. Danziger-Isakov L, Kumar D ,The A. S. T. I. D. Community of Practice. Vaccination of solid organ transplant candidates and recipients: Guidelines from the American society of transplantation infectious diseases community of practice. *Clinical Transplantation*, 2019. 33(9): p. e13563.
56. Di Sabatino A, Carsetti R ,Corazza GR. Post-splenectomy and hyposplenic states. *The Lancet*, 2011. 378(9785): p. 86-97.
57. Aberg JA, Gallant JE, Ghanem KG, et al. Primary care guidelines for the management of persons infected with HIV: 2013 update by the HIV Medicine Association of the Infectious Diseases Society of America. *Clinical Infectious Diseases*, 2014. 58(1): p. e1-34.
58. Mathew R, Mason D ,Kennedy JS. Vaccination issues in patients with chronic kidney disease. *Expert Rev Vaccines*, 2014. 13(2): p. 285-98.
59. Neuhaus TJ. Immunization in children with chronic renal failure: a practical approach. *Pediatric Nephrology*, 2004. 19(12): p. 1334-9.
60. Park SJ ,Shin JI. Complications of nephrotic syndrome. *Korean Journal of Pediatrics*, 2011. 54(8): p. 322-8.
61. Lin SY, Liu JH, Lin CL, et al. A comparison of herpes zoster incidence across the spectrum of chronic kidney disease, dialysis and transplantation. *American Journal of Nephrology*, 2012. 36(1): p. 27-33.
62. Ministry of Health. 2019. *Guidelines for Tuberculosis Control in New Zealand, 2019* (ed.), Wellington: Ministry of Health. URL: <https://www.tewhatauora.govt.nz/publications/guidelines-for-tuberculosis-control-in-new-zealand-2019> (accessed 8 April 2024)
63. Institute of Environmental Science and Research (ESR). 2019 *Tuberculosis in New Zealand Annual Report 2016*. Porirua. URL: [https://surv.esr.cri.nz/PDF\\_surveillance/AnnTBReports/TBannualreport2016.pdf](https://surv.esr.cri.nz/PDF_surveillance/AnnTBReports/TBannualreport2016.pdf). (accessed 3 July 2020)

# 5 Coronavirus disease (COVID-19)

## Key information

Modes of transmission	Inhalation of respiratory droplets and aerosolised particles, deposits of respiratory droplets and particles on mucous membranes
Incubation period	Most commonly 2–5 days (range 1–14 days).
Period of communicability	Infectious period varies based on individual factors and variants. May be infectious 1-2 days prior to symptom onset. Asymptomatic spread is documented.
Incidence and burden of disease	Global pandemic ongoing. The burden of disease predominantly lies with older adults and those with comorbidities. Children generally experience milder disease.
Funded vaccines	mRNA-CV: Comirnaty (manufacturer Pfizer/BioNTech).
Dose, presentation, route (see sections 5.4.4 and 5.4.5)	<b>mRNA CV: Comirnaty</b> <u>Omicron XBB.1.5 mRNA-CV (30 µg)</u> <ul style="list-style-type: none"><li>• 0.3 mL dose</li><li>• no dilution required - multi-dose vial (dark grey cap) and single-dose vial (light grey cap)</li><li>• intramuscular injection</li><li>• storage once thawed:<ul style="list-style-type: none"><li>– unopened vial +2° to 8°C expiry 10 weeks</li><li>– multi-dose vial, punctured +2° to 30°C expiry 12 hours or drawn up +2° to 30°C expiry 6 hours</li><li>– single dose vial – use immediately after puncture</li></ul></li></ul>

*Continued overleaf*

Dose, presentation, route (continued)	<p><u>XBB.1.5 mRNA-CV (10 µg) – paediatric</u></p> <ul style="list-style-type: none"> <li>• 0.3 mL dose</li> <li>• no dilution required – single dose vial (light blue cap)</li> <li>• Intramuscular injection</li> <li>• Storage once thawed: <ul style="list-style-type: none"> <li>– unopened vial +2° to 8°C expiry 10 weeks</li> <li>– use immediately after puncture</li> </ul> </li> </ul> <p><u>XBB.1.5 mRNA-CV (3 µg)- paediatric</u></p> <ul style="list-style-type: none"> <li>• 0.2 mL (maroon cap)</li> <li>• dilution required – multidose vials (yellow or maroon cap)</li> <li>• Intramuscular injection</li> <li>• Storage once thawed: <ul style="list-style-type: none"> <li>– undiluted, +2° to 8°C expiry 10 weeks</li> <li>– diluted, in vial +2° to 8°C expiry 12 hours or drawn up +2° to 30°C expiry 6 hours</li> </ul> </li> </ul>
Funded vaccine indications and schedule (see section 5.5)	<p><u>XBB.1.5 mRNA-CV (30 µg)– for ages 12 years and over</u></p> <p><u>XBB.1.5 mRNA-CV (10 µg) – for ages 5 to 11 years</u></p> <ul style="list-style-type: none"> <li>• For anyone previously unvaccinated or have only partially completed a primary course – give one dose</li> <li>• For those with severe immunocompromise from age 5 years (see section 5.5.2) complete three primary doses, given at least 8 weeks apart</li> <li>• For those who are eligible age 5 years and over, an additional dose is given after at least 6 months, regardless of number of previous COVID-19 vaccine doses received since the primary course (see section 5.5.3 for eligibility and recommended groups)</li> </ul> <hr/> <p><u>XBB.1.5 mRNA-CV (3 µg) – for ages 6 months to 4 years</u></p> <ul style="list-style-type: none"> <li>• Three doses as a primary course – dose two is given at least 3 weeks after first, then dose three at least 8 weeks later</li> <li>• For use in infants and young children with severe immunocompromise or complex/multiple health conditions that increase their risk of severe COVID-19 (see section 5.5.2)</li> <li>• An additional dose can be given at least 6 months after any primary course.</li> </ul>
Contraindications (see section 5.6.1)	mRNA-CV: A history of anaphylaxis to any component or previous dose.
Precautions (see section 5.6.2)	<p>mRNA-CV: A definite history of anaphylaxis to any other product is a precaution not contraindication.</p> <p>Defer further doses if individual develops myocarditis/pericarditis after any dose of mRNA-CV or recombinant CV. Seek specialist immunisation advice regarding future COVID-19 vaccination doses.</p>
Potential responses to vaccine (see section 5.7.1)	<p>Generally mild or moderate: injection site pain, headache, fever, muscle aches, dizziness and nausea, a day or two after vaccination. These responses are more commonly reported after second dose and in younger adults (&lt;55 years). Responses to subsequent doses are generally similar or milder than after the second dose.</p>

*Continued overleaf*

Vaccine effectiveness  
(see section 5.4.3)

mRNA-CV (30 µg): Clinical trial data (original formulation in 2020) showed efficacy against confirmed symptomatic COVID-19 of 90–98% after two doses.  
mRNA-CV (10 µg): Clinical trial data showed efficacy against confirmed, symptomatic COVID-19 of 68–98% after two doses in children aged 5–11 years.  
mRNA-CV (3 µg): Clinical trial data showed combined efficacy against confirmed symptomatic COVID-19 of 80.4 percent (14.1–96.7 percent) for ages 6 months to 4 years.  
Effectiveness of these vaccines is maintained against severe disease with recommended additional doses but wanes for mild disease over a period of weeks after each dose.

Public health measures

For current information refer to [www.tewhatauora.govt.nz/for-the-health-sector/covid-19-information-for-health-professionals/](http://www.tewhatauora.govt.nz/for-the-health-sector/covid-19-information-for-health-professionals/)

## 5.1 Virology

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a member of the Coronaviridae family and the *Betacoronavirus* genus. This enveloped, positive-strand RNA virus encodes four major structural proteins – spike (S), membrane (M), envelope (E) and a helical nucleocapsid (N). To enter host cells, the spike protein, which forms the characteristic crown-like (Latin: *corona*) surface structures, binds to the angiotensin-converting enzyme-2 (ACE2) receptor most frequently found on human respiratory tract epithelium.<sup>1, 2</sup> SARS-CoV-2 was first detected in late 2019 in China and is thought to be a zoonotic disease of an unidentified origin.

As with most RNA viruses, mutations occur and variant strains of SARS-CoV-2 have been identified that have increased transmissibility, altered virulence, or have reduced the effectiveness of public health measures. WHO has classified genetic variants into three classes: variants of concern, variants of interest and variants under monitoring.<sup>3</sup> Emergence of new variants is monitored in New Zealand by ESR through whole genome sequencing of specimens taken from hospitalised cases and wastewater sampling. For more information on COVID-19 variants see the ESR wastewater surveillance at [esr.cri.nz/digital-library/wastewater-dashboard/](http://esr.cri.nz/digital-library/wastewater-dashboard/).

## 5.2 Clinical features

Coronavirus disease 2019 (COVID-19) is caused by the SARS-CoV-2 virus, which infects the respiratory tract and is transmitted human to human primarily through respiratory droplets and aerosols. Documented transmission has also occurred through direct contact and rarely fomites (objects or materials that can carry infection).

The symptoms of COVID-19 range widely from asymptomatic infection or from a mild to severe respiratory tract infection and pneumonia, which can lead to severe inflammatory disease and respiratory failure. The most common symptoms of COVID-19 are like those of other common respiratory illnesses and include a new or worsening dry cough, sneezing and rhinorrhoea or nasal congestion, fever, sore throat, shortness of breath and fatigue. Unlike other respiratory viral infections, COVID-19 is frequently associated with a temporary loss of smell or altered sense of

taste. Some cases have reported gastrointestinal symptoms including nausea, diarrhoea, vomiting and abdominal pain, headache, muscle aches, malaise, chest pain, joint pain, and confusion or irritability; these symptoms almost always occur with one or more of the common symptoms. For most cases COVID-19 is a mild disease, but some can develop more severe disease or exacerbation of comorbidities. As for influenza and other respiratory viruses, some of those with laboratory-confirmed infection remain asymptomatic.

In the early stages, it is difficult to distinguish COVID-19 symptoms from other common viral infections. The most reliable common diagnostic test has been detection of viral mRNA from a nasopharyngeal swab, using PCR assay and rapid antigen tests (RATs).

The incubation period is typically around two to five days (up to 14 days). Individuals may be infectious from up to two days before becoming symptomatic.<sup>4</sup> Unlike previous coronavirus outbreaks (SARS and MERS), transmission of SARS-CoV-2 can also occur before the onset of symptoms or from asymptomatic individuals.<sup>5</sup> Viral loads and infectiousness are highest immediately after symptom onset, and most transmission occurs in household settings.<sup>6, 7</sup>

It is currently unclear what level and duration of protection is provided by infection with SARS-CoV-2. Early in the pandemic, neutralising antibodies were shown to remain relatively stable between eight to 11 months after primary infection.<sup>8, 9</sup> Frequently, reinfection occurs due to exposure to different variants of SARS-CoV-2 that are better able to evade the immune response and when inadequately matched neutralising antibody immunity has waned. The risk of reinfection is less in recently vaccinated individuals, and hybrid immunity, from both infection and vaccine, reduces the risk of COVID-19 hospitalisation.<sup>10, 11</sup> The degree of protection is highly variable depending on individual risk for severe disease. To maintain effective neutralising antibody levels, additional COVID-19 vaccination with a variant-matched vaccine is recommended, particularly for high-risk groups.

## 5.2.1 Children and young adults

Overall, the incidence of severe or fatal disease in children is significantly lower than in adults, with fewer hospitalisations and shorter hospital stays. The incidence is less for the Omicron variants than the previous variants.<sup>12, 13</sup> Children at highest risk of more severe disease are predominantly those living with pre-existing significant health conditions and those living in areas with highest levels of deprivation.<sup>13</sup> Pre-existing conditions in children associated with increased risk from COVID-19 include obesity, diabetes, cardiac and pulmonary diseases, immune disorders, metabolic disease, cancer, neurological, neurodevelopmental (in particular, Down syndrome [trisomy 21]) and neuromuscular conditions.<sup>14, 15</sup> Although these risk factors are prevalent in New Zealand children, particularly for some Māori and Pacific children,<sup>16, 17</sup> during the first wave of sustained Omicron transmission in New Zealand, hospitalisations of predominantly COVID-19-naïve children were of short duration (0-2 days) with few intensive care admissions.<sup>18</sup>

### Paediatric multisystem inflammatory syndrome

Paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 (PIMS-TS or MIS-C) is a rare, delayed complication of COVID-19 following largely asymptomatic SARS-CoV-2 infection in children and adolescents.<sup>19, 20</sup> Surveillance in England has found that, despite the very high numbers of COVID-19 cases associated with the Omicron variants, the risk of PIMS-



TS is extremely low due to most children having immunity to SARS-CoV-2 through previous infection and vaccination.<sup>13</sup>

## 5.2.2 Risk groups

Risk factors for severe disease include older age, male, smoking,<sup>21</sup> obesity and chronic medical conditions, including diabetes,<sup>22</sup> cancer, chronic respiratory disease, cardiovascular disease, chronic kidney disease, hypertension, immunocompromise,<sup>23</sup> and pregnancy (see below). Increased incidence is well documented in some ethnic groups but seems primarily related to prevalence of the risk factors listed above. Increasing age is the most important risk factor for severe disease, due to declining immune function and high prevalence of comorbidities. The highest risk group for severe illness and mortality is those aged over 70 years,<sup>24</sup> although Māori and Pacific populations experience age-related risk at a younger age than other ethnicities.

### Pregnancy

Pregnancy can increase the risk of severe disease and death compared with age-matched non-pregnant women.<sup>25-28</sup> While the absolute risk of severe outcomes during pregnancy is low compared with absolute risk due to advanced age, adverse pregnancy and perinatal outcomes, including acute renal failure, acute respiratory distress, mechanical ventilation, ICU admission, and preterm labour with preterm delivery, occur at a higher rate in pregnant people with COVID-19 during delivery hospitalisations than those without.<sup>29</sup> A healthcare database review including almost three million pregnant people found that although the risk was considerably lower than during the Delta predominant period, those with Omicron infection during hospital delivery were five times more likely to die during delivery than those without COVID-19. During the Omicron period, the risk for all adverse outcomes was significantly higher at delivery for those with COVID-19 than those without, except for thromboembolic disease and acute cardiac events (comparison of 26,053 with Omicron and 1,270,490 without COVID-19).<sup>29</sup> Unvaccinated pregnant people are at four times the risk of hospitalisation with moderate to severe COVID-19 than those who had received three doses of vaccine.<sup>30</sup> One international study found that the risk for referral to ICU or death was over 20 times higher for unvaccinated pregnant women with Omicron COVID-19.<sup>31</sup> Obesity, hypertension, asthma, autoimmune disease, diabetes and older age are also associated with severe COVID-19 in pregnancy and postpartum.<sup>32</sup>

Infants born to those with COVID-19 are at increased risk of preterm birth, particularly due to maternal COVID-19 severity leading to early induction, and neonatal ICU admission.<sup>26, 32</sup> Early studies do not suggest intrauterine transmission, but transmission during birth has been shown in around 3 percent of neonates.<sup>33</sup> Most neonatal infections are asymptomatic or mild, but around 12 percent experience severe disease with dyspnoea and fever as the most commonly reported signs.<sup>34</sup>

## 5.2.3 Post-infection complications

Post-acute COVID-19 sequelae or commonly called 'long COVID' is characterised by persistent symptoms lasting for more than three months and appears to affect around 10 percent of those infected, particularly those with at least five symptoms in the first week of illness.<sup>35-37</sup> Post-acute



manifestations include cardiovascular, pulmonary and neurological effects, including chronic fatigue, dyspnoea, specific organ dysfunction and depression.<sup>38</sup>

Long COVID-19 is not well described in children, and although WHO formally agreed an international clinical case definition in February 2023, it was very broad.<sup>39</sup> In the UK in 2023, according to national statistics, the difference in prevalence of the most common persistent symptoms of long COVID-19 in children was 0.2 percent in 2-11 year olds and 1.0 percent in 12-16 year-olds between cases and controls.<sup>13</sup> Unfortunately, the broadly inclusive criteria for post-COVID-19 conditions fail to identify children who genuinely experience adverse complications of SARS-CoV-2 infection, such as chronic fatigue, respiratory compromise and cognitive difficulties.<sup>13</sup>

For further information see the HealthNZ website: [info.health.nz/conditions-treatments/infectious-diseases/covid-19/long-covid/](https://info.health.nz/conditions-treatments/infectious-diseases/covid-19/long-covid/)

## 5.3 Epidemiology

### 5.3.1 Global burden of disease

SARS-CoV-2 was first identified in January 2020 following clusters of distinctive pneumonia cases observed in Wuhan, China during December 2019. This virus has genetic and clinical similarity to the coronavirus causing the severe acute respiratory syndrome (SARS) epidemic from 2002 to 2004. A public health emergency of international concern (PHEIC) was announced in late January 2020. By the time the COVID-19 pandemic was declared by the World Health Organization (WHO) on 11 March 2020, there were 118,000 reported COVID-19 cases and 4,291 associated deaths in 114 countries. The global death toll surpassed one million by late September 2020. Case numbers and death continued to increase, with a rapid peak in cases at the end of December 2021 due to the more infectious omicron variant. As of 8 November 2022, WHO reported over 6.5 million cumulative COVID-19 deaths.

See the WHO Coronavirus Disease (COVID-19) Dashboard ([covid19.who.int](https://covid19.who.int)) for the latest official data. Actual rates are expected to be considerably higher than officially reported rates, especially since milder infections may not be reported.

The infection-fatality rate, while still high particularly in the older age groups, has reduced since the start of the pandemic, partly due to changes in the prevalent variants but also due to public health measures that include vaccination, improved clinical recognition and management and the use of therapies of demonstrated value, such as dexamethasone and antiviral medications such as nirmatrelvir with ritonavir.

The use of vaccines has reduced the global burden of COVID-19 significantly. The first phase I clinical trial for a COVID-19 vaccine commenced in March 2020 and the first public vaccination dose was administered in the United Kingdom on 8 December 2020. By late 2022, 11 COVID-19 vaccines had been granted emergency use listing or approval by the WHO.

In May 2023, the WHO declared an end to the PHEIC and moved forward to update its Strategic Preparedness and Response plan for 2023-2025 to transition from the emergency response to longer-term sustained COVID-19 protection, control and management.<sup>40</sup>

### 5.3.2 New Zealand epidemiology

The first case of COVID-19 was reported in New Zealand on 28 February 2020. Border restrictions were implemented on 16 March 2020 as cases numbers increased and clusters of transmission were identified. On 25 March 2020, New Zealand entered a nationwide lockdown ('Alert level four'). With rapid contact tracing and the public health COVID-19 protection framework, the spread of SARS-CoV-2 was restricted during 2020 and 2021. Only 19 percent of the introductions of virus in 2020 resulted in ongoing transmission or more than one additional case.<sup>41</sup> Prior to the outbreak of the Delta variant in August 2021, most of the reported cases during 2021 were imported from overseas (over 95 percent from 1 January to 9 August 2021).

From 16 August 2021, the number of cases in New Zealand began to increase sharply due initially to the highly infectious Delta variant. From January 2022, when the more infectious Omicron variant entered the community, case numbers rose sharply but at this stage around 90 percent of the population aged from 12 years had been vaccinated with at least two doses of COVID-19 vaccine. In late February 2023, almost three years after the first reported case, there were over 2.2 million cases recorded, over 26,000 hospitalisations, and 711 ICU admissions for COVID-19. There were 1,599 deaths coded with COVID-19 as the underlying cause, and the vast majority (96 percent) were aged over 59 years.

The COVID-19 Mortality Report published September 2022 found that although COVID-19-attributed mortality was highest in older age groups, based on age-adjusted estimates, the risk of mortality for those aged under 60 years was 3.7 times higher for those Māori and 3.9 times higher for those of Pacific ethnicities than of European and Other ethnicities.<sup>42</sup> Comorbidity in those under the age of 60 years significantly increased the risk of mortality by 78 times, and explained 59 percent of the increased risk for Māori and 69 percent for Pacific ethnicities. Vaccination was shown to have a strong protective effect: after adjusting for age, sex, comorbidities and vaccination status (>2 doses), mortality risk was lowered but still 1.7 times higher in Māori and 1.9 times higher for Pacific compared with European/Other ethnicities.<sup>42</sup>

Emergence of new variants is monitored in New Zealand by ESR through whole genome sequencing of specimens taken from hospitalised cases and wastewater sampling. For current details on case demographics see **Health New Zealand COVID-19 data and statistics** and for the mortality report see **[health.govt.nz/publications/covid-19-mortality-aotearoa-new-zealand-inequities-risk](https://health.govt.nz/publications/covid-19-mortality-aotearoa-new-zealand-inequities-risk)**.

## 5.4 Vaccines

### 5.4.1 Introduction

Clinical trials for COVID-19 vaccine candidates began shortly after the pandemic was announced in March 2020. Between October to December 2020, the New Zealand Government signed advanced purchase agreements for four vaccine candidates, with purchase dependent on approval for use from the New Zealand Medicines and Medical Devices Safety Authority (Medsafe). This is an ongoing process and, therefore, the availability and eligibility for these different vaccines may change.

Medsafe continues to review for each COVID-19 vaccine candidate, examining clinical trial and post-marketing surveillance data. Provisional consent imposes conditions on these vaccines to restrict their use by health professionals according to the available data at time of approval. This approval status allows New Zealanders early access to medicines with significant unmet clinical need under the Medicines Act.

### 5.4.2 Available vaccines

#### Funded vaccines

The mRNA-CV, Comirnaty, consists of messenger ribonucleic acid (mRNA) encoding the full-length spike glycoprotein of the SARS-CoV-2 virus, inside a lipid nanoparticle. The spike protein mRNA has an adjuvant effect, so no additional adjuvant is included. The original version was designated BNT162b2 in clinical trials conducted by Pfizer and BioNTech. This mRNA vaccine delivers the instructions for human cells to build the viral antigen, SARS-CoV-2 spike protein. The mRNA is temporarily protected from degradation by the lipid nanoparticle that also facilitates fusion with the recipient's cell wall.<sup>43, 44</sup>

#### **mRNA-CV – Comirnaty (Pfizer/BioNTech)**

*Omicron XBB.1.5 mRNA-CV (30 µg) – from age 12 years (grey caps)*

This Omicron XBB.1.5 formulation replaces the original (tozinameran) mRNA-CV (30µg) and bivalent (tozinameran/famtozinameran) mRNA-CV (15/15µg) formulations.

Each 0.3 mL dose of mRNA-CV contains:

- 30 µg of raxtozinameran, a single-stranded 5'-capped mRNA encoding pre-fusion stabilised SARS-CoV-2 full-length spike glycoprotein (Omicron XBB.1.5 variant) embedded in a lipid nanoparticle. The mRNA is produced using cell-free in vitro transcription from DNA templates.
- The lipid nanoparticle contains ALC-0315 ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)), ALC-0159 (2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide), distearoylphosphatidylcholine (DSPC) and cholesterol.
- Also contains Tris/sucrose buffer: tromethamine (also known as Tris), tromethamine hydrochloride, sucrose and water for injection.

*XBB.1.5 mRNA-CV (10 µg), for children aged 5 to 11 years (blue cap)*

This paediatric formulation replaces the original (tozinameran) mRNA-CV (10 µg) vaccine.

Each 0.3 mL dose contains:

- 10 µg of raxtozinameran (nucleoside modified mRNA encoding Omicron XBB.1.5 SARS-CoV-2 spike protein, as described for 30 µg formulation).
- Lipid nanoparticle – as above.
- Tris/sucrose buffer – as above.

*XBB.1.5 mRNA-CV (3 µg), for children aged 6 months to 4 years (maroon cap)*

This paediatric formulation replaces the original (tozinameran) mRNA-CV (3 µg) vaccine.

Each 0.2 mL (maroon) dose contains:

- 3 µg of raxtozinameran (nucleoside modified mRNA encoding Omicron XBB.1.5 SARS-CoV-2 spike protein, as described for 30 µg formulation)
- Lipid nanoparticle – as above.
- Tris/sucrose buffer – as above.

## History of approved vaccines

On 3 February 2021, the first COVID-19 vaccine to receive provisional consent approval in New Zealand was Comirnaty (abbreviation mRNA-CV, manufactured by Pfizer/BioNTech). It contained 30 µg of a modified mRNA expressing the original SARS-CoV-2 spike protein (designated tozinameran). mRNA-CV (30µg) vaccine was widely used for the COVID-19 vaccination programme from February 2021 to February 2023, for primary and early booster vaccinations of those aged 12 years and over.

A paediatric formulation of mRNA-CV (10 µg) was introduced from January 2022 for a primary course in children aged 5-11 years. Then in February 2023, mRNA-CV (3 µg) became available for children aged 6 months – 4 years with complex health conditions or severe immunocompromise.

Medsafe approved bivalent mRNA-CV (15/15 µg) on 21 December 2022 as an additional dose. This vaccine contained modified mRNA expressing the original spike protein (tozinameran) and the Omicron BA.4-5 variant spike protein (famtozinameran). At the same time, to match the paediatric vaccines, mRNA-CV vaccines changed to a more stable Tris-sucrose buffer formulation. The bivalent mRNA-CV (15/15 µg) was used for additional doses and the monovalent mRNA-CV (30µg) was used for the primary course from 1 March 2023 to March 2024. In January 2024, Medsafe approved the use of an XBB.1.5 mRNA-CV (30 µg) vaccine containing Omicron XBB.1.5 mRNA (raxtozinameran). The original monovalent and bivalent versions of mRNA-CV were replaced by Omicron XBB.1.5 mRNA-CV (30 µg) in April 2024 and the Omicron XBB.1.5 paediatric formulations (10 µg and 3 µg) in June 2024.

Other vaccines were granted provisional approval and used in the COVID-19 immunisation programme. In July 2021, two adenoviral vector COVID-19 vaccines were provisionally approved

for use: Vaxzevria (manufactured by AstraZeneca, ChAd-CV) was offered as an alternative to mRNA-CV from November 2021 to September 2022; COVID-19 Vaccine Janssen (Ad26-CV) was not used in the programme. Provisionally approved for use in February 2022, an adjuvanted recombinant spike protein subunit COVID-19 vaccine (rCV; trade name Nuvaxovid) replaced Vaxzevria as an alternative to mRNA-CV. It was sponsored in New Zealand by Biocelect on behalf of the manufacturer Novavax. In July 2024, Novavax withdrew its application for the approval an XBB.1.5 version of Nuvaxovid, leaving Comirnaty (Pfizer/BioNTech) as the only COVID-19 vaccine offered in New Zealand.

See [medsafe.govt.nz/COVID-19/status-of-applications](https://medsafe.govt.nz/COVID-19/status-of-applications) for Medsafe approval status of COVID-19 vaccines.

### 5.4.3 Efficacy and effectiveness

This section of the COVID-19 chapter reflects the development of the COVID-19 vaccines and the changing behaviour and variants of the SARS-CoV-2 infection during the COVID-19 pandemic. Further data is emerging. There is much heterogeneity in the immunity of different populations, many people have hybrid immunity to the wild-type infection as well as a range of booster doses, which make effectiveness measures challenging. Overall, COVID-19 vaccines continue to perform very well against severe disease and mortality, and in the short term can help to prevent symptomatic illness and infection.

#### mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

##### Immunogenicity

Compared with convalescent sera from those who had SARS-CoV-2 infection (original variant), the only group with lower antibody responses were older people (aged 55 – 85 years) but they had higher average neutralising antibody levels.<sup>45</sup> Clinical studies continued to assess immunogenicity in each age group in which the vaccines were used.<sup>46-48</sup> As SARS-CoV-2 variants evolved to become more immune evasive, higher levels of neutralising antibody were required to prevent infection. This was particularly evident in older people and those with comorbidities that affected the immune response. This was circumvented by offering booster doses and adapting the vaccine to better match circulating variants (ie bivalent and XBB.1.5 vaccines).

##### Efficacy – clinical trial data

Early in the pandemic, efficacy studies were straightforward as most individuals were naïve of SARS-CoV-2 vaccine. Efficacy of mRNA-CV 30 µg (BNT162b2) was first assessed during 2020 in the phase III component of a large, clinical trial. A total of 43,448 participants aged 16–85 years across six countries were randomised to receive vaccine or saline placebo, with a primary series of two doses given 21 days apart.<sup>49</sup> Interim data, based on the early SARS-CoV-2 variants, indicated a very high efficacy against symptomatic PCR-confirmed COVID-19 of 94.8 percent (95% CI: 89.8–97.6 percent) and consistent across all subgroups (defined by age, sex, race, ethnicity, baseline BMI and presence of co-existing conditions).<sup>49</sup> Efficacy in younger age groups was also high. For adolescents aged 12–15 years vaccinated with two doses of mRNA-CV (30 µg) efficacy of 100 percent (95% CI 75.3–100) was observed against symptomatic COVID-19 in 2020/2021.<sup>46</sup> A lower



dose vaccine, mRNA-CV (10 µg) showed efficacy of 90.7 percent (95% CI 67.7–98.3) against symptomatic COVID-19 from seven days after dose two in 1,305 children aged 5–11 years.<sup>47</sup> Due to few cases in young children aged under 5 years, efficacy of mRNA-CV (3µg) was less well established. Combined for children aged 6–23 months and 2–4 years, vaccine efficacy of 80.4 percent (14.1–96.7 percent) was reported during a period of Omicron prevalence in the US.<sup>48, 50</sup>

As the pandemic progressed, more hybrid immunity (with infection and vaccination) developed making placebo-controlled efficacy trials obsolete.

### Effectiveness of primary course – real-world experience

At the start of the COVID-19 immunisation programmes in late 2020/early 2021, mRNA-CV (30 µg) was highly effective at preventing severe COVID-19 and COVID-19-related death, in line with efficacy observed during clinical trials.<sup>51</sup>

As the Delta variant emerged from mid-2021, effectiveness against symptomatic COVID-19 reduced (ranging from around 78–93 percent),<sup>52</sup> but the vaccine remained highly effective against hospitalisation (73–94 percent), severe disease and death (80–97 percent) in a range of groups in the UK.<sup>53</sup> With time following the two-dose primary series, the waning antibody levels were less effective against the Omicron variant and booster doses were required to help prevent symptomatic infection and reinfection (see below).

Vaccination with mRNA-CV in pregnancy reduces the risk of severe COVID-19 and provides passive immunity to the infant for the first few months of life.<sup>54–56</sup> During Delta, systematic review showed 70 percent reduction in SARS-CoV-2 infection in infants of vaccinated mothers for up to 6 months; vaccine effectiveness was much lower for omicron variants and the numbers of infants infected were very low.<sup>57–59</sup>

### Duration of immunity and additional doses

A decline in vaccine effectiveness was observed after the primary course against SARS-CoV-2 infection and mild disease, particularly with emerging Omicron variants, but protection against severe disease has been maintained and enhanced with the use of additional doses for around 6–9 months, at least.<sup>60,61</sup> It is unclear how long-lived immunity is following immunisation or natural infection. Many people now have hybrid immunity from both vaccination and infection.

Although neutralising antibody levels wane,<sup>62</sup> and lower levels are less effective against the emerging variants such as Omicron lineages, T cell responses and memory are maintained in vaccine recipients (for mRNA-CV and rCV),<sup>63, 64</sup> and this is likely to correspond to the observed the rate of disease being reduced. The greatest waning in immunity is observed in those aged over 65 years and those aged 40–64 years with underlying medical conditions compared with healthy adults.<sup>65</sup>

Across all age groups, at least three exposures to SARS-CoV-2 spike protein through vaccination and infection (hybrid immunity), provide significant protection against Omicron-associated hospitalisation and death. Further doses help to maintain a high level of immunity in elderly adults, particularly if they have exposed through infection previous. A Canadian cohort study of people with previous exposure to Omicron (BA.1 and BA.2 predominance) estimated protection

at one to two months post vaccination to be 96 percent (95% CI 92-98) after a fourth dose of vaccine.<sup>66</sup>

Booster dose programmes were accelerated following the emergence of the Omicron variant from late 2021, including in New Zealand. Variant specific vaccines, including Omicron variant vaccines (eg BA.4/5 and XBB.1.5), are being used as additional doses to enhance protection against more immune-evasive omicron variants.<sup>64, 67</sup>

### mRNA COVID-19 vaccine – additional doses

A range of cohort studies in the US has demonstrated a relative improvement in effectiveness of booster doses against severe COVID-19, especially for previously well-vaccinated older adults, when bivalent mRNA-CV was given.<sup>68-70</sup> Due to varying exposures to SARS-CoV-2 variants, timing since vaccine doses and in different populations, comparison between these studies is not possible and they did not provide evidence comparing monovalent original vaccine with the bivalent one.

Data from the Netherlands during October 2023 to January 2024 estimated effectiveness of the XBB.1.5 mRNA-CV (30 µg) vaccine to be around 41 percent against Omicron infection for those aged 18-59 years and 50 percent for ages 60-85 years who had received at least one previous booster.<sup>71</sup> Earlier data, from October 2023 to December 2023 in the Netherlands, found XBB.1.5 mRNA-CV (30 µg) vaccine to be around 70 percent effective against hospitalisation and ICU admission (95% CI 67-74 percent and 42-88 percent, respectively) within the first two months of vaccination in adults aged 60 years and over.<sup>72</sup> In the US, the overall VE against symptomatic infection was 58 percent (48-65 percent) up to 59 days after vaccination and 49 percent (36-58 percent from 60-119 days after vaccination).<sup>73</sup> Since the XBB.1.5 vaccine formulations were created, Omicron variants have evolved but the vaccines are still demonstrating effectiveness against symptomatic disease and inducing a good neutralising antibody response against these newer variants, including BA.2.86 and JN.1.<sup>73, 74</sup>

## 5.4.4 Transport, storage and handling

### mRNA COVID-19 vaccines – Comirnaty (3 µg, 10 µg and 30 µg)

These vaccines require storage at ultra-low temperatures (-90°C to -60°C) and at this temperature has a shelf-life of 18 months. Store unopened vials at +2°C to 8°C for up to 10 weeks within the 18 months shelf-life. Do not freeze.

Transport according to the National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2<sup>nd</sup> edition) [www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)

It is recommended that each vaccine is prepared as needed, always stored in the fridge and, where practical, doses are drawn up as required.

For single dose vials, store at +2°C to 8°C.



Store punctured multi-dose vials at +2°C to 30°C for a maximum of 12 hours, or store vaccine drawn-up in syringe for a maximum of six hours at +2°C to 30°C. Discard any vaccine exceeding these times, accordingly. For further details, see also the IMAC COVID-19 information and factsheets available from [immune.org.nz](https://www.immune.org.nz).

**For those that require dilution prior to use (see Table 5.1):** once an undiluted vial is taken out of the refrigerator, allow a few minutes for the vaccine to reach room temperature prior to dilution. Store diluted vaccine in vials at +2°C to 8°C for a maximum of 12 hours, or store vaccine drawn-up in syringe for a maximum of six hours at +2°C to 30°C. Discard any vaccine exceeding these times, accordingly.

## 5.4.5 Dosage and administration

### mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

**Table 5.1 Summary of preparation and dosages for mRNA-CV (Comirnaty) formulations**

Description	XBB.1.5 mRNA-CV (30 µg)	XBB.1.5 mRNA-CV (10 µg)	XBB.1.5 mRNA-CV (3 µg) <sup>a</sup>
Vial cap colour:			
multidose vial	<b>Dark grey</b>	-	<b>Maroon</b>
single dose vial	<b>Light grey</b>	<b>Light blue</b>	-
Age range	12 years and over	5 to 11 years	6 months – 4 years <sup>a</sup>
Active ingredient (nucleoside modified mRNA)	raxtozinameran (Omicron XBB.1.5)	raxtozinameran	raxtozinameran
mRNA/per dose	30 µg	10 µg	3 µg
Buffer	Tris/sucrose	Tris/sucrose	Tris/sucrose
Unopened vial volume:			
multidose vial	2.25 mL	-	0.2 mL
single dose vial	0.3 mL	0.48 mL	-
Dilution require (volume of NaCl to add)	No	No	Yes (2.2 mL)
Volume per dose	0.3 mL	0.3 mL	0.2 mL
Doses per multidose vial	6	-	10
Primary course doses	1	1	3

- a. Only available for certain infants and children at increased risk of severe COVID-19 (see the Starship guidelines for children with complex or multiple health conditions at increased risk of severe COVID-19 ([starship.org.nz/guidelines/covid-19-disease-in-children](https://www.starship.org.nz/guidelines/covid-19-disease-in-children))).

#### XBB.1.5 mRNA-CV (30 µg) for ages from 12 years

Each dose of mRNA-CV (30 µg) is 0.3 mL to be administered intramuscularly.

**One dose** is given to individuals aged 12 years or older who have not received any previous COVID-19 vaccination. According to eligibility, additional doses are given six months after the first. This interval can be reduced to a minimum three months in certain circumstances. For additional dose eligibility see section 5.5.3.

Each single dose vial (with light grey cap) contains 0.3 mL of vaccine to supply a single 0.3 mL dose.

Each multi-dose vial (with dark grey cap) contains 2.25 ml of vaccine to supply six doses of 0.3 mL. If the amount of vaccine remaining in the vial cannot provide a full 0.3 mL dose, discard the vial and any excess volume. Do not pool excess vaccine from multiple vials.

An observation period following vaccination of at least 15 minutes is recommended (see section 5.6.2). This is to ensure that any anaphylactic-type reactions can receive prompt treatment.

This vaccine is latex-free. The vial stopper is made with synthetic rubber (bromobutyl), not natural rubber latex.

### XBB.1.5 mRNA-CV (10 µg) for ages 5 to 11 years

Each 0.3 ml dose mRNA-CV (10 µg) is to be administered intramuscularly. One dose is given to individuals aged 5 to <12 years.

Each single dose vial (with light blue cap) contains 0.48 mL of vaccine to supply a single 0.3 mL dose.

### XBB.1.5 mRNA-CV (3 µg) for ages 6 months – 4 years

Each **0.2 ml dose** of mRNA-CV (3 µg) is to be administered intramuscularly. **Three doses** are given to individuals aged 6 months to under 5 years. It is recommended to administer dose two at least three weeks after dose one followed by dose three at least eight weeks after dose two.

Each multidose vial (with a maroon cap) contains 0.4 ml of vaccine and **should be diluted with 2.2 ml** of 0.9 percent NaCl. Once reconstituted, each reconstituted vial will supply ten doses of 0.2 mL. If the amount of vaccine remaining in the vial cannot provide a full 0.2 mL dose, discard the vial and any excess volume. Do not pool excess vaccine from multiple vials.

An observation period following vaccination of at least 15 minutes is recommended (see section 5.6.2). This is to ensure that any anaphylactic-type reactions can receive prompt treatment.

This vaccine is latex-free. The vial stopper is made with synthetic rubber (bromobutyl), not natural rubber latex.

### Preparing mRNA-CV multi-dose vial

Note that the process for drawing up mRNA-CV differs from the recommendations for other multi-dose vial vaccines as described in section A7.2 in Appendix 7. To follow international guidance around the use of low dead space needles, the needle used to draw up mRNA-CV is also used to administer the injection. Unless you plan to administer the vaccine dose

immediately, carefully replace the needle guard and place labelled syringe onto a ridged tray for storage, for example, if all available doses are prepared at one go in a mass vaccination setting.

For detailed instructions for mRNA-CV multi-dose vial preparation and administration see the most current IMAC Comirnaty factsheets available from [immune.org.nz](https://www.immune.org.nz).

## Coadministration with other vaccines

There are no anticipated safety concerns regarding coadministration any of the currently available COVID-19 vaccines with other vaccines. These vaccines can be administered at any time before, after or simultaneously (in separate syringes, at separate sites) with other Schedule vaccines including PCV13, DTaP-IPV-HepB/Hib, DTaP-IPV, MMR, VV, influenza, HPV, Tdap and meningococcal vaccines.

For children aged 6 months – 4 years, it is recommended to give mRNA-CV (3 µg) in a different limb to MenB or MenACWY due to each vaccine's reactogenicity. If feasible, spacing of at least three days is suggested. This is less important if antipyretic prophylaxis (eg paracetamol) is given as recommended to those aged under 2 years with MenB (see section Usual childhood schedule 13.5.1).

TST/Mantoux testing for tuberculosis can also be conducted at any time before, after or simultaneously with mRNA-CV.

## 5.5 Recommended immunisation schedule

The COVID-19 vaccines were initially only available according to a prioritisation schedule for defined groups, however, since January 2022, all individuals in New Zealand aged from 5 years are eligible to be vaccinated with a primary course. Vaccination was also introduced for certain high-risk infants aged from 6 months to 4 years, inclusively, in February 2023. See Table 5.2 and Table 5.3 for the recommended schedules.

For up-to-date details around vaccine policy statements and further clinical guidance for the COVID-19 Vaccine Immunisation Programme refer to [www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/about-immunisation-in-new-zealand/immunisation-policy-statements](https://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/about-immunisation-in-new-zealand/immunisation-policy-statements).

**Table 5.2: Recommended schedule for COVID-19 vaccination for healthy individuals, from March 2024**

	<b>Age<sup>a</sup></b>	<b>No prior vaccination</b>	<b>Previously vaccinated (with at least a partially or completed primary course)</b>
		<b>Primary dose(s)</b>	<b>Additional doses (for new variants)</b>
<b>Healthy population</b>			
	6 months – 4 years	-	-
	5–11 years	One dose	- b
	12–15 years	One dose	- b
	16–29 years		<b>One</b> dose, give from 6 months after a first dose(s) <sup>c</sup> (or disease, see below)
	From 30 years		Given at least 6 months after any previous dose (or disease, see below)
Frontline health care, age care or disability workers	16 years – 29 years	One dose	<b>One</b> dose, given at least 6 months after first dose(s) <sup>c</sup> (or disease, see below)
	from 30 years		Given at least 6 months after any previous dose (or disease, see below)
<b>Any group following SARS-CoV-2 infection</b>			
<b>Following SARS-CoV-2 infection</b>	Any age, from 5 years	Complete vaccination course as recommended (see sections 5.5.3 and 5.5.4).	
		If previously unvaccinated, give one dose 6 months after recovery from acute illness or positive SARS-CoV-2 test if asymptomatic.	For additional doses, as appropriate, defer next dose for at least 6 months after recovery from acute illness or positive SARS-CoV-2 test if asymptomatic,

- a. mRNA-CV can be given from age 5 years.
- b. If have only partially completed a primary course of any COVID-19 vaccine and have received no additional doses, can give one dose of XBB.1.5 mRNA-CV (as age appropriate).
- c. Including for individuals who had a two-dose primary course with original mRNA-CV.

**Table 5.3 Recommended schedule for COVID-19 vaccination for individuals at higher risk from COVID-19, from March 2024**

Age <sup>a</sup>	No prior vaccination Primary dose (s)	Previously vaccinated (with at least a partial or completed primary course) Additional doses (for new variants) <sup>b</sup>	
<b>Severely immune compromised <sup>c</sup></b>			
6 months to 4 years <sup>c</sup>	Three doses, give first two doses 3 weeks apart and third dose 8 weeks <sup>e</sup> after dose two.	<b>One</b> dose given 6 <sup>f</sup> months after previous dose or disease (see below)	
5–11 years <sup>c,d</sup>	Give three doses, 8 weeks apart <sup>e</sup>	<b>One</b> dose given 6 <sup>f</sup> months after previous dose (or disease, see below)	
From 12 years <sup>c,d</sup>	Give three doses, 8 weeks apart <sup>e</sup>	From 6 <sup>f</sup> months after any previous dose (or disease, see below)	
<b>Additional groups at increased risk of severe COVID-19<sup>h</sup></b>			
6 months to 4 years <sup>c</sup>	Three doses, given first two doses 3 weeks apart and third dose 8 weeks <sup>e</sup> after dose two.	<b>One</b> dose given 6 <sup>f</sup> months after previous dose (or disease, see below)	
5–11 years <sup>c</sup>	One dose	<b>One</b> dose from 6 <sup>f</sup> months after any previous dose (or disease, see below)	
from 12 years <sup>c,g</sup>	One dose	From 6 <sup>f</sup> months after any previous dose (or disease, see below)	
<b>Other risk groups</b>			
Older adults	from 65 years	One dose give from 6 months after any previous dose (or disease, see below)	
Māori or Pacific People	from 50 years		
Resident of age or disability care facility	from 16 years		
Pregnant people	See below <sup>h</sup>	One dose, at any stage of pregnancy	give from 6 months after any previous dose (or disease, see below)
<b>Any group following SARS-CoV-2 infection</b>			
<b>Following SARS-CoV-2 infection</b>	Any age, from 6 months	Complete vaccination course as recommended (see sections 5.5.2 and 5.5.4).  If previously unvaccinated, give first dose(s) 6 months <sup>f</sup> after recovery from acute illness or positive SARS-CoV-2 test if asymptomatic.	For additional doses, as appropriate, defer next dose for 6 months <sup>f</sup> after recovery from acute illness or positive SARS-CoV-2 test if asymptomatic.

- mRNA-CV can be given from age 5 years and mRNA-CV (3µg) is available for certain children aged from 6 months – 4 years.
- Including for individuals who had a two-dose primary course with original mRNA-CV.
- See Starship guidelines for children with complex or multiple health conditions at increased risk of severe COVID-19 ([starship.org.nz/guidelines/covid-19-disease-in-children](https://starship.org.nz/guidelines/covid-19-disease-in-children)).
- Certain individuals with severe immunosuppressive conditions or treatments are eligible for three primary doses and additional doses). See section 5.5.2.
- The timing of the second and third doses also needs to consider current or planned immunosuppressive therapies. If the period of least immunosuppression is less than eight weeks, the third vaccination can be given any time from three weeks after dose two. See section 5.5.2.
- This spacing can be reduced to at least three months, on a case-by-case basis, where there is a clinical need. Preferred spacing is at least 6 months between additional doses or COVID-19 infection.

- g. Including those with medical condition or living with disability with significant or complex health needs. See section 5.5.3 for groups, including those eligible for funded influenza vaccine recommended additional dose due to increased risk of severe breakthrough COVID-19.
- h. One dose is recommended for any pregnant person who is unvaccinated. An additional dose is recommended to be given in pregnancy for those who were previously vaccinated, particularly for those with comorbidities that increase risk for severe COVID-19. See section 5.5.5.

## 5.5.1 mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

### XBB.1.5 mRNA-CV (30 µg) for ages from 12 years (grey caps)

Individuals from the age of 12 years who have not previously received any doses of COVID-19 vaccine are recommended to receive a single dose of mRNA-CV (30 µg). For additional primary doses for severely immunocompromised, see section 5.5.2.

All individuals aged from 16 years can be offered a single dose after receiving a primary dose(s) of any COVID-19 vaccine, at least three months later. See section 5.5.3 for additional dose recommendations.

*Individuals who have started but not completed a primary course.*

Individuals aged 12 years and over who have started but not completed a primary course of any COVID-19 vaccine, including original mRNA-CV (30 µg), and have received no additional doses can be offered a dose of XBB.1.5 mRNA-CV (30 µg), given from six months after the first dose

### XBB.1.5 mRNA-CV (10 µg) for ages 5 to 11 years (blue cap)

Individuals from the age of 5 years who have not previously received any doses of COVID-19 vaccine can have a single dose of mRNA-CV (10 µg) and, if eligible, a further dose given at least three months later. See section 5.5.2 for primary course recommendations for those who are severely immunocompromised. For additional doses see section 5.5.3.

Individuals aged 5 years to 11 years who have started but not completed a primary course of any COVID-19 vaccine, including original mRNA-CV (10 µg), and have received no additional doses can be offered a dose of XBB.1.5 mRNA-CV (10 µg), given from six months after the first dose.

For children who are severely immunocompromised and eligible for three primary doses (as described in section 5.5.2), who turn 12 years after their first or second dose, continue with the same dose of paediatric vaccine (ie, mRNA-CV (10 µg)) for subsequent doses, if it is less than three months since previous dose. If it is longer than 3 months, give age-appropriate vaccine (ie, mRNA-CV (30µg)). Give an additional dose mRNA-CV (30µg) 6 months later.



## XBB.1.5 mRNA-CV (3 µg) for ages 6 months to 4 years (maroon)

A paediatric formulation, mRNA-CV (3µg), is available for use for certain children aged 6 months to 4 years in New Zealand. **Three doses** are given for the primary series individuals aged 6 months to under 5 years. Dose two is administered at least three weeks after dose one followed by dose three at least eight weeks after dose two.

The use of this vaccine is limited to young children who are at highest risk of severe disease if they were to catch COVID-19 such as those with severe immunocompromise (see section 5.5.2) or with complex and/or multiple health conditions (see the [starship.org.nz/guidelines/covid-19-disease-in-children/](https://starship.org.nz/guidelines/covid-19-disease-in-children/)).

Children who started the primary course with the original (tozinameran) mRNA-CV (3 µg) vaccine can complete the three-dose series with XBB.1.5 mRNA-CV (3 µg).

Children who start their primary course aged under 5 years need three doses even if they turn 5 years part way through the course. For children who turn 5 years after their first or second dose, continue with the same dose of paediatric vaccine (ie, mRNA-CV (3 µg)) for subsequent primary doses, if it is less than three months since previous dose: dose two is given at least three weeks after first dose and dose three is given at least 8 weeks after previous dose. If it is longer than 3 months between their primary doses, give an age-appropriate vaccine (ie. mRNA-CV (10µg)).

## 5.5.2 Individual with immunodeficiencies or receiving immunosuppressive agents

There are no safety concerns around administering mRNA-CV to individuals who are immunocompromised and/or receiving immunosuppressive agents. As with other non-live vaccines, the antibody response to these vaccines may be reduced and protection may be suboptimal but, it is likely to be adequate to protect against severe disease. It is recommended to discuss the optimal timing for vaccination with a specialist before the vaccine appointment for those who are severely immunocompromised. Ideally, vaccination should be conducted prior to any planned immunosuppression (see section 4.3.6).

It is important that all household members and other close contacts of immunocompromised individuals aged from 5 years are up to date with immunisations. Household members and other close contacts aged from 16 years can also receive an additional dose at least six months after any previous doses or SARS-CoV-2 infection. For additional doses, see section 5.5.3.

### Individuals who are severely immunocompromised

#### Severely immunocompromised individuals aged 5 years and over.

Three primary doses of mRNA-CV (10 µg or 30 µg, as age-appropriate) are indicated for certain individuals aged from 5 years who are severely immunocompromised who are likely to have not responded adequately to the first doses (for children younger than 5 years, see note below). Serology is not recommended. A second and third primary dose is distinct from a booster or additional doses (for additional doses see section 5.5.3).



Preferably, a second dose is given eight weeks after dose one, and a third dose given a further at least eight weeks after the second dose. However, the timing also needs to consider current or planned immunosuppressive therapies. Consider vaccination during a treatment 'holiday' or at a nadir of immunosuppression between doses of treatment. If the period of least immunosuppression is less than eight weeks, vaccine doses can be given any time from three weeks apart.

For children who turn 12 years after their first or second dose, continue with the same dose of paediatric vaccine (ie, mRNA-CV (10 µg)) for subsequent doses, if it is less than three months since the previous dose. If the spacing is greater than 3 months, complete the primary course with an age-appropriate vaccine (ie mRNA-CV (30 µg)). Give an additional dose mRNA-CV (30µg) 6 months later.

If a significant adverse reaction to mRNA-CV has occurred, it is recommended to seek advice from IMAC to determine whether further doses are contraindicated.

### Children aged 6 months to 4 years with severely immunocompromise or complex or multiple health conditions.

Note: For children aged 6 months to 4 years, three doses of mRNA-CV (3 µg) is available for those who are severely immunocompromised, including those given in Table 5.4, and for those who have complex or multiple health conditions that increase their risk from COVID-19 (see the [starship.org.nz/guidelines/covid-19-disease-in-children/](https://starship.org.nz/guidelines/covid-19-disease-in-children/)), such as:

- chronic lung disease including bronchiectasis, cystic fibrosis, BiPAP for obstructive sleep apnoea (not asthma)
- complex congenital heart disease, acquired heart disease or congestive heart failure
- diabetes (insulin-dependent)
- chronic kidney disease (GFR <15 ml/min/1.73m<sup>2</sup>)
- severe cerebral palsy (or severe neurodisability including neuromuscular disorders)
- complex genetic, liver, metabolic disease or multiple congenital anomalies, including trisomy 21/Down Syndrome
- primary or acquired immunodeficiency, including HIV infection
- haematological malignancy and/or post-transplant (solid organ or HSCT in last 24 months)
- on immunosuppressive treatment including chemotherapy, high-dose corticosteroids, biologic agents or DMARDS.

### Examples of severe immunocompromising conditions recommended three primary doses

Table 5.4 provides guidance on types of immunocompromise for which three primary doses are recommended for those aged from 5 years, and for children aged 6 months to 4 years with immunocompromise eligible for mRNA-CV (3 µg). For further information on corticosteroid

indicative dosages and examples of non-corticosteroid agents considered immunosuppressive, see section below.

**Table 5.4: Individuals with severe immunocompromise aged 6 months or older recommended to receive three primary doses of mRNA-CV (3 µg, 10 µg or 30 µg, as age-appropriate).**

This list is not exhaustive but provides guidance on scenarios where three primary doses are recommended. There is variation between individuals in response to immunosuppressive or immunomodulating therapy. Clinicians may use their judgement for conditions or medications that are not listed here that are associated with severe immunocompromise.

Eligible group / indication	Treatments or health status
<b>Individuals with primary or acquired immunodeficiency states at the time of vaccination</b>	
Acute and chronic leukaemia and clinically aggressive lymphomas (including Hodgkin's Lymphoma)	under treatment, or within 12 months of achieving cure or remission
Chronic lymphoproliferative disorders, including haematological malignancies <sup>a</sup> and plasma cells dyscrasias	under specialist follow up
Active HIV infection / AIDS	current CD4 count <200 cells/µl
Primary or acquired cellular and combined immune deficiencies	lymphopenia (<1,000 lymphocytes/µl) or functional lymphocyte disorder.
Allogenic or autologous haematopoietic stem cell transplant	received in previous 24 months or received >24 months ago but had ongoing immunosuppression or graft-versus-host disease.
Persistent agammaglobulinaemia due to primary immunodeficiency and secondary to disease/therapy	IgG <3 g/L
<b>Individuals on, or recently on, immunosuppressive therapy at the time of vaccination</b>	
Following a solid organ transplant	receiving therapy
B cell depleting biologic therapy, including rituximab	receiving or received therapy in the previous 6 months
Biologics or targeted therapy <sup>b</sup> for autoimmune or autoinflammatory disease	received within the previous 3 months
Immunosuppressive cytotoxic chemotherapy or immunosuppressive radiotherapy for any indication	received within the previous 6 months

*Continued overleaf*

Eligible group / indication	Treatments or health status
<b>Individuals with chronic immune-mediated inflammatory disease who were receiving or had received immunosuppressive therapy prior to vaccination</b>	
High-dose or long-term moderate dose corticosteroids (for indicative dosages, see below)	for more than a week in the month before vaccination
For select immunosuppressant drugs <sup>b,c</sup>	in previous 3 months
Certain combination therapies at where cumulative effect is severely immunosuppressive, as determined by clinical judgment	in previous 3 months
<b>Individuals receiving long term haemodialysis or peritoneal dialysis</b>	
<p>a. Such as indolent lymphoma, chronic lymphoid leukaemia, myeloma, Waldenstrom’s macroglobulinemia and other plasma cell dyscrasias. <b>Note</b> this list is not exhaustive but provides an indication of conditions where an individual is recommended to receive a third primary dose.</p> <p>b. For examples, see Table 5.5</p> <p>c. Excluding hydroxychloroquine, sulfasalazine, or mesalazine, when used as monotherapy.</p>	

## Individuals receiving corticosteroids

A three primary doses of mRNA-CV is recommended for individuals with chronic immune-mediated inflammatory disease who are receiving or have received high dose or long-term moderate doses of corticosteroids prior to vaccination, for example:

- high dose – equivalent to at least 20 mg prednisolone per day for more than ten days, in previous month
- moderate dose – equivalent to at least 10 mg prednisolone per day for more than four weeks, in previous three months
- also includes for those who received high dose corticosteroids for any reason – equivalent to at least 40 mg per day for more than a week, in the previous month.

Individuals for whom three primary doses **are not** routinely recommended include those who require:

- brief corticosteroid therapy, for example for asthma, chronic obstructive pulmonary disease or COVID-19 – equivalent to 40 mg or less prednisolone per day
- low locally acting corticosteroids, inhaled or topical
- replacement corticosteroid treatment for adrenal insufficiency.

Clinical judgement is required to determine the level of immunosuppression and these dosages are only indicative examples. In some cases, combinations of therapies can have a cumulative effect that is severely immunosuppressive.

## Individuals receiving non-corticosteroid immunomodulatory agents

Three primary doses of mRNA-CV are recommended for individuals with chronic immune-mediated inflammatory diseases who were receiving or had received immunosuppressive therapy prior to primary COVID-19 vaccination. Indicative examples are given in Table 5.5. Clinical judgement is required to determine the level of immunosuppression. In some cases, combinations of therapies can have a cumulative effect that is severely immunosuppressive.

**Table 5.5: Examples of non-corticosteroid immunosuppressant therapies for which three primary doses of mRNA-CV are recommended or not routinely recommended**

**Clinicians may use their judgement** for conditions or medications that are not listed here that are associated with severe immunocompromise and in some cases based on dosages or combinations of therapies

### Examples of non-corticosteroid agents for which a third dose is recommended

Agent	Example
Mycophenolate, methotrexate, leflunomide, 6-mercaptopurine	
Thiopurines	azathioprine
Alkylating agents	cyclophosphamide
Systemic calcineurin inhibitors	cyclosporin, tacrolimus
BTK inhibitors	ibrutinib
JAK inhibitors	ruxolitinib
Anti CD20 antibodies	rituximab, obinutuzumab, ocrelizumab
Sphingosine 1-phosphate receptor modulators	fingolimod
Anti-CD52 antibodies	alemtuzumab
Anti-complement antibodies	eculizumab
Anti-thymocyte globulin	

### Examples of non-corticosteroid agents<sup>a</sup> for which three primary doses are not routine recommended

Agent	Example
Anti-integrins	natalizumab
Anti-TNF- $\alpha$ antibodies	infliximab, adalimumab, etanercept
Anti-IL-1 antibodies	anakinra
Anti-IL-6 antibodies	tocilizumab
Anti-IL-17 antibodies	secukinumab
Anti-IL-4 antibodies	dupilumab
Anti-IL-23 antibodies	ustekinumab

a. For immune checkpoint inhibitors see section 4.3.8

## 5.5.3 Additional doses after primary course

NB: Certain individuals with severe immunosuppression are recommended to receive three primary doses (see section 5.5.2; this is part of the primary course and not the same as additional doses described in this section). Following the three-dose primary course, these individuals are also eligible for additional doses as described here.

A dose of XBB.1.5 mRNA-CV (30µg) is available for all adults aged from 30 years and age appropriate XBB.1.5 mRNA-CV (10 µg or 30 µg) is recommended for those aged 5 years and over who are at increased risk of severe COVID-19, regardless of number prior doses received. This additional dose can be given at least six months after the previous dose of COVID-19 vaccine or at least six months after a recovery from acute COVID-19 illness or a positive SARS-CoV-2 test (see section 5.5.4).

Clinical discretion can be applied, case by case, when considering vaccination given less than six months after infection or previous dose. A shorter spacing of a minimum of three months may be appropriate for those individuals considered to be at very high risk of severe disease from COVID-19 re-infection. Spacing of at least six months is preferred.

Due to the risk from waning protection, those at highest risk from severe breakthrough COVID-19 are particularly recommended to have a dose of XBB.1.5 mRNA-CV (30 µg or 10 µg, as age-appropriate) to extend and provide broader protection. This includes:

- people of Māori or Pacific ethnicities aged 50 years and over
- all other individuals aged 65 years and over
- residents aged 16 years and over living in aged care and disability care facilities
- severely immunocompromised people who were eligible to receive three primary doses (see section 5.5.2) aged 5 years and over
- individuals aged 5 years and over who are eligible for influenza vaccination, including those:
  - who have certain medical conditions that increase the risk of severe breakthrough COVID-19 illness (see section 5.5.2 and Table 5.6)
  - who live with disability with significant or complex health needs or multiple comorbidities (see Table 5.6)
  - who are severely obese (BMI  $\geq 40$  kg/m<sup>2</sup>) or severely underweight (BMI  $< 16.5$  kg/m<sup>2</sup>).
  - who are pregnant (see section 5.5.5).

Children aged from 6 months to 4 years who are severely immunocompromised or who have complex or multiple health conditions that increase their risk from COVID-19 and have received a three-dose primary series (as described in section 5.5.2) can be given an additional dose, six months after a previous COVID-19 vaccine or SARS-CoV-2 infection (reduced to a least 3 months with clinical discretion).

For further information see <https://info.health.nz/immunisations/vaccines-aotearoa/covid-19-vaccines/> For underlying health conditions that increase risk for severe COVID-19 in

adolescents see [starship.org.nz/guidelines/covid-19-disease-in-children/](https://starship.org.nz/guidelines/covid-19-disease-in-children/). This list is not exhaustive and clinicians may use their judgement for conditions that are not listed.

In addition, anyone aged 16 years or over who has not yet received an additional dose since completion of the primary course is recommended to receive a single dose of XBB.1.5 mRNA-CV (30µg), if not contraindicated.

**Table 5.6: Groups recommended an additional dose of COVID-19 vaccine (adapted from ATAGI)**

People in these groups are likely to have ongoing increased risk of severe COVID-19 after previous vaccination. These examples are not exhaustive, and providers may include individuals with conditions similar to those listed below, based on clinical judgement.

Category	Examples
Immunocompromising conditions	including people living with HIV infection
Cancer	Non-haematological cancer including those diagnosed within the past 5 years or on chemotherapy, radiotherapy, immunotherapy or targeted anti-cancer therapy (active treatment or recently completed) or with advanced disease regardless of treatment. Survivors of childhood cancer.
Chronic inflammatory conditions requiring medical treatment with disease-modifying anti-rheumatic drugs (DMARDs) or immune-suppressive or immunomodulatory therapies.	Systemic lupus erythematosus, rheumatoid arthritis, Crohn's disease, ulcerative colitis, and similar who are being treated.
Chronic lung disease	Chronic obstructive pulmonary disease, cystic fibrosis, interstitial lung disease and severe asthma (defined as requiring frequent hospital visits or the use of multiple medications).
Chronic liver disease	Cirrhosis, autoimmune hepatitis, non-alcoholic fatty liver disease, alcoholic liver disease.
Severe chronic kidney disease (stage 4 or 5)	
Chronic neurological disease	Stroke, neurodegenerative disease (eg, dementia, motor neurone disease, Parkinson's disease), myasthenia gravis, multiple sclerosis, cerebral palsy, myopathies, paralytic syndromes, epilepsy.
Diabetes mellitus requiring medication	
Chronic cardiac disease	Ischaemic heart disease, valvular heart disease, congestive cardiac failure, cardiomyopathies, poorly controlled hypertension, pulmonary hypertension, complex congenital heart disease.
People with disability with significant or complex health needs or multiple comorbidities which increase risk of poor outcome from COVID-19	Particularly those with trisomy 21 (Down Syndrome) or complex multi-system disorders.
Severe obesity with BMI $\geq 40$ kg/m <sup>2</sup>	
Severe underweight with BMI $< 16.5$ kg/m <sup>2</sup>	



## 5.5.4 Vaccination following SARS-CoV-2 infection

Vaccination should be offered regardless of an individual's history of symptomatic or asymptomatic SARS-CoV-2 infection. As the duration of protection post infection alone, is currently unknown, vaccination is recommended. Hybrid immunity from at least three exposures to both vaccination and infection provides longer lasting protection against hospitalisation and death than vaccine or infection alone.<sup>66</sup> Although, there are no specific safety concerns around giving mRNA-CV to individuals with a history of symptomatic COVID-19 or asymptomatic SARS-CoV-2 infection, those who have had recent infection can experience more systemic reactogenicity after the first dose of mRNA-CV (see section 5.7.1).<sup>75</sup> Viral or serological testing is not required before vaccination.

For most healthy, previously vaccinated people under the age of 50 years, SARS-CoV-2 infection can boost their immunity to a level like that following a dose of vaccine and are unlikely to require further vaccine doses for at least 12 months after infection.<sup>76</sup>

A person aged from 5 years (or from age 6 months for special groups) who has had prior SARS-CoV-2 infection, and is at increased risk of complications, is recommended to complete the recommended course of mRNA-CV (or another COVID-19 vaccine, as available). Individuals are advised to wait 6 months after SARS-CoV-2 infection (after recovery from acute illness or from the first confirmed positive test if asymptomatic) before receiving a recommended dose of COVID-19 vaccine. Based upon clinical discretion, where the individual is at increased risk of severe disease from reinfection and has not completed the recommended doses, vaccination can be shortened to a minimum of three months after SARS-CoV-2 infection.

**For all other vaccines, vaccination can commence as soon as the individual is no longer acutely unwell.**

## 5.5.5 Pregnancy

Anyone who is pregnant or planning pregnancy is encouraged to be routinely vaccinated with mRNA-CV at any stage of pregnancy. The risk of an adverse outcomes from COVID-19 infection during pregnancy is significantly higher compared to age-matched non-pregnant adults (see section 5.2.2).<sup>32</sup> International evidence from large quantities of safety surveillance has found no safety concerns with administering mRNA-CV in any stage of pregnancy including no safety concerns for the infant.<sup>77-81</sup> There is also evidence of antibody transfer in cord blood and breast milk which can offer protection to infants through passive immunity.<sup>56, 82-84</sup> Infants born to those vaccinated in pregnancy have some protection from COVID-19-associated hospitalisation for up to six months.<sup>85</sup>

Individuals who have not received any COVID-19 vaccination, are recommended to have one dose of mRNA-CV at any stage during pregnancy. Previously vaccinated individuals at increased risk of complications are recommended to receive one XBB.1.5 mRNA-CV (30µg) dose during pregnancy, at least 6 months after previous vaccination or SARS-CoV-2 infection.

People who are trying to become pregnant do not need to avoid pregnancy after receiving mRNA-CV.



## Additional doses in pregnancy

XBB.1.5 mRNA-CV (30 µg) vaccine can be used in pregnancy and while breastfeeding. Pregnant women who have completed the primary course can receive an additional dose of mRNA-CV at any stage of pregnancy, regardless of the number of previous doses given (from six months after a previous last dose or SARS-CoV-2 infection, whichever is later).

If previously unvaccinated, a single dose of XBB.1.5 mRNA-CV (30 µg) can be given at any stage during the current pregnancy.

An additional dose is particularly recommended for older ages in pregnancy (usually considered those aged 35 years and older) or any age with underlying medical conditions, including hypertension, diabetes, and obesity, or who meet other eligibility criteria given above (see section 5.5.3).

Although there is no data available yet for the use of the XBB.1.5 mRNA-CV (30 µg) formulation in pregnancy, the safety of XBB.1.5 mRNA-CV in pregnancy is inferred from the large quantity of reassuring data from the use of the original (30µg) and bivalent (15/15 µg) mRNA-CVs in pregnant people. Observational data for these vaccines show no increased risk of adverse pregnancy outcomes or increased risk of miscarriage in first trimester. The safety profile of additional doses of original mRNA COVID-19 vaccines given in pregnancy is as seen with the primary course.<sup>86</sup> During use in clinical trials and in real-world use from the age of 12 years, no clinically meaningful difference in safety profiles has been shown between the monovalent and the bivalent mRNA COVID-19 vaccines. There is no theoretically plausible reason for there to be any increased risk in pregnancy because the differences between these vaccine formulations are confined to mRNA spike protein sequences.

### 5.5.6 Breastfeeding

As with all schedule vaccines, there are no safety concerns about giving mRNA-CV to those lactating.

### 5.5.7 Frail elderly individuals

It is highly recommended that all eligible adults including the frail and elderly with comorbidities are offered vaccination against COVID-19, if there are no contraindications to its administration (see section 5.6.1), to provide protection for the individual as well as their community, especially when living in residential care facilities.

### 5.5.8 Individuals receiving cardiology care

It is recommended that all previously unvaccinated individuals from age 5 years to receive one dose of mRNA-CV (30 µg or 10 µg, as age appropriate). Pre-existing cardiac conditions, in

general, **are not** regarded as precautions or contraindications to vaccination. This includes pre-existing rheumatic heart disease. Note that many cardiac conditions increase the risk from COVID-19 infection.

Individuals aged from 5 years with a history of pericarditis or myocarditis, unrelated to mRNA-CV, can have the vaccine once the condition is completely resolved, (ie, no symptoms and no evidence of ongoing cardiac inflammation).

Infants and young children aged from 6 months to 4 years with complex congenital heart disease, acquired heart disease or congestive heart failure are recommended to receive three doses of mRNA-CV (3 µg), dose two given at least three weeks after dose one and dose three given at least eight weeks later. An additional dose can be considered at 6 months after the previous vaccine dose or SARS-CoV-2 infection. For young children with a history of inflammatory heart disease, discuss with cardiologist/specialist paediatrician.

For those with a history of myocarditis and pericarditis related to mRNA-CV, seek specialist immunisation advice on a case-by-case basis to consider appropriate vaccination options and timing of any further doses. See section 5.6.2 for those who have myocarditis associated with mRNA-CV.

### 5.5.9 Revaccination

Individuals from age 6 months who have undergone haematopoietic stem cell transplantation since their first course can be revaccinated with a three-dose primary course of a COVID-19 vaccine, plus additional doses as age appropriate (preferably with age-appropriate mRNA-CV).

Based on clinical discretion, if all scheduled doses have been completed prior to commencement of chemotherapy or solid organ transplant, a single further dose of mRNA-CV can be given.

## 5.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

### 5.6.1 Contraindications

Vaccination with mRNA-CV is contraindicated for individuals with a history of anaphylaxis to any component or previous dose of the same vaccine.

## 5.6.2 Precautions

A definite history of immediate allergic reaction to any other product is considered as a precaution but not a contraindication to vaccination with COVID-19 vaccines (mRNA-CV). A slightly increased risk of a severe allergic response in individuals who have had a previous anaphylaxis-type reaction needs to be balanced against the risk of SARS-CoV-2 exposure and severe COVID-19. These individuals can still receive a COVID-19 vaccine, if not contraindicated, and observation extended to 30 minutes after vaccination in health care settings, where anaphylaxis can be immediately treated with adrenaline.

### Myocarditis or pericarditis

If myocarditis, myopericarditis or pericarditis occurs after a dose of COVID-19 vaccine (mRNA-CV or another COVID-19 vaccine) defer further doses of COVID-19 vaccination. Seek specialist immunisation advice, on a case-by-case basis, to consider an appropriate alternative vaccine or no further vaccination, and about timing for further doses. Vaccination is not recommended for anyone with current active cardiac inflammation.

The risk of myocarditis following vaccination is not thought to be greater in children aged 6 months to 4 years than any other group, acknowledging that background rates of myocarditis from any cause in infants (aged under 1 year) are generally higher than in older children. There is no current evidence of a safety concern with this vaccine in young children or infants, overall.

## 5.7 Potential responses and AEFIs

### 5.7.1 Potential responses

#### mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

Commonly reported responses to mRNA-CV (30 µg) are injection-site pain, headache, dizziness and fatigue; other responses included muscle aches, feeling generally unwell, chills, fever, chest discomfort, joint pain, nausea and axillar lymph node swelling. These occurred most often after dose two and in younger adults (aged 18–55 years), and within one or two days of vaccination. Most are mild or moderate in severity and are self-limiting.<sup>49, 80</sup> According to Australian AusVaxSafety active surveillance data, the responses to XBB.1.5 mRNA-CV, given as a single primary dose or as an additional dose, are similar or milder than the previous mRNA-CV vaccines.<sup>87</sup> No new adverse reactions have been identified in clinical trials and real-world usage.<sup>88</sup> Analgesia, such as paracetamol or ibuprofen (as appropriate), can be taken for pain and discomfort following vaccination. It is advisable to limit vigorous exercise if feeling unwell.

Responses to the paediatric formulation mRNA-CV (10 µg) in children aged 5–11 years are similar to those seen for the adult formulation mRNA-CV (30 µg) in those age 16–25 years. During clinical trials, reactions were generally mild to moderate and short-lived. Pain at injection site was commonly reported (by over 70 percent) after dose one and two. Overall fewer children reported systemic reactions than seen after the 30 µg dose in adults, with fever, fatigue, headache, chills

and muscle ache as the most common and more frequent after the second dose.<sup>47</sup> These responses were mirrored in reports to VAERS and V-safe after 8.7 million doses given routinely to children in the US.<sup>89</sup> As with adults, the responses to paediatric XBB.1.5 mRNA-CV, given as a single primary dose or as an additional dose, are expected to be similar to the earlier mRNA-CV.

In clinical trials for paediatric mRNA-CV (3 µg), the most frequent responses seen in infants (aged 6–23 months) were irritability, decreased appetite, injection-site tenderness and redness, and fever; and in children aged 2–4 years, injection-site pain and redness, fatigue and fever. Less common responses included lymphadenopathy, diarrhoea, vomiting and nausea. Consistent with the clinical trial, systemic reactions were more frequently reported to V-safe in the US for infants (ages 6 months – 2 years) than those aged 3–5 years.<sup>90</sup>

See chapter 2 (section 2.3.3) for immunisation-stress related responses (ISRR).

## Breast screening and CT scans

Transient unilateral axillary adenopathy, a known response to vaccination, was particularly noted following vaccination with mRNA-CV due to the scale of the roll-out and age groups being immunised. Early estimates suggest that 12–16 percent of vaccine recipients experience axillary adenopathy after vaccination with mRNA-CV, starting one or two days after vaccination and which can persist for several weeks.<sup>91, 92</sup> Lymphadenopathy has also been commonly reported after additional doses of mRNA-CV.<sup>93</sup>

When attending breast screening appointments, including MRI scans and mammography, it is recommended that individuals advise the radiographer or doctor that they have received a COVID-19 vaccine recently. It is advised to monitor any lymph node changes that persist for longer than six weeks after vaccination.<sup>91</sup>

Likewise, individuals undergoing FDG PET/CT or MRI scans for cancer screening are advised to inform the radiologist or their oncologist that they have been recently vaccinated, or, if possible, to have COVID-19 vaccination at least two weeks before a scheduled scan or as soon as possible afterwards. Treatment should not be delayed.

## 5.7.2 AEFIs

Adverse events following immunisation (AEFIs) with the COVID-19 vaccines are being closely monitored during clinical trials and by post marketing surveillance. A dedicated COVID-19 vaccine AEFI reporting tool is available online from CARM (see section 1.6.3). Medsafe reports weekly on the AEFI reported to CARM after COVID-19 vaccinations (see [medsafe.govt.nz/COVID-19/vaccine-report-overview.asp](https://www.medsafe.govt.nz/COVID-19/vaccine-report-overview.asp)).

A list of adverse events of special interest (AESIs), including those previously associated with immunisation in general and with the individual vaccine platforms, was created by Safety Platform for Emergency Vaccines (SPEAC) in collaboration with the Coalition for Epidemic Preparedness Innovations (CEPI) and based on existing and new Brighton Collaboration case definitions. For further information, see [brightoncollaboration.us/covid-19](https://brightoncollaboration.us/covid-19). Global pharmacovigilance and active safety monitoring systems continue to watch for both AESI and unexpected AEFI.

## mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

Overall, no AESI signals were detected by the Vaccine Safety Datalink in the US up to 21 days after vaccination, following the administration of over 13 million doses of mRNA-CV (Comirnaty), however, subgroup analyses did find mRNA-CV to be associated with a slight increase in myocarditis and pericarditis in younger people (aged under 30 years).<sup>94, 95</sup>

Preliminary phase II/III clinical trial safety data reported lymphadenopathy in 64 (0.3%) vaccine recipients and six (<0.1%) placebo recipients (follow-up of up to 14 weeks after second dose of a subset of 18,860 participants who received at least one dose of mRNA-CV). Four vaccine-related adverse events were recorded (namely, shoulder injury related to vaccine administration, lymphadenopathy local to injection site, paroxysmal ventricular arrhythmia and right leg paraesthesia). No deaths were related to either the vaccine or the placebo.<sup>49</sup> During clinical trial follow-up to 1 February 2021, acute peripheral facial paralysis (Bell's palsy) was reported by four vaccinated participants and none in the placebo group.<sup>96</sup> No safety signal has been detected for this condition as an AESI,<sup>97</sup> and safety monitoring is ongoing.

No vaccine-related severe adverse events were seen during the phase II/III clinical trial of mRNA-CV (10 µg) and mRNA-CV (3 g). In 1,518 children aged 5–11 years, lymphadenopathy was reported in ten (0.9 percent) of mRNA-CV (10 µg) recipients. Rashes, with no consistent pattern, considered related to the vaccination were observed in four participants; these were mild and self-limiting with typical onset seven or more days after vaccination. No differences were apparent in vaccine safety between the children who had baseline evidence of previous SARS-CoV-2 infection.<sup>47</sup> Following administration of approximately 8.7 million doses of mRNA-CV (10 µg) in children aged 5–11 years in the US, the majority of reports to VAERS (97.6 percent) were non-serious and 2.4 percent were serious. The most common non-serious reports were due to vaccine administration errors. Of the serious reports, 11 verified cases of myocarditis were reported to VAERS but no chart-confirmed myocarditis cases were reported through the Vaccine Safety Datalink in this age group.<sup>89</sup> Post-licensure surveillance is ongoing internationally.

## Bivalent mRNA and XBB.1.5 COVID-19 vaccines

Safety monitoring in the US was evaluated following of use bivalent mRNA-CV as a booster dose (approximately 14.4 million doses bivalent Comirnaty and 8.2 million doses of bivalent Moderna) given to those who had received at least two doses of monovalent original mRNA-CV.<sup>88</sup> Of the 5,542 VAERS reports, 34% of events were vaccine administration and handling errors and 95% non-serious AEFI. V-safe reports, from almost 211,959 participants aged at least 12 years who received age-appropriate bivalent booster doses, were consistent with those reported following monovalent booster doses. Most people were receiving their fourth or fifth COVID-19 vaccine dose and 98.3 percent received influenza vaccine at the same visit. Adverse events were less common and less serious than the health impacts associated with COVID-19 illness.<sup>88</sup>



A Danish data linking study, covering a cohort of over one million adults aged 65 years and over (mean 74.7 years  $\pm$  7.4 years), reported no increased risk for 28 predetermined adverse events were observed within 28 days following XBB.1.5 mRNA-CV given as a fifth COVID-19 vaccine dose.<sup>98</sup> For example, incidence rate ratio of hospital contact was 0.96 (95% CI 0.87-1.07) for an ischaemic cardiac event, 0.87 (0.79-0.96) for cerebral infarction and 0.60 (0.14-2.66) for myocarditis.<sup>98</sup>

### Myocarditis and pericarditis

A small increase in incidence of myocarditis, myopericarditis and pericarditis has been observed following the second dose of mRNA-CV vaccination (40.6 cases per million doses in young males and 4.2 cases per million in young females, aged 12–29 years, decreasing to 2.4 and 1.0 per million, respectively, in men and women aged over 30 years).<sup>99</sup> Very rarely, myocarditis has also been reported in boys aged 5–11 years after dose two in the US (reporting rate of 2.2 cases per million doses).<sup>100</sup> Most cases occur within 14 days of vaccination typically with full recovery after standard treatment and rest.<sup>101, 102</sup> A review of clinical records in the US observed the median time to onset for myocarditis was 3.5 days (interquartile range 3.0–10.8 days) after vaccination and a median of 20 days (range 6.0–41 days) for pericarditis.<sup>102</sup> Wider spacing between doses (ie, eight weeks) has been shown to significantly lower the risk of myocarditis in young adults in Canada.<sup>103</sup> Following 22.6 million doses of bivalent mRNA-CV given to individuals aged from 12 years in the US, three out of five cases of myocarditis and four cases of pericarditis reported to VAERS were medically verified. These early data confirm that myocarditis and pericarditis post vaccine dose is an extremely rare event and suggests that this rate is the same or lower than after the primary doses.<sup>88</sup>

Myocarditis and pericarditis are uncommon conditions considered to be associated with viral infection, including COVID-19. Recently vaccinated individuals should seek immediate medical attention if they experience new onset of (acute and persisting) chest pain, shortness of breath or arrhythmia (palpitations). Diagnosis is based on elevated troponin, C-reactive protein and electrocardiogram and/or MRI findings. Report all suspected cases to CARM as Medsafe continues to monitor this AEFI closely. Defer further doses of mRNA-CV if myocarditis or pericarditis occurs after vaccination. Seek specialist immunisation advice, on a case-by-case basis, to consider an appropriate alternative vaccination option, and timing for further doses (see section 5.6.2).

### Anaphylaxis

Following approval for use in the US, the VAERS detected 47 cases of anaphylaxis after administration of just under ten million doses (around five cases per million doses) mRNA-CV (Pfizer/BioNTech). The median interval to symptom onset was ten minutes (range <1–1140 minutes), almost 90 percent occurred within 30 minutes of vaccination.<sup>104</sup> All were successfully treated with adrenaline. See section 5.6 for contraindications and precautions.

A placebo-controlled trial evaluated the recurrence of systemic allergic reactions after a second or third dose of mRNA-CV in individuals who reported anaphylactic reactions after previous dose.<sup>105</sup> It found that immunisation stress-related (ISRR) responses were significantly more common (more than five times higher), including in the placebo group, than recurrent serious

allergic reactions following revaccination. Increased levels of anxiety prior to vaccination were a risk factor for ISRR.<sup>105</sup>

See chapter 2 (section 2.3.3) for immunisation-stress related responses.

### History of Guillain-Barré Syndrome

There is no evidence of a higher rate of reporting of Guillain-Barré syndrome (GBS) following COVID-19 vaccination in individuals who have previously had GBS. Vaccination with mRNA-CV is preferred.

## 5.8 Public health measures

Although the official WHO public health emergency has ended, SARS-CoV-2 continues to have an impact on population health globally. During the early stages of the pandemic, New Zealand implemented control measures to limit the spread of SARS-CoV-2 in the community.

Immunisation using COVID-19 vaccines continues to be part of the public health strategy aimed at reducing the risk of severe disease, to minimise the burden on the health care system and slowing the rate of transmission during community outbreaks.

## 5.9 Variations from the vaccine data sheets

## References

1. V'Kovski P, Kratzel A, Steiner S, et al. Coronavirus biology and replication: implications for SARS-CoV-2. *Nature Reviews: Microbiology*, 2021. 19(3): p. 155-170.
2. Walls AC, Park YJ, Tortorici MA, et al. Structure, function, and antigenicity of the SARS-CoV-2 spike glycoprotein. *Cell*, 2020. 181(2): p. 281-292 e6.
3. World Health Organization. 2021 *Tracking SARS-CoV-2 variants*. WHO; 2021 [updated 13 December 2021]; URL: <https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/>. (accessed 17 December)
4. Cevik M, Tate M, Lloyd O, et al. SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis. *The Lancet Microbe*, 2021. 2(1): p. e13-e22.
5. Bai Y, Yao L, Wei T, et al. Presumed asymptomatic carrier transmission of COVID-19. *JAMA*, 2020. 323(14): p. 1406-07.
6. Liu Y, Yan LM, Wan L, et al. Viral dynamics in mild and severe cases of COVID-19. *Lancet Infectious Diseases*, 2020. 20(6): p. 656-7.



7. Piccoli L, Ferrari P, Piumatti G, et al. Risk assessment and seroprevalence of SARS-CoV-2 infection in healthcare workers of COVID-19 and non-COVID-19 hospitals in Southern Switzerland. *The Lancet Regional Health - Europe*, 2021. 1.
8. McGregor R, Craigie A, Jack S, et al. The persistence of neutralising antibodies up to 11 months after SARS CoV-2 infection in the southern region of New Zealand. *New Zealand Medical Journal*, 2022. 135(1550): p. 162-166.
9. Whitcombe AL, McGregor R, Craigie A, et al. Comprehensive analysis of SARS-CoV-2 antibody dynamics in New Zealand. *Clin Transl Immunology*, 2021. 10(3): p. e1261.
10. Lewis N, Chambers LC, Chu HT, et al. Effectiveness associated with vaccination after COVID-19 recovery in preventing reinfection. *JAMA Netw Open*, 2022. 5(7): p. e2223917-e2223917.
11. Nordstrom P, Ballin M, Nordstrom A. Risk of SARS-CoV-2 reinfection and COVID-19 hospitalisation in individuals with natural and hybrid immunity: a retrospective, total population cohort study in Sweden. *The Lancet Infectious Diseases*, 2022. 22(6): p. 781-790.
12. World Health Organization. 2021 *Interim statement on COVID-19 vaccination for children and adolescents*. WHO; 2021 [updated 29 November 2021]; URL: <https://www.who.int/news/item/24-11-2021-interim-statement-on-covid-19-vaccination-for-children-and-adolescents>. (accessed 2021 December 14)
13. Powell AA, Dowell AC, Moss P, Ladhani SN. Current state of COVID-19 in children: 4 years on. *Journal of Infection*, 2024. 88(5): p. 106134.
14. Shi Q, Wang Z, Liu J, et al. Risk factors for poor prognosis in children and adolescents with COVID-19: A systematic review and meta-analysis. *EClinicalMedicine*, 2021. 41.
15. Tsankov BK, Allaire JM, Irvine MA, et al. Severe COVID-19 infection and pediatric comorbidities: A systematic review and meta-analysis. *International Journal of Infectious Diseases*, 2021. 103: p. 246-256.
16. Ministry of Health. 2021 *Regional Data Explorer 2017-2020: New Zealand Health Survey*. URL: <https://www.health.govt.nz/publication/regional-results-2017-2020-new-zealand-health-survey>. (accessed 14 December 2021)
17. Murray S. 2019 *The state of wellbeing and equality for disabled people, their families, and whānau*. URL: <https://apo.org.au/node/270566>. (accessed 14 December 2021)
18. Taylor A, Best EJ, Walls T, et al. COVID-19-related hospitalizations among Aotearoa, New Zealand children during the Omicron era of SARS-CoV-2. *IJID Reg*, 2024. 12: p. 100408.
19. Carter MJ, Shankar-Hari M, Tibby SM. Paediatric inflammatory multisystem syndrome temporally-associated with SARS-CoV-2 infection: an overview. *Intensive Care Medicine*, 2021. 47(1): p. 90-93.
20. Jiang L, Tang K, Levin M, et al. COVID-19 and multisystem inflammatory syndrome in children and adolescents. *Lancet Infectious Diseases*, 2020. 20(11): p. e276-e288.
21. Reddy RK, Charles WN, Sklavounos A, et al. The effect of smoking on COVID-19 severity: A systematic review and meta-analysis. *Journal of Medical Virology*, 2021. 93(2): p. 1045-1056.
22. Barron E, Bakhai C, Kar P, et al. Associations of type 1 and type 2 diabetes with COVID-19-related mortality in England: a whole-population study. *Lancet Diabetes Endocrinol*, 2020. 8(10): p. 813-822.
23. Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature*, 2020. 584(7821): p. 430-436.
24. Maze M, Williman J, Best E, et al. 2023 *Clinical and Demographic Predictors of COVID-19 Severity in New Zealand*. Christchurch, New Zealand. (accessed
25. Kotlar B, Gerson E, Petrillo S, et al. The impact of the COVID-19 pandemic on maternal and perinatal health: a scoping review. *Reprod Health*, 2021. 18(1): p. 10.
26. Mullins E, Hudak ML, Banerjee J, et al. Pregnancy and neonatal outcomes of COVID-19: co-reporting of common outcomes from PAN-COVID and AAP SONPM registries. *Ultrasound in Obstetrics and Gynecology*, 2021. 57(4): p. 573-581.

27. Villar J, Ariff S, Gunier RB, et al. Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection: The INTERCOVID Multinational Cohort Study. *JAMA Pediatr*, 2021. 175(8): p. 817-826.
28. Vousden N, Bunch K, Morris E, et al. The incidence, characteristics and outcomes of pregnant women hospitalized with symptomatic and asymptomatic SARS-CoV-2 infection in the UK from March to September 2020: A national cohort study using the UK Obstetric Surveillance System (UKOSS). *PLoS One*, 2021. 16(5): p. e0251123.
29. Carlson J, Simeone RM, Ellington S, et al. Pre-Delta, Delta, and Omicron periods of the Coronavirus Disease 2019 (COVID-19) pandemic and health outcomes during delivery hospitalization. *Obstetrics and Gynecology*, 2024. 143(1): p. 131-138.
30. Engjom HM, Ramakrishnan R, Vousden N, et al. Severity of maternal SARS-CoV-2 infection and perinatal outcomes of women admitted to hospital during the omicron variant dominant period using UK Obstetric Surveillance System data: prospective, national cohort study. *BMJ Medicine*, 2022. 1(1): p. e000190.
31. Villar J, Soto Conti CP, Gunier RB, et al. Pregnancy outcomes and vaccine effectiveness during the period of omicron as the variant of concern, INTERCOVID-2022: a multinational, observational study. *Lancet*, 2023. 401(10375): p. 447-457.
32. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ*, 2020. 370: p. m3320.
33. Adhikari EH, Moreno W, Zofkie AC, et al. Pregnancy outcomes among women with and without severe acute respiratory syndrome coronavirus-2 infection. *JAMA Netw Open*, 2020. 3(11): p. e2029256.
34. Liguoro I, Pilotto C, Bonanni M, et al. SARS-COV-2 infection in children and newborns: a systematic review. *Eur. J. Pediatrics*, 2020. 179(7): p. 1029-1046.
35. Greenhalgh T, Knight M, A'Court C, et al. Management of post-acute covid-19 in primary care. *BMJ*, 2020. 370: p. m3026.
36. Sivan M, Taylor S. NICE guideline on long COVID. *BMJ*, 2020. 371: p. m4938.
37. Sudre CH, Murray B, Varsavsky T, et al. Attributes and predictors of long COVID. *Nature Medicine*, 2021. 27(4): p. 626-631.
38. Del Rio C, Collins LF, Malani P. Long-term health consequences of COVID-19. *JAMA*, 2020. 324(17): p. 1723-1724.
39. World Health Organization. 2023 *A clinical case definition for post COVID-19 condition in children and adolescents by expert consensus, 16 February 2023*. URL: <https://www.who.int/publications/i/item/WHO-2019-nCoV-Post-COVID-19-condition-CA-Clinical-case-definition-2023-1>. (accessed 5 April 2024)
40. World Health Organization. 2023 *From emergency response to long-term COVID-19 disease management: sustaining gains made during the COVID-19 pandemic*. WHO; 2023 [updated 3 May 2023]; WHO/WHE/SPP/2023.1:[URL: <https://www.who.int/publications/i/item/WHO-WHE-SPP-2023.1>]. (accessed February 7)
41. Geoghegan JL, Ren X, Storey M, et al. Genomic epidemiology reveals transmission patterns and dynamics of SARS-CoV-2 in Aotearoa New Zealand. *Nat Commun*, 2020. 11(1): p. 6351.
42. Public Health Agency. 2022 *COVID-19 mortality in Aotearoa New Zealand: Inequities in risk*. Wellington. URL: <https://www.health.govt.nz/publication/covid-19-mortality-aotearoa-new-zealand-inequities-risk>. (accessed 1 November 2022)
43. Callaway E. The race for coronavirus vaccines: a graphical guide. *Nature*, 2020. 580(7805): p. 576-7.
44. Flanagan KL, Best E, Crawford NW, et al. Progress and pitfalls in the quest for effective SARS-CoV-2 (COVID-19) vaccines. *Frontiers in Immunology*, 2020. 11: p. 579250.
45. Walsh EE, Frenck RW, Jr., Falsey AR, et al. Safety and Immunogenicity of Two RNA-Based Covid-19 Vaccine Candidates. *New England Journal of Medicine*, 2020. 383(25): p. 2439-2450.

46. Frenck RW, Klein NP, Kitchin N, et al. Safety, immunogenicity, and efficacy of the BNT162b2 COVID-19 vaccine in adolescents. *New England Journal of Medicine*, 2021. 385(3): p. 239-250.
47. Walter EB, Talaat KR, Sabharwal C, et al. Evaluation of the BNT162b2 COVID-19 vaccine in children 5 to 11 years of age. *New England Journal of Medicine*, 2021. 386(1): p. 35-46.
48. Fleming-Dutra KE, Wallace M, Moulia DL, et al. Interim recommendations of the Advisory Committee on Immunization Practices for use of Moderna and Pfizer-BioNTech COVID-19 vaccines in children aged 6 months–5 years — United States, June 2022. *MMWR. Morbidity and Mortality Weekly Report*, 2022. 71(26): p. 859-868.
49. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. *New England Journal of Medicine*, 2020. 383(27): p. 2603-2615.
50. Vaccines and Related Biological Products Advisory Committee Meeting. 2022 *FDA briefing document. EUA amendment request for Pfizer-BioNTech COVID-19 vaccine for use in children 6 months through 4 years of age*. URL: <https://www.fda.gov/media/159195/download>. (accessed 2 February 2023)
51. Dagan N, Barda N, Kepten E, et al. BNT162b2 mRNA Covid-19 vaccine in a nationwide mass vaccination setting. *New England Journal of Medicine*, 2021. 384(15): p. 1412-1423.
52. Lopez Bernal J, Andrews N, Gower C, et al. Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant. *New England Journal of Medicine*, 2021. 385(7): p. 585-594.
53. Lopez Bernal J, Andrews N, Gower C, et al. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study. *BMJ*, 2021. 373: p. n1088.
54. Birol Ilter P, Prasad S, Berkkan M, et al. Clinical severity of SARS-CoV-2 infection among vaccinated and unvaccinated pregnancies during the Omicron wave. *Ultrasound in Obstetrics and Gynecology*, 2022. 59(4): p. 560-562.
55. Intensive Care National Audit and Research Centre (ICNARC). 2022 *ICNARC report on COVID-19 in critical care: England, Wales and Northern Ireland, 8 July 2022*. London, UK. URL: <https://www.icnarc.org/our-audit/audits/cmp/reports>. (accessed 21 July 2022)
56. Kugelman N, Nahshon C, Shaked-Mishan P, et al. Third trimester messenger RNA COVID-19 booster vaccination upsurge maternal and neonatal SARS-CoV-2 immunoglobulin G antibody levels at birth. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 2022. 274: p. 148-154.
57. Rahmati M, Yon DK, Lee SW, et al. Effects of COVID-19 vaccination during pregnancy on SARS-CoV-2 infection and maternal and neonatal outcomes: A systematic review and meta-analysis. *Reviews in Medical Virology*, 2023. 33(3).
58. Zerbo O, Ray GT, Fireman B, et al. Maternal SARS-CoV-2 vaccination and infant protection against SARS-CoV-2 during the first six months of life. *Nat Commun*, 2023. 14(1): p. 894.
59. Zerbo O, Ray GT, Fireman B, et al. Effectiveness of COVID-19 vaccination during pregnancy by circulating viral variant. *AJOG Glob Rep*, 2023. 3(4): p. 100264.
60. Andrews N, Stowe J, Kirsebom F, et al. Effectiveness of COVID-19 vaccines against the Omicron (B.1.1.529) variant of concern. *medRxiv*, 2021 (preprint): p. 2021.12.14.21267615.
61. Buchan SA, Chung H, Brown KA, et al. Effectiveness of COVID-19 vaccines against Omicron or Delta symptomatic infection and severe outcomes. *medRxiv*, 2022 (preprint): p. 2021.12.30.21268565.
62. Mallory RM, Formica N, Pfeiffer S, et al. Safety and immunogenicity following a homologous booster dose of a SARS-CoV-2 recombinant spike protein vaccine (NVX-CoV2373): a secondary analysis of a randomised, placebo-controlled, phase 2 trial. *The Lancet Infectious Diseases*, 2022.
63. Tarke A, Coelho CH, Zhang Z, et al. SARS-CoV-2 vaccination induces immunological T cell memory able to cross-recognize variants from Alpha to Omicron. *Cell*, 2022.
64. Liu J, Chandrashekar A, Sellers D, et al. Vaccines elicit highly conserved cellular immunity to SARS-CoV-2 Omicron. *Nature*, 2022. 603(7901): p. 493-496.

65. Andrews N, Tessier E, Stowe J, et al. Duration of protection against mild and severe disease by COVID-19 vaccines. *New England Journal of Medicine*, 2022.
66. Wu S, Li Y, Baral S, et al. Protection of prior SARS-CoV-2 infection, COVID-19 boosters, and hybrid immunity against Omicron severe illness: A population-based cohort study of five million residents in Canada. *PloS One*, 2024. 19(2): p. e0299304.
67. Carreño JM, Alshammary H, Tcheou J, et al. Activity of convalescent and vaccine serum against SARS-CoV-2 Omicron. *Nature*, 2021.
68. Lin DY, Xu Y, Gu Y, et al. Effectiveness of bivalent boosters against severe Omicron infection. *New England Journal of Medicine*, 2023. 388(8): p. 764-766.
69. Surie D, DeCuir J, Zhu Y, et al. Early estimates of bivalent mRNA vaccine effectiveness in preventing COVID-19-associated hospitalization among immunocompetent adults aged ≥65 Years - IVY Network, 18 States, September 8-November 30, 2022. *MMWR: Morbidity and Mortality Weekly Report*, 2022. 71(5152): p. 1625-1630.
70. Tenforde MW, Weber ZA, Natarajan K, et al. Early estimates of bivalent mRNA vaccine effectiveness in preventing COVID-19-associated emergency department or urgent care encounters and hospitalizations among immunocompetent adults - VISION Network, nine states, September-November 2022. *MMWR: Morbidity and Mortality Weekly Report*, 2022. 71(5152): p. 1616-1624.
71. Huiberts AJ, Hoeve CE, De Gier B, et al. Effectiveness of Omicron XBB.1.5 vaccine against infection with SARS-CoV-2 Omicron XBB and JN.1 variants, prospective cohort study, the Netherlands, October 2023 to January 2024. *Eurosurveillance*, 2024. 29(10).
72. van Werkhoven CH, Valk AW, Smagge B, et al. Early COVID-19 vaccine effectiveness of XBB.1.5 vaccine against hospitalisation and admission to intensive care, the Netherlands, 9 October to 5 December 2023. *Euro Surveillance*, 2024. 29(1).
73. Link-Gelles R, Ciesla AA, Mak J, et al. Early estimates of updated 2023-2024 (monovalent XBB.1.5) COVID-19 vaccine effectiveness against symptomatic SARS-CoV-2 infection attributable to co-circulating omicron variants among immunocompetent adults - Increasing Community Access to Testing Program, United States, September 2023-January 2024. *MMWR: Morbidity and Mortality Weekly Report*, 2024. 73(4): p. 77-83.
74. Wang Q, Guo Y, Bowen A, et al. XBB.1.5 monovalent mRNA vaccine booster elicits robust neutralizing antibodies against XBB subvariants and JN.1. *Cell Host Microbe*, 2024.
75. Menni C, Klaser K, May A, et al. Vaccine side-effects and SARS-CoV-2 infection after vaccination in users of the COVID Symptom Study app in the UK: a prospective observational study. *Lancet Infectious Diseases*, 2021.
76. Bobrovitz N, Ware H, Ma X, et al. Protective effectiveness of previous SARS-CoV-2 infection and hybrid immunity against the omicron variant and severe disease: a systematic review and meta-regression. *The Lancet Infectious Diseases*, 2023. 23(5): p. 556-567.
77. Blakeway H, Prasad S, Kalafat E, et al. COVID-19 vaccination during pregnancy: coverage and safety. *American Journal of Obstetrics and Gynecology*, 2021.
78. Lipkind HS, Vazquez-Benitez G, DeSilva M, et al. Receipt of COVID-19 vaccine during pregnancy and preterm or small-for-gestational-age at birth - Eight integrated health care organizations, United States, December 15, 2020-July 22, 2021. *MMWR: Morbidity and Mortality Weekly Report*, 2022. 71(1): p. 26-30.
79. Sadarangani M, Soe P, Shulha HP, et al. Safety of COVID-19 vaccines in pregnancy: a Canadian National Vaccine Safety (CANVAS) network cohort study. *The Lancet Infectious Diseases*.
80. Shimbabukuro T, CDC-COVID-19 Vaccine Task Force. 2021 COVID-19 vaccine safety update. . (ACIP) ACoIP. URL: <https://www.cdc.gov/vaccines/acip/meetings/slides-2021-1-27-21.html>. (accessed 5 February 2021)
81. Faherty EAG, Wilkins KJ, Jones S, et al. Pregnancy outcomes among pregnant persons after COVID-19 vaccination: Assessing vaccine safety in retrospective cohort analysis of U.S. National COVID Cohort Collaborative (N3C). *Vaccines (Basel)*, 2024. 12(3): p. 289.



82. Perl SH, Uzan-Yulzari A, Klainer H, et al. SARS-CoV-2-specific antibodies in breast milk after COVID-19 vaccination of breastfeeding women. *JAMA*, 2021. 325(19): p. 2013-2014.
83. Prabhu M, Murphy EA, Sukhu AC, et al. Antibody response to Coronavirus Disease 2019 (COVID-19) messenger RNA vaccination in pregnant women and transplacental passage into cord blood. *Obstetrics & Gynecology*, 2021. 138(2): p. 278-280.
84. Rottenstreich A, Zarbiv G, Oiknine-Djian E, et al. Efficient maternofetal transplacental transfer of anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike antibodies after antenatal SARS-CoV-2 BNT162b2 messenger RNA vaccination. *Clin Inf Dis*, 2021. 73(10): p. 1909-1912.
85. Halasa N, Olson S, Staat M, et al. Effectiveness of maternal vaccination with mRNA COVID-19 vaccine during pregnancy against COVID-19-associated hospitalization in infants aged <6 months — 17 States, July 2021–January 2022. *MMWR: Morbidity and Mortality Weekly Report*, 2022. 71(Early Release).
86. Moro PL, Olson CK, Zhang B, et al. Safety of booster doses of Coronavirus Disease 2019 (COVID-19) vaccine in pregnancy in the Vaccine Adverse Event Reporting System. *Obstetrics and Gynecology*, 2022. 140(3): p. 421-427.
87. AusVaxSafety. *Pfizer monovalent Omicron XBB.1.5 COVID-19 vaccine safety data – all participants*. [updated 15 April 2024]; URL: <https://ausvaxsafety.org.au/covid-19-vaccines/pfizer-monovalent-omicron-xbb15-covid-19-vaccine-safety-data-all-participants>. (accessed 2 May 2024)
88. Hause AM, Marquez P, Zhang B, et al. Safety monitoring of bivalent COVID-19 mRNA vaccine booster doses among persons aged ≥12 years - United States, August 31–October 23, 2022. *MMWR: Morbidity and Mortality Weekly Report*, 2022. 71(44): p. 1401-1406.
89. Hause AM, Baggs J, Marquez P, et al. COVID-19 vaccine safety in children aged 5–11 years - United States, November 3–December 19, 2021. *MMWR: Morbidity and Mortality Weekly Report*, 2021. 70(5152): p. 1755-1760.
90. Hause AM, Marquez P, Zhang B, et al. COVID-19 mRNA vaccine safety among children aged 6 months–5 years - United States, June 18, 2022–August 21, 2022. *MMWR: Morbidity and Mortality Weekly Report*, 2022. 71(35): p. 1115-1120.
91. Edmonds CE, Zuckerman SP, Conant EF. Management of unilateral axillary lymphadenopathy detected on breast MRI in the era of coronavirus disease (COVID-19) vaccination. *AJR: American Journal of Roentgenology*, 2021.
92. Garreffa E, Hamad A, O'Sullivan CC, et al. Regional lymphadenopathy following COVID-19 vaccination: Literature review and considerations for patient management in breast cancer care. *European Journal of Cancer*, 2021. 159: p. 38-51.
93. Medsafe. *2022 Adverse events following immunisation with COVID-19 vaccines: Safety Report #40 – 31 January 2022*. online. URL: <https://www.medsafe.govt.nz/COVID-19/safety-report-40.asp>. (accessed 25 February 2022)
94. Klein N. 2021 *Rapid cycle analysis to monitor the safety of COVID-19 vaccines in near real-time within the Vaccine Safety Datalink: myocarditis and anaphylaxis*. Advisory Committee on Immunization Practices (ACIP). URL: <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-08-30/04-COVID-Klein-508.pdf>. (accessed 20 September 2021)
95. Gargano J, Wallace M, Hadler S, et al. Use of mRNA COVID-19 vaccine after reports of myocarditis among vaccine recipients: Update from Advisory Committee on Immunization Practices - United States, June 2021. *MMWR: Morbidity and Mortality Weekly Report*, 2021. 70(27): p. 977-982.
96. Pfizer New Zealand. 2021 *New Zealand Datasheet: Comirnaty COVID-19 vaccine*. Medsafe. URL: <https://www.medsafe.govt.nz/profs/Datasheet/c/comirnatyinj.pdf>. (accessed 10 November 2021)

97. Renoud L, Khouri C, Revol B, et al. Association of facial paralysis with mRNA COVID-19 vaccines: A disproportionality analysis using the World Health Organization pharmacovigilance database. *JAMA Intern Med*, 2021. 181(9): p. 1243-1245.
98. Andersson NW, Thiesson EM, Hviid A. Adverse Events After XBB.1.5-Containing COVID-19 mRNA Vaccines. *JAMA*, 2024. 331(12): p. 1057-1059.
99. World Health Organization. 2021 *COVID-19 subcommittee of the WHO Global Advisory Committee on Vaccine Safety (GACVS): updated guidance regarding myocarditis and pericarditis reported with COVID-19 mRNA vaccines.*: WHO; 2021 [updated 9 July 2021]; URL: <https://www.who.int/news/item/09-07-2021-gacvs-guidance-myocarditis-pericarditis-covid-19-mrna-vaccines>. (accessed 12 July 2021)
100. Hause AM, Shay DK, Klein NP, et al. Safety of COVID-19 vaccination in United States children ages 5 to 11 years. *Pediatrics*, 2022. 150(2).
101. Mevorach D, Anis E, Cedar N, et al. Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel. *New England Journal of Medicine*, 2021. 385(23): p. 2140-2149.
102. Diaz GA, Parsons GT, Gering SK, et al. 2021. Myocarditis and pericarditis after vaccination for COVID-19. *JAMA*. DOI: 10.1001/jama.2021.13443 (accessed 16 August 2021)
103. Buchan SA, Seo CY, Johnson C, et al. Epidemiology of myocarditis and pericarditis following mRNA vaccination by vaccine product, schedule, and interdose interval among adolescents and adults in Ontario, Canada. *JAMA Netw Open*, 2022. 5(6): p. e2218505.
104. Shimabukuro TT, Cole M, Su JR. Reports of anaphylaxis after receipt of mRNA COVID-19 vaccines in the US-December 14, 2020-January 18, 2021. *JAMA*, 2021. 325(11): p. 1101-1102.
105. Khalid MB, Zektser E, Chu E, et al. A randomized double-blinded trial to assess recurrence of systemic allergic reactions following COVID-19 mRNA vaccination. *Journal of Allergy and Clinical Immunology*, 2024.

# 6 Diphtheria

## Key information

Mode of transmission	Contact with respiratory droplets or infected skin of a case or carrier or, more rarely, contaminated objects.	
Incubation period	Usually 2–5 days, occasionally longer.	
Period of communicability	Variable; usually 2 weeks or less, seldom more than 4 weeks. Carriers may shed for longer. Effective antimicrobial therapy promptly terminates shedding.	
Funded and available vaccines	DTaP-IPV-HepB/Hib (Infanrix-hexa). DTaP-IPV (Infanrix-IPV). Tdap (Boostrix).	
Dose, presentation, route	0.5 mL per dose. DTaP-IPV-HepB/Hib: pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. DTaP-IPV, Tdap: pre-filled syringe. Intramuscular injection.	
Funded vaccine indications and schedule	During each pregnancy (recommended from 16 weeks' gestation) for pertussis protection	Tdap
	6 weeks, 3 months and 5 months	DTaP-IPV-HepB/Hib
	4 years	DTaP-IPV
	11 years	Tdap
	45 years (catch-up, if individual has not received 4 previous tetanus doses)	Tdap
	65 years	Tdap
	Parents or primary caregivers of infants admitted to neonatal intensive or specialist baby care units for more than 3 days and whose mothers had not received Tdap at least 14 days prior to birth for pertussis protection	Tdap
	For vaccination of previously unimmunised or partially immunised patients	DTaP-IPV-HepB/Hib, DTaP-IPV or Tdap
	For (re)vaccination of eligible patients	
Vaccine effectiveness	Protection of 87–98 percent has been demonstrated using population-based analysis. Immunised cases have been shown to have less severe disease  To prevent major community outbreaks at least 70 percent of the childhood population must be immune to diphtheria	
Public health measures	All cases of diphtheria must be notified immediately on suspicion (see section 6.8)	
Post exposure prophylaxis	Antimicrobial prophylaxis should be administered to contacts as appropriate (see section 6.8)	



## 6.1 Bacteriology

Diphtheria is a serious, often fatal, toxin-mediated disease caused by *Corynebacterium diphtheriae*, a non-sporulating, non-encapsulated, gram-positive bacillus. Rarely, it may also be caused by other toxin-carrying *Corynebacteria* species, such as *Corynebacterium ulcerans*. Both toxigenic and non-toxigenic strains can occur during outbreaks, during which non-toxigenic strains can convert to toxigenic strains by infection with *tox*-gene containing  $\beta$ -corynebacteriophage.<sup>1</sup>

## 6.2 Clinical features

Classic diphtheria characteristically involves membranous inflammation of the upper respiratory tract with involvement of other tissues, especially the myocardium and peripheral nerves. The organism itself is rarely invasive, but a potent exotoxin, diphtheria toxin, is produced by some toxigenic strains that causes tissue damage through local and systemic actions. There is also a cutaneous form of diphtheria, which is typically less severe. The detection of either *C. diphtheriae* or *C. ulcerans* is notifiable to the medical officer of health, and the isolates should be referred to the Institute of Environmental Science and Research (ESR) for toxin detection. Non-toxigenic diphtheria strains can circulate but these do not secrete diphtheria toxin and are not associated with disease nor preventable by immunisation with diphtheria toxoid vaccine.

Transmission is by respiratory tract droplets, or by direct contact with skin lesions or contaminated articles. Cutaneous toxigenic diphtheria is more efficiently transmitted than respiratory toxigenic diphtheria and can cause respiratory infection in others.<sup>2,3</sup> Humans are the only known host for diphtheria, and the disease is usually spread by close personal contact with a case or carrier, or occasionally by fomites or food. The disease remains communicable for up to four weeks after infection, but carriers of *C. diphtheriae* may continue to shed the organism and be a source of infection for much longer.

Classic diphtheria has a gradual onset after an incubation period of two to five days. Symptoms and signs may be mild at first, but progress over one to two days with the development of a mildly painful tonsillitis or pharyngitis with an associated greyish membrane. Diphtheria should be suspected particularly if the membrane extends to the uvula and soft palate. The nasopharynx may also be obstructed by a greyish membrane, which leaves a bleeding area if disturbed. The breath of a patient with diphtheria has a characteristic mousy smell.

The major complication of diphtheria is respiratory obstruction, although most deaths result from the effects of diphtheria toxin on various organs. Of importance is the toxicity to the myocardium (leading to myocarditis and heart failure), peripheral nerves (resulting in demyelination and paralysis), and kidneys (resulting in tubular necrosis). The neuropathy begins two to eight weeks after disease onset, while the myocarditis can be early or late. Neurological complications occur in 15–20 percent of cases and can cause paralysis up to two months after disease onset.<sup>1</sup>

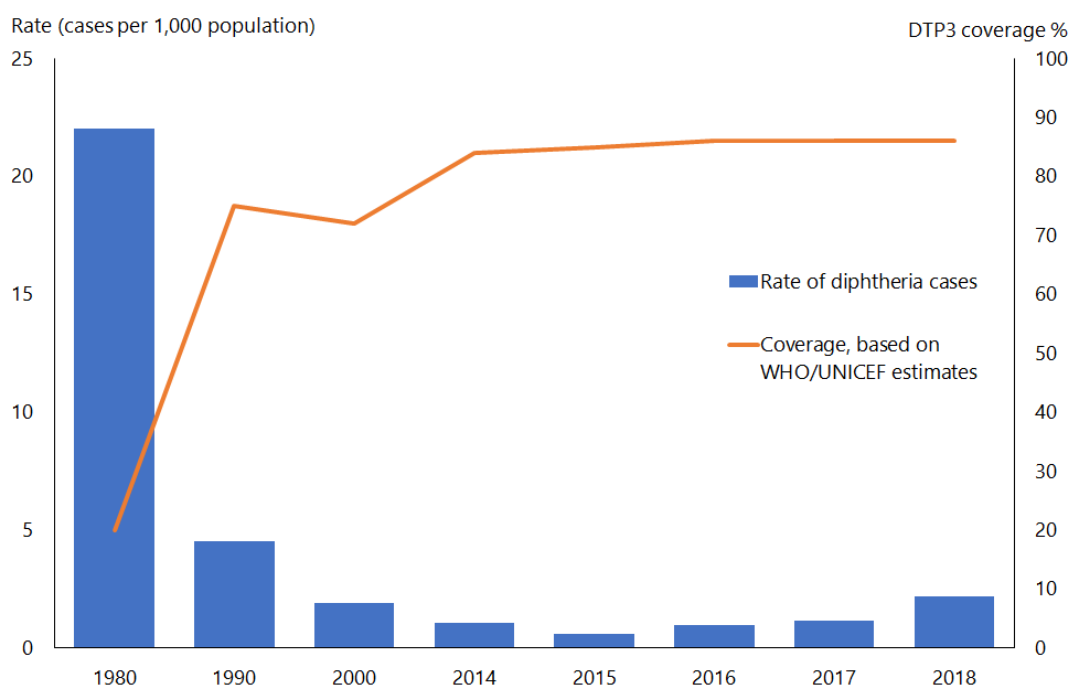
## 6.3 Epidemiology

### 6.3.1 Global burden of disease

In the pre-immunisation era, diphtheria was predominantly a disease of children aged under 15 years; most adults acquired immunity without experiencing clinical diphtheria. Asymptomatic carriage was common (3–5 percent) and important in perpetuating both endemic and epidemic diphtheria. The global incidence of diphtheria dropped dramatically during the 20th century. Immunisation played a large part but may not be wholly responsible for this reduction (see Figure 6.1). The estimated total number of diphtheria cases globally fell from just under 100,000 cases in 1980 to around 4,500 in 2015, but increased to over 16,500 cases in 2018.<sup>4</sup>

Diphtheria remains a significant health issue in countries with low immunisation coverage. Around 14 percent of children globally are not fully immunised against diphtheria and all countries have pockets of unvaccinated children.<sup>5</sup> Most cases of diphtheria reported during 2011–2015 were in South-East Asia, in particular India and Indonesia, but under-reporting has been shown for Africa and Eastern Mediterranean regions.<sup>5</sup>

**Figure 6.1: Diphtheria global annual reported cases and DTP3\* immunisation coverage, 1980–2018**



\* Three doses of diphtheria, tetanus and pertussis vaccine in infancy.

Source: WHO/UNICEF as of December 2019

Immunisation leads to the disappearance of circulating toxigenic strains, but non-toxigenic strains infected with the  $\beta$ -corynebacteriophage can become toxigenic during outbreaks. The return of epidemic diphtheria is a real threat when herd immunity is insufficient, as happened in the states of the former Soviet Union during 1990–1997. Factors contributing to this epidemic included a large population of susceptible adults, decreased childhood immunisation, suboptimal socioeconomic conditions and high population movement.<sup>6</sup>

Most reported cases were unvaccinated or incompletely vaccinated adolescents and adults (40 percent of cases were age over 15 years in high-incidence countries and 66 percent in low incidence countries) due to historically low coverage and a lack of booster doses to maintain protection in adolescents and adults. This vulnerability in adults was highlighted by a recent outbreak in Indonesia.<sup>7</sup> However, continuing endemic cutaneous diphtheria in indigenous communities has been reported from the US, Canada and Australia. Small diphtheria outbreaks occurring in high-income countries often appear to be caused by non-immune individuals travelling to endemic countries.<sup>1</sup>

The overall case fatality rate for clinical diphtheria is 5–10 percent, with higher death rates (up to 20 percent) among persons younger than 5 and older than 40 years. The case-fatality rate for diphtheria has changed very little during the last 50 years.<sup>8</sup>

Diphtheria remains rare in high-income countries such as New Zealand due to widespread use of diphtheria toxoid-containing vaccines. Falling immunisation coverage rates worldwide increases the risk for diphtheria outbreaks.

## 6.3.2 New Zealand epidemiology

Diphtheria infection was common in New Zealand until the 1960s. The last case of toxigenic respiratory diphtheria was reported in 1998.<sup>9</sup> Low numbers of cutaneous toxigenic diphtheria are regularly notified in New Zealand: two confirmed cases were notified in 2015 in refugees from Afghanistan<sup>10</sup> and one case was notified in 2019 in an immunised child from Papua New Guinea.

Non-toxigenic *C. diphtheria* isolates continue to be identified; for example, there were seven throat and 41 cutaneous non-toxigenic isolates and seven from other sites in 2019 (ESR, 8 June 2020). These strains do not cause diphtheria disease.

Travel to endemic countries is an important risk factor for infection, but transmission within New Zealand can occur to susceptible contacts of cutaneous cases. Tattooing practices in the Pacific Islands have also been implicated in outbreaks in New Zealand.<sup>11</sup>

The 2005–2007 National Serosurvey of Vaccine Preventable Diseases found that 61 percent of 6–10-year-olds, 77 percent of 11–15-year-olds, 71 percent of 16–24-year-olds, 48 percent of 25–44-year-olds and 46 percent of  $\geq 45$ -year-olds had presumed protective levels of diphtheria antibody.<sup>12</sup> The decline apparent with age suggests there is likely to be a large and increasing pool of older adults who may be susceptible to diphtheria in New Zealand, despite the introduction of adult tetanus and diphtheria (Td) vaccination in 1994.

For details of diphtheria notifications, refer to the most recent ESR notifiable disease annual tables and reports (available at [www.esr.cri.nz/digital-library/notifiable-disease-dashboard/](http://www.esr.cri.nz/digital-library/notifiable-disease-dashboard/)).

## 6.4 Vaccines

Diphtheria toxoid is prepared from cell-free purified diphtheria toxin treated with formaldehyde. It is a relatively poor immunogen, which, to improve its efficacy, is usually adsorbed onto an adjuvant, either aluminium phosphate or aluminium hydroxide.

Diphtheria toxoid is only available as a component of combination vaccines (in New Zealand as DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap).

See Appendix 1 for the history of diphtheria toxoid-containing vaccines in New Zealand.

### 6.4.1 Available vaccines

#### Funded diphtheria vaccines

The diphtheria toxoid-containing vaccines funded as part of the Schedule are as follows.

DTaP-IPV-HepB/Hib (Infanrix-hexa, GSK): diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and *Haemophilus influenzae* type b vaccine, which contains:

- not less than 30 IU of diphtheria and 40 IU of tetanus toxoids and three purified Bordetella pertussis antigens (25 µg of pertussis toxoid; 25 µg of filamentous hemagglutinin; 8 µg of pertactin, a 69 kilodalton outer membrane protein) adsorbed onto aluminium salts
- three types of inactivated polio viruses: 40 D-antigen units of type 1 (Mahoney), 8 D-antigen units of type 2 (MEF-1) and 32 D-antigen units of type 3 (Saukett)
- 10 µg of purified major surface antigen (HBsAg) of the hepatitis B virus (HBV)
- 10 µg of purified polyribosylribitol phosphate (PRP) capsular polysaccharide of *Haemophilus influenzae* type b (Hib), covalently bound to 20–40 µg tetanus toxoid, adsorbed onto aluminium salts
- lactose, sodium chloride, Medium 199, potassium chloride, disodium phosphate, monopotassium phosphate, polysorbate 20 and 80, glycine, formaldehyde, neomycin sulphate and polymyxin B sulphate, which are also present as other components or as trace residuals from the manufacturing process.

DTaP-IPV (Infanrix-IPV, GSK): diphtheria, tetanus, acellular pertussis and inactivated polio vaccine, in the same quantities as for Infanrix-hexa above. Other components and residuals include sodium chloride, aluminium salts, Medium 199, potassium chloride, disodium phosphate, monopotassium phosphate, polysorbate 80, glycine, formaldehyde, neomycin sulphate and polymyxin B sulphate.

Tdap (Boostrix, GSK): a smaller adult dose of diphtheria toxoid and pertussis antigens together with tetanus toxoid. Tdap contains not less than 2 IU of diphtheria toxoid, not less than 20 IU of tetanus toxoid, 8 µg of pertussis toxoid, 8 µg of filamentous hemagglutinin and 2.5 µg of pertactin, adsorbed onto aluminium salts. Other components and trace residuals include sodium chloride, formaldehyde, polysorbate 80 and glycine.

## Other vaccines

Other diphtheria toxoid-containing vaccines registered (approved for use) and available (marketed) in New Zealand are:

- Tdap: Adacel (Sanofi)
- Tdap-IPV: Adacel Polio (Sanofi).

## 6.4.2 Efficacy and effectiveness

Immunity against toxigenic diphtheria occurs via an antibody-mediated response to the diphtheria toxin and is primarily of the IgG type. Antitoxin antibodies can pass through the placenta to provide passive immunity to the newborn.

Although there are no randomised controlled studies on the efficacy of the vaccine, between 87 and 98 percent protection has been demonstrated using population-based analyses. Immunised cases have been shown to have less severe disease, as highlighted during the outbreak in the former Soviet Union.

Vaccines combining pertussis antigens with diphtheria and tetanus toxoids have been gradually introduced into immunisation schedules throughout the world. Immunogenicity data for these combination vaccines is discussed in section 16.4.2.

### Herd immunity

Immunisation is more effective at preventing disease, by neutralising diphtheria toxin, than preventing infection. Herd immunity is created by reducing carriage and transmission from symptomatic patients.<sup>13, 14</sup> To prevent major community outbreaks, it has been suggested that 70 percent or more of the childhood population must be immune to diphtheria.<sup>15, 16</sup> Herd immunity in adults is likely to depend on the size of the reservoir of disease in children.<sup>1</sup> This may explain the control of diphtheria in New Zealand despite historically relatively poor coverage.

### Duration of immunity

Diphtheria antitoxin levels decline over time in children after they have received a primary series of vaccines, and a booster dose is required. In countries where diphtheria immunisation is common practice and high coverage rates are achieved, there will be no natural boosting from circulating disease, and antitoxin levels declining with increasing age may result in a susceptible older adult population.<sup>5</sup> WHO identified that adults in countries with long-standing childhood immunisation programmes were likely to be susceptible without booster doses to overcome waning immunity due to lack of exposure to diphtheria. Waning immunity contributed to the high number of cases in adults observed during the outbreak in the former Soviet Union.<sup>17</sup>

Despite apparent immunity gaps, there has been minimal disease in high-income countries, suggesting that the established correlates of seroprotection based on antitoxin levels may not be reliable guides for protection and that other factors may be operating.<sup>18</sup> For example, a high proportion of the adult German population have low antibody levels, indicating susceptibility, yet diphtheria outbreaks have not occurred despite Germany's relative geographical proximity to high rates of disease in the former Soviet Union.<sup>19</sup>

The duration of protection after Tdap boosters is unknown, but the results of an Australian study have shown that five years after the Tdap booster dose, 94.4 percent of adults had seroprotective levels of antibodies against diphtheria, compared with 93.7 percent who received Td vaccine.<sup>20</sup> It has been predicted that 95 percent of the

adult population in the US would maintain seroprotection for more than 30 years without requiring further booster doses.<sup>21</sup>

### 6.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at [www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

Store at +2°C to +8°C. Do not freeze. DTaP-IPV-HepB/Hib and Tdap should be stored in the dark.

DTaP-IPV-HepB/Hib (Infanrix-hexa) must be reconstituted by adding the entire contents of the supplied container of the DTaP-IPV-HepB vaccine to the vial containing the Hib-PRP pellet. After adding the vaccine to the pellet, the mixture should be shaken until the pellet is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.

### 6.4.4 Dosage and administration

The dose of DTaP-IPV-HepB/Hib, DTaP-IPV or Tdap vaccine is 0.5 mL, administered by intramuscular injection (see section 2.2.3).

#### Co-administration with other vaccines

DTaP-IPV-HepB/Hib, DTaP-IPV or Tdap vaccine can be administered simultaneously (at separate sites) with other vaccines or IGs.



## 6.5 Recommended immunisation schedule

**Table 6.1: Immunisation schedule for diphtheria-containing vaccines (excluding catch-up)**

Age	Vaccine	Comment
Pregnant women – recommended from 16 weeks' gestation of every pregnancy, preferably in the second trimester (funded when given any time in second or third trimester)	Tdap	Booster for mother <sup>a</sup> Passive immunity for infant
6 weeks	DTaP-IPV-HepB/Hib	Primary series
3 months	DTaP-IPV-HepB/Hib	Primary series
5 months	DTaP-IPV-HepB/Hib	Primary series
4 years	DTaP-IPV	Booster
11 years	Tdap	Booster
45 years (individuals who have not received 4 tetanus vaccinations in their lifetime)	Tdap	Booster
65 years	Tdap	Booster

a Tdap booster during pregnancy is to protect against mother and newborn against pertussis (see section 4.1.2).

### 6.5.1 Usual childhood schedule

A primary course of diphtheria vaccine is given as DTaP-IPV-HepB/Hib (Infanrix-hexa) at ages 6 weeks, 3 months and 5 months, followed by a dose of DTaP-IPV (Infanrix-IPV) at age 4 years (Table 6.1). A booster is given at age 11 years (school year 7), which includes a pertussis component given as the vaccine Tdap (Boostrix).

If a course of immunisation is late or interrupted for any reason, it may be resumed without repeating prior doses (see Appendix 2).

### 6.5.2 Catch-ups for individuals aged 10 years and older

For previously unimmunised individuals aged 10 years and older, a primary immunisation course consists of three doses of a diphtheria toxoid-containing vaccine at intervals of not less than four weeks (see Appendix 2). For children aged under 18 years, a booster dose is recommended at least six months after the third dose.

Children aged under 18 years may receive Tdap (funded from age 7 to under 18 years); adults aged 18 years and older may receive Tdap (funded). Although Tdap is not approved for use (registered) as a primary course, there are expected to be no safety concerns.

### 6.5.3 Booster doses for adolescents and adults

Studies overseas show that many adults lack protective levels of the antitoxin, and this has led to concern about waning immunity and recommendations for booster doses beyond childhood (see also section 6.3.2). Most authorities recommend maintaining diphtheria immunity by periodic reinforcement using a combined Td vaccine.<sup>1</sup> A single booster dose of Tdap induces seroprotective levels of antibodies to diphtheria and tetanus in virtually all children and adolescents, and in a high proportion of adults and elderly individuals at approximately one month post-vaccination, irrespective of their vaccination history.<sup>22</sup>

Tdap is recommended and funded:

- as a booster dose to all adolescents at school year 7 or age 11 years
- as a booster dose for vaccination of individuals aged 65 years old
- as a single dose for catch-up vaccination of individuals aged 45 years old who have not had four previous tetanus-containing doses.

These age-specific recommendations may facilitate the linkage of adult immunisation to the delivery of other preventive health measures.

#### Booster doses before travel

If someone is travelling to an area endemic for diphtheria, or there is another reason to ensure immunity, a booster dose is recommended (but not funded) if it is more than 10 years since the last dose. For website sources on travel vaccines, see Appendix 8.

### 6.5.4 Pregnancy and breastfeeding

Pregnant women should receive a dose of Tdap in every pregnancy so that antibodies can pass to the fetus to provide pertussis protection from birth (funded when given any time in second or third trimester). It is recommended to be given from 16 weeks' gestation of every pregnancy, preferably in the second trimester to protect both the mother and her infant from pertussis (see section 17.5.2).<sup>23</sup>

Tdap vaccine may also be given to pregnant women when catch-up is needed for an under-immunised woman, or for management of a tetanus-prone wound (see section 22.5.5).<sup>23, 24</sup>

Tdap vaccines can be given to breastfeeding women.<sup>24</sup>

## 6.5.5 (Re)vaccination

Diphtheria toxoid-containing vaccines are funded for (re)vaccination of eligible patients as follows, including prior to planned or following immunosuppression. See also sections 4.3.6 and 4.3.7.

### DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV)

Up to an additional four doses (as appropriate) of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for (re)vaccination of patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- prior to planned or following other severely immunosuppressive regimens.

Up to an additional four doses (as appropriate) of DTaP-IPV-HepB/Hib are funded for children aged 10 years to under 18 years for (re)vaccination of patients post HSCT. This is an off-label use of this vaccine which requires a prescription from an authorised prescriber or the patient's specialist. In this group, all prior immunity will have been lost and revaccination is equivalent to a primary immunisation schedule. DTaP-IPV-HepB/Hib not recommended for other severely immunocompromised individuals aged 10-18 years that require revaccination as they may have residual immune memory.

### Tdap (Boostrix)

An additional four doses (as appropriate) of Tdap (Boostrix) are funded for patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- prior to planned or following other severely immunosuppressive regimens.

## 6.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

### 6.6.1 Contraindications

There are no specific contraindications to diphtheria vaccine (as Tdap or DTaP), except for anaphylaxis to a previous dose or any component of the vaccine.

Most other cases of hypersensitivity that have been reported for tetanus-containing vaccines were in individuals who have had an excessive number of booster injections outside the guidelines noted above (see section 22.6.2).

### 6.6.2 Precautions

See section 16.6.2 for precautions for pertussis-containing vaccines and section 22.6.2 for precautions for tetanus-containing vaccines.

## 6.7 Potential responses and AEFIs

Despite the widespread use of diphtheria toxoid, the 1994 Institute of Medicine review of vaccine reactions did not identify any reaction for which the evidence favoured or established a causal relationship with diphtheria toxoid.<sup>25</sup> However, local and systemic reactions do occur with diphtheria toxoid-containing vaccine, especially when the infant vaccine is used in older children and adults. Mild discomfort or pain at the injection site persisting for up to a few days is common.<sup>24</sup>

See also sections 16.7 and 22.7 for potential responses and AEFIs to DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap.

## 6.8 Public health measures

It is a legal requirement that all cases of diphtheria be notified immediately on suspicion to the local medical officer of health. Notification should not await confirmation.

All isolates of *C. diphtheriae* and *C. ulcerans* are notifiable until toxigenicity is determined, including cutaneous isolates. If the isolate is determined to be non-toxicogenic, the case should be de-notified.

All contacts should have cultures taken. Contacts who have a positive laboratory result should be isolated as if they are a case until proven bacteriologically negative.

For detailed information about public health control measures and case definition see the diphtheria chapter of the Communicable Disease Control Manual at [www.tewhaturora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/diphtheria/](http://www.tewhaturora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/diphtheria/)

### 6.8.1 Antimicrobial prophylaxis

All contacts, after cultures have been taken and **regardless of immunisation status**, require antimicrobial prophylaxis. For more information see the Communicable Disease Control Manual at [www.tewhaturora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/diphtheria/](http://www.tewhaturora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/diphtheria/).

### 6.8.2 Vaccination of contacts

All close contacts should also be offered a complete course of vaccine or a booster according to the following schedule.

- Fully immunised children up to and including 6 years of age who have only received three doses of diphtheria toxoid-containing vaccine: give one injection of a DTaP-IPV.
- Fully immunised individuals aged 7 years and older who have not received a booster dose of a diphtheria toxoid-containing vaccine within the last five years: give one injection of Tdap – funded if aged 10–17 years; unfunded if aged 18 years or older (see section 6.5).
- Unimmunised individuals: see Appendix 2.

## 6.9 Variations from the vaccine data sheets

See section 16.9 for variations from the DTaP-IPV-HepB/Hib (Infanrix-hexa), DTaP-IPV (Infanrix-IPV) and Tdap (Boostrix) data sheets.

### References

1. Tiwari TSP ,Wharton M. 2018. Diphtheria Toxoid, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
2. Belsey MA, Sinclair M, Roder MR,LeBlanc DR. *Corynebacterium diphtheriae* skin infections in Alabama and Louisiana. A factor in the epidemiology of diphtheria. *New England Journal of Medicine*, 1969. 280(3): p. 135-41.
3. Koopman JS ,Campbell J. The role of cutaneous diphtheria infections in a diphtheria epidemic. *Journal of Infectious Diseases*, 1975. 131(3): p. 239-44.
4. World Health Organization. *Diphtheria reported cases to 2018*. [updated 10 December 2019 ]; URL: [http://apps.who.int/immunization\\_monitoring/globalsummary/timeseries/tsincidencediphtheria.html](http://apps.who.int/immunization_monitoring/globalsummary/timeseries/tsincidencediphtheria.html). (accessed 19 February 2020 )
5. World Health Organization. Diphtheria vaccine: WHO position paper - August 2017. *Weekly Epidemiological Record*, 2017. 92(31): p. 417-35.
6. Vitek CR ,Wharton M. Diphtheria in the former Soviet Union: reemergence of a pandemic disease. *Emerging Infectious Diseases*, 1998. 4(4): p. 539-50.
7. Rengganis I. Adult Diphtheria Vaccination. *Acta Medica Indonesiana*, 2018. 50(3): p. 268-272.
8. Centers for Disease Control and Prevention. 2012. Diphtheria. in *Epidemiology and Prevention of Vaccine-Preventable Diseases (12th edition)*, Atkinson W, Hamborsky J, Wolfe S, and al e (eds). Washington, DC. URL: <https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/dip.pdf>. (accessed 10 May 2022)
9. Baker M, Taylor P ,Wilson E. A case of diphtheria in Auckland: implications for disease control. *New Zealand Public Health Report*, 1998. 5(10): p. 73-6.
10. Institute of Environmental Science and Research Ltd. 2016. *Notifiable Diseases in New Zealand: Annual Report 2015* (ed.), Porirua, New Zealand: The Institute of Science and Environmental Research Ltd. URL: [https://surv.esr.cri.nz/PDF\\_surveillance/AnnualRpt/AnnualSurv/2015/2015AnnualReportFinal.pdf](https://surv.esr.cri.nz/PDF_surveillance/AnnualRpt/AnnualSurv/2015/2015AnnualReportFinal.pdf) (accessed 3 July 2020)
11. Sears A, McLean M, Hingston D, et al. Cases of cutaneous diphtheria in New Zealand: implications for surveillance and management. *New Zealand Medical Journal*, 2012. 125(1350): p. 64-71.
12. Weir R, Jennings L, Young S,et al. 2009. *National Serosurvey of Vaccine Preventable Diseases*. <https://www.health.govt.nz/system/files/documents/publications/national-serosurvey-of-vaccine-preventable-diseases-may09.pdf> (accessed 30 June 2020)
13. Fine PE. Herd immunity: history, theory, practice. *Epidemiologic Reviews*, 1993. 15(2): p. 265-302.

14. Fine P, Mulholland K, Scott J, Edmunds W. 2018. Community Protection, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
15. Smith JW. Diphtheria and tetanus toxoids. *British Medical Bulletin*, 1969. 25(2): p. 177-82.
16. Ad-hoc Working Group. Susceptibility to diphtheria. *The Lancet*, 1978. 311(8061): p. 428-30.
17. Strategic Advisory Group of Experts on Immunisation (SAGE). 2017 *Diphtheria vaccine. Review of evidence on vaccine effectiveness and immunogenicity to assess the duration of protection  $\geq 10$  years after the last booster dose*. Geneva. URL: [https://www.who.int/immunization/sage/meetings/2017/april/presentations\\_background\\_docs/en/](https://www.who.int/immunization/sage/meetings/2017/april/presentations_background_docs/en/). (accessed 18 June 2020)
18. Bowie C. Tetanus toxoid for adults--too much of a good thing. *Lancet*, 1996. 348(9036): p. 1185-6.
19. Stark K, Barg J, Molz B, et al. Immunity against diphtheria in blood donors in East Berlin and West Berlin. *Lancet*, 1997. 350(9082): p. 932.
20. McIntyre PB, Burgess MA, Egan A, et al. Booster vaccination of adults with reduced-antigen-content diphtheria, Tetanus and pertussis vaccine: immunogenicity 5 years post-vaccination. *Vaccine*, 2009. 27(7): p. 1062-6.
21. Hammarlund E, Thomas A, Poore EA, et al. Durability of Vaccine-Induced Immunity Against Tetanus and Diphtheria Toxins: A Cross-sectional Analysis. *Clinical Infectious Diseases*, 2016. 62(9): p. 1111-1118.
22. McCormack PL. Reduced-antigen, combined diphtheria, tetanus and acellular pertussis vaccine, adsorbed (Boostrix®). A review of its properties and use as a single-dose booster immunization. *Drugs*, 2012. 72(13): p. 1765-1791.
23. Havers FP, Moro PL, Hunter P, et al. Use of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccines: updated recommendations of the Advisory Committee on Immunization Practices – United States, 2019. *MMWR: Morbidity and Mortality Weekly Report*, 2020. 69(3): p. 77-83.
24. Australian Technical Advisory Group on Immunisation. 2018. *Australian Immunisation Handbook* (ed.), Canberra: Australian Government Department of Health. URL: <https://immunisationhandbook.health.gov.au/> (accessed October 2019)
25. Stratton KR, Howe CJ, Johnston RB, Jr. Adverse events associated with childhood vaccines other than pertussis and rubella. Summary of a report from the Institute of Medicine. *JAMA*, 1994. 271(20): p. 1602-5.



# 7 *Haemophilus influenzae* type b (Hib) disease

## Key information

Mode of transmission	By inhalation of respiratory tract droplets or by direct contact with respiratory tract secretions.
Incubation period	Unknown, but probably 2–4 days.
Period of communicability	May be prolonged. Non-communicable within 24–48 hours after starting effective antimicrobial therapy.
Burden of disease	Children aged under 5 years, particularly those aged under 1 year: meningitis, epiglottitis, pneumonia and bacteraemia.
Funded vaccines	DTaP-IPV-HepB/Hib (Infanrix-hexa). Hib-PRP (Act-HIB).
Dose, presentation, route	DTaP-IPV-HepB/Hib and Hib-PRP: <ul style="list-style-type: none"><li>• 0.5 mL per dose after reconstitution</li><li>• pre-filled syringe and glass vial – the vaccines must be reconstituted prior to injection</li><li>• intramuscular injection (Hib-PRP can also be administered subcutaneously).</li></ul>
Funded vaccine indications and schedule	Usual childhood schedule: <ul style="list-style-type: none"><li>• at ages 6 weeks, 3 months and 5 months: DTaP-IPV-HepB/Hib</li><li>• at age 15 months: Hib-PRP.</li></ul> For (re)vaccination of eligible patients: <ul style="list-style-type: none"><li>• up to 4 additional doses of DTaP-IPV-HepB/Hib (for eligible children &lt;10 years); or</li><li>• 1 additional dose of Hib-PRP.</li></ul> For children <10 years receiving solid organ transplantation: up to 5 doses of DTaP-IPV-HepB/Hib. For testing for primary immune deficiencies: Hib-PRP.
Vaccine effectiveness	Hib disease has been almost eliminated in countries where Hib vaccine is used.
Public health measures	All cases of Hib disease be notified immediately on suspicion. (see section 7.8) All child contacts should have their immunisation status assessed and updated as appropriate.
Post exposure prophylaxis	Antimicrobial prophylaxis should be administered to contacts as appropriate (see section 7.8).

## 7.1 Bacteriology

*Haemophilus influenzae* is a gram-negative coccobacillus, which occurs in typeable and non-typeable (NTHi) forms. There are six antigenically distinct capsular types (a–f), of which type b is the most important. Before the introduction of the vaccine, *H. influenzae* type b (Hib) caused 95 percent of *H. influenzae* invasive disease in infants and children.

## 7.2 Clinical features

Transmission is by inhalation of respiratory tract droplets or by direct contact with respiratory tract secretions. Hib causes meningitis and other focal infections (such as pneumonia, septic arthritis and cellulitis) in children, primarily those aged under 2 years, while epiglottitis was more common in children over 2 years. Invasive Hib disease was rare over the age of 5 years, but could occur in adults. In the absence of vaccination these presentations may still occur. There have always been a small number of cases of *H. influenzae* invasive disease in adults, and these continue to occur. The incubation period of the disease is unknown, but is probably from two to four days.

Immunisation against Hib does not protect against infections due to other *H. influenzae* types or NTHi strains. Non-typeable *H. influenzae* (NTHi) organisms usually cause non-invasive mucosal infections, such as otitis media, sinusitis and bronchitis, but can occasionally cause bloodstream infection, especially in neonates. They are frequently present (60–90 percent) in the normal upper respiratory tract flora.

Young infants (aged under 2 years) do not produce an antibody response following Hib invasive disease, so a course of Hib-PRP vaccine is recommended when they have recovered (see section 7.5.3).

Hib and NTHi strains also cause diseases (including pneumonia and septicaemia) in the elderly.

## 7.3 Epidemiology

### 7.3.1 Global burden of disease

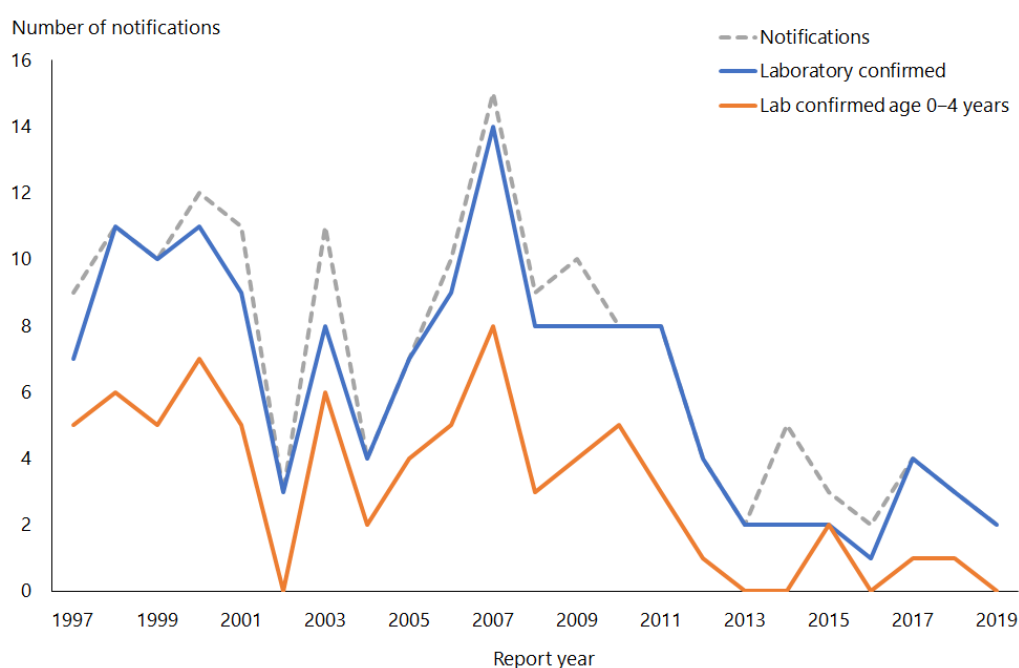
The source of the organism is the upper respiratory tract. Immunisation with a protein conjugate vaccine reduces the frequency of asymptomatic colonisation by Hib. Before the introduction of the vaccine, Hib was the most common cause of bacterial meningitis in children. Worldwide immunisation coverage is increasing, with approximately 194 countries having fully or partially introduced Hib onto their schedules by July 2019 (98 percent of all WHO member states).<sup>1</sup> The estimated global coverage for three doses of Hib is 72 percent as of July 2019.<sup>2</sup>

## 7.3.2 New Zealand epidemiology

Hib-PRP was introduced in 1994 (see Appendix 1). In 1993, 101 children aged under 5 years had laboratory-confirmed invasive Hib disease (an age-specific rate of 36.4 per 100,000 population). By 1999 only five children in this age group had laboratory-confirmed disease (1.7 per 100,000) (Figure 7.1).

Two cases of Hib were notified and laboratory confirmed in 2019 (ESR, 8 June 2020). The cases were aged 50–59 and 60–69 years, both were unvaccinated. There were seven deaths from Hib between 1997 and 2019 (ESR, 8 June 2020), the most recent was in 2012 in an adult over 70 years of age.<sup>3</sup>

**Figure 7.1: Number of notifications and culture-positive cases of *Haemophilus influenzae* type b invasive disease, 1997–2019**



Source: ESR

For details of Hib notifications, refer to the most recent ESR notifiable disease annual tables and reports (available at [www.esr.cri.nz/digital-library/notifiable-disease-dashboard/](http://www.esr.cri.nz/digital-library/notifiable-disease-dashboard/)).

## 7.4 Vaccines

Antibodies to PRP, a component of the polysaccharide cell capsule of Hib, are protective against invasive Hib disease. To induce a T-cell dependent immune response, the polyribosylribitol phosphate (PRP) polysaccharide has been linked (conjugated) to a variety of protein carriers. These conjugate Hib vaccines are immunogenic and effective in young infants (see also section 1.4.3). The protein carriers used are either an outer membrane protein of *Neisseria meningitidis* (Hib-PRP-OMP vaccine), or a tetanus toxoid (Hib-PRP vaccine).

Note that the protein conjugates used in Hib vaccines are not themselves expected to be immunogenic and do not give protection against *N. meningitidis* or tetanus.

## 7.4.1 Available vaccines

### Funded vaccines

The Hib vaccines funded as part of the Schedule are:

- Hib-PRP, given as the hexavalent vaccine DTaP-IPV-HepB/Hib (Infanrix-hexa, GSK). It contains diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and *Haemophilus influenzae* type b vaccine (see section 6.4 for more information)
- Hib-PRP given as monovalent Hib vaccine (Act-HIB, Sanofi). It contains 10 µg of purified Hib capsular PRP polysaccharide conjugated to 18-30 µg of tetanus protein. Other components (excipients) include trometamol and sucrose and sterile saline solution in the diluent.

### Other vaccines

No other Hib vaccines are available currently. Hib-PRP (Hiberix, GSK) was the funded vaccine prior to October 2024.

## 7.4.2 Efficacy and effectiveness

The high efficacy and effectiveness of Hib-PRP vaccines have been clearly demonstrated by the virtual elimination of Hib in countries implementing the vaccine,<sup>4-6</sup> including New Zealand. Hib-PRP vaccines are highly effective after a primary course of two or three doses.<sup>7-9</sup> Disease following a full course of Hib-PRP is rare.

Conjugate vaccines reduce carriage in immunised children and as a result also decrease carriage and disease in unimmunised people (herd immunity). These vaccines will not protect against infection with NTHi strains, and therefore do not prevent the great majority of otitis media, recurrent upper respiratory tract infections, sinusitis or bronchitis.

(See also section 16.4.2 for information about the DTaP-IPV-HepB/Hib vaccine.)

### Duration of immunity

A primary series followed by a booster dose in the second year of life should provide sufficient antibody levels to protect against invasive Hib disease to at least the age of 5 years.<sup>10</sup>

### 7.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at [www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

Store at +2°C to +8°C. Do not freeze. DTaP-IPV-HepB/Hib should be stored in the dark.

DTaP-IPV-HepB/Hib vaccine (Infanrix-hexa) must be reconstituted by adding the entire contents of the pre-filled syringe containing DTaP-IPV-HepB vaccine to the vial containing the Hib powder. After adding the vaccine to the powder, the mixture should be shaken until the powder is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.

Monovalent Hib-PRP vaccine (Act-HIB) must be reconstituted with the supplied diluent and used immediately after reconstitution.

### 7.4.4 Dosage and administration

The dose of DTaP-IPV-HepB/Hib and Hib-PRP vaccines is 0.5 mL administered by intramuscular injection. Hib-PRP can also be administered subcutaneously if indicated (see section 2.2.3).

#### Co-administration

DTaP-IPV-HepB/Hib and Hib-PRP vaccines can be co-administered with other routine vaccines on the Schedule, in separate syringes and at separate sites.

## 7.5 Recommended immunisation schedule

### 7.5.1 Usual childhood schedule

Hib vaccine is funded for all children aged under 5 years. Three doses of DTaP-IPV-HepB/Hib (Infanrix-hexa) vaccine are given as the primary course, with a booster of monovalent Hib-PRP at age 15 months (see Table 7.1).

**Table 7.1: Usual childhood Hib schedule (excluding catch-up)**

Age	Vaccine	Comment
6 weeks	DTaP-IPV-HepB/Hib	Primary series
3 months	DTaP-IPV-HepB/Hib	Primary series
5 months	DTaP-IPV-HepB/Hib	Primary series
15 months	Hib-PRP	Booster

For children aged under 5 years who, for whatever reason, have missed out on Hib vaccine in infancy, a catch-up schedule is recommended. The total number of doses of Hib vaccine required is determined by the age at which Hib immunisation commences. Where possible, the combined available vaccines should be used, but individual immunisation schedules based on the recommended national schedule may be required for children who have missed some immunisations (see Appendix 2).

## 7.5.2 Special groups

### Children

Because of an increased risk of infection, it is particularly important that the following groups of children, whatever their age, receive the Hib vaccine as early as possible (see also sections 4.2 and 4.3):

- children with anatomical or functional asplenia, or who are suffering from sickle cell disease (if possible, it is recommended that children be immunised prior to splenectomy)
- children with partial immunoglobulin deficiency, Hodgkin's disease or following chemotherapy (note, however, that response to the vaccine in these children is likely to be suboptimal)
- children with nephrotic syndrome
- HIV-positive children.

### Recommendations for Hib vaccine for older children and adults with asplenia

Although there is no strong evidence of an increased risk of invasive Hib disease in asplenic older children and adults, some authorities recommend Hib immunisation for these individuals.<sup>11, 12</sup> The Hib PRP-T vaccine has been shown to be immunogenic in adults.

- Monovalent Hib-PRP vaccine is funded for older children and adults pre- or post-splenectomy or with functional asplenia; one dose of vaccine is recommended (see also section 4.3.3) if childhood vaccine schedule is incomplete or unknown.

Note: Pneumococcal, meningococcal, influenza, varicella and pertussis-containing vaccines are also recommended for these individuals; see section 4.3 and the relevant disease chapters.

## 7.5.3 Children who have recovered from invasive Hib disease

Children aged under 2 years with Hib disease do not reliably produce protective antibodies and need to receive a complete course of Hib-PRP. The number of doses required will depend on the age at which the first dose after the illness is given, **ignoring** any doses given before the illness (follow the age-appropriate catch-up schedules in Appendix 2).

Commence immunisation approximately four weeks after the onset of disease.

Any immunised child who develops Hib disease or who experiences recurrent episodes of Hib invasive disease requires immunological investigation by a paediatrician.

## 7.5.4 (Re)vaccination

Hib-PRP-containing vaccines are funded for vaccination and revaccination of eligible patients, as follows. See also section 4.3.

### DTaP-IPV-HepB/Hib (Infanrix-hexa)

Up to an additional four doses (as appropriate) of DTaP-IPV-HepB/Hib are funded for vaccination or revaccination of children aged under 10 years:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- prior to planned or following other severely immunosuppressive regimens.

Up to an additional four doses (as appropriate) of DTaP-IPV-HepB/Hib are funded for children aged 10 years to under 18 years for (re)vaccination of patients post HSCT. This is an off-label use of this vaccine which requires a prescription from an authorised prescriber or the patient's specialist. In this group, all prior immunity will have been lost and revaccination is equivalent to a primary immunisation schedule. DTaP-IPV-HepB/Hib not recommended for other severely immunocompromised individuals aged 10-18 years that require revaccination as they may have residual immune memory.

### Monovalent Hib-PRP

One additional dose of monovalent Hib-PRP is funded for vaccination or revaccination of patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy or with functional asplenia
- pre- or post-solid organ transplant
- pre- or post-cochlear implants



- undergoing renal dialysis
- prior to planned or after other severely immunosuppressive regimens.

## 7.5.5 Pregnancy and breastfeeding

Hib-PRP is not routinely recommended for pregnant or breastfeeding women. However, for women with asplenia see the 'Recommendations for Hib vaccine for older children and adults with asplenia' in section 7.5.2.

## 7.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general vaccine contraindications. Anaphylaxis to a previous vaccine dose or any component of the vaccine is an absolute contraindication to further vaccination with that vaccine.

See section 16.6 for contraindications and precautions to DTaP-IPV-HepB/Hib vaccine.

Hib-PRP vaccines should not be administered to people with a history of an anaphylactic reaction to a prior dose of Hib vaccine or to a vaccine component. Significant hypersensitivity reactions to Hib vaccines appear to be extremely rare.

## 7.7 Potential responses and AEFIs

See section 16.7.1 for potential responses and AEFIs with DTaP-IPV-HepB/Hib vaccine.

### 7.7.1 Potential responses

Adverse reactions to Hib-PRP conjugate vaccines are uncommon. Pain, redness and swelling at the injection site occur in approximately 25 percent of recipients, but these symptoms typically are mild and last less than 24 hours.<sup>13</sup>

### 7.7.2 AEFIs

A meta-analysis of trials of Hib-PRP vaccination from 1990 to 1997 found that serious adverse events were rare.<sup>14</sup> No serious vaccine-related adverse experiences were observed during clinical trials of Hib vaccine alone. There have been rare reports, not proven to be causally related to Hib vaccine, of transverse myelitis, thrombocytopenia and Guillain-Barré syndrome (GBS).<sup>15</sup>

## 7.8 Public health measures

It is a legal requirement that all cases of Hib disease be notified immediately on suspicion to the local medical officer of health, who will arrange for contact tracing, immunisation and administration of prophylactic rifampicin, where appropriate.

For detailed information see the Communicable Disease Control Manual at [www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/haemophilus-influenzae-type-b-invasive-disease/](http://www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/haemophilus-influenzae-type-b-invasive-disease/)

### 7.8.1 Management of contacts

All child contacts should have their immunisation status assessed and updated, as appropriate.

Immunisation reduces – but does not necessarily prevent – the acquisition and carriage of Hib. Therefore, immunised children still need antimicrobial prophylaxis, when indicated, to prevent them transmitting infection to their contacts. All contacts need to be assessed for the need for antimicrobial prophylaxis.

For further information, see the Communicable Disease Control Manual at [www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/haemophilus-influenzae-type-b-invasive-disease/](http://www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/haemophilus-influenzae-type-b-invasive-disease/)

## 7.9 Variations from the vaccine data sheets

The Hib-PRP data sheet states that the vaccine is indicated for use in children aged up to 5 years. However, Health New Zealand | Te Whatu Ora recommends that all children and asplenic adults (see section 7.5.2) or those with specified immunocompromised conditions (see section 7.5.4) receive Hib-PRP vaccine.<sup>11, 16</sup> There are not expected to be any safety concerns in regard to use in older age groups.

See section 16.9 for variations from the DTaP-IPV-HepB/Hib (Infanrix-hexa) data sheet.

## References

1. World Health Organization ,UNICEF. 2019 *Progress and challenges with achieving universal immunisation coverage: 2018 WHO/UNICEF estimates of National Immunization Coverage*. Monitoring and Surveillance Monitoring and Surveillance; 2019 [updated July 2019]; URL: [https://www.who.int/immunization/monitoring\\_surveillance/who-immuniz.pdf?ua=1](https://www.who.int/immunization/monitoring_surveillance/who-immuniz.pdf?ua=1). (accessed 3 July 2020)
2. World Health Organization ,UNICEF. 2019 *Global and regional immunization profile*. URL: [https://www.who.int/immunization/monitoring\\_surveillance/data/gloprofile.pdf?ua=1](https://www.who.int/immunization/monitoring_surveillance/data/gloprofile.pdf?ua=1). (accessed 3 July 2020)
3. Institute of Environmental Science and Research Ltd. 2013. *Notifiable and Other Diseases in New Zealand: Annual Report 2012* (ed.), Porirua: Institute of Environmental Science and Research Ltd. URL: [https://surv.esr.cri.nz/PDF\\_surveillance/AnnualRpt/AnnualSurv/2012/2012AnnualSurvRpt.pdf](https://surv.esr.cri.nz/PDF_surveillance/AnnualRpt/AnnualSurv/2012/2012AnnualSurvRpt.pdf) (accessed 3 July 2020)
4. Ladhani SN. Two decades of experience with the *Haemophilus influenzae* serotype b conjugate vaccine in the United Kingdom. *Clinical Therapeutics*, 2012. 34(2): p. 385–99.
5. Bisgard KM, Kao A, Leake J, et al. *Haemophilus influenzae* invasive disease in the United States, 1994–1995: near disappearance of a vaccine-preventable childhood disease. *Emerging Infectious Diseases*, 1998. 4(2): p. 229–37.
6. MacNeil JR, Cohn AC, Farley M, et al. Current epidemiology and trends in invasive *Haemophilus influenzae* disease – United States, 1989–2008. *Clinical Infectious Diseases*, 2011. 53(12): p. 1230–6.
7. Griffiths UK, Clark A, Gessner B, et al. Dose-specific efficacy of *Haemophilus influenzae* type b conjugate vaccines: a systematic review and meta-analysis of controlled clinical trials. *Epidemiology & Infection*, 2012. 140(8): p. 1343–55.
8. O’Loughlin RE, Edmond K, Mangtani P, et al. Methodology and measurement of the effectiveness of *Haemophilus influenzae* type b vaccine: systematic review. *Vaccine*, 2010. 28(38): p. 6128–36.
9. Kalies H, Grote V, Siedler A, et al. Effectiveness of hexavalent vaccines against invasive *Haemophilus influenzae* type b disease: Germany’s experience after 5 years of licensure. *Vaccine*, 2008. 26(20): p. 2545–52.
10. Khatami A, Snape MD, John TM, et al. Persistence of immunity following a booster dose of *Haemophilus influenzae* type B-meningococcal serogroup C glycoconjugate vaccine: follow-up of a randomized controlled trial. *Pediatric Infectious Disease Journal*, 2011. 30(3): p. 197–202.
11. Centers for Disease Control and Prevention. 2014. Prevention and control of *Haemophilus influenzae* type b disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morbidity and Mortality Weekly Report: Recommendations and Reports*. 63(RR-1): p. 1–14. URL: <https://www.cdc.gov/mmwr/pdf/rr/rr6301.pdf> (accessed 3 July 2020)
12. Australian Technical Advisory Group on Immunisation (ATAGI). 2018. *Haemophilus influenzae* type b (Hib). in *Australian Immunisation Handbook*. Canberra. URL: <https://immunisationhandbook.health.gov.au/vaccine-preventable-diseases/haemophilus-influenzae-type-b-hib>. (accessed 6 July 2020)
13. American Academy of Pediatrics. 2018. *Haemophilus influenzae* infections. in *Red Book: 2018 Report of the Committee on Infectious Diseases*, Kimberlin D, Brady M, Jackson M, and Long S (eds). URL: <https://redbook.solutions.aap.org/redbook.aspx>. (accessed 3 July 2020)

14. Obonyo CO, Lau J. Efficacy of *Haemophilus influenzae* type b vaccination of children: a meta-analysis. *European Journal of Clinical Microbiology & Infectious Diseases*, 2006. 25(2): p. 90–97.
15. Nanduri S, Sutherland A, Gordon L, Santosham M. 2018. *Haemophilus influenzae* type b vaccines, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
16. Public Health England. 2016. Immunisation of individuals with underlying medical conditions. in *The Green Book*. URL: [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/566853/Green\\_Book\\_Chapter7.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/566853/Green_Book_Chapter7.pdf). (accessed 1 April 2017)

# 8 Hepatitis A

## Key information

Mode of transmission	Faecal–oral route, either from person-to-person contact or through contaminated food or drink. It is also occasionally spread by injected drug use.
Incubation period	28–30 days average (range 15–50 days).
Period of communicability	The 1–2 weeks before and the first few days after the onset of jaundice.
Burden of disease	Infants and children are usually asymptomatic. Severity in adults increases with age. The disease is more serious in those with chronic liver disease and the immunocompromised. There is no carrier state.
Funded vaccines	Monovalent inactivated hepatitis A virus (HAV) vaccine: Havrix.
Other available vaccines	Monovalent inactivated hepatitis A virus (HAV) vaccine: Avaxim. Combined inactivated HAV-recombinant HBsAg protein vaccine: Twinrix. Combined HAV-purified <i>Salmonella typhi</i> Vi polysaccharide vaccine: Vivaxim.
Dose, presentation, route	Havrix 1440, Twinrix, Vivaxim: 1.0 mL per dose. Havrix Junior, Twinrix Junior, Avaxim: 0.5 mL per dose. Pre-filled syringe. Intramuscular injection.
Funded vaccine indications and recommended schedule	HepA vaccine (Havrix 1440) is recommended and funded for: <ul style="list-style-type: none"> <li>• transplant patients – 2 doses</li> <li>• children with chronic liver disease – 2 doses</li> <li>• close contacts of hepatitis A cases – 1 dose.</li> </ul>
Recommended, unfunded	Individuals working with children, exposed to faeces or contaminated water, or with non-human primates Armed forces personnel and travellers visiting high-risk countries Adults with chronic liver disease, including with chronic hepatitis B and C infection Men who have sex with men Food handlers during community outbreaks
Vaccine efficacy	High efficacy: HAV infection has been almost eliminated in immunised populations.
Public health measures	All cases of hepatitis A must be notified immediately on suspicion to local medical officer of health
Post-exposure prophylaxis	In an outbreak (if within 2 weeks of exposure): <ul style="list-style-type: none"> <li>• age &lt;12 months: human normal immunoglobulin is recommended</li> <li>• ≥12 months: age-appropriate vaccination is recommended. (See section 8.8)</li> </ul>

## 8.1 Virology

Hepatitis A virus (HAV) is a ribonucleic acid (RNA) virus belonging to the picornavirus group, which also contains enteroviruses and rhinoviruses. The virus is usually transmitted by the faecal–oral route, either from person-to-person contact or through contaminated food or drink.

HAV primarily replicates in the liver and is excreted in large quantities via the biliary tract into the faeces. It is a hardy virus and can survive outside the body for prolonged periods in food and water. It causes a self-limiting illness with no carrier state.

## 8.2 Clinical features

The incubation period between ingestion of the virus and clinical symptoms is 15 to 50 days, with an average of 28 to 30 days. The virus can be detected in blood and faeces within a few days of ingestion, and it increases to a peak in the two weeks prior to the onset of clinical illness, which is the time that subjects are most likely to spread the infection. Faecal viral shedding continues for one to three weeks in adults, but has been reported to last longer in young children. Virus excretion falls sharply in the week following the onset of hepatitis.

In infants and preschool children, most infections are either asymptomatic or cause only mild, non-specific symptoms without jaundice. Most adults and adolescents develop symptomatic disease, the severity of which generally increases with age. Symptomatic HAV infection is characterised by an acute febrile illness with jaundice, anorexia, nausea, abdominal discomfort, malaise and dark urine. Signs and symptoms usually last less than two months, although 10–15 percent of symptomatic persons have prolonged or relapsing illness lasting up to six months. Liver enzymes almost always return to normal by six months after the illness, and often much sooner. The disease is more serious in people with chronic liver disease or those who are immunocompromised (including people with HIV infection). Chronic carrier states do not occur following hepatitis A infection and persisting liver damage is very rare.

## 8.3 Epidemiology

### 8.3.1 Global burden of disease

HAV is common in areas with poor sanitary conditions and limited access to clean water.<sup>1</sup> In highly endemic areas, such as parts of Africa and Asia, the disease is virtually confined to early childhood and is not an important cause of morbidity.<sup>1, 2</sup> Almost all adults in these areas are immune, and hepatitis A epidemics are uncommon. In intermediate endemicity areas, such as Central and South America, Eastern Europe and parts of Asia, children may not be infected in early childhood and reach adulthood without immunity. A high proportion of adolescents and adults are susceptible and large outbreaks are common. In low endemicity areas, such as the US and Western Europe, infection is less common but can occur in high-risk groups. Large outbreaks are rare, due to high levels of sanitation that stops person-to-person transmission.

Viral spread occurs readily in households, in early childhood services and in residential facilities that care for the chronically ill, disabled or those with a weakened immune system. In early childhood services, typically the adult guardian develops symptomatic disease while the primary source, the infected young child, is asymptomatic. The risk of spread in early childhood centres is proportional to the number of children aged under 2 years wearing nappies. Infection in these early childhood services is an important source of outbreaks for whole communities.

Other groups at the highest risk of contracting the disease include people in close contact with an infected person, and travellers to areas with high or intermediate rates of hepatitis A infection. Others also at greater risk of contracting HAV are people who have oral–anal sexual contact, illicit drug users, those with chronic liver disease, food handlers and laboratory staff working with the virus.

Universal and targeted programmes for childhood immunisation have been introduced in several countries, including Israel, the US and Australia. Acute HAV infection has almost been eradicated in areas with HAV immunisation programmes.

### 8.3.2 New Zealand epidemiology

The rate of HAV in New Zealand declined from 145.7 per 100,000 in 1971 to 1.2 per 100,000 in 2019 (ESR, 8 June 2020).<sup>3, 4</sup> This fall in rate is attributable to the use of HAV vaccination in travellers and a reduction in HAV prevalence overseas.

In 2019, 58 cases were notified compared with 68 in 2018 (ESR, 8 June 2020). Hospitalisation status was recorded for 57 cases, of which, 36 (63 percent) were hospitalised.

The highest rates occurred in the 15–19 years (2.2 per 100,000) and 1–4- and 20–29-years age groups (both 2.0 per 100,000). Of the 56 cases with ethnicity information



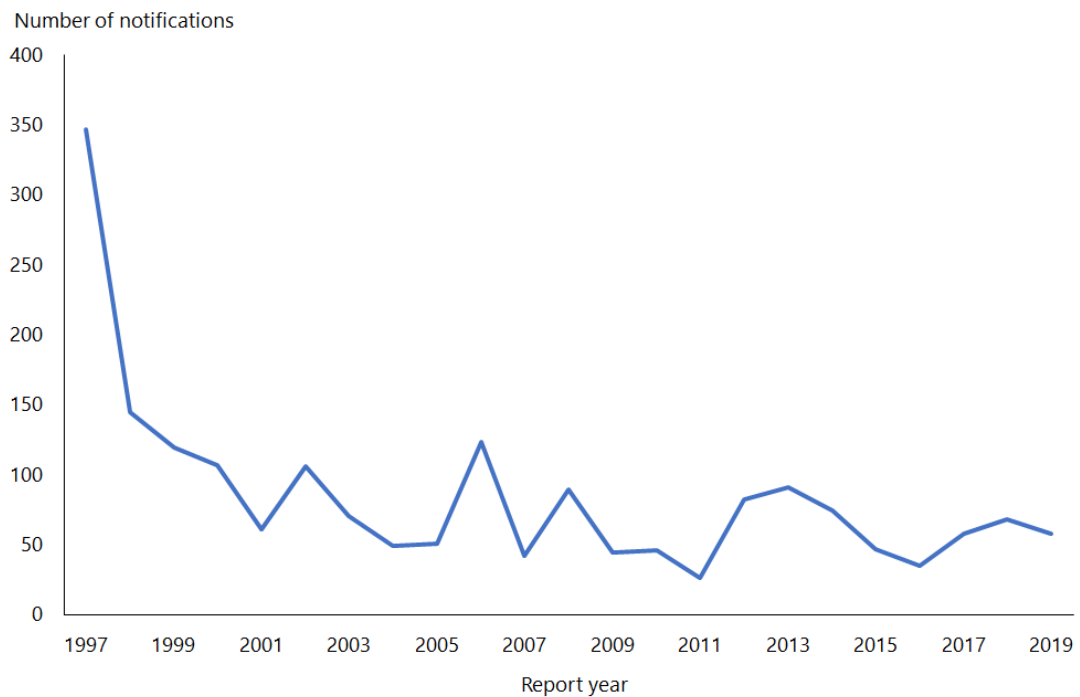
recorded, Pacific peoples had the highest notification rate (5.4 per 100,000), followed by the Asian (3.1 per 100,000) ethnic groups (ESR, 8 June 2020).

Overseas travel information was recorded for 55 cases: 32 cases (58.2 percent) had travelled overseas during the incubation period of the disease (ESR, 8 June 2020). The countries most frequently visited included India and Samoa (7 cases each), Fiji (5 cases), Indonesia (4 cases) and Tonga (3 cases). Four cases reported travel to more than one country.

Hepatitis A outbreaks continue to occur. There was one outbreak in 2019, involving 10 cases (ESR, 8 June 2020).

Figure 8.1 illustrates the overall national downward trend since a peak of notifications in 1997.

**Figure 8.1: Hepatitis A notifications, by year, 1997–2019**



Source: ESR

For further details of hepatitis A notifications in New Zealand, refer to the most recent notifiable disease annual reports from ESR (available at [www.esr.cri.nz/digital-library/notifiable-disease-dashboard/](http://www.esr.cri.nz/digital-library/notifiable-disease-dashboard/)).

## 8.4 Vaccines

### 8.4.1 Available vaccines

Two inactivated HAV vaccines (HepA) are currently registered (approved for use) and available (marketed) in New Zealand, as well as a combined HepA-HepB vaccine and a combined HepA-typhoid vaccine.

#### Funded vaccine

Hepatitis A vaccine (HepA) is not on the Schedule, but is recommended and funded for certain high-risk groups, as shown in Table 8.1.

Each 1.0 mL dose of Havrix 1440 (GSK) contains 1,440 EU (enzyme-linked immunosorbent assay units) of inactivated hepatitis A virus (HAV) adsorbed onto aluminium hydroxide. Each 0.5 mL dose of Havrix Junior contains 720 EU of inactivated HAV. Other components and residuals include neomycin sulphate, 2-phenoxyethanol, polysorbate 20, amino acid supplement in a phosphate buffered saline solution.

#### Other vaccines

##### Inactivated HAV vaccine

Avaxim (Sanofi) contains 160 antigen units of inactivated HAV in each 0.5 mL dose; other components and residuals include aluminium hydroxide, phenoxyethanol, formaldehyde, Medium 199, neomycin and bovine serum albumin.

##### Combined HAV and HBV vaccine

Twinrix (GSK) contains 720 EU of inactivated HAV and 20 µg of recombinant DNA HBsAg vaccine in each 1.0 mL dose. The Twinrix Junior preparation (0.5 mL per dose) contains half these amounts. The vaccines are adsorbed onto aluminium adjuvants. Other components and residuals include aluminium hydroxide, aluminium phosphate, sodium chloride, amino acids, dibasic sodium phosphate, formaldehyde, monobasic sodium phosphate, neomycin sulphate, polysorbate 20 and trometamol.

##### Combined HAV and typhoid vaccines

Vivaxim (Sanofi) contains 160 antigen units of inactivated HAV and 25 µg of purified *Salmonella typhi* Vi polysaccharide in each 1.0 mL dose; other components and residuals include sodium chloride, sodium phosphate, aluminium hydroxide, phenoxyethanol, formaldehyde, Medium 199, neomycin and bovine serum albumin.

## 8.4.2 Efficacy and effectiveness

After one dose of monovalent HepA in healthy people, protective levels of antibody have been demonstrated by two weeks, and 94–100 percent of people vaccinated will seroconvert by four weeks.<sup>5</sup>

A second dose 6 to 18 months after the first is thought to be important for long-term protection, particularly in the absence of exposure to HAV.<sup>6, 7</sup> In subjects with an impaired immune system, adequate anti-HAV antibody titres may not be obtained after a single dose.

Hep A vaccines have not yet been approved for children aged under 12 months. This is due to the potential interference from maternal antibody which may affect long term immunity.<sup>8</sup> However, HepA vaccines have been shown to be safe and efficacious in infants as young as 2 months.<sup>9</sup> Such that the CDC recommends HepA vaccination for infants aged 6–11 months travelling outside of the US.<sup>10</sup>

HepA vaccines are highly effective in preventing clinical disease, with recorded efficacy measures of around 94–100 percent from six weeks post-vaccination. Where children, adolescents and young adults have been vaccinated in targeted and/or national programmes, there has been a rapid decline in disease incidence. This decline is through both direct and indirect (herd immunity) effects.<sup>6</sup>

### Duration of immunity

Antibodies to two doses of HepA have been shown to persist in vaccinated adults for at least 17 years after vaccination, and up to 15 years in vaccinated children and adolescents.<sup>11</sup> Mathematical models estimate that following completion of a two-dose series, protective levels of antibody persist for 40 years or longer in adults and 14–20 years in children.<sup>11</sup> Given that HAV has a long incubation period, it is possible that immune memory with no detectable circulating antibody may be sufficient for protection, as is the case with HBV and HepB.

## 8.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at [www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

Store at +2°C to +8°C. Do not freeze.

## 8.4.4 Dosage and administration

See Table 8.2 for dosage and scheduling information.

The monovalent HepA and HepA combination vaccines should be administered by intramuscular injection into the deltoid region of the upper arm in adults and older children, or the anterolateral aspect of the thigh in younger children (see section 2.2.3).

### Co-administration with other vaccines

The monovalent HepA and HepA-combination vaccines may be administered concurrently with other vaccines.<sup>11, 12</sup> The vaccines should be given in separate syringes and at different injection sites.

### Interchangeability of hepatitis A vaccines

The monovalent HepA vaccines may be used interchangeably to complete a two-dose course.<sup>12</sup>

## 8.5 Recommended immunisation schedule

### 8.5.1 Recommendations

Hepatitis A vaccines are not on the Schedule, but are funded for the high-risk groups as shown in the shaded section of Table 8.1. They may also be employer-funded or funded during an outbreak (see section 8.8).

**Table 8.1: Hepatitis A vaccine recommendations**

Note: **Funded individuals are in shaded rows.** See the Pharmaceutical Schedule ([pharmac.govt.nz/](http://pharmac.govt.nz/)) for any changes to the funding decisions.

<b>Recommended and funded</b>
Transplant patients <sup>a</sup>
Children with chronic liver disease <sup>a</sup>
Close contacts <sup>b</sup> of hepatitis A cases
Recommended but not funded
Adults with chronic liver disease: <ul style="list-style-type: none"><li>• chronic hepatitis B or C infection</li><li>• other chronic liver disease</li></ul>
Men who have sex with men
Travellers – including occupational <sup>c</sup> and recreational travel
Occupational groups <sup>c</sup> exposed to faeces, including: <ul style="list-style-type: none"><li>• employees of early childhood services, particularly where there are children too young to be toilet trained</li><li>• sewage workers</li><li>• those who work with non-human primates (eg, zoos, research laboratories).</li></ul>
Food handlers <sup>c</sup> during community outbreaks.
Armed forces personnel <sup>c</sup> who are likely to be deployed to high-risk areas.

a. See also section 4.3.10.

b. Only one dose is funded for close contacts as protection is only required for the duration of the outbreak. For long-term protection, contacts may seek a second (unfunded) dose, after an interval of at least 6 months. See the Hepatitis A chapter of *Communicable Disease Control Manual* for a definition of contacts (at [www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/hepatitis-a/](http://www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/hepatitis-a/)).

c. May be employer-funded. See also section 4.8.

## Individuals with chronic liver disease

HepA is recommended and funded for children with chronic liver disease and for children and adults undergoing transplants (see sections 4.3.10 and 4.5). People with chronic liver disease are not at increased risk for hepatitis A, but acute hepatitis A can have serious or fatal consequences.<sup>6</sup>

## Chronic hepatitis B or C infection

Studies have shown that in these individuals, super-infection with HAV leads to increased morbidity and mortality.<sup>6</sup>

## Other chronic liver disease

Non-immune individuals who have not been vaccinated should receive HepA before liver decompensation. It should be given as early as possible before liver transplantation; vaccination may be performed after transplantation, although the response is unlikely to be as good as early in liver disease.<sup>13, 14</sup>

## Travellers

The first dose of HepA should be given as soon as travel is considered.<sup>11</sup> The high and intermediate endemicity areas listed in section 8.3.1 may be used as a guide for recommending hepatitis A vaccination for travel, but there are limits to the data that informs these listings, and variation within countries. Even in low prevalence countries there is a risk of foodborne hepatitis A. In addition, decreasing prevalence in formerly endemic countries leads to large numbers of susceptible people and the risk of large outbreaks, as has recently been reported. The vaccine may be considered for all travellers. Although licensed from age 1 year, HepA could also be considered for use in infants younger than 1 year if at significant risk of infection.<sup>10</sup>

Immunoglobulin is not normally available or recommended in New Zealand for pre-travel use.

## Certain occupational groups

Immunisation with HepA is recommended (but not funded) for people in occupational groups exposed to faeces, as listed in Table 8.1 above.

## Others at higher risk

Pre-immunisation screening for anti-HAV antibodies is not routinely recommended. There is no danger in vaccinating an already immune person, but some groups with higher probability of prior infection may wish to avoid the expense of vaccination. These include:

- those who are likely to have been exposed as children (born in a country of high endemicity) or in the course of their employment
- those with a history of jaundice.

Consider HepA for the following groups:

- intravenous drug users (who account for 30 percent of cases in communities during outbreaks)<sup>6</sup>
- men who have sex with men.

## Routine immunisation for children

HepA is not routinely recommended and is not on the Schedule for children in New Zealand. It should, however, be considered during community outbreaks (see section 8.8).

## 8.5.2 Immunisation schedule

Immunisation schedules for HAV-containing vaccines are provided in Table 8.2. See the manufacturers' data sheets for more information. For monovalent HepA, the first dose is for primary immunisation and the second dose is a booster.

**Table 8.2: Hepatitis A-containing vaccines: by age, dose and schedule**

Note: Havrix 1440 and Havrix Junior are funded for eligible individuals<sup>a</sup> (see Table 8.1).

Age	Vaccine	Dose	Volume (mL)	Number of doses	Schedule
<b>Hepatitis A vaccines</b>					
1–15 years	Havrix Junior <sup>a</sup>	720 EU	0.5	2	0 and 6–12 months <sup>b</sup>
2 years–adult	Avaxim	160 antigen units	0.5	2	0 and 6–36 months
≥16 years	Havrix 1440 <sup>a</sup>	1,440 EU	1	2	0 and 6–12 months <sup>b</sup>
<b>Hepatitis A–Hepatitis B combined vaccine</b>					
1–15 years	Twinrix <sup>c</sup>	720 EU of HAV and 20 µg of HBsAg	1.0	2	0 and 6–12 months
	Twinrix Junior <sup>d</sup>	360 EU of HAV and 10 µg of HBsAg	0.5	3	0, 1 and 6 months
≥16 years	Twinrix	720 EU of HAV and 20 µg of HBsAg	1.0	3	0, 1 and 6 months; or 0, 7, and 21 days plus a booster at 1 year
<b>Hepatitis A–Typhoid combined vaccines</b>					
≥16 years	Vivaxim	160 antigen units of HAV and 25 µg of Vi	1.0	1	At least 14 days before departure; then boost with HepA at 6–36 months <sup>e</sup>

Key: EU = enzyme-linked immunosorbent assay (ELISA) units of hepatitis A virus protein; HAV = hepatitis A virus; HBsAg = recombinant hepatitis B surface antigen; Vi = *Salmonella typhi* polysaccharide

### Notes

- Note that two doses of HepA are funded for transplant patients and children with chronic liver disease (see sections 4.3.10 and 4.5); one dose is funded for close contacts of hepatitis A cases.
- Even after a longer interval between the first and second doses, there is no need to restart the series. A substantial anamnestic response occurs after a second dose given up to 8 years after the initial dose.<sup>15</sup>
- For children not previously exposed to the hepatitis A or B viruses. Source: GlaxoSmithKline NZ Ltd. 2016. Twinrix and Twinrix Junior New Zealand Data Sheet. URL: [www.medsafe.govt.nz/profs/datasheet/t/Twinrixinj.pdf](http://www.medsafe.govt.nz/profs/datasheet/t/Twinrixinj.pdf) (accessed 19 June 2020).
- Use when the child is at immediate risk of exposure to hepatitis B (eg, travellers) and did not receive a primary course of HepB as an infant. Source: GlaxoSmithKline NZ Ltd. 2019. Twinrix and Twinrix Junior New Zealand Data Sheet. URL: [www.medsafe.govt.nz/profs/datasheet/t/Twinrixinj.pdf](http://www.medsafe.govt.nz/profs/datasheet/t/Twinrixinj.pdf) (accessed 19 June 2020).
- If the individual remains at risk from typhoid fever, a single dose of the typhoid vaccine is recommended every 3 years.



### 8.5.3 Pregnancy and breastfeeding

The safety of HepA during pregnancy and while breastfeeding has not been determined. However, because HepA is produced from inactivated HAV, there is not expected to be any risk to the developing fetus and infant. As a precaution, HepA should be used during pregnancy only when clearly needed, such as when travelling to a country where HAV is endemic.

## 8.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

### 8.6.1 Contraindications

Administration of HepA should be delayed in individuals suffering from acute febrile illness. HepA should not be administered to people with a history of an anaphylactic reaction to a prior dose of HepA or to a vaccine component.

### 8.6.2 Precautions

In individuals with an impaired immune system, adequate anti-HAV antibody titres may not be obtained after a single dose.

Pregnancy is a precaution – see section 8.5.3.

## 8.7 Potential responses and AEFIs

### 8.7.1 Potential responses

Soreness, redness and swelling at the injection site; fever; malaise; headache; nausea; and loss of appetite have been reported for monovalent HepA, but these responses are usually mild and brief.<sup>16</sup> Similar responses are seen with HepA–HepB combination vaccines, and HepA–typhoid combination vaccines.

## 8.7.2 AEFIs

Review of data from multiple sources has not identified any serious adverse events among children and adults that could be attributed to HepA.<sup>16</sup>

# 8.8 Public health measures

It is a legal requirement that all cases of hepatitis A be notified immediately on suspicion to the local medical officer of health.

For further details on public health control measures, see the *Communicable Disease Control Manual* at [www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/hepatitis-a/](http://www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/hepatitis-a/)

## 8.8.1 Post-exposure prophylaxis and outbreak control

### Vaccination

Age-appropriate vaccine is recommended for all close contacts aged older than 1 year. If time allows, consider pre-vaccine serology if there is a history or likelihood of previous HepA vaccination or infection (eg, previous residence in an endemic country). Post-exposure prophylaxis with vaccine should be offered to contacts as soon as possible, and within two weeks of last exposure to an infectious case. The efficacy of vaccine when administered more than two weeks after exposure has not been established.

### Immunoglobulin

Where vaccine is contraindicated (or not immediately available), human normal immunoglobulin may be offered to a close contact who may have a reduced response to vaccine or has risk factors for severe disease. The dose is 0.03 mL/kg given by intramuscular injection. Post-exposure prophylaxis should be offered to contacts as soon as possible, and within two weeks of last exposure to an infectious case.

For post-exposure prophylaxis, close contacts aged under 1 year may require human normal immunoglobulin. This should be discussed with the appropriate infectious disease physician.

Human normal immunoglobulin is available from the New Zealand Blood Service. For further information, see the medicine data sheets or the New Zealand Blood Service website ([nzblood.co.nz](http://nzblood.co.nz)).

## Early childhood services and other institutional outbreaks

If an outbreak occurs in an early childhood service, vaccination (and/or immunoglobulin if appropriate) may be indicated for all previously unimmunised staff and children at the service and unimmunised new staff and children for up to six weeks after the last case has been identified, including cases in the household of attendees.

For more details on control measures, see the 'Hepatitis A' chapter of the *Communicable Disease Control Manual* (available at [www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/hepatitis-a/](http://www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/hepatitis-a/)).

## 8.9 Variations from the vaccine data sheets

Havrix Junior is licensed from ages 1 to 15 years of age. However, for infants travelling to areas at high risk of hepatitis A infection and pre-exposure prophylaxis, Health New Zealand | Te Whatu Ora recommends that HepA vaccination (Havrix Junior) can be given under 1 year of age at least two weeks prior to departure.

## References

1. Nelson N, Murphy T. 2016. Hepatitis A. in *CDC Health Information for International Travel (Yellow Book)*, Brunette GW (ed) (eds). URL: <https://wwwnc.cdc.gov/travel/yellowbook/2020/travel-related-infectious-diseases/hepatitis-a>. (accessed 10 May 2022)
2. World Health Organization. *Hepatitis A Factsheet*. [updated 21 July 2021]; URL: <https://www.who.int/en/news-room/fact-sheets/detail/hepatitis-a>. (accessed 10 May 2022)
3. Institute of Environmental Science and Research Ltd. 2016. *Notifiable Diseases in New Zealand: Annual Report 2015* (ed.), Porirua, New Zealand: The Institute of Science and Environmental Research Ltd. URL: [https://surv.esr.cri.nz/PDF\\_surveillance/AnnualRpt/AnnualSurv/2015/2015AnnualReportFinal.pdf](https://surv.esr.cri.nz/PDF_surveillance/AnnualRpt/AnnualSurv/2015/2015AnnualReportFinal.pdf) (accessed 3 July 2020)
4. Institute of Environmental Science and Research Ltd. 2019 *Notifiable Diseases in New Zealand: Annual Report 2017*. Porirua, New Zealand. URL: [https://surv.esr.cri.nz/PDF\\_surveillance/AnnualRpt/AnnualSurv/2017/2017AnnualNDReport\\_FINAL.pdf](https://surv.esr.cri.nz/PDF_surveillance/AnnualRpt/AnnualSurv/2017/2017AnnualNDReport_FINAL.pdf). (accessed 3 July 2020)
5. Centers for Disease Control and Prevention. 2006. Prevention of Hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morbidity and Mortality Weekly Report: Recommendations and Reports*. 55(RR07): p. 1–23. URL: (accessed 3 July 2020)

6. Averhoff F, Khudyakov Y, Nelson N. 2018. Hepatitis A vaccines, in *Plotkin's Vaccines (7th Edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
7. Van Damme P, Banatvala J, Fay O, et al. Hepatitis A booster vaccination: is there a need? *Lancet*, 2003. 362(9389): p. 1065-71.
8. Bell BP, Negus S, Fiore AE, et al. Immunogenicity of an inactivated hepatitis A vaccine in infants and young children. *Pediatric Infectious Disease Journal*, 2007. 26(2): p. 116-22.
9. Dagan R, Amir J, Mijalovsky A, et al. Immunization against hepatitis A in the first year of life: priming despite the presence of maternal antibody. *Pediatric Infectious Disease Journal*, 2000. 19(11): p. 1045-52.
10. Nelson NP, Link-Gelles R, Hofmeister MG, et al. Update: Recommendations of the Advisory Committee on Immunization Practices for Use of Hepatitis A Vaccine for Postexposure Prophylaxis and for Preexposure Prophylaxis for International Travel. *MMWR: Morbidity and Mortality Weekly Report*, 2018. 67(43): p. 1216-1220.
11. American Academy of Pediatrics. 2018. Hepatitis A. in *Red Book: 2018 Report of the Committee on Infectious Diseases*, Kimberlin D, Brady M, Jackson M, and Long S (eds). URL: <https://redbook.solutions.aap.org/redbook.aspx>. (accessed 3 July 2020)
12. Australian Technical Advisory Group on Immunisation (ATAGI). 2018. Hepatitis A. in *Australian Immunisation Handbook*. Canberra. URL: <https://immunisationhandbook.health.gov.au/vaccine-preventable-diseases/hepatitis-a>. (accessed 25 May 2020)
13. Arslan M, Wiesner RH, Poterucha JJ, Zein NN. Safety and efficacy of hepatitis A vaccination in liver transplantation recipients. *Transplantation*, 2001. 72(2): p. 272-6.
14. Arguedas MR, Johnson A, Eloubeidi MA, Fallon MB. Immunogenicity of hepatitis A vaccination in decompensated cirrhotic patients. *Hepatology*, 2001. 34(1): p. 28-31.
15. Iwarson S, Lindh M, Widerstrom L. Excellent booster response 4 to 8 years after a single primary dose of an inactivated hepatitis A vaccine. *Journal of Travel Medicine*, 2004. 11(2): p. 120-1.
16. Irving GJ, Holden J, Yang R, Pope D. Hepatitis A immunisation in persons not previously exposed to hepatitis A. *Cochrane Database Syst Rev*, 2012. CD009051.(7).

# 9 Hepatitis B

## Key information

Mode of transmission	Contact with infected blood or body fluids during childbirth (vertical transmission); sexual intercourse, intravenous drug use or contact with broken skin (horizontal transmission).
Incubation period	45–180 days, commonly 60–90 days.
Period of communicability	Potentially infectious 2–3 weeks before the onset of symptoms, during the clinical disease and usually for 2–3 months after acute hepatitis B illness; or for as long as HBsAg continues to be present in blood (chronic hepatitis B carrier state).
Incidence and burden of disease	New Zealand is a country with a low overall prevalence of hepatitis B carriage, but it contains certain populations with high prevalence. All pregnant women and high-risk groups should be screened for chronic HBV infection. HBV acquisition in infancy is very likely to lead to chronic infection. Chronic HBV infection can progress to cirrhosis and liver cancer.
Funded vaccines	HepB (Engerix-B) DTaP-IPV-HepB/Hib (Infanrix-hexa).
Dose, presentation, route	HepB: <ul style="list-style-type: none"><li>• 20 µg presentation – 1.0 mL per dose, pre-filled syringe</li><li>• 10 µg presentation – 0.5mL per dose, pre-filled syringe (paediatric dose)</li><li>• intramuscular or subcutaneous injection.</li></ul> DTaP-IPV-HepB/Hib: <ul style="list-style-type: none"><li>• 0.5 mL per dose</li><li>• pre-filled syringe and glass vial – the vaccine must be reconstituted prior to injection.</li><li>• intramuscular injection.</li></ul>
Funded vaccine indications and schedule	At ages 6 weeks, 3 months and 5 months: DTaP-IPV-HepB/Hib. Infants born to HBsAg-positive mothers should receive HepB vaccine plus HBIG at birth, then the usual childhood schedule. Serological testing at age 9 months (anti-HBs and HBsAg). Individuals with eligible conditions or close household contacts of infected individuals: HepB (see section 9.5).
Recommended, unfunded	Those with increased risk from occupational or sexual exposure to body fluids and faeces, or receiving regular blood products. Those with developmental disability, current or prior injectable drug users, prison inmates, and travellers to and from high-prevalence countries.
Vaccine effectiveness	In general, efficacy is 85–95 percent in high-risk groups, though likely to be lower in older individuals and those with immunocompromise. Protection is expected to be lifelong and boosters are not required.

*Continued overleaf*

Public health measures	Notify all cases of acute hepatitis B infection (see section 9.8).
Post-exposure prophylaxis	Vaccination and immunoglobulin prophylaxis of close contacts, as appropriate (see section 9.8).

## 9.1 Virology

The hepatitis B virus (HBV) is a partially double-stranded DNA virus belonging to the Hepadnaviridae family. Three major subunits make up the structural components:

- the HBV genome, a small, circular, partially double-stranded DNA molecule, in association with a polymerase enzyme
- the nucleocapsid core, which surrounds the genome and consists of core protein (hepatitis B core antigen, HBcAg)
- the outer lipoprotein envelope, which contains the hepatitis B surface antigen (HBsAg).

The genome has four genes (S, C, X and P). Both the core nucleocapsid protein (HBcAg) and the 'early' protein (which makes HBeAg) are translated from the C gene. HBcAg is essential for viral packaging and is an integral part of the nucleocapsid. HBeAg is a soluble protein that is not part of the virus particle. Detection of HBeAg in the serum is correlated with viral replication and is a marker for severe disease. It is most commonly found in those with acute hepatitis B and those with chronic HBV infection with high viral load.<sup>1</sup>

## 9.2 Clinical features

There is a broad spectrum of clinical disease with HBV infection, from subclinical through to fulminant hepatitis. Persistent infection can lead to chronic liver disease, potentially causing cirrhosis or hepatocellular carcinoma.

### 9.2.1 Serological markers of infection

The HBV antigens and their associated antibodies are serological markers of HBV infection or vaccination (Table 9.1). At least one serological marker is present during the different phases of infection (Table 9.2).

**Table 9.1: HBV antigens and their respective antibodies**

Antigen	Antibody (IgM, IgG and total)
HBsAg (hepatitis B surface antigen)	Anti-HBs
HBcAg (hepatitis B core antigen)	Anti-HBc
HBeAg (hepatitis B e antigen)	Anti-HBe

**Table 9.2: Interpretation of serology for HBV infection**

HBsAg	Serological marker			Interpretation
	Total anti-HBc	IgM anti-HBc	Anti-HBs	
-	-	-	-	Never infected
+	-	-	-	Early acute infection; transient (up to 18 days) after vaccination
+	+	+	-	Acute infection
-	+	+	+ or -	Acute resolving infection
-	+	-	+	Recovered from past infection and is immune
+	+	-	-	Chronic infection <sup>a</sup>
-	-	-	+	Immune if $\geq 10$ IU/L vaccinated or natural infection

Key: Anti-HBc = antibody to hepatitis B core antigen; anti-HBs = antibody to hepatitis B surface antigen (HBsAg); IgM = immunoglobulin M; + = positive test result; - = negative test result.

a HBeAg positive (HBeAg+) correlates with high viral load and increased risk of transmission; HBeAg negative (HBeAg-) correlates with lower viral load and reduced risk of developing cirrhosis or cancer.

Adapted from: Van Damme P, Ward J, Shouval D, et al. 2018. Hepatitis B vaccines. In: Plotkin SA, Orenstein WA, Offit PA (eds). *Plotkin's Vaccines* (7th edition). Philadelphia, US: Elsevier. Table 25.1.

Any difficulties with interpreting serological results for cases and contacts should be discussed with an infectious diseases physician or the laboratory. See the 'Hepatitis B' chapter of the *Communicable Disease Control Manual* for recommendations for HBV case and contact management (available at [www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual](http://www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual)).

## 9.2.2 Acute hepatitis

The virus preferentially infects liver cells, multiplying in the liver and releasing large amounts of HBsAg, which is present in the blood of people with active infection. The incubation period varies between 45 and 180 days and is commonly 60 to 90 days.

HBV is not directly cytopathic; the host's immune response leads to death of infected liver cells. Most infected people mount an effective immune response that leads to eradication of infection over a period of several months. Approximately 80 percent of



adults with acute infection have symptomatic hepatitis, and the remaining 20 percent can be asymptomatic (but these proportions vary).<sup>2</sup>

The common symptoms of acute hepatitis B illness are fever, jaundice, malaise, anorexia, nausea, vomiting, myalgia and abdominal pain. Jaundice usually develops within two weeks of onset of the illness, and dark urine and/or clay coloured stools might appear up to five days before clinical jaundice. Clinical signs and symptoms of acute hepatitis B usually resolve one to three months later.<sup>1</sup>

There is a small risk of liver failure (less than 1 percent) with acute infection; if failure occurs, almost half will die or require emergency liver transplantation.

### 9.2.3 Chronic HBV infection

The main burden of HBV disease occurs in people with chronic HBV infection. Chronically infected people are identified by presence and persistence of HBsAg in their serum for at least six months. The age of acquisition of HBV is strongly associated with the risk of developing chronic HBV infection. Approximately 90 percent of those infected perinatally or in infancy develop chronic HBV infection, compared with 30 percent of children infected between ages 1 and 4 years and less than 5 percent of people infected as adults.

Infants seldom mount an immune response to HBV infection, and infection in infancy is often asymptomatic. Asymptomatic chronic infection stimulates persistent immune responses that may eventually lead to cirrhosis (decades later); cirrhosis and chronic infection increase the risk of development of hepatocellular carcinoma.

**Table 9.3: Characteristics and phases of chronic hepatitis B virus infection**

Phases of HBV infection	Features
Immune tolerance phase	Prolonged period of active viral replication without active liver disease. Seen in children who acquire infection perinatally.
Immune clearance phase	Active viral replication and active liver disease
Inactive chronic HBV infection	Low or absent viral replication and remission of active liver disease
Reactivation	HBV replication after inactivity, seen in some patients

There are up to four phases of chronic infection as in Table 9.3 show; not all are present in all infections.<sup>1</sup> The initial phase of infection may last 10 to 30 years, during which spontaneous clearance rates of HBeAg in the serum are less than 1 percent per year.

Chronically infected people who are HBsAg positive can also have detectable HBeAg in the serum; this combination is considered most infectious. Although recent evidence suggests HBeAg negative patients are less infectious, it is dependent on HBV DNA levels. Whatever the case, both groups can be an ongoing source of infection to susceptible individuals. In the early years of chronic infection, high rates of viral replication are common, and both HBeAg and high levels of HBV DNA are present in

the blood. In later years, HBeAg may be absent from the blood, and HBV DNA levels (viral load) are usually lower, both of which correspond with lower rates of viral replication.

It is estimated that 4.5 percent of HBsAg positive individuals (12 million people worldwide) have been co-infected with hepatitis D virus (HDV), which is a significant contributor to HBV-associated cirrhosis and hepatocellular carcinoma.<sup>3</sup> The highest prevalence is seen in those with hepatitis C and HIV, and in certain geographic areas.

## 9.2.4 Routes of transmission

HBV is usually transmitted through contact with infected blood or body fluids during childbirth, contact with broken skin, sexual intercourse or intravenous drug use. Although HBV can be found in all body fluids, blood has the highest concentration and saliva the lowest. HBV in dried blood remains infective for at least one week.<sup>4</sup>

### Perinatal (vertical) transmission

The primary source of HBV infection is perinatal exposure from mothers with chronic HBV infection. Transmission usually occurs at the time of birth. The *in utero* transmission of HBV is relatively rare, accounting for less than 2 percent of infections transmitted from mother to infant.<sup>5</sup>

If no prophylaxis is given to the infant, the baby of an HBeAg positive mother has a 70–90 percent risk of infection, while the baby of an HBeAg negative HBsAg positive carrier mother has a 5–20 percent risk of infection. Over 90 percent of infants who acquire infection perinatally become chronic carriers.

### Person-to-person (horizontal) transmission

Non-sexual person-to-person transmission probably occurs from inadvertent percutaneous or mucosal contact with blood or infectious body fluids among people in close daily contact (household members).

The main sources of transmission are:

- sexual contact with an infected individual
- percutaneous exposure to blood or infectious body fluids
- needle-stick injuries or sharing needles.

Those travelling to high endemic countries are at higher risk of exposure (see below).

## 9.3 Epidemiology

### 9.3.1 Global burden of disease

Approximately two billion people worldwide had been exposed to HBV in 1995. In 2015, based on serological data, around 3.5 percent of the general population globally were infected with HBV and more than 250 million people were estimated to have chronic infection and these people remain at risk of developing cirrhosis and hepatocellular carcinoma.<sup>6, 7</sup> More than 90 percent of individuals with chronic HBV resided in the Asia–Pacific region, where most countries have high prevalence rates of HBV infection (the population rate of HBsAg positivity is between 5 and 20 percent) and more than 99 percent of HBV-infected people in this region acquired infection through vertical transmission from their mother (usually at the time of delivery) or in early childhood.<sup>8</sup> As an example of this risk, 22.8 million out of 80 million people living in China with chronic HBV infection are women of child-bearing age.<sup>9</sup> Acquisition of HBV during adulthood (usually via sexual transmission or injecting drug use) is associated with a high rate of symptomatic hepatitis but a low rate of chronic infection.

The introduction of universal childhood HBV immunisation has changed the epidemiology of chronic infection in many countries, but it will be several decades (one to two human generations) before the full benefits are realised. In China, for example, within 20 years since the introduction of HBV immunisation, mother-to-child transmission has been cut by 97 percent; 120 million new HBV infections and 28 million chronic infections have been averted.<sup>9</sup> Thirty years after the introduction of a HepB immunisation programme for newborns in Taiwan, infant fulminant hepatitis mortality and, in those aged 5 to 29 years, chronic liver disease and hepatocellular carcinoma mortality had all decreased by more than 90 percent.<sup>10</sup>

The world can be divided into regions with high (8 percent and over), high-moderate (5–7 percent), low-moderate (2–4 percent) and low (less than 2 percent) prevalence of chronic infection, defined as the presence of HBsAg in serum.<sup>11, 12</sup> In regions with a high prevalence of chronic infection, the lifetime risk of exposure to HBV is almost 80 percent, with most infections occurring in the first decade of life. The Pacific Islands and most of Asia (except Japan and India) are high-prevalence regions. Other high-prevalence regions include Sub-Saharan Africa and Latin America.<sup>12</sup> In contrast, in countries with a low HBsAg prevalence, the lifetime risk of HBV exposure is less than 20 percent, with most infections acquired in adulthood. New Zealand has a low overall prevalence of hepatitis B carriage but contains certain populations with high prevalence (see section 9.3.2 below).

## 9.3.2 New Zealand epidemiology

Before the introduction of HBV immunisation in New Zealand, HBV transmission was common among preschool and school-aged children. The exact mode of transmission is uncertain, but is thought to be related to close contact. In the eastern Bay of Plenty region almost half of the population were infected by age 15 years.<sup>13, 14</sup> Even after the introduction of universal HepB in 1988 (see Appendix 1), there were regions in New Zealand where children were still at risk of HBV infection due to poor immunisation coverage rates.<sup>15-17</sup>

### Acute HBV infection

Only acute hepatitis B is a notifiable disease in New Zealand; notification rates do not describe the burden of chronic HBV infections.

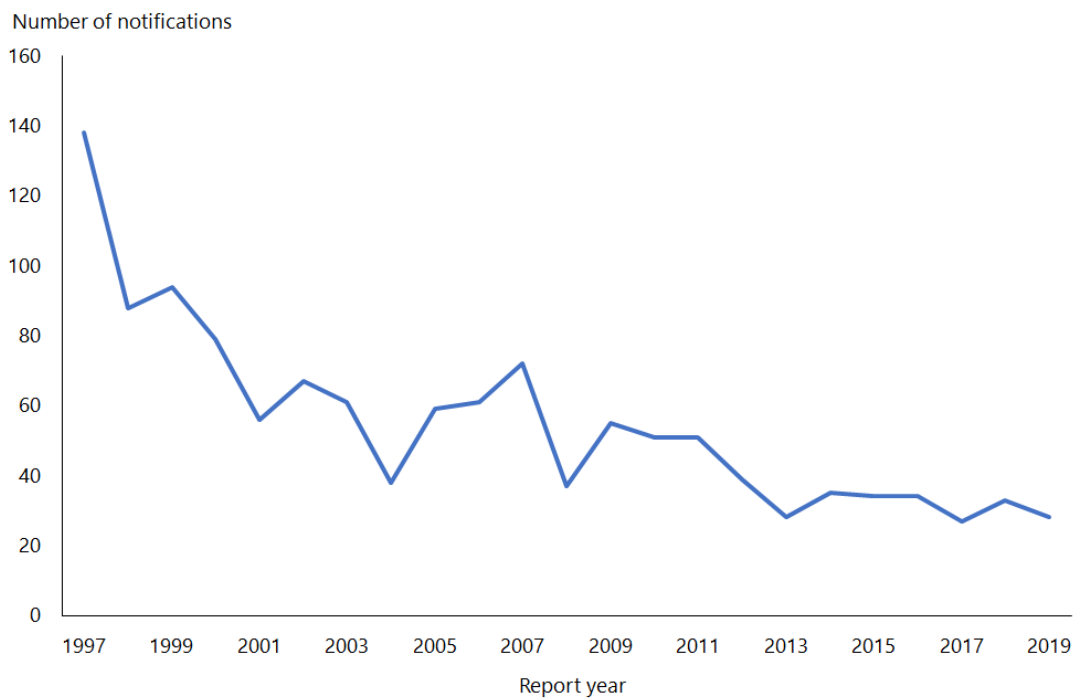
The HBV notification rate in 2019 was 0.6 per 100,000 population (28 cases), similar to the 2018 rate (0.7 per 100,000, 33 cases). The highest notification rate was in the 30–39 years age group (1.1 per 100,000) followed by 50–59 years and 70 years and over (both 0.8 per 100,000). The notification rate was higher for males (0.9 per 100,000) than for females (0.3 per 100,000) (ESR, 8 June 2020).

Ethnicity was recorded for all cases. The Māori (1.3 per 100,000) ethnic group had the highest hepatitis B notification rate followed by the Asian (0.7 per 100,000) ethnic group.

The most common reported risk factors were overseas travel, migration and sexual contact with a confirmed case or carrier.

Hepatitis B notifications have declined from 609 cases in 1984 to 28 cases in 2019 (see Figure 9.1). While difficult to quantify accurately, the introduction of universal infant immunisation in 1988 has contributed to the dramatic decline in the number of newly notified cases of HBV infection.

**Figure 9.1: Notifications of hepatitis B, 1997–2019**



Source: ESR

For recent data on acute hepatitis B notifications, refer to the most recent notifiable disease annual reports from ESR (available at [www.esr.cri.nz/digital-library/notifiable-disease-dashboard/](http://www.esr.cri.nz/digital-library/notifiable-disease-dashboard/)).

## Chronic HBV infection

The Hepatitis Foundation of New Zealand reports that around 120,000 people in New Zealand are living with chronic HBV infection, around 50 percent are diagnosed, but only around 7,000 are being treated. Based on 2016 data, around 1,000 new cases are diagnosed each year nationally. Mathematical modelling anticipated that the prevalence of chronic HBV infection would drop from 3.3 percent in 2016 to 2.4 percent by 2030, falling short of the elimination targets set by the WHO in 2016.<sup>18</sup>

The National Hepatitis B Screening Programme found that between 1999 and 2002 in the North Island, the highest rates of chronic HBV infection were among Chinese (9.1 percent), Pacific peoples (8.5 percent) and Māori (5.8 percent). Although Europeans were not specifically targeted in this screening programme, they have an estimated prevalence rate of 1 percent (higher than in Australia, North America and Europe), reflecting an increased risk of childhood horizontal transmission.<sup>19</sup>

A New Zealand-based modelling study estimated that until the year 2100, people with chronic HBV infection will continue to provide a source of infection to susceptible people.<sup>20</sup> Increased immigration from high-prevalence countries in the Asia-Pacific region is also likely to influence HBV prevalence in New Zealand.

Because people who acquire chronic HBV infection in childhood usually do not develop hepatocellular carcinoma until aged 40 years or older, the introduction of a universal HBV vaccination in 1988 is unlikely to have a significant effect on the incidence of hepatocellular carcinoma until approximately 2030.

A retrospective laboratory data study of antenatal HBsAg tests from the Midlands region (Bay of Plenty, Eastern Bay of Plenty, Waikato and Rotorua) between 1997 and 2009 found a declining prevalence of HBV infection. This decrease was seen across all age groups, but was most marked in antenatal tests of women aged under 20 years, due to receipt of funded HepB in childhood.<sup>21</sup>

A long-term follow-up study in New Zealand showed that horizontally acquired HBV infection during childhood in Māori and Pacific peoples correlates with increased rates of hepatocellular carcinoma and liver-related mortality.<sup>22</sup> This study emphasises the importance of early protection of the infant with vaccination.

## Strategy for prevention

In 1988 New Zealand was one of the first countries to introduce universal infant hepatitis B immunisation. As of 31 December 2019, 93 percent of New Zealand children aged 2 years had completed a primary course of HepB, which confers lifelong immunity in approximately 95 percent of those vaccinated.

# 9.4 Vaccines

## 9.4.1 Available vaccines

The specific monovalent and combination HepB vaccines licensed (approved for use) and available (marketed) in New Zealand contain recombinant HBsAg (HepB).

### Funded vaccines

- HepB (Engerix-B, GSK): contains 20 µg HBsAg per 1 mL dose (10 µg HBsAg per 0.5 mL paediatric dose); it does not contain a preservative. Other components and residuals include aluminium hydroxide, sodium chloride, sodium phosphate dehydrate, sodium dihydrogen phosphate and traces of polysorbate 80.
- DTaP-IPV-HepB/Hib (Infanrix-hexa, GSK): diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and *Haemophilus influenzae* type b vaccine (see section 6.4.1 for more information).

## Other vaccines

HepA-HepB (hepatitis A and hepatitis B vaccine): Twinrix and Twinrix Junior (GSK) (see also section 8.4.1).

### 9.4.2 Efficacy and effectiveness

Clinical trials in high-risk groups have shown a vaccine efficacy of 85–95 percent for HepB vaccines.<sup>8</sup>

See also section 16.4.2 for information about the DTaP-IPV-HepB/Hib vaccine.

#### Immunogenicity

Serum anti-HBs antibody  $\geq 10$  IU/L, measured 1–2 months after immunisation, is considered by WHO as a correlate of long-term protection.<sup>8</sup> In the primary care setting, individuals who have had a documented seroconversion after three injections are expected to have lifelong immunity with no need for further boosters, even if circulating antibody is subsequently not detectable.

Smoking, obesity, HIV infection and chronic disease (including renal failure) all reduce vaccine efficacy, but age is the primary factor affecting the response. At least 98 percent of infants, 95 percent of children and 90 percent of adolescents develop protective levels of antibody after three doses of vaccine. Some non-responders will not produce adequate antibody levels to the initial vaccination course, but most respond to further vaccine doses.

However, some people are persistent non-responders. Persistent non-responders often have an impaired immune system, such as organ transplant recipients and those with HIV infection or chronic disease, including advanced cirrhosis, renal failure or those undergoing haemodialysis. A small percentage (approximately 2–3 percent) of the immunocompetent population may also fail to elicit an antibody response. High-risk individuals who fail to respond adequately are recommended further vaccinations (see section 9.5.7).

#### Effectiveness of birth dose given to babies born to HBsAg-positive mothers

Infants vaccinated at birth born to infected mothers were 3.5 times less likely to be infected with HBV than those who did not receive a birth vaccination.<sup>8, 23</sup> For babies of HBeAg-positive mothers, controlled trials have shown that vaccine at birth provides 75 percent protection from infection, while administration of HBIG in addition to vaccination provides 85–95 percent protection against transmission.<sup>23, 24</sup> Transmission following HBIG/HepB prophylaxis at birth almost exclusively occurs in HBeAg-positive mothers with high HBV DNA levels (above  $2 \times 10^5$  IU/ml or 1 million copies/ml) and/or HBsAg levels above 4–4.5  $\log_{10}$  IU/ml.<sup>25</sup> In this situation, administration of tenofovir (an antiviral agent) to the mother during the last trimester is recommended and funded.



## Duration of immunity

The development of anti-HBs antibodies after a primary vaccination course (three injections and seroconversion) indicates development of immune memory. The quantity of antibody in serum is thought to determine the length of time the antibody titre can be detected in the blood, although any reading  $\geq 10$  IU/L post-vaccination course is considered protective.<sup>26, 27</sup> Children who are given booster doses up to 12 years after the primary series show strong anamnestic (secondary) responses, indicating that booster is unnecessary once a seroprotective level is reached after the three-dose primary vaccination course.<sup>26, 27</sup>

Long-term protection from clinical infection, despite loss of detectable neutralising antibody, is thought to reflect a strong cellular memory immune response following HBV vaccination.<sup>28</sup> Even though a large proportion of vaccine recipients may have undetectable antibody within seven years of vaccination, there is evidence from Germany,<sup>28</sup> Taiwan,<sup>29</sup> Alaska<sup>30</sup> and Hawaii<sup>31</sup> that boosters of HepB are unnecessary following completion of infant immunisation.

Sustained immune memory, including circulating memory B and T cells, and long-term protection have been shown 20–30 years after complete primary immunisation of immune competent adults in the absence of natural or artificial boosting.<sup>24</sup>

In general, vaccine recipients who are subsequently infected with HBV do not develop clinical illness but may have anti-HBc present in plasma.<sup>1</sup>

## Impact on chronic HBV infection

In all populations, where it has been measured, immunisation has led to a dramatic drop in HBV chronic infection.<sup>32</sup> For example, chronic HBV infection dropped from 16 percent to zero in Alaska as a result of 96 percent immunisation coverage. In Taiwan, the incidence of hepatocellular carcinoma also decreased as a result of the immunisation programme in children.<sup>33, 34</sup> Adolescents and adults who were offered universal HBV vaccination in infancy had more than 75 percent lower prevalence of HBV infection and anti-HBc prevalence than those for whom immunisation was unavailable.<sup>35</sup>

### 9.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at

[www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

Store at +2°C to +8°C. Do not freeze. DTaP-IPV-HepB/Hib and HepB vaccines should be stored in the dark.

DTaP-IPV-HepB/Hib (Infanrix-hexa) must be reconstituted by adding the entire contents of the supplied container of the DTaP-IPV-HepB vaccine to the vial containing the Hib-PRP pellet. After adding the vaccine to the pellet, the mixture should be shaken until the pellet is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.

## 9.4.4 Dosage and administration

### DTaP-IPV-HepB/Hib

Each 0.5 mL dose of DTaP-IPV-HepB/Hib (Infanrix-hexa) vaccine contains 10 µg of HBsAg, and is administered by intramuscular injection (see section 2.2.3).

### HepB

The dose of HepB vaccine varies according to the vaccine manufacturer, the age of the individual and/or their health status (see section 9.5 for recommendations):

- Engerix-B 20 µg (GSK): 20 µg HBsAg per 1.0 mL
- Engerix-B paediatric 10 µg (GSK): 10 µg per 0.5 mL.

HepB vaccine is administered by intramuscular injection. It can be also administered by subcutaneous injection, if indicated for bleeding disorders (see section 2.2.3).

### Co-administration with other vaccines

Hepatitis B vaccines may be given at the same time as all other vaccines on the Schedule, including measles, mumps and rubella (MMR) vaccine.

If a course of vaccine is interrupted, it may be resumed without repeating prior doses (see Appendix 2).

## 9.5 Recommended immunisation schedule

**Table 9.4: Hepatitis B vaccine recommendations, funded and unfunded**

Note: **Funded individuals and situations are in the shaded rows.** See the Pharmaceutical Schedule ([pharmac.govt.nz](http://pharmac.govt.nz)) for any changes to funding decisions.

<b>Recommended and funded</b>
Household or sexual contacts of HBsAg-positive patients (ie, patients with acute or chronic HBV infection)
Babies of HBsAg-positive mothers (ie, mothers with acute or chronic HBV infection) – require a birth dose plus the three-dose primary series (HBIG is also given to these babies at birth)
Children and adolescents aged under 18 years who are considered not to have achieved a positive serology by 1 month after vaccination and require additional vaccination or require a primary course of vaccination <sup>a</sup>
Individuals who are HIV-positive <sup>b</sup>
Individuals who are hepatitis C-positive <sup>c</sup>
Following non-consensual sexual intercourse
Prior to planned or following immunosuppression <sup>b,d</sup>
Prior to or following solid organ transplant <sup>b,d</sup>
Individuals post-HSCT <sup>b</sup>
Following needle-stick injury
Patients on dialysis <sup>b,d</sup>
<b>Recommended, not funded</b>
Adults at occupational risk (see section 4.8)
Adults at risk of infection by sexual exposure: <ul style="list-style-type: none"> <li>• people seeking evaluation or treatment for a sexually transmitted infection</li> <li>• people with a high number of sexual partners</li> <li>• people who have sex with commercial sex workers</li> <li>• men who have sex with men</li> </ul>
Individuals with haemophilia and other regular recipients of blood products
Prison inmates
Current or recent injecting drug users
Individuals with developmental disabilities
Migrants from HBV endemic countries (HBsAg prevalence $\geq 2$ percent) <sup>f</sup>
Travellers to HBV endemic regions (HBsAg prevalence $\geq 2$ percent) <sup>f</sup>

- a. Serological testing is not routinely recommended, see Figure 9.3.
- b. See also section 4.3.2.
- c. Hepatitis C patients should also receive hepatitis A vaccine, although this is not currently funded.
- d. The period of immunosuppression due to steroid or other immunosuppressive therapy must be longer than 28 days.
- e. 40 µg of HepB is recommended for adult dialysis patients or for adult liver or kidney transplant patients.<sup>36</sup> See Table 9.5.
- f. See the Centers for Disease Control and Prevention website for countries with an HBsAg prevalence  $\geq 2$  percent (<https://wwwnc.cdc.gov/travel/yellowbook/2020/travel-related-infectious-diseases/hepatitis-b>). Consider combined Hep A and B vaccination for travellers to these regions.

## 9.5.1 Usual childhood schedule

A primary course of hepatitis B vaccination is given as three doses of DTaP-IPV-HepB/Hib at ages 6 weeks, 3 months and 5 months (Table 9.5). If a course of immunisation is interrupted for any reason, it may be resumed without repeating prior doses (see section 9.5.3 and Appendix 2).

**Table 9.5: Usual childhood schedule for hepatitis B-containing vaccine (excluding catch-up)**

Age	Vaccine	Comment
6 weeks	DTaP-IPV-HepB/Hib	Primary series
3 months	DTaP-IPV-HepB/Hib	Primary series
5 months	DTaP-IPV-HepB/Hib	Primary series

### Preterm infants of HBsAg-negative women

Some low birthweight or preterm infants may have a reduced response to HepB vaccine at birth.<sup>37</sup> However, by the chronological age of 1 month, all medically stable preterm infants, regardless of initial birthweight or gestational age, respond to HepB as well as term and larger infants.<sup>38</sup> Because New Zealand's Schedule starts at age 6 weeks, low birthweight and preterm infants are expected to respond to HepB content in the DTaP-IPV-HepB/Hib vaccine. (See also sections 4.2.1 and 4.2.2.)

### Infants with liver or renal disease

HepB vaccine is funded for liver or kidney transplant patients and for dialysis patients. For infants requiring transplants, see 'Solid organ transplantation' in section 4.3.10. For infants undergoing dialysis, see 'Chronic kidney disease' in section 4.4.

## 9.5.2 Infants born to HBsAg-positive mothers

The routine schedule for these infants is a birth dose of monovalent HepB plus HBIG, then three routine doses of DTaP-IPV-HepB/Hib at ages 6 weeks, 3 months and 5 months.

All pregnant women should receive antenatal screening for hepatitis B infection by testing for HBsAg. Infants of HBsAg-positive mothers are to be notified at birth using the form **HE1446: Consent for hepatitis B vaccine and hepatitis B immunoglobulin and notification to the Medical Officer of Health**, available from [health.govt.nz](http://health.govt.nz) or the local authorised health education resource provider or public health unit.

Infants born to HBsAg-positive mothers should receive:

- 100–110 IU HBIG neonatal, at or as close as possible to birth
- a birth dose of HepB which should be given at or as close as possible to birth (preferably within 12 hours).

If HBIG and/or HepB is inadvertently omitted, administer as soon as the omission is recognised. HBIG can be administered up to seven days post-delivery. If there is a delay for longer than seven days, seek specialist advice.

These infants should then continue as per the Schedule at ages 6 weeks, 3 months and 5 months. Serological testing is required at 9 months of age (see below).

The vitamin K injection may also be given at the same time, in the same limb as the HBIG, but not at the same site.

Occasionally women have not been tested for their HBsAg status during the antenatal period. If a woman's HBsAg status is unknown at the time of delivery, the baby should be given HepB at the time of delivery while waiting for the result of an urgent HBsAg test on the mother. If she is found to be HBsAg positive, the baby should be given HBIG as soon as possible, up to seven days post-delivery. Immunoprophylaxis is most effective when given within 12 hours of delivery.<sup>38</sup> Subsequent vaccine doses are given as per the Schedule.

It is essential to take blood to determine whether the baby has seroconverted (anti-HBs positive) or has become infected despite immunoprophylaxis (HBsAg positive), or is neither infected nor immune (ie, HBsAg negative and anti-HBs negative). Testing should be performed at 9 months of age to avoid detection of anti-HBs from HBIG administered during infancy and to maximise the likelihood of detecting late onset HBV infections.<sup>38</sup> Infants of HBsAg-positive mothers should be placed on a practice recall system to have their blood tested at 9 months of age. Check at the 12-month immunisation event to ensure that testing has occurred. The serology results should be interpreted as in Figure 9.2.

**Figure 9.2: Management of an infant of an HBsAg-positive woman**

<p><b>Screen all women in early pregnancy for hepatitis B carriage</b></p> <p>Woman is HBsAg positive    <b>No</b>    .....&gt;    See section 9.5.1: 'Usual childhood schedule'</p> <p><b>Yes</b></p> <p style="text-align: center;">↓</p> <p>All HBsAg-positive pregnant women should also be tested for HBeAg and should have HBV DNA measured. The results should be discussed with a specialist or the woman should immediately be referred to a specialist for ongoing care.</p> <p>Give the baby hepatitis B protection as follows.</p>	
<b>At age</b>	<b>Action to be taken</b>
Birth	Give HBIG 100–110 IU <b>and</b> HepB
6 weeks	DTaP-IPV-HepB/Hib
3 months	DTaP-IPV-HepB/Hib
5 months	DTaP-IPV-HepB/Hib
9 months	<p>Take a blood test to check for hepatitis B infection (HBsAg) and for vaccine-induced immunity (anti-HBs).</p> <p>If HBsAg is negative and anti-HBs level is <math>\geq 10</math> IU/L at age 9 months, immunity is proven.</p> <p>If HBsAg is positive, the infant has become infected despite prophylaxis: refer to an appropriate specialist.</p> <p>If HBsAg is negative and anti-HBs level is <math>&lt; 10</math> IU/L at age 9 months, give a further 3 doses of HepB at least 4 weeks apart. Recheck serology 4 weeks after the last dose. If there is no seroconversion after the third further dose of HepB (ie, if anti-HBs is still <math>&lt; 10</math> IU/L), discuss with a specialist.</p>
<b>All other vaccines should be administered as per the Schedule.</b>	

Neonatal HBIG plus vaccine will fail to prevent vertical HBV transmission in up to 20 percent of infants born to HBsAg-positive mothers with serum HBV DNA levels greater than  $10^8$  IU/mL (or  $2 \times 10^7$  copies/mL). These mothers are usually young, with normal alanine transaminase, and are HBeAg-positive. If the mother's HBV DNA level is greater than 200,000 IU/mL<sup>39-41</sup>, administration of tenofovir (an antiviral agent) during the last trimester is funded.

The number of such high-risk pregnancies appears to be increasing in this country as a result of the immigration of young Asian women of childbearing age, of whom approximately 8 percent are HBsAg-positive with the majority of those also HBeAg-positive. In contrast, the number of HBsAg-positive Māori and Pacific women of childbearing age has decreased markedly due to infant vaccination. In addition, most HBsAg-positive Māori and Pacific women are HBeAg-negative, with lower HBV DNA levels (below  $10^8$  IU/mL).

Infants born to mothers who received oral antiviral therapy for chronic HBV must still receive the recommended neonatal HBIG/vaccine schedule. All other vaccines are administered as per the Schedule.

See Appendix 6 and section 9.8.1 for more information about passive immunisation and HBIG.

## Preterm and low birthweight infants of HBsAg-positive women

Preterm and low birthweight infants of HBsAg-positive women should be managed as above, regardless of birthweight or gestation.

### 9.5.3 Catch-ups for children and adolescents

HepB is recommended and funded for everyone aged under 18 years. If HepB is not given during the first year of life, three doses of vaccine are recommended given 0, 1 and 6 months.

For adolescents aged 10–15 years, an alternative two-dose hepatitis B catch-up schedule may be considered using the monovalent HepB with the second dose given six months after the first.

See Appendix 2 for catch-up schedules.

### Children and adolescents with liver or kidney disease

HepB vaccine is funded for liver or kidney transplant patients (recommend six months post-transplant) and for dialysis patients.

See Figure 9.3 and Figure 9.4 for serological testing and vaccination recommendations. If non-immune, children aged under 16 years should receive three doses of HepB; those aged 16 years and older should receive four doses of HepB given at 0, 1, 2 and 12 months. If there is an inadequate immune response to the initial three-dose HepB series (see Figure 9.4), give a further three doses, as appropriate for age.

See also 'Solid organ transplantation' in section 4.3.10, 'Chronic kidney disease' in section 4.4 and 'Chronic liver disease' in section 4.5.

### 9.5.4 Eligible adults aged 18 years and older

**Table 9.6: Hepatitis B vaccine schedules for eligible adults aged 18 years and older**

Who	Vaccine	Dose	Volume (mL)	Number of doses	Schedule
Dialysis patients, liver or kidney transplant patients	HepB	40 µg	1.0 (x2)	3	0, 1 and 6 months
HIV patients	HepB	20 µg	1.0	4	0, 1, 2 and 12 months
Other eligible adults (see Table 9.4)	HepB	20 µg	1.0	3	0, 1 and 6 months

**Adult** 1 dose (1 mL, 20 micrograms), according to schedule in table above; in *adults on dialysis, or who are liver or kidney transplant patients*, give two doses at separate sites (1 mL each, total dose 40 micrograms)



## Adult dialysis or adult liver or kidney transplant patients

These adults may have a reduced response to HepB,<sup>36,42</sup> so three higher doses (40 µg per dose) are recommended and funded.

See section 9.5.7 for information about post-vaccination serology.

(See also 'Solid organ transplantation' in section 4.3.10 and recommendations provided in IMAC factsheet '*Immunisation for adults pre-dialysis, on dialysis or pre-/post-kidney transplant*' available at [immune.org.nz/resources/factsheets](https://immune.org.nz/resources/factsheets).)

## Adult HIV patients

Adult HIV patients should receive four doses of HepB (20 µg per dose) at 0, 1, 2 and 12 months.

(See also 'HIV infection' in section 4.3.12 and recommendations provided in IMAC factsheet '*Immunisation for adults with HIV infection*' available from [immune.org.nz/resources/factsheets](https://immune.org.nz/resources/factsheets).)

## Other eligible adults

The optimal dosing regime is three doses of 20 µg HepB given at 0, 1 and 6 months. See the manufacturer's data sheet for sub-optimal accelerated HepB schedules if dosing is time constrained. For other eligible adults, see Table 4.8 'Other special groups' in section 4.6.

## 9.5.5 Pregnancy and breastfeeding

HepB may be given during pregnancy and while breastfeeding. Acute HBV infection in pregnant women may result in severe acute hepatitis for the mother, with associated increased risk of fetal loss or neonatal infection. Vaccination should not be withheld from a susceptible pregnant woman at increased risk of acquiring hepatitis B (eg, the sexual partner of an injecting drug user, or known infected male).

## 9.5.6 (Re)vaccination

Hepatitis B-containing vaccines are funded for vaccination and revaccination of eligible children, as follows. See also sections 4.2 and 4.3.

## DTaP-IPV-HepB/Hib (Infanrix-hexa)

An additional four doses (as appropriate) of DTaP-IPV-HepB/Hib are funded for vaccination or revaccination of children aged under 10 years:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- prior to planned or following other severely immunosuppressive regimens.

Up to an additional four doses (as appropriate) of DTaP-IPV-HepB/Hib are funded for children aged 10 years to under 18 years for (re)vaccination of patients post HSCT. This is an off-label use of this vaccine which requires a prescription from an authorised prescriber or the patient's specialist. In this group, all prior immunity will have been lost and revaccination is equivalent to a primary immunisation schedule. DTaP-IPV-HepB/Hib not recommended for other severely immunocompromised individuals aged 10-18 years that require revaccination as they may have residual immune memory.

## Monovalent HepB

HepB is funded for children aged under 18 years who are considered not to have achieved a positive serology and require additional vaccination.

### 9.5.7 Serological testing

- Serological testing is **not** routinely recommended – immunisation is highly effective.
- Most people with documented evidence of three HepB vaccinations will be immune for life.
- Unnecessary testing leads to unnecessary extra vaccination.
- Infants born to HBsAg-positive mothers and some individuals who require protection in relation to their employment (eg, health care professionals) require post-vaccination serology.
- Where there is concern about immunity follow Figure 9.3.

## Screening for chronic infection

Screening for the antigen (HBsAg) is useful where there is increased likelihood of the individual already being infected.

The Hepatitis Foundation of New Zealand recommends that the following individuals are most at risk of HBV:<sup>43</sup>

- people of Māori, Pacific or Asian ethnicity, unless fully vaccinated with HepB vaccine as an infant
- people born in an area of high hepatitis B endemicity, including Asia, the Pacific Islands, Africa, the Middle East, southern Europe or the northern or eastern parts of New Zealand's North Island
- people born to a mother or who have a close family member who has chronic HBV infection
- people who live with someone who has HBV
- people who have had unprotected sexual contact with an HBV-infected person
- people who have ever injected drugs
- people who have received a tattoo using unsterile equipment.

Screening for HBsAg is also part of routine antenatal care (see section 9.5.2).

All HBsAg-positive individuals should be offered follow-up under the Hepatitis Foundation Hepatitis B Follow-up Programme to enable early diagnosis and treatment of the complications of severe liver disease and hepatocellular carcinoma. Vaccination is funded for household or sexual contacts of HBsAg-positive people (ie, contacts of people with acute or chronic HBV infection).

To confirm chronic HBV status, repeat testing after 6 months and if still positive, refer patient to The Hepatitis Foundation.

## Serological testing for high-risk groups

Serological testing is **not** routinely recommended – immunisation is highly effective.

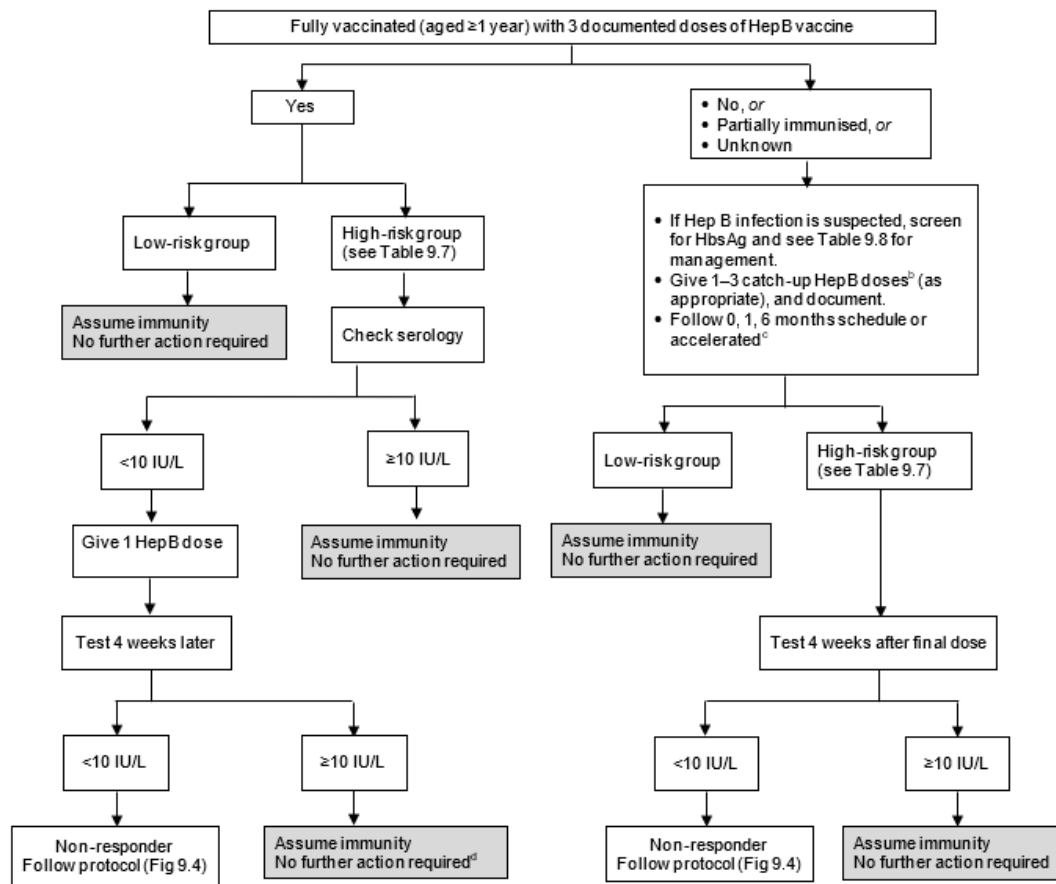
- Serological testing is only indicated in high-risk groups (see Table 9.7). These high-risk groups are at higher risk of exposure to HBV, at higher risk of having severe disease or are more susceptible to disease.
- A flow diagram (Figure 9.3) is included to assist in deciding whether pre- and/or post-vaccination serological testing is indicated. Figure 9.3 may be used for any individual aged 12 months or older, such as for the management of blood and body fluid exposures, or when an adult presents to primary care.

**Table 9.7: Individuals at high-risk of hepatitis B infection, for whom serological testing is indicated**

Household or sexual contacts of HBsAg-positive patients (ie, patients with acute or chronic HBV infection)
Current or recent injecting drug users
Individuals who change sexual partners frequently (eg, sex workers)
Immunocompromised individuals, including HIV-positive patients
Following non-consensual sexual intercourse
Individuals prior to planned immunosuppressive therapies for 28 days or more
Individuals following immunosuppressive therapies for 28 days or more
Solid organ and post-HSCT patients
Following percutaneous injury (eg, needle-stick injury)
Adults at occupational-related risk (see section 4.8)
Individuals with haemophilia and other regular recipients of blood products
Inmates of custodial institutions
Individuals with developmental disabilities
People with chronic disease (eg, chronic renal failure requiring haemodialysis, or chronic liver disease)
Migrants from HBV endemic regions (where HBsAg prevalence is $\geq 2$ percent)*

\* See the Centers for Disease Control and Prevention website for countries with an HBsAg prevalence  $\geq 2\%$  (<https://wwwnc.cdc.gov/travel/yellowbook/2020/travel-related-infectious-diseases/hepatitis-b>). Consider combined Hep A and B vaccination for individuals travelling to these regions.

**Figure 9.3: Flow diagram for serological testing for hepatitis B**



- HBIG may be recommended for non-immune individuals. See Table 9.8.
- Do not count any birth doses of HepB vaccine. See Table 9.4 for the list of funded conditions for HepB vaccine.
- See the manufacturer's data sheet for accelerated HepB schedules.
- Haemodialysis patients need annual testing and boosting if required.

## The non-responder protocol

Most vaccine recipients will develop a high anti-HBs titre, usually greater than 100 IU/L, which usually wanes over time.

Fully vaccinated individuals (ie, those who have received three documented doses of HepB) who have at any time had anti-HBs antibody titre of  $\geq 10$  IU/L do not need any booster doses, even if antibodies subsequently wane to undetectable levels, which occurs in most individuals by seven years after the last vaccination. Adults have been shown to have an anamnestic antibody and cellular immune response to a HepB dose given 20–30 years after the primary immunisation.<sup>24</sup> If exposed to HBV, they will have a secondary anamnestic immune response that will prevent replication of the virus.<sup>1, 44</sup>

Note: Some laboratories may require a higher anti-HBs antibody level for proof of immunity. Please follow the testing laboratory's interpretative comments.

If a high-risk individual does not achieve a titre of  $\geq 10$  IU/L by four weeks following one HepB dose, they should be considered a non-responder and follow the non-responder protocol (Figure 9.4).

**Figure 9.4: The non-responder protocol**

Individual is high-risk (see Table 9.7), has received three documented doses of HepB plus a booster dose and has an anti-HBs antibody titre  $< 10$  IU/L:

- Check serology for HBsAg and anti-HBc antibody to exclude chronic infection.
- Complete a second course with two further HepB vaccine doses, given at 1 and 6 months after booster dose.
- Repeat the serology four weeks after the final HepB vaccine dose
- If anti-HBs  $\geq 10$  IU/L, assume immunity. No further action is required.
- Where there is expertise available to administer intradermal injections, deliver 0.25 ml (5  $\mu$ g) of HepB intradermally<sup>45, 46</sup> at four sites (e.g. each deltoid and anterior thigh) ensuring a pale wheal is formed on the skin.
- Repeat serology four weeks later.
- If anti-HBs remains at  $\leq 10$  IU/L, repeat intradermal doses.
- Repeat serology 4 weeks later.
- If, after a second intramuscular three-dose course of HepB followed by two intradermal HepB doses given across multiple injection-sites, the individual has not achieved anti-HBs  $\geq 10$  IU/L, they should be considered a persistent non-responder to vaccination.
- Persistent non-responders with no immunocompromise who have completed the primary series and further courses of three vaccine doses should be monitored for wild-type disease, but literature reports disease from vaccine failures are rare. They should be considered 'unprotected' against hepatitis B and advised to minimise the chance of exposures. Parenteral or mucosal exposure to HBV requires HBIG within 72 hours.

## 9.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

The only specific contraindication to HepB is anaphylaxis following a previous dose, or individuals with a history of allergic reactions to yeast or any of the vaccine's components. Immunisation of previously infected subjects is wasteful, but not harmful.

See section 16.6 for contraindications and precautions to DTaP-IPV-HepB/Hib vaccine.

## 9.7 Potential responses and AEFIs

See section 16.7 for potential responses and AEFIs with DTaP-IPV-HepB/Hib vaccine.

### 9.7.1 Potential responses

Minor side-effects – including local tenderness and redness, nausea, diarrhoea, general malaise and fever – are more common in adults than in children and, except for local reactions, occur at rates close to those seen with a placebo. Minor reactions reported after receiving the vaccine include a temperature  $>37.7^{\circ}\text{C}$  in 1–6 percent; pain in 3–29 percent; and erythema, headache or swelling in 3 percent of vaccine recipients.

### 9.7.2 AEFIs

Allergic reactions have been reported but are rare. Anaphylaxis following vaccination is extremely rare (estimated to be 1.1 cases per million doses).<sup>47</sup>

A number of studies have examined and failed to find disease events linked to hepatitis B immunisation.<sup>48</sup> These studies have documented no increased risk of multiple sclerosis,<sup>49-51</sup> diabetes, chronic fatigue syndrome,<sup>52</sup> encephalomyelitis or hair loss.<sup>53</sup> Rarely, transient thrombocytopenia<sup>54</sup> and myalgia and arthralgia<sup>55, 56</sup> have been reported after HepB vaccination.

## 9.8 Public health measures

The elimination of HBV transmission is now a realistic public health goal<sup>7, 57</sup> especially with the proven effectiveness and safety record of HepB.<sup>58</sup> Achievement of this goal is being facilitated by the implementation of triple elimination strategies in the Western Pacific Region to prevent mother-to-child transmission of HIV, HBV and syphilis,<sup>8</sup> and the use of birth dosing HepB regimes, either universally or as directed.

It is important to ensure vaccination programmes are maintained for the at-risk populations, especially babies of mothers with chronic hepatitis B infection.

It is a legal requirement that all cases of acute hepatitis B infection be notified to the local medical officer of health.

Babies born to HBsAg-positive mothers should be notified at birth. The prevention of perinatal transmission is covered in section 9.5.2.

For further information about public health measures, see the *Hepatitis B* chapter of the *Communicable Disease Control Manual* at [www.tewhatauora.govt.nz/for-the-](http://www.tewhatauora.govt.nz/for-the-)



## 9.8.1 Passive immunisation

HBIG is prepared from donated blood plasma and contains high levels of anti-HBs antibody (see Appendix 6). It is given after exposure to HBV and provides passive anti-HBs antibody protection against acute and chronic HBV disease. HBIG prophylaxis should be given in combination with the HepB to confer both passive and active immunity after exposure.

The efficacy of HBIG alone in preventing clinical hepatitis B infection is about 75 percent in adults, but the protection lasts only for a few months.<sup>1</sup>

Whenever immediate protection is required, immunisation with a vaccine should be combined with simultaneous administration of HBIG at a different site. It has been shown that passive immunisation with HBIG does not suppress the active immune response to vaccination. A single dose of HBIG is sufficient (usually 400 IU for adults, 100–110 IU for newborns). If infection has already occurred at the time of the first immunisation, virus replication is unlikely to be inhibited completely, but severe illness and, more importantly, the development of chronic HBV infection may be prevented, particularly in the infants of HBsAg-positive mothers.

The management of contacts is summarised in Table 9.8.

**Table 9.8: Management of contacts of hepatitis B cases**

Contact	Serological testing of contact (HBsAg, anti-HBs, anti-HBc, IgM and IgG)	Immunoglobulin (if within 7 days of onset of case's symptoms)	Immunisation
Any sexual contact, including protected sex	Yes	Yes, immediately after blood taken	Yes, immediately after blood taken
Household, mucosal or percutaneous	Yes	Yes, if serology negative	Yes, if serology negative
Other	Yes	No	Yes, if serology negative

Source: Health New Zealand | Te Whatu Ora. *Communicable Disease Control Manual*. Wellington: Health New Zealand | Te Whatu Ora. URL: [www.tewhaturora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual](http://www.tewhaturora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual) (accessed 24 July 2024).

For further definitions and details see the Communicable Disease Control Manual at [www.tewhaturora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/hepatitis-b/](http://www.tewhaturora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/hepatitis-b/)

## 9.9 Variations from the vaccine data sheet

See section 16.9 for variations from the DTaP-IPV-HepB/Hib (Infanrix-hexa) data sheet.

Health New Zealand | Te Whatu Ora advises that two doses Enderix-B 20 µg, given six months apart, may be given to adolescents aged 10–15 years. The manufacturer's data sheet recommends three doses of 10 µg given at 0, 1 and 6 months, but in circumstances where compliance may not be assured, giving 20 µg per dose increases the proportion of recipients protected after the first and second doses.

Although the Health New Zealand and the data sheet recommend 0.5 ml Enderix-B 10 µg (paediatric formulation) for neonates born to HBV infected mothers, where the paediatric presentation is unavailable, the data sheet advises that Enderix-B 20 µg can be given to children from birth up to the age of 10 years.

Health New Zealand recommends giving three doses of 40 µg HepB (ie, two doses of Enderix-B 20 µg per visit) to be given 0, 1, and 6 months for adult renal dialysis patients, liver or kidney transplant patients. For adults with HIV, four doses of Enderix-B 20 µg is recommended given at 0, 1, 2 and 12 months. The data sheet advises four doses of 40 µg (ie, two doses for Enderix-B 20 µg per visit) given at 0, 1, 2 and 6 months for chronic haemodialysis patients and other individuals who have an impairment of their immune system.

## References

1. Van Damme P, Ward J, Shouval D, Zanetti P. 2018. Hepatitis B Vaccines, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
2. McMahon BJ, Alward WL, Hall DB, et al. Acute hepatitis B virus infection: relation of age to the clinical expression of disease and subsequent development of the carrier state. *Journal of Infectious Diseases*, 1985. 151(4): p. 599-603.
3. Stockdale AJ, Kreuels B, Henrion MYR, et al. The global prevalence of hepatitis D virus infection: systematic review and meta-analysis. *Journal of Hepatology*, 2020.
4. Bond WW, Favero MS, Petersen NJ, et al. Survival of hepatitis B virus after drying and storage for one week. *Lancet*, 1981. 1(8219): p. 550-1.
5. Alter HJ. To have B or not to have B: vaccine and the potential eradication of hepatitis B. *Journal of Hepatology*, 2012. 57(4): p. 715-7.
6. Papastergiou V, Lombardi R, MacDonald D, Tsochatzis EA. Global epidemiology of hepatitis B Virus (HBV) infection. *Current Hepatology Reports*, 2015. 14(3): p. 171-178.
7. World Health Organization. 2016. *WHO Global Health Sector Strategy on Viral Hepatitis 2016–2021* (ed.), Geneva, Switzerland: World Health Organization. URL: <https://apps.who.int/iris/handle/10665/246177> (accessed 10 May 2022)
8. World Health Organization. Hepatitis B vaccines: WHO position paper - July 2017. *Weekly Epidemiological Record*, 2017. 92(27): p. 369-392.

9. World Health Organization. *China steers towards zero new hepatitis B infections (Press release)*. World Health Organization. 30 March 2019 URL: <https://www.who.int/hepatitis/news-events/china-hbv-childhood-vaccination/en/>. (accessed 3 July 2020)
10. Chiang CJ, Yang YW, You SL, et al. Thirty-year outcomes of the national hepatitis B immunization program in Taiwan. *JAMA*, 2013. 310(9): p. 974-6.
11. Harris AM. 2020. Hepatitis B. in *CDC 2020 Yellow Book. Health Information for International Travel*. New York, New York. URL: <https://wwwnc.cdc.gov/travel/yellowbook/2020/travel-related-infectious-diseases/hepatitis-b>. (accessed 3 July 2020)
12. Ott JJ, Stevens GA, Groeger J, Wiersma ST. Global epidemiology of hepatitis B virus infection: new estimates of age-specific HBsAg seroprevalence and endemicity. *Vaccine*, 2012. 30(12): p. 2212-9.
13. Milne A, Allwood GK, Moyes CD, et al. Prevalence of hepatitis B infections in a multiracial New Zealand community. *New Zealand Medical Journal*, 1985. 98(782): p. 529-32.
14. Moyes C, Milne A. Hepatitis B markers in 14–15 year olds in the Bay of Plenty. *The New Zealand Medical Journal*, 1986. 99(809): p. 662–4.
15. Rainger W, Solomon N, Jones N. Immunisation coverage and risk factors for immunisation failure in Auckland and Northland. *New Zealand Public Health Report*, 1998. 5(7): p. 49–51.
16. Ramadas D, Moyes CD, Ramadas G. Immunisation status of children in the eastern Bay of Plenty. *New Zealand Medical Journal*, 1992. 105(942): p. 378-9.
17. Stehr-Green P, Briasco C, Baker M. How well are we protecting our children? An immunisation coverage survey in Hawke's Bay. *The New Zealand Medical Journal*, 1992. 105(938): p. 277–9.
18. The Hepatitis Foundation of New Zealand. *2030 Targets*. The Hepatitis Foundation of New Zealand,; URL: <https://www.hepatitisfoundation.org.nz/2030-targets>. (accessed 11 May 2020)
19. Robinson T, Bullen C, Humphries W, et al. The New Zealand Hepatitis B Screening Programme: screening coverage and prevalence of chronic hepatitis B infection. *New Zealand Medical Journal*, 2005. 118(1211): p. U1345.
20. Mann J, Roberts M. Modelling the epidemiology of hepatitis B in New Zealand. *J Theor Biol*, 2011. 269(1): p. 266-72.
21. Addidle M. Impact of universal hepatitis B vaccination on antenatal hepatitis B prevalence in the Midlands region of the North Island, New Zealand. *New Zealand Medical Journal*, 2011. 124(1332): p. 40-4.
22. Lim TH, Gane E, Moyes C, et al. Serological and clinical outcomes of horizontally transmitted chronic hepatitis B infection in New Zealand Maori: results from a 28-year follow-up study. *Gut*, 2015. 64(6): p. 966-72.
23. Lee C, Gong Y, Brok J, et al. Effect of hepatitis B immunisation in newborn infants of mothers positive for hepatitis B surface antigen: systematic review and meta-analysis. *BMJ*, 2006. 332(7537): p. 328-36.
24. Van Damme P, Dionne M, Leroux-Roels G, et al. Persistence of HBsAg-specific antibodies and immune memory two to three decades after hepatitis B vaccination in adults. *Journal of Viral Hepatitis*, 2019. 26(9): p. 1066-1075.
25. Gruber C, Warner J, Hill D, et al. Early atopic disease and early childhood immunization--is there a link? *Allergy*, 2008. 63(11): p. 1464-72.
26. Moyes CD, Milne A, Waldon J. Very low dose hepatitis B vaccination in the newborn: anamnestic response to booster at four years. *Journal of Medical Virology*, 1990. 30(3): p. 216-8.

27. West DJ ,Calandra GB. Vaccine induced immunologic memory for hepatitis B surface antigen: implications for policy on booster vaccination. *Vaccine*, 1996. 14(11): p. 1019-27.
28. Van Der Meeren O, Bleckmann G ,Crasta PD. Immune memory to hepatitis B persists in children aged 7-8 years, who were vaccinated in infancy with 4 doses of hexavalent DTPa-HBV-IPV/Hib (Infanrix hexa) vaccine. *Human Vaccines & Immunotherapeutics*, 2014. 10(6): p. 1682-7.
29. Su WJ, Liu CC, Liu DP, et al. Effect of age on the incidence of acute hepatitis B after 25 years of a universal newborn hepatitis B immunization program in Taiwan. *Journal of Infectious Diseases*, 2012. 205(5): p. 757-62.
30. McMahon BJ, Bulkow LR, Singleton RJ, et al. Elimination of hepatocellular carcinoma and acute hepatitis B in children 25 years after a hepatitis B newborn and catch-up immunization program. *Hepatology*, 2011. 54(3): p. 801-7.
31. Perz JF, Elm JL, Jr., Fiore AE, et al. Near elimination of hepatitis B virus infections among Hawaii elementary school children after universal infant hepatitis B vaccination. *Pediatrics*, 2006. 118(4): p. 1403-8.
32. Chen D-S. Hepatitis B vaccination: The key towards elimination and eradication of hepatitis B. *Journal of Hepatology*, 2009. 50(4): p. 805-16.
33. Chang M-H. 2011. Hepatitis B virus and cancer prevention, in *Clinical Cancer Prevention*, Senn H-J, Otto F (eds). Springer: Berlin & Heidelberg.
34. Lee CL ,Ko YC. Hepatitis B vaccination and hepatocellular carcinoma in Taiwan. *Pediatrics*, 1997. 99(3): p. 351-3.
35. Whitford K, Liu B, Micallef J, et al. Long-term impact of infant immunization on hepatitis B prevalence: a systematic review and meta-analysis. *Bulletin of the World Health Organization*, 2018. 96(7): p. 484-497.
36. el-Reshaid K, al-Mufti S, Johny KV, Sugathan TN. Comparison of two immunization schedules with recombinant hepatitis B vaccine and natural immunity acquired by hepatitis B infection in dialysis patients. *Vaccine*, 1994. 12(3): p. 223-34.
37. Committee on Infectious Diseases. Update on timing of hepatitis B vaccination for premature infants and for children with lapsed immunisation. *Pediatrics*, 1994. 94(3): p. 403-4.
38. American Academy of Pediatrics. 2018. Hepatitis B. in *Red Book: 2018 Report of the Committee on Infectious Diseases*, Kimberlin D, Brady M, Jackson M, and Long S (eds). URL: <https://redbook.solutions.aap.org/redbook.aspx>. (accessed 3 July 2020)
39. Scheller NM, Svanstrom H, Pasternak B, et al. Quadrivalent HPV vaccination and risk of multiple sclerosis and other demyelinating diseases of the central nervous system. *JAMA*, 2015. 313(1): p. 54-61.
40. Benarroch EE. Postural tachycardia syndrome: a heterogeneous and multifactorial disorder. *Mayo Clinic Proceedings*, 2012. 87(12): p. 1214-25.
41. Borucki AN ,Greco CD. An update on complex regional pain syndromes in children and adolescents. *Current Opinion in Pediatrics*, 2015. 27(4): p. 448-52.
42. Roukens AH ,Visser LG. Hepatitis B vaccination strategy in vaccine low and non-responders: a matter of quantity of quality? *Hum Vaccin*, 2011. 7(6): p. 654-7.
43. Hepatitis Foundation of New Zealand. *Hepatitis B for health professionals*. URL: <https://www.hepatitisfoundation.org.nz/health-professionals/hepatitis-b-health-professionals>. (accessed 20 January 2020)
44. European Consensus Group on Hepatitis B Immunity. Are booster immunisations needed for lifelong hepatitis B immunity? European Consensus Group on Hepatitis B Immunity. *Lancet*, 2000. 355(9203): p. 561-5.
45. Yousaf F, Gandham S, Galler M, et al. Systematic review of the efficacy and safety of intradermal versus intramuscular hepatitis B vaccination in end-stage renal disease

- population unresponsive to primary vaccination series. *Renal Failure*, 2015. 37(7): p. 1080-8.
46. David MC, Ha SH, Paynter S, Lau C. A systematic review and meta-analysis of management options for adults who respond poorly to hepatitis B vaccination. *Vaccine*, 2015. 33(48): p. 6564-9.
  47. Bohlke K, Davis RL, Marcy SM, et al. Risk of anaphylaxis after vaccination of children and adolescents. *Pediatrics*, 2003. 112(4): p. 815-20.
  48. Institute of Medicine: Committee to Review Adverse Effects of Vaccines. 2012. *Adverse effects of vaccines: Evidence and causality* (ed.), Washington, DC: The National Academies Press. URL: <https://www.nap.edu/catalog/13164/adverse-effects-of-vaccines-evidence-and-causality> (accessed January 2020)
  49. Expanded Programme on Immunization (EPI). Expanded programme on immunization (EPI). Lack of evidence that hepatitis B vaccine causes multiple sclerosis. *Weekly Epidemiological Record*, 1997. 72(21): p. 149-52.
  50. Mouchet J, Begaud B. Hepatitis B vaccination and central demyelination - History, description and observed/expected analyses of 624 cases reported to the French pharmacovigilance over a 20-year period. *Vaccine*, 2019. 37(15): p. 2142-2148.
  51. Sadovnick AD, Scheifele DW. School-based hepatitis B vaccination programme and adolescent multiple sclerosis. *The Lancet*, 2000. 355(9203): p. 549-50.
  52. Health and Welfare Canada. Report of the working group on the possible relationship between hepatitis B vaccination and the chronic fatigue syndrome. *Canadian Communicable Disease Report*, 1993. 19(4): p. 25-8.
  53. Wise RP, Kiminyo KP, Salive ME. Hair loss after routine immunizations. *JAMA*, 1997. 278(14): p. 1176-8.
  54. Ronchi F, Cecchi P, Falcioni F, et al. Thrombocytopenic purpura as adverse reaction to recombinant hepatitis B vaccine. *Archives of Disease in Childhood*, 1998. 78(3): p. 273-4.
  55. Fisher MA, Eklund SA, James SA, Lin X. Adverse events associated with hepatitis B vaccine in U.S. children less than six years of age, 1993 and 1994. *Annals of Epidemiology*, 2001. 11(1): p. 13-21.
  56. McMahon BJ, Helminiak C, Wainwright RB, et al. Frequency of adverse reactions to hepatitis B vaccine in 43,618 persons. *American Journal of Medicine*, 1992. 92(3): p. 254-6.
  57. Ni YH, Chang MH, Wu JF, et al. Minimization of hepatitis B infection by a 25-year universal vaccination program. *Journal of Hepatology*, 2012. 57(4): p. 730-5.
  58. Romanò L, Paladini S, Van Damme P, Zanetti AR. The worldwide impact of vaccination on the control and protection of viral hepatitis B. *Digestive and Liver Disease*, 2011. 43 Suppl 1(Suppl 1): p. S2-7.

# 10 Human papillomavirus

## Key information

Mode of transmission	Skin-to-skin contact, predominantly sexual, with a person with human papillomavirus (HPV) infection.
Period of communicability	HPV infection is very common, with initial infection occurring soon after sexual debut and a lifetime risk of over 80%. Recurrent infection and co-infection with multiple types are possible.
Incidence and burden of disease	HPV is linked to almost all cervical cancers and to about 69% of vulvar, 75% of vaginal, 63% of penile, 90% of anal and 70% of oropharyngeal cancers.
Funded vaccine	HPV9 (Gardasil 9) is a recombinant subunit vaccine containing virus-like particles (VLPs). HPV9 contains HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58.
Dose, presentation, route	0.5 mL per dose. Pre-filled syringe. Intramuscular injection.
Funded indications and recommended schedules	2 doses, at 0 and 6–12 months for children aged 14 years and under. 3 doses, at 0, 2 and 6 months, for individuals: <ul style="list-style-type: none"><li>aged 15–26 years inclusive</li><li>aged 9–26 years inclusive:<ul style="list-style-type: none"><li>with confirmed HIV infection or</li><li>who are transplant (including stem cell) patients</li></ul></li></ul> An additional dose for individuals aged 9–26 years post-chemotherapy. NB: Individuals who were previously fully vaccinated with HPV4 are not eligible for HPV9.
Vaccine effectiveness	The incidence of HPV infection, precancerous lesions and genital warts is significantly reduced in immunised populations (in women and men). There is evidence for herd immunity (reductions in HPV infection and genital warts in unimmunised populations).
Precautions and special considerations	HPV vaccines are not recommended for pregnant women; however, enquiring about the possibility of pregnancy is not necessary before vaccination.
Potential responses to vaccine	Syncope (fainting) and other immunisation-related stress reactions are associated with giving vaccine to adolescents.
Public health measures	Measures for cancer prevention (see section 10.8): <ul style="list-style-type: none"><li>HPV immunisation.</li><li>Regular cervical screening for women.</li><li>Safer sex approaches.</li></ul>



## 10.1 Virology and the causal link to cancer

Human papillomaviruses (HPVs) are small, non-enveloped DNA viruses from the Papillomavirus family. There are about 150 different HPV serotypes. They vary in their preference for infecting squamous epithelium at different sites, thereby causing the various types of HPV infection (eg, common, palmar, plantar or anogenital). More than 40 HPV types can infect the anogenital tract.<sup>1,2</sup>

Data from the US cancer registry indicates that HPV is causally associated with almost all cervical cancers, about 69 percent of vulvar, 75 percent of vaginal, 63 percent of penile, 90 percent of anal and 70 percent of oropharyngeal cancers (see Table 10.1).<sup>3</sup>

Based on their causal link to cancer, HPVs are divided into low-risk and high-risk types. There are approximately 12 high-risk types, which include 16, 18 and types 31, 33, 52, 58 and 45 that are genetically related to 16 and 18.<sup>4</sup> Types 16 and 18 are most frequently associated with cervical cancer but are also causally associated with other cancers. In the US, HPV types 16 and 18 are estimated to cause 66 percent of invasive cervical cancers, 80 percent of anal, 49 percent of vulvar, 55 percent of vaginal, 48 percent of penile and 60 percent of oropharyngeal cancers annually (Table 10.1).<sup>3</sup>

Low-risk types (especially types 6 and 11) are predominantly associated with non-malignant lesions, such as genital warts, and recurrent respiratory papillomatosis.



**Table 10.1: Average annual percentage of cancer cases attributable to HPV, by anatomic site and sex, United States, 2008–2010**

Anatomic site <sup>c</sup>	Cancers attributable to any HPV <sup>a, b</sup> %	Cancers attributable to HPV 16, 18 <sup>a, b</sup> %	Cancers attributable to HPV 31, 33, 45, 52, 58 <sup>a, b</sup> %
Cervix	90.6 <sup>d</sup>	66.2	14.7
Vulva	68.8	48.6	14.2
Vagina	75.0	55.1	18.3
Penis	63.3	47.9	9.0
Anus			
• women	92.5	79.5	10.8
• men	88.7	79.1	3.8
Oropharyngeal			
• women	63.3	50.8	9.5
• men	72.4	63.4	4.4

a. Data is from 2008–2010 diagnosis years from population-based cancer registries that participate in the National Program of Cancer Registries and/or the Surveillance, Epidemiology, and End Results Program.

b. These estimates do not consider future changes in incidence, population structure or the percentage of cancers that are HPV positive.

c. International Classification of Diseases (ICD) codes: Cervix C53; Vulva C51; Vagina C52; Penis C60; Anus C21; Oropharyngeal (includes cancers of the soft palate, walls of pharynx, tonsils and base of tongue) C01.9, C02.4, C02.8, C05.1, C05.2, C05.9, C09.0, C09.1, C09.8, C09.9, C10.0, C10.2, C10.8, C10.9, C14.0, C14.2, and C14.8.

d. Although HPV is accepted to be a necessary factor in the causal pathway to invasive cervical cancer, HPV is not always detected in tumour specimens from women who receive a diagnosis of invasive cervical cancer due to a variety of reasons, including misclassification of tissue specimens as cervix, quality of tissue specimens, assay sensitivity, and a small proportion of HPV-negative, cervical cancers.

Adapted from: Saraiya M, Unger ER, Thompson TD, et al. 2015. US Assessment of HPV types in cancers: Implications for current and 9-valent HPV vaccines. *Journal of the National Cancer Institute* 107(6), DOI: 10.1093/jnci/djv086 Table 4.

## 10.2 Clinical features

### 10.2.1 Infection

Infection results from predominantly sexual skin-to-skin contact with a person with HPV infection. Transmission in the genital region may occur even when condoms are used and does not necessarily require penetrative intercourse. HPV may also be transmitted perinatally from mother to newborn baby.

Clinically apparent warts are probably more infectious than subclinical infection. The virus penetrates micro-abrasions in the epithelium to reach the basal epithelial cells, where it causes the infected cells to produce proteins that delay cellular maturation. Continued replication of these infected cells in the intermediate epithelial layer, followed by virus replication in the superficial epithelial layer, results in the cellular overgrowth typical of warts.

For most people, HPV infection is transient and becomes undetectable by DNA testing within 6 to 12 months, but in some cases, HPV infection remains latent and may reactivate years later. As it is difficult to detect HPV in its latent stage, it is impossible to know whether the immune system can completely clear the virus or whether, in some cases, undetectable latent virus is capable of later re-emerging.

## Acquisition of HPV

Infection with oncogenic serotypes of HPV is common, with an estimated 70–80 percent of sexually active individuals becoming infected at some stage during their life. Initial infection occurs soon after sexual debut.

Most episodes of infection become undetectable by DNA testing within two years of acquisition; the average duration of infection is one year. Previous infection does not necessarily create long-term immune memory so does not prevent future re-infection with the same HPV type.

At any one time, approximately 10 percent of women have at least one HPV infection. The HPV serotypes that cause more prolonged infection tend to be those that more frequently result in the development of histological abnormalities.<sup>5, 6</sup>

Two US studies found that incidence of genital HPV infection was higher in men than for similar cohorts of young women. In university students (age 18–20 years), the cumulative incidence of first-time infection at 24 months was 32 percent (95% CI: 28.0–37.1) for females compared with 62.4 percent (95% CI: 52.6–72.2) in heterosexually active male students. Frequent new sexual partners and a history of smoking were associated with an elevated risk of HPV acquisition for both.<sup>7, 8</sup>

There are differences between the sexes in the immune response to HPV. A smaller proportion of men are HPV-seropositive, and men have lower antibody titres than women.<sup>9</sup> In contrast to women, for whom the risk for HPV acquisition increases with age through the early 20s and then decreases, studies have demonstrated HPV prevalence in men seems to peak at slightly older ages and remains constant or decreases slightly with increasing age, suggesting persistent HPV infection or a higher rate of re-infection.<sup>10, 11</sup>

Men who have sex with men, especially those who are HIV-positive, are at higher risk for HPV infection, anal cancer and high-grade anal intraepithelial neoplasia.<sup>12</sup> In teenage men who have sex with men (aged 16–20 years), early and high per-partner HPV transmission occurs between men soon after their first sexual experiences.<sup>13</sup>

Individuals who are immunocompromised (due to medical conditions or treatment) are more likely to develop a persistent HPV infection and to subsequently progress to HPV-related disease.<sup>14, 15</sup> Those with confirmed HIV infection are more at risk of HPV infection.<sup>16</sup> HPV is less likely to become undetectable in individuals coinfecting with HIV.<sup>17, 18</sup> A direct relationship has been identified between low CD4+ cell count and an increased risk of cervical cancer in HIV-infected women.<sup>19</sup>

## 10.2.2 Cervical cancer

HPV rapidly becomes undetectable in the first 6–12 months of acquisition of infection, with 80–90 percent undetectable by two years. Following this, a very small fraction of persistent infection progresses to cervical intraepithelial neoplasia (CIN); these are non-invasive precancerous lesions, which are categorised as either low- or high-grade CIN. Invasive cervical cancer occurs when the lesions invade the cervical tissue, and is graded from stage I to IV, depending on how far the cancer has spread beyond the cervix into surrounding tissue or organs.

Cervical cancer does not usually develop until decades after acquisition of infection with an oncogenic (cancer-causing) HPV serotype. Persistent HPV infection is detected in almost all women with cervical cancer.<sup>20</sup>

HPV infection is essential, but not sufficient by itself, for the development of cervical cancer. Other factors have been described that may be associated with HPV persistence and high-grade lesions including smoking, early onset sexual activity, older age, contraceptive use, multiple sexual partners and genetic factors.<sup>21, 22</sup>

## 10.2.3 Oropharyngeal and other cancers

The clinical features of other HPV-associated cancers and their precancerous lesions in the anogenital and oropharyngeal regions vary, and also depend on the anatomical site. The progression from HPV-associated precancer lesions to cancers in these sites is less well understood than the process in the cervix.

Oropharyngeal cancers include cancers of the soft palate, the walls of the pharynx, the tonsils and the base of the tongue. The risk factors for oropharyngeal cancer are similar to those for cervical cancer, including the number of sexual partners, younger age at first sexual intercourse, practice of oral sex, history of genital warts and younger age.<sup>23</sup>

## 10.2.4 Genital warts and recurrent respiratory papillomatosis

HPV 6 and 11 account for around 90 percent of all genital wart cases. Most warts cases are self-limited, although some may persist for several years. Persistence is more common in patients with impaired cell-mediated immunity.<sup>2</sup>

Perinatal transmission of HPV (usually types 6 or 11) can cause laryngeal infection in infants, which in rare cases can result in recurrent respiratory papillomatosis in children. Respiratory papillomatosis is characterised by multiple warty growths on the mucosal surface of the respiratory tract, which can cause hoarseness and significantly obstruct the airways and require repeated surgery.<sup>2</sup>

## 10.3 Epidemiology

### 10.3.1 Global burden of disease

HPV is an important carcinogenic infection. The 12 high-risk types are reported to be the second most common infectious cause of cancer worldwide after *Helicobacter pylori*.<sup>24</sup> It has been estimated that 4.5 percent of all cancers (630,000 new cancer cases per year) are attributable to HPV; over 70 percent are attributable to HPV types 16 and 18, and 90 percent to types contained within the HPV9 vaccine. The greatest burden is in India and sub-Saharan Africa, where there is limited access to both screening and vaccination, and more than 20 percent of cancers in women are attributable to HPV infection.<sup>25</sup>

#### Onset of sexual activity

Most HPV infections occur within the first two years of onset of sexual activity; more than 40 percent of individuals become infected during this period. The first sexual relationship carries a substantial risk.<sup>26</sup>

#### Cervical cancer

Cervical cancer is the fourth cause of female cancer and cancer deaths in the world and is the second most common cause of female cancer and cancer deaths in women aged 15–44 years; the estimated incidence rate of cervical cancer cases attributable to HPV across Oceania was 10.1 (range 5.6–28.3) per 100,000 across all ages; the estimated annual mortality was 4.6 (range 1.6–18.6) per 100,000 in 2020.<sup>27</sup>

Persistent HPV infection can lead to high-grade CIN. Approximately one-third of CIN3 progresses to invasive cervical cancer within 10–20 years. A 2010 study reported that more than one-quarter (26.7 percent; 95% CI: 21.1–31.8) of those with persistent HPV16 and nearly one in five (19.1 percent; 95% CI: 10.4–27.3) of those with persistent HPV18 developed CIN3 or cancer within 12 years.<sup>28</sup> A multi-national study across 38 countries found HPV types 16, 18, 31, 33, 45, 52 and 58 in 85 percent of invasive cervical cancer cases, 71 percent (95% CI: 70–72) of cervical adenocarcinomas were positive for HPV16 and 18 and 94 percent (95% CI: 92–96) were positive for HPV16, 18 and 45.<sup>20</sup>

#### Other HPV-related cancers

Oncogenic HPV types are linked to other cancers in women and men, including vulval, vaginal, penile, anal and oropharyngeal cancers (see Table 10.1).

## Anal cancers

Anal cancer remains relatively rare compared to other cancers, but the global incidence has increased among both men and women, particularly in high-income regions (the average worldwide incidence is 0.5 per 100,000 population in 2020).<sup>27</sup> Women have a higher incidence of anal cancer than men. The incidence is highest among men who have sex with men, women with history of cervical or vulvar cancer, and immunosuppressed populations, including those who are HIV-infected and patients with a history of organ transplantation.<sup>27</sup>

## Oropharyngeal cancers

There has been an increase in the incidence of head and neck cancers over the past few decades. This increase is mainly due to an unexpected increase in HPV-related oropharyngeal cancers, primarily in males aged 40–55 years with exposure to alcohol and tobacco.<sup>29</sup>

Most recent data suggest that around one-quarter of all oropharyngeal cancers are attributable to HPV infection; the most frequent type is HPV16.<sup>25, 27</sup> (see Table 10.1).

## Vulval and vaginal cancer

Vulval and vaginal cancers are rare worldwide, representing 4 percent and 2 percent of all gynaecological cancers. Incidence is highest in less developed countries.<sup>27</sup>

## Genital warts

Genital warts, which are most commonly due to infection with HPV6 or HPV11, have a prevalence of approximately 1 percent of adults in the US.<sup>30, 31</sup> Scandinavian countries have reported rates as high as 10 percent.<sup>32</sup>

## 10.3.2 New Zealand epidemiology

### Onset of sexual activity

Data from the Youth'12 survey suggests that approximately 8 percent of New Zealand adolescents may have had sexual intercourse before the age of 13 years.<sup>33, 34</sup> This increases to 24 percent by the age of 15 years and 46 percent by age 17 years.

Compared to 2001, students were more likely to delay sexual debut in 2012 but less likely to use condoms and contraception consistently.<sup>35</sup> Māori (OR 0.7; 95% CIs: 0.6–0.8) and Pacific (OR 0.5; 95% CIs: 0.4–0.7) students used condoms less frequently than NZ European students; those from socioeconomically deprived communities (school decile 1) used condoms less frequently (OR 0.7; 95% CIs: 0.5–0.9) than students from wealthier communities (school decile 10).<sup>35</sup>

## Cervical cancer

### HPV prevalence in precancerous lesions and invasive cervical cancer

The prevalence of HPV infection and distribution of HPV types among New Zealand women with histologically confirmed CIN 2/3<sup>36, 37</sup> or invasive cervical cancer<sup>38</sup> was broadly consistent with that seen internationally. During 2011–2012, 97 percent (95% CI: 94–98) of women with histologically confirmed CIN 2/3 were HPV-positive, and the prevalence of any high-risk HPV was 96 percent (95% CI: 91–99).<sup>36</sup> In women with histologically confirmed invasive cervical cancer during 2004–2010, 88.5 percent (95% CI: 83.7–92.4) were HPV-positive, and the prevalence of any high-risk HPV was 87.2 percent (95% CI: 82.2–91.3).<sup>38</sup> For both CIN 2/3 and invasive cervical cancer, the overall distribution of HPV types was similar in Māori and non-Māori women, with HPV16 being the most commonly detected HPV type in both groups.<sup>36, 38</sup>

### Cervical cancer registrations and deaths

In 2018 (provisional), there were 191 new cervical cancer registrations, an increase from 164 in 2017.<sup>39</sup> In 2017, the age-standardised registration rate was 6.0 per 100,000 population, similar to the 2016 rate (6.4 per 100,000). The registration rate for Māori women was 9.4 per 100,000, 1.7 times greater than the rate for non-Māori women (5.4 per 100,000).<sup>39</sup>

There were 55 cervical cancer deaths in 2016. In 2014, when there were 46 deaths (1.4 deaths per 100,000 population) and the mortality rate for Māori women was 3.0 per 100,000, 2.7 times greater than for non-Māori women (1.1 per 100,000).<sup>40</sup>

### Other HPV-related cancers

The most recent New Zealand data available for other HPV-related cancers is from 2017 (see Table 10.2). Note that this data is for new cancer registrations only; the tumours have not been analysed for the presence of HPV.

**Table 10.2: Number and age-standardised rate of new registrations for other cancers known to be associated with HPV in New Zealand, 2017**

Anatomic site*	Number of new registrations	Rate of new registrations (per 100,000)
Vulva	52	1.2
Vagina	19	0.5
Penis	18	0.5
Anus		
• women	40	1.1
• men	21	0.6
Oropharynx		
• women	4	0.1
• men	10	0.3
Tonsils		
• women	21	0.6
• men	85	2.7

\* ICD codes: Vulva C51; Vagina C52; Penis C60; Anus C21; Oropharynx C10; Tonsils C09. (Note that in Table 10.1, the US definition for oropharyngeal cancer combines multiple cancers, using 4-character ICD codes. At the time of writing, New Zealand data for 2017 was only available at the 3-character ICD code level.)

Source: Ministry of Health. 2019. *New cancer registrations 2017*. Wellington: Ministry of Health URL: [www.health.govt.nz/publications/new-cancer-registrations-2017](http://www.health.govt.nz/publications/new-cancer-registrations-2017) (accessed 20 June 2020).

## Anal cancers

For the period 2008–2012, the age-standardised rate for anal cancer was 0.6 and 1.1 per 100,000 persons per year among men and women in New Zealand, respectively.<sup>27</sup> It remained the same in 2017 (see Table 10.2).

## Oropharyngeal cancers

A retrospective review of New Zealand cancer registry data for the period 1981–2010 showed a rapid rise in oropharyngeal cancers in men (mainly in those aged 40 years or older), particularly from 2005 onwards.<sup>41</sup> The rate of oropharyngeal cancers was almost four times greater in men (1.87 per 100,000) than in women (0.47 per 100,000). The incidence rates for oral cavity cancer, which is generally associated with alcohol and tobacco consumption, remained relatively stable in both sexes during that time. (Note that this study included both oropharyngeal and oral cavity cancers.)

A significant increase in HPV-positive oropharyngeal cancer (OR 5.65; 95% CI: 2.60–12.30) was detected in biopsies taken during 1996–1998 and 2010–2012 and occurring at a younger age (OR 0.55; 95% CI: 0.33–0.99) aged 61 or older and age 60 years or younger). Most cases attributable to HPV were HPV16-positive (98.5 percent); there was also one case each of HPV 33 and 35.<sup>42</sup>



## Genital warts

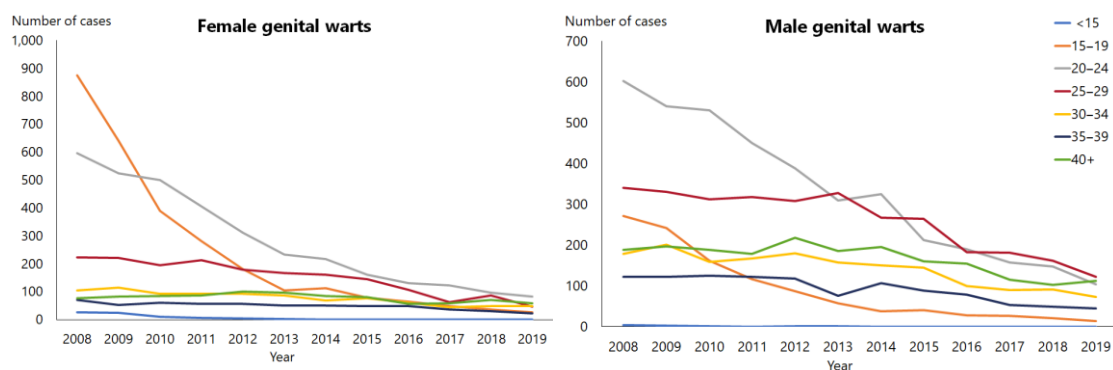
Many sexually transmitted infections (STIs), including genital warts, are not notifiable in New Zealand. ESR cautions that the number of cases of genital warts reported through the clinic-based surveillance system likely underestimates the true burden of disease in New Zealand because a substantial percentage of STIs are diagnosed by other health care providers.

Following the introduction of HPV4 vaccine to females in 2008 and the introduction of HPV9 vaccine for males and females in 2017, from 2008 to 2019 genital warts clinical case counts reported by sexual health clinics have decreased by 79.5 percent (from 3,681 to 756 cases) and case counts reported by family planning clinics decreased by 77.8 percent (from 573 to 127 cases) (ESR 26 June 2020). Since the introduction of the HPV vaccination programme, there have been decreases in the number of genital warts diagnoses in all ethnic groups in sexual health clinics and in all ethnic groups, except 'Other', in family planning clinics.

In sexual health clinics, the decrease was most notable in the 15–19 years and 20–24 years age groups, and there was a moderate decrease in the 25–29 years age group, in both sexes (Figure 10.1). A marked decrease was following the extension of vaccination to males in 2017. From 2016 to 2019, reported cases decreased by 50 percent (from 28 to 14 cases) in the younger males aged 15–19 years and 45.3 percent (from 190 to 104 cases) in those aged 20–24 years (ESR, 26 June 2020). A decrease in cases seen in older age groups suggests that immunisation is also providing some herd immunity to unvaccinated individuals. A decline in the number of prescriptions for treating genital warts (imiquimod and podophyllum resin-based products) supports this evidence for a herd immunity effect.<sup>43</sup> The largest decline was seen in women aged under 20 years.

A study in Auckland sexual health clinics found a similar population effect in genital wart cases over five years following the introduction of HPV4 to women in 2009. A significant reduction in new genital warts cases was observed in a vaccine-eligible age group of females (aged <20 years), not observed in older age-groups (those aged over 20 years) or in males, not eligible to receive vaccination at that time. There was a smaller but not statistically significant decrease in genital warts cases in younger males (age <20 years) compared with that seen in older males.<sup>44</sup>

**Figure 10.1: Number of genital warts (first presentation) in sexual health clinics, by sex and age group, 2008–2019**



Source: ESR

For further details of genital wart notifications, refer to the most recent STI quarterly and annual reports from ESR (available [www.esr.cri.nz/digital-library/sti-quarterly-dashboard/](http://www.esr.cri.nz/digital-library/sti-quarterly-dashboard/)).

## 10.4 Vaccines

### 10.4.1 Available vaccines

One HPV vaccine, HPV9 (Gardasil 9, Seqirus/MSD), is approved for use (registered) and is available for distribution (marketed) in New Zealand.

HPV9 is registered for use in females and males aged 9–45 years as a two-dose schedule in individuals aged 14 years and under, and as a three-dose schedule in older individuals and immunocompromised individuals from age 9 years.

The vaccine contains HPV virus-like particles (VLPs), which are composed of the L1 protein (a component of the virus outer layer) aggregated into clumps that mimic the outer structure of the HPV virion. The VLPs do not contain viral DNA and are incapable of causing infection. The L1 proteins are produced by genetically engineered yeast cells.

#### Funded HPV vaccine

Each 0.5 mL dose of HPV9 vaccine (Gardasil 9, Seqirus/MSD) contains:

- 30 µg of HPV6 L1 VLP, 40 µg of HPV11 L1 VLP, 60 µg of HPV16 L1 VLP, 40 µg of HPV18 L1 VLP, 20 µg of HPV31 L1 VLP, 20 µg of HPV33 L1 VLP, 20 µg of HPV45 L1 VLP, 20 µg of HPV52 L1 VLP and 20 µg of HPV58 L1 VLP
- 500 µg of aluminium hydroxyphosphate sulphate.

The vaccine does not contain any preservative or antibiotics.

#### Other vaccine

HPV4 (Gardasil) was used prior to the introduction of HPV9 (Gardasil 9) in January 2017. See also section A1.3.4 in Appendix 1 for the history of HPV vaccines in New Zealand.

In other countries, including Australia and in Europe, a bi-valent HPV vaccine (Cervarix, GSK) is available to protect against HPV types 16 and 18 only. This vaccine is unavailable in New Zealand.

## 10.4.2 Efficacy and effectiveness

Most HPV vaccine clinical trials do not collect direct data about clinical outcomes, like cancer or precancer, for young adolescents, because it is unethical to collect samples from the cervix of vaccinated girls who are sexually naïve and because precancerous lesions do not appear for years after the HPV infection has occurred. Also, since treatment is offered as precancers develop, progression to cervical cancer is rare even in those not vaccinated and requires a very long time for follow-up. Therefore, immunological bridging is used to infer efficacy against cervical and anal cancer. Efficacy is also inferred for the younger age group because immunogenicity (antibody responses) is non-inferior to that seen in older age groups.

### Immunogenicity

Although there is no known correlate of protection (ie, an established antibody level required for protection against HPV-related disease), HPV vaccines generate excellent antibody responses in most recipients.

#### HPV4

Immunisation with three doses of HPV4 vaccine produces antibody responses against HPV16, HPV18, HPV6 and HPV11 in more than 99 percent of vaccine recipients. The peak antibody titres following three doses of HPV vaccine are greater than that following natural infection.

A Cochrane systematic review found the immunogenicity of two- and three-dose HPV vaccination schedules in young females to be comparable.<sup>45</sup> Two doses of HPV4 are more immunogenic in recipients aged between 9 and under 15 years than in older groups aged over 15 years and comparable to three doses in older recipients (those over 15 years).<sup>46</sup> In young females, two doses have been found to be non-inferior to three doses for at least 21 months after vaccination, particularly when the interval between doses is at least six months.<sup>47, 48</sup> The immunogenicity of three doses of HPV4 vaccine has been established to be robust and long-lasting.<sup>49-51</sup> Anamnestic responses have been demonstrated out to at least 8.5 years.<sup>51</sup>

Differences in seroconversion rates and antibody titres were seen in immunocompromised individuals. The immune response to HPV4 among immunocompromised children appears adequate,<sup>52, 53</sup> although antibody titres were lower than those in healthy children of the same age groups.<sup>52</sup> Seroconversion among HIV-infected individuals has been demonstrated to be robust and higher among those with lower HIV loads or on antiretroviral therapy.<sup>54-56</sup>

While some immunosuppression regimes can attenuate the immune response to HPV4, patients with autoimmune diseases generally appear to respond well to the vaccine.<sup>57</sup> In contrast, adult solid organ transplant recipients produce suboptimal responses to HPV4.<sup>58</sup>

## HPV9

The immunogenicity of HPV9 vaccine was initially assessed in women aged 16–26 years.<sup>59</sup> Antibody responses generated by the HPV9 were non-inferior to HPV4 against HPV types 6, 11, 16 and 18; and in girls and boys aged 9–15 years.<sup>60</sup> Antibody responses to all nine vaccine HPV types in girls and boys aged 9–15 years and men aged 16–26 years were non-inferior to women aged 16–26 years.<sup>61, 62</sup>

Men who have sex with men appear to produce lower antibody titres than heterosexual men (although seroconversion rates to all nine vaccine types were greater than 99 percent in both groups).<sup>61</sup> This lower antibody response is possibly due to greater exposure to the virus, highlighting the importance of vaccination at a young age.

The immunogenicity of two doses of HPV9 in girls and boys aged 9–14 years was non-inferior to three doses in women aged 16–26 years, the age group in which efficacy was demonstrated.<sup>63</sup>

## Efficacy

### HPV-related cancers

HPV4 and HPV9 vaccines offer similar protection against cervical, vaginal and vulval precancerous lesions or cancer in women vaccinated at 15–26 years.<sup>45</sup> Protection is greatest among young women not initially infected with HPV 16/18 prior to vaccination (vaccine efficacy of 95 percent [95% CI: 83–99] against vaginal and vulval lesions).<sup>64</sup>

HPV9 efficacy was studied in women aged 16–26 years and compared with HPV4.<sup>59</sup> HPV9 prevented cervical, vulvar and vaginal disease and persistent infection related to HPV types 31, 33, 45, 52 and 58 (the five additional serotypes in HPV9). The antibody response and incidence of disease related to HPV types 6, 11, 16 and 18 were similar in the two vaccine groups.

Protection against CIN 2/3 or adenocarcinoma *in situ* is widely accepted as a surrogate for protection against invasive cancer, since study participants who develop these precancerous lesions require treatment to prevent progression to invasive cancer. Bivalent and quadrivalent HPV vaccines have been shown to be highly effective in preventing these HPV16- and HPV18-related precancerous lesions in females.<sup>1, 65</sup> In the pivotal efficacy trial in women aged 15–26 years, HPV4 vaccine efficacy for the prevention of precancerous lesions related to HPV16 or HPV18 was 98 percent (95% CI: 86–100) in the per-protocol susceptible population.<sup>66</sup>

A phase III clinical trial among Asian and Latin American women found population-specific vaccine efficacy to be more than 96 percent against any grade of cervical, vulvar and vaginal disease and more than 93 percent efficacy against six-month persistent HPV infection.<sup>67</sup>

Studies in males, including men who have sex with men, have shown that HPV4 vaccine is efficacious against anal HPV infection and associated precancerous lesions.<sup>9, 68, 69</sup> HPV4 protects men vaccinated between ages 16–26 years against genital warts or external genital lesions compared with unvaccinated dummy controls.<sup>45</sup>

## Effectiveness

A 2016 systematic review of published literature summarised the global experiences with HPV4 from 1 January 2007 to 29 February 2016.<sup>70</sup> It assessed the global effect of HPV4 vaccine on HPV infection, genital warts and cervical abnormalities based on 57 publications across nine countries. The greatest impact was seen in countries with high vaccine uptake and among girls vaccinated prior to HPV exposure. Maximal reductions of around 90 percent were reported for vaccine-type HPV infections (6, 11, 16, 18) and genital wart cases.

For women vaccinated before the age of 20 years, the risk of CIN2+ was significantly lower than in unvaccinated women (effectiveness of at least one dose is 58–77 percent).<sup>71-73</sup>

## Duration of protection

As vaccination programmes have only been in place for little over a decade, the duration of protection is not yet fully known. Follow-up studies 8–10 years after HPV vaccination have shown no waning of protection.<sup>1</sup> Long-term studies are ongoing to determine the duration of efficacy for all HPV vaccines.

## Herd immunity and population impact

In January 2019, WHO began considering a global strategy to eliminate cervical cancer and established clear targets to 2030. This is only achievable with high vaccination coverage and access to regular screening for all women.<sup>74, 75</sup>

Australia saw a reduction in the prevalence of vaccine-type HPV infections (6, 11, 16, 18) in unvaccinated young men after the introduction of the vaccine to young women, supporting the role of herd immunity.<sup>76-78</sup> There was also a significant decrease in the prevalence of vaccine-type HPV infections in unvaccinated women (aged 25 years or younger).<sup>79</sup> Vaccination of females has provided herd immunity against oropharyngeal HPV16 prevalence in unvaccinated males in the UK.<sup>80</sup>

In a study of sexual health clinic data in Melbourne, the researchers noted the near disappearance of genital warts in women and heterosexual men aged under 21 years.<sup>78</sup> In addition, the data indicated that the basic reproductive rate (see section 1.2.1) had fallen below one. This reduction in cases occurred without any corresponding reduction in women aged over 30 years, men who have sex with men and non-residents. Similar trends were noted in the data from the Australian genital warts national surveillance network.

Eleven years after the introduction of HPV4 vaccine in the US, HPV4 types declined by 81 percent in vaccinated women and 40 percent in unvaccinated women. As well as direct protection from HPV9 vaccine, potential cross-protection from HPV4 was also observed in vaccinated women with a 71 percent decline in prevalence of the additional, genetically related HPV9 types.<sup>4</sup>

### Previous exposure to HPV

While efficacy is unclear, there are no safety concerns in offering vaccination to women who have had HPV-related disease and would like to use the vaccine to reduce the risk of further disease.

A retrospective analysis of the HPV4 vaccine's pivotal efficacy trial data (Future I and Future II) studied a group of women who were vaccinated before they had their first treatment for HPV-related disease.<sup>81</sup> This showed a reduction in subsequent HPV-related disease in vaccinated women aged 15–26 years who had received treatment for cervical, vulvar or vaginal disease during the trial. The study showed a 46.2 percent reduction (95% CI: 22.5–63.2) after cervical surgery of any HPV-related disease and 35.2 percent reduction (95% CI: 18.8–51.8) after diagnosis of genital warts or vaginal or vulvar disease.

In contrast, a systematic review found that there was no evidence that HPV vaccines were effective in preventing vaccine-type HPV-associated precancer in pre-exposed women. This review explored efficacy against CIN3+ precancers in women with evidence of prior vaccine-type HPV exposure in three randomised controlled trials and two post-trial cohort studies.<sup>82</sup> Despite these findings, it was concluded that longer-term benefits in preventing re-infection could not be excluded (ie, the vaccine is not therapeutic but may prevent future infection, emphasising the importance of vaccination prior to sexual debut).

## 10.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at [www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

Store in the dark at +2°C to +8°C. Do not freeze.

## 10.4.4 Dosage and administration

The dose of HPV vaccine is 0.5 mL, administered by intramuscular injection in the deltoid area (see section 2.2.3).

## Co-administration with other vaccines

HPV vaccine may be co-administered with any live or inactivated vaccine indicated at the same visit.<sup>1</sup>

## Interchangeability

All HPV vaccines may be used interchangeably for completion of a course.<sup>83</sup>

# 10.5 Recommended immunisation schedule

## 10.5.1 Recommended and funded

From 1 January 2017 males and females aged 26 years and under became eligible for HPV vaccine. Including males in a routine vaccination programme is expected to increase the benefit to the population in terms of reduction for both HPV-related cancer outcomes and genital warts.

Immunisation should preferably be completed before the onset of sexual activity. The optimal time for HPV administration is at age 9–13 years, as the immunogenicity is more effective when given younger and as most males and females in this age group would be naïve to all HPV types. However, individuals who have begun sexual activity may still benefit from vaccination. The decision to vaccinate older age groups should follow an assessment of the potential benefits of vaccination – based on their likely previous HPV exposure and future risks.

See Table 10.3 for HPV vaccine recommendations and schedules. A two-dose schedule of HPV at 0 and 6–12 months is recommended for individuals who receive the first dose before their 15th birthday, even if they are 15 years or older at the time of the second dose. Three doses are required for this age group if they have confirmed HIV infection or are transplant or chemotherapy patients, or if the minimum dosing interval is not met (see below). Older individuals from age 15 years receive three doses of HPV vaccine, at 0, 2 and 6 months.



**Table 10.3: HPV vaccine recommendations and schedules**

Note: HPV vaccine may be offered from age 9 years, but the usual Schedule will be at age 11/12 years (school years 7/8). **Funded individuals are in shaded rows.** See the Pharmaceutical Schedule ([pharmac.govt.nz](http://pharmac.govt.nz)) for any changes to the funding decisions.

Recommended and funded	Doses	HPV Schedule <sup>a</sup>
Children aged 14 years and under <sup>a</sup>	2 <sup>a</sup>	0 and 6–12 <sup>a</sup> months
Individuals aged 15–26 years <sup>a,b</sup>	3	0, 2 and 6 months <sup>c</sup>
Individuals aged 9–26 years:		
• with confirmed HIV infection <sup>d</sup>	3	0, 2 and 6 months
• transplant (including stem cell) <sup>d</sup>		
• post-chemotherapy patients <sup>d</sup>	An additional dose	At least 1 month after the last dose of chemotherapy
Recommended but not funded	Doses	HPV Schedule
Individuals aged 27 years and older: <sup>a,b,e</sup>	3	0, 2 and 6 months <sup>e</sup>
• who have had little previous exposure to HPV and are now likely to be exposed		
• who are men who have sex with men		
• with HIV.		

- See note in text for two-dose schedules, age groups and continuation of courses.
- The decision to vaccinate older age groups should follow an assessment of the potential benefits of vaccination – based on their likely previous HPV exposure and future risks.
- If a shortened schedule is required, the three doses can be given with a minimum of 4 weeks between doses one and two, and the third dose given at least 12 weeks after dose two.
- For more information see sections 4.3.8 and 4.3.9.
- HPV vaccines are approved for use in females and males aged 9–45 years.

## Note

For the two-dose HPV schedule for children aged 14 years and under:

- a two-dose schedule at least 6–12 months apart is recommended for individuals who receive the first dose before their 15th birthday, even if they are 15 years or older at the time of the second dose
- the second dose is preferably given at least 6–12 months after the first; if the second dose is given less than five months after the first, a third HPV dose is recommended and funded – give the third HPV dose at least five months after the first.

Individuals who started with HPV4 may complete their remaining doses with HPV9.

Individuals who were fully vaccinated with HPV4 do not require further vaccination with HPV9. Any further protection is likely to be limited, particularly, if they have already been exposed through sexual contact. Most HPV-associated cancers result from infection with HPV types 16 and 18, which are covered by HPV4 (see Table 10.1).

Individuals who were under age 27 years when they commenced HPV vaccination are currently funded to complete the three-dose course, even if they are older than 27 years when they complete it.

Non-residents who were under age 18 years when they commenced HPV vaccination are currently funded to complete the course, even if they are older than 18 years when they complete it.

## 10.5.2 Recommended but not funded

### Individuals aged 27 years and older

The decision to vaccinate older age groups should follow an assessment of the potential benefits of vaccination – based on their likely previous HPV exposure and future risks. HPV9 is approved for use in females and males aged 9–45 years.

The data from the pivotal studies for HPV4 has demonstrated potential benefit to some women older than 25 years and the vaccine was shown to be effective at preventing infection and disease from the vaccine types in women aged 24–45 years who were uninfected at baseline.<sup>84</sup> However, pre-vaccination testing for cervical cytological abnormalities or for HPV infection is not recommended.

## 10.5.3 Pregnancy and breastfeeding

HPV vaccines are not recommended for pregnant women; however, enquiring about the possibility of pregnancy is not necessary before vaccination.<sup>85</sup>

Data to date shows no adverse effects of HPV vaccines on pregnancy outcomes.<sup>1, 86, 87</sup> However, if a vaccine dose has been administered around the time of conception or during pregnancy, health professionals are advised to report this to CARM (see section 1.6.3) and the vaccine manufacturer to assist with ongoing safety monitoring. If a woman is found to be pregnant after starting the HPV vaccine schedule, the remaining doses should be delayed until after pregnancy.

HPV vaccines may be given to breastfeeding women.<sup>88</sup>

# 10.6 Contraindications and precautions

See section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

## 10.6.1 Contraindications

HPV vaccine should not be administered to people with a history of an anaphylactic reaction to a prior dose of HPV vaccine or to a vaccine component. HPV vaccines

contain HPV proteins produced by genetically engineered yeast cells. They should not, therefore, be given to people with a history of an immediate hypersensitivity to yeast.

## 10.6.2 Precautions

Pregnancy is a precaution – see section 10.5.3.

# 10.7 Potential responses and AEFIs

HPV vaccines have excellent safety profiles internationally. There have been no safety signals raised since the vaccines were licensed, and a number of large investigations have been carried out to assess specific outcomes, particularly autoimmune conditions.<sup>89-93</sup> Post-marketing surveillance systems globally continue to monitor the safety of HPV vaccination programmes.<sup>94-96</sup> The WHO's Global Advisory Committee on Vaccine Safety has systematically reviewed HPV vaccine safety and has not found any safety issue that would alter its recommendations for use.<sup>97, 98</sup> The main challenge with HPV vaccine is communicating its excellent safety profile.<sup>99</sup> (See also the HPV discussion in section 3.2.4.)

Syncope (fainting) occurs frequently in adolescents following vaccination, but this is a stress response to being vaccinated, not a reaction to the vaccine.<sup>2, 100, 101</sup> WHO recognises immunisation-related stress responses as potential responses to HPV vaccination (see section 2.3.3).<sup>102</sup>

Safety has been evaluated in approximately 15,000 subjects in the HPV9 clinical development programme and no new safety signals have been shown through post-marketing surveillance.<sup>83, 103</sup> The vaccine is well-tolerated, and most adverse events were injection-site-related pain, swelling, and erythema that were mild to moderate in intensity. The safety profile of HPV9 is like HPV4. Female HPV9 recipients had more injection-site adverse events than female HPV4 recipients, including swelling (40.3 percent compared to 29.1 percent in HPV4 recipients) and erythema (34 percent compared to 25.8 percent in HPV4 recipients). Male recipients had fewer injection-site adverse events and were similar following either vaccine. Rates of injection-site swelling and erythema both increased following each successive dose of HPV9.

In summary, HPV9 is well-tolerated in all age groups, although it is slightly more reactogenic than HPV4.<sup>59, 61, 83</sup> The most common adverse events are pain, swelling, erythema, pruritus, headache and pyrexia. The frequency of these common adverse events is increased slightly (up to two-fold) when concurrent vaccinations are given.<sup>104</sup>

## 10.8 Cancer prevention measures

For women, HPV immunisation is part of a three-pronged approach to cervical cancer prevention that also includes regular cervical screening and safer sex approaches. For men, HPV immunisation and safer sex approaches are expected to contribute to the prevention of HPV-related cancers and disease that affect men, as well as cervical cancer prevention in women.

### 10.8.1 HPV immunisation

By preventing infection with oncogenic HPV types, HPV vaccination can reduce the incidence of precursor lesions that may lead to cancer. Vaccination needs to be administered before HPV infection occurs to prevent atypia and malignancy. Because genital HPVs are so common and so readily transmitted, in practical terms vaccination should be offered before the onset of sexual activity; that is, during or prior to early adolescence.

HPV immunisation does not reduce the progression of established disease but can be used in therapeutic situations by preventing the reactivation of latent infection or acquiring new infections.

### 10.8.2 Regular cervical screening for women

A successful HPV immunisation programme for men and women will reduce the community prevalence of HPV infection and thus the incidence of cervical cancer in women. However, HPV immunisation alone will not completely eliminate cervical cancer, because some women will not have been vaccinated, a few will not develop immunity despite vaccination, and some will be infected prior to vaccination or with oncogenic types not included in the vaccine.

Consequently, women will need to continue to undergo regular cervical screening to detect those precancerous lesions that occur despite vaccination. Cervical screening programmes are based on regular cytological screening or HPV testing to detect, monitor and treat at an early-stage precancerous lesion, or CIN. These programmes have been successful in reducing invasive disease and mortality.

Although the frequency of abnormal cytology is lower in the vaccinated group, women who have received HPV immunisation should still take part in the National Cervical Screening Programme. Three-yearly cervical smears are recommended for women between the ages of 25 and 70 years who have ever been sexually active.

### 10.8.3 Safer sex approaches

To minimise the risk of HPV infection (plus other sexually transmitted infections), practitioners should remind individuals of safer sex approaches, including sexual abstinence, monogamous relationships, delayed sexual debut and minimising the number of sexual partners.<sup>1</sup> Consistent and correct use of condoms can decrease the risk of anogenital HPV infection when infected areas are covered or protected by the condom. However, HPV transmission in the genital region may occur even when condoms are used and does not necessarily require penetrative intercourse.<sup>8</sup>

## 10.9 Variations from the vaccine data sheets

For the three-dose schedules, the HPV vaccine data sheets recommend that all three doses are given within a 12-month period. Health New Zealand | Te Whatu Ora recommends that if the three-dose schedule has been interrupted, prior doses do not need to be repeated regardless of how long ago the previous doses were given (see Appendix 2).

The HPV9 data sheet states that there are no studies on the interchangeability of HPV vaccines. Health New Zealand recommends that all HPV vaccines may be used interchangeably for completion of a course.<sup>83</sup> Those individuals who started with HPV4 may complete their remaining doses with HPV9.

## References

1. American Academy of Pediatrics. 2018. Human papillomaviruses. in *Red Book: 2018 Report of the Committee on Infectious Diseases*, Kimberlin D, Brady M, Jackson M, and Long S (eds). URL: <https://redbook.solutions.aap.org/redbook.aspx>. (accessed 3 July 2020)
2. Schiller JT, Markowitz LE, Hildesheim A, Lowy DR. 2018. Human papillomavirus vaccines, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
3. Saraiya M, Unger ER, Thompson TD, et al. US assessment of HPV types in cancers: implications for current and 9-valent HPV vaccines. *Journal of the National Cancer Institute*, 2015. 107(6): p. djv086.
4. Spinner C, Ding L, Bernstein DI, et al. Human Papillomavirus Vaccine Effectiveness and Herd Protection in Young Women. *Pediatrics*, 2019. 143(2).
5. Ministry of Health. 2007. *High Grade Squamous Intra-epithelial Lesions (HSIL) in New Zealand* (ed.), Wellington: Ministry of Health, National Cervical Screening Programme, National Screening Unit. URL: <https://www.nsu.govt.nz/system/files/resources/hsil-in-new-zealand.pdf> (accessed 3 July 2020)

6. McFadden K, McConnell D, Salmond C, et al. Socioeconomic deprivation and the incidence of cervical cancer in New Zealand: 1988–1998. *New Zealand Medical Journal*, 2004. 117(1206): p. U1172.
7. Partridge JM, Hughes JP, Feng Q, et al. Genital human papillomavirus infection in men: incidence and risk factors in a cohort of university students. *Journal of Infectious Diseases*, 2007. 196(8): p. 1128-36.
8. Winer RL, Lee SK, Hughes JP, et al. Genital human papillomavirus infection: incidence and risk factors in a cohort of female university students. *American Journal of Epidemiology*, 2003. 157(3): p. 218-26.
9. Giuliano AR, Palefsky JM, Goldstone S, et al. Efficacy of quadrivalent HPV vaccine against HPV Infection and disease in males. *New England Journal of Medicine*, 2011. 364(5): p. 401-11.
10. Centers for Disease Control and Prevention. 2012. Human papillomavirus-associated cancers – United States, 2004–2008. *Morbidity and Mortality Weekly Report*. 61(15): p. 258–61. URL: (accessed 3 July 2020)
11. Smith JS, Gilbert PA, Melendy A, et al. Age-specific prevalence of human papillomavirus infection in males: a global review. *Journal of Adolescent Health*, 2011. 48(6): p. 540-52.
12. Machalek DA, Poynten M, Jin F, et al. Anal human papillomavirus infection and associated neoplastic lesions in men who have sex with men: a systematic review and meta-analysis. *Lancet Oncology*, 2012. 13(5): p. 487-500.
13. Zou H, Tabrizi SN, Grulich AE, et al. Early acquisition of anogenital human papillomavirus among teenage men who have sex with men. *Journal of Infectious Diseases*, 2014. 209(5): p. 642-51.
14. Vajdic CM, van Leeuwen MT, Jin F, et al. Anal human papillomavirus genotype diversity and co-infection in a community-based sample of homosexual men. *Sexually Transmitted Infections*, 2009. 85(5): p. 330-5.
15. Grulich AE, van Leeuwen MT, Falster MO, Vajdic CM. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. *Lancet*, 2007. 370(9581): p. 59-67.
16. Wilkin T, Lee JY, Lensing SY, et al. Safety and immunogenicity of the quadrivalent human papillomavirus vaccine in HIV-1-infected men. *Journal of Infectious Diseases*, 2010. 202(8): p. 1246-53.
17. Beachler DC, Weber KM, Margolick JB, et al. Risk factors for oral HPV infection among a high prevalence population of HIV-positive and at-risk HIV-negative adults. *Cancer Epidemiology, Biomarkers and Prevention*, 2012. 21(1): p. 122-33.
18. Begue R. Immunization recommendations for the HIV-infected adolescent. *HIV Clinician*, 2012. 24(2): p. 15-21.
19. Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. Human papillomavirus disease. in *Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-infected Adults and Adolescents: Recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America*. URL: [https://aidsinfo.nih.gov/contentfiles/lvguidelines/adult\\_oi.pdf](https://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf). (accessed 3 July 2020)
20. de Sanjose S, Quint WG, Alemany L, et al. Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. *Lancet Oncology*, 2010. 11(11): p. 1048-56.
21. Sarian LO, Derchain SF, Pitta Dda R, et al. Factors associated with HPV persistence after treatment for high-grade cervical intra-epithelial neoplasia with large loop excision of the transformation zone (LLETZ). *Journal of Clinical Virology*, 2004. 31(4): p. 270-4.



22. Safaeian M, Hildesheim A, Gonzalez P, et al. Single nucleotide polymorphisms in the PRDX3 and RPS19 and risk of HPV persistence and cervical precancer/cancer. *PloS One*, 2012. 7(4): p. e33619.
23. Syrjanen S. The role of human papillomavirus infection in head and neck cancers. *Annals of Oncology*, 2010. 21 Suppl 7(Suppl 7): p. vii243-5.
24. Plummer M, de Martel C, Vignat J, et al. Global burden of cancers attributable to infections in 2012: a synthetic analysis. *Lancet Glob Health*, 2016. 4(9): p. e609-16.
25. de Martel C, Plummer M, Vignat J, Franceschi S. Worldwide burden of cancer attributable to HPV by site, country and HPV type. *International Journal of Cancer*, 2017. 141(4): p. 664-670.
26. Winer RL, Feng Q, Hughes JP, et al. Risk of female human papillomavirus acquisition associated with first male sex partner. *Journal of Infectious Diseases*, 2008. 197(2): p. 279-82.
27. Bruni L, Albero G, Serrano B, et al. 2019. *Human Papillomavirus and Related Diseases in the World. Summary Report* (ed.), Barcelona, Spain: ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). URL: <https://hpcvcentre.net/statistics/reports/XWX.pdf> (accessed 12 March 2020)
28. Kjaer SK, Frederiksen K, Munk C, Iftner T. Long-term absolute risk of cervical intraepithelial neoplasia grade 3 or worse following human papillomavirus infection: role of persistence. *Journal of the National Cancer Institute*, 2010. 102(19): p. 1478-88.
29. Mallen-St Clair J, Alani M, Wang MB, Srivatsan ES. Human papillomavirus in oropharyngeal cancer: The changing face of a disease. *Biochimica et Biophysica Acta*, 2016. 1866(2): p. 141-150.
30. Wiley DJ, Douglas J, Beutner K, et al. External genital warts: diagnosis, treatment, and prevention. *Clinical Infectious Diseases*, 2002. 35(Suppl 2): p. S210-24.
31. Koutsky L. Epidemiology of genital human papillomavirus infection. *American Journal of Medicine*, 1997. 102(5A): p. 3-8.
32. Kjaer SK, Tran TN, Sparen P, et al. The burden of genital warts: a study of nearly 70,000 women from the general female population in the 4 Nordic countries. *Journal of Infectious Diseases*, 2007. 196(10): p. 1447-54.
33. Clark TC, Fleming T, Bullen P, et al. 2013. *Youth'12 Overview: The health and wellbeing of New Zealand secondary school students in 2012* (ed.), Auckland, New Zealand: The University of Auckland. URL: <https://www.fmhs.auckland.ac.nz/assets/fmhs/faculty/ahrg/docs/2012-overview.pdf> (accessed 13 March 2020)
34. Clark TC, Fleming T, Bullen P, et al. 2013. *Youth'12 Prevalence Tables: The health and wellbeing of New Zealand secondary school students in 2012* (ed.), Auckland, New Zealand: The University of Auckland. URL: <https://www.fmhs.auckland.ac.nz/assets/fmhs/faculty/ahrg/docs/2012prevalence-tables-report.pdf> (accessed 13 March 2020)
35. Clark TC, Lucassen MF, Fleming T, et al. Changes in the sexual health behaviours of New Zealand secondary school students, 2001-2012: findings from a national survey series. *Australian and New Zealand Journal of Public Health*, 2016. 40(4): p. 329-36.
36. Kang YJ, Lewis H, Smith MA, et al. Pre-vaccination type-specific HPV prevalence in confirmed cervical high grade lesions in the Maori and non-Maori populations in New Zealand. *BMC Infectious Diseases*, 2015. 15(365): p. 365.
37. Simonella LM, Lewis H, Smith M, et al. Type-specific oncogenic human papillomavirus infection in high grade cervical disease in New Zealand. *BMC Infectious Diseases*, 2013. 13: p. 114.



38. Sykes P, Gopala K, Tan AL, et al. Type distribution of human papillomavirus among adult women diagnosed with invasive cervical cancer (stage 1b or higher) in New Zealand. *BMC Infectious Diseases*, 2014. 14: p. 374.
39. Ministry of Health. 2019. *Selected Cancers 2015, 2016, 2017* (ed.): Ministry of Health. URL: <https://www.health.govt.nz/publication/selected-cancers-2015-2016-2017> (accessed 13 March 2020)
40. Ministry of Health. 2016 *Mortality 2014 data tables*. 2016; URL: <https://www.health.govt.nz/publication/mortality-2014-data-tables>. (accessed 3 July 2020)
41. Chelimo C ,Elwood JM. Sociodemographic differences in the incidence of oropharyngeal and oral cavity squamous cell cancers in New Zealand. *Australian and New Zealand Journal of Public Health*, 2015. 39(2): p. 162-7.
42. Lucas-Roxburgh R, Benschop J, Lockett B, et al. The prevalence of human papillomavirus in oropharyngeal cancer in a New Zealand population. *PloS One*, 2017. 12(10): p. e0186424.
43. Wilson N, Morgan J ,Baker MG. Evidence for effectiveness of a national HPV vaccination programme: national prescription data from New Zealand. *Sexually Transmitted Infections*, 2014. 90(2): p. 103.
44. Oliphant J, Stewart J, Saxton P, et al. Trends in genital warts diagnoses in New Zealand five years following the quadrivalent human papillomavirus vaccine introduction. *New Zealand Medical Journal*, 2017. 130: p. 1452.
45. Bergman H, Buckley BS, Villanueva G, et al. Comparison of different human papillomavirus (HPV) vaccine types and dose schedules for prevention of HPV-related disease in females and males. *Cochrane Database Syst Rev*, 2019. 2019(11).
46. Donken R, Knol MJ, Bogaards JA, et al. Inconclusive evidence for non-inferior immunogenicity of two- compared with three-dose HPV immunization schedules in preadolescent girls: A systematic review and meta-analysis. *Journal of Infection*, 2015. 71(1): p. 61-73.
47. Sankaranarayanan R, Prabhu PR, Pawlita M, et al. Immunogenicity and HPV infection after one, two, and three doses of quadrivalent HPV vaccine in girls in India: a multicentre prospective cohort study. *Lancet Oncology*, 2016. 17(1): p. 67-77.
48. D'Addario M, Redmond S, Scott P, et al. Two-dose schedules for human papillomavirus vaccine: Systematic review and meta-analysis. *Vaccine*, 2017. 35(22): p. 2892-2901.
49. Joura EA, Kjaer SK, Wheeler CM, et al. HPV antibody levels and clinical efficacy following administration of a prophylactic quadrivalent HPV vaccine. *Vaccine*, 2008. 26(52): p. 6844-51.
50. Einstein MH, Baron M, Levin MJ, et al. Comparison of the immunogenicity and safety of Cervarix and Gardasil human papillomavirus (HPV) cervical cancer vaccines in healthy women aged 18-45 years. *Hum Vaccin*, 2009. 5(10): p. 705-19.
51. Rowhani-Rahbar A, Alvarez FB, Bryan JT, et al. Evidence of immune memory 8.5 years following administration of a prophylactic human papillomavirus type 16 vaccine. *Journal of Clinical Virology*, 2012. 53(3): p. 239-43.
52. MacIntyre CR, Shaw P, Mackie FE, et al. Immunogenicity and persistence of immunity of a quadrivalent Human Papillomavirus (HPV) vaccine in immunocompromised children. *Vaccine*, 2016. 34(36): p. 4343-50.
53. Gomez-Lobo V, Whyte T, Kaufman S, et al. Immunogenicity of a prophylactic quadrivalent human papillomavirus L1 virus-like particle vaccine in male and female adolescent transplant recipients. *Pediatric Transplantation*, 2014. 18(3): p. 310-5.
54. Giacomet V, Penagini F, Trabattoni D, et al. Safety and immunogenicity of a quadrivalent human papillomavirus vaccine in HIV-infected and HIV-negative adolescents and young adults. *Vaccine*, 2014. 32(43): p. 5657-61.

55. Kahn JA, Xu J, Kapogiannis BG, et al. Immunogenicity and safety of the human papillomavirus 6, 11, 16, 18 vaccine in HIV-infected young women. *Clinical Infectious Diseases*, 2013. 57(5): p. 735-44.
56. Kojic EM, Kang M, Cespedes MS, et al. Immunogenicity and safety of the quadrivalent human papillomavirus vaccine in HIV-1-infected women. *Clinical Infectious Diseases*, 2014. 59(1): p. 127-35.
57. Jacobson DL, Bousvaros A, Ashworth L, et al. Immunogenicity and tolerability to human papillomavirus-like particle vaccine in girls and young women with inflammatory bowel disease. *Inflammatory Bowel Diseases*, 2013. 19(7): p. 1441-9.
58. Kumar D, Unger ER, Panicker G, et al. Immunogenicity of quadrivalent human papillomavirus vaccine in organ transplant recipients. *American Journal of Transplantation*, 2013. 13(9): p. 2411-7.
59. Joura EA, Giuliano AR, Iversen OE, et al. A 9-valent HPV vaccine against infection and intraepithelial neoplasia in women. *New England Journal of Medicine*, 2015. 372(8): p. 711-23.
60. Vesikari T, Brodzski N, van Damme P, et al. A randomized, double-blind, phase III study of the immunogenicity and safety of a 9-valent human papillomavirus L1 virus-like particle vaccine (V503) versus Gardasil® in 9-15-year-old girls. *Pediatric Infectious Disease Journal*, 2015. 34(9): p. 992-8.
61. Castellsagué X, Giuliano AR, Goldstone S, et al. Immunogenicity and safety of the 9-valent HPV vaccine in men. *Vaccine*, 2015. 33(48): p. 6892-901.
62. Van Damme P, Olsson SE, Block S, et al. Immunogenicity and Safety of a 9-Valent HPV Vaccine. *Pediatrics*, 2015. 136(1): p. e28-39.
63. Seqirus/MSD. 2016 *Gardasil 9 data sheet*. URL: <https://www.medsafe.govt.nz/profs/datasheet/g/gardasil9inj.pdf>. (accessed 10 May 2022)
64. Xu L, Selk A, Garland SM, et al. Prophylactic vaccination against human papillomaviruses to prevent vulval and vaginal cancer and their precursors. *Expert Rev Vaccines*, 2019. 18(11): p. 1157-1166.
65. Lehtinen M, Paavonen J, Wheeler CM, et al. Overall efficacy of HPV-16/18 AS04-adjuvanted vaccine against grade 3 or greater cervical intraepithelial neoplasia: 4-year end-of-study analysis of the randomised, double-blind PATRICIA trial. *Lancet Oncology*, 2012. 13(1): p. 89-99.
66. Future II Study Group. Quadrivalent vaccine against human papillomavirus to prevent high-grade cervical lesions. *New England Journal of Medicine*, 2007. 356(19): p. 1915-27.
67. Toh ZQ, Kosasih J, Russell FM, et al. Recombinant human papillomavirus nonavalent vaccine in the prevention of cancers caused by human papillomavirus. *Infect Drug Resist*, 2019. 12: p. 1951-1967.
68. Palefsky JM, Giuliano AR, Goldstone S, et al. HPV vaccine against anal HPV infection and anal intraepithelial neoplasia. *New England Journal of Medicine*, 2011. 365(17): p. 1576-85.
69. Swedish KA, Factor SH, Goldstone SE. Prevention of recurrent high-grade anal neoplasia with quadrivalent human papillomavirus vaccination of men who have sex with men: a nonconcurrent cohort study. *Clinical Infectious Diseases*, 2012. 54(7): p. 891-8.
70. Garland SM, Kjaer SK, Munoz N, et al. Impact and effectiveness of the quadrivalent human papillomavirus vaccine: a systematic review of 10 years of real-world experience. *Clinical Infectious Diseases*, 2016. 63(4): p. 519-27.
71. Dehlendorff C, Sparen P, Baldur-Felskov B, et al. Effectiveness of varying number of doses and timing between doses of quadrivalent HPV vaccine against severe cervical lesions. *Vaccine*, 2018. 36(43): p. 6373-6378.

72. Racey CS, Albert A, Donken R, et al. Cervical Intraepithelial Neoplasia Rates in British Columbia Women: A Population-Level Data Linkage Evaluation of the School-Based HPV Immunization Program. *Journal of Infectious Diseases*, 2020. 221(1): p. 81-90.
73. Silverberg MJ, Leyden WA, Lam JO, et al. Effectiveness of catch-up human papillomavirus vaccination on incident cervical neoplasia in a US health-care setting: a population-based case-control study. *Lancet Child Adolesc Health*, 2018. 2(10): p. 707-714.
74. Simms KT, Steinberg J, Caruana M, et al. Impact of scaled up human papillomavirus vaccination and cervical screening and the potential for global elimination of cervical cancer in 181 countries, 2020-99: a modelling study. *Lancet Oncology*, 2019. 20(3): p. 394-407.
75. World Health Organization. 2020 *Cervical cancer: Eliminating cervical cancer*. 2020; URL: [https://www.who.int/health-topics/cervical-cancer#tab=tab\\_2](https://www.who.int/health-topics/cervical-cancer#tab=tab_2). (accessed 12 March 2020)
76. Chow EPF, Machalek DA, Tabrizi SN, et al. Quadrivalent vaccine-targeted human papillomavirus genotypes in heterosexual men after the Australian female human papillomavirus vaccination programme: a retrospective observational study. *Lancet Infectious Diseases*, 2017. 17(1): p. 68-77.
77. Donovan B, Franklin N, Guy R, et al. Quadrivalent human papillomavirus vaccination and trends in genital warts in Australia: analysis of national sentinel surveillance data. *Lancet Infectious Diseases*, 2011. 11(1): p. 39-44.
78. Read TR, Hocking JS, Chen MY, et al. The near disappearance of genital warts in young women 4 years after commencing a national human papillomavirus (HPV) vaccination programme. *Sexually Transmitted Infections*, 2011. 87(7): p. 544-7.
79. Chow EPF, Danielewski JA, Fehler G, et al. Human papillomavirus in young women with *Chlamydia trachomatis* infection 7 years after the Australian human papillomavirus vaccination programme: a cross-sectional study. *The Lancet Infectious Diseases*, 2015. 15(11): p. 1314-1323.
80. Mehanna H, Bryant TS, Babrah J, et al. Human papillomavirus (HPV) vaccine effectiveness and potential herd immunity for reducing oncogenic oropharyngeal HPV-16 prevalence in the United Kingdom: A cross-sectional study. *Clinical Infectious Diseases*, 2019. 69(8): p. 1296-1302.
81. Joura EA, Garland SM, Paavonen J, et al. Effect of the human papillomavirus (HPV) quadrivalent vaccine in a subgroup of women with cervical and vulvar disease: retrospective pooled analysis of trial data. *BMJ*, 2012. 344(e1401): p. e1401.
82. Miltz A, Price H, Shahmanesh M, et al. Systematic review and meta-analysis of L1-VLP-based human papillomavirus vaccine efficacy against anogenital pre-cancer in women with evidence of prior HPV exposure. *PloS One*, 2014. 9(3): p. e90348.
83. Petrosky E, Bocchini JA, Jr., Hariri S, et al. Use of 9-valent human papillomavirus (HPV) vaccine: updated HPV vaccination recommendations of the advisory committee on immunization practices. *MMWR: Morbidity and Mortality Weekly Report*, 2015. 64(11): p. 300-4.
84. Muñoz N, Manalastas R, Jr., Pitisuttithum P, et al. Safety, immunogenicity, and efficacy of quadrivalent human papillomavirus (types 6, 11, 16, 18) recombinant vaccine in women aged 24-45 years: a randomised, double-blind trial. *Lancet*, 2009. 373(9679): p. 1949-57.
85. Bonde U, Joergensen JS, Lamont RF, Mogensen O. Is HPV vaccination in pregnancy safe? *Human Vaccines & Immunotherapeutics*, 2016. 12(8): p. 1960-1964.
86. Moreira ED, Jr., Block SL, Ferris D, et al. Safety Profile of the 9-Valent HPV Vaccine: A Combined Analysis of 7 Phase III Clinical Trials. *Pediatrics*, 2016. 138(2): p. e20154387.

87. Wang A, Liu C, Wang Y, et al. Pregnancy outcomes after human papillomavirus vaccination in periconceptional period or during pregnancy: A systematic review and meta-analysis. *Human Vaccines & Immunotherapeutics*, 2019: p. 1-9.
88. Australian Technical Advisory Group on Immunisation. 2018. *Australian Immunisation Handbook* (ed.), Canberra: Australian Government Department of Health. URL: <https://immunisationhandbook.health.gov.au/> (accessed October 2019)
89. Arnheim-Dahlstrom L, Pasternak B, Svanstrom H, et al. Autoimmune, neurological, and venous thromboembolic adverse events after immunisation of adolescent girls with quadrivalent human papillomavirus vaccine in Denmark and Sweden: cohort study. *BMJ*, 2013. 347: p. f5906.
90. Chao C, Klein NP, Velicer CM, et al. Surveillance of autoimmune conditions following routine use of quadrivalent human papillomavirus vaccine. *Journal of Internal Medicine*, 2012. 271(2): p. 193-203.
91. Grimaldi-Bensouda L, Guillemot D, Godeau B, et al. Autoimmune disorders and quadrivalent human papillomavirus vaccination of young female subjects. *Journal of Internal Medicine*, 2014. 275(4): p. 398-408.
92. Langer-Gould A, Qian L, Tartof SY, et al. Vaccines and the risk of multiple sclerosis and other central nervous system demyelinating diseases. *JAMA Neurol*, 2014. 71(12): p. 1506-13.
93. Scheller NM, Svanstrom H, Pasternak B, et al. Quadrivalent HPV vaccination and risk of multiple sclerosis and other demyelinating diseases of the central nervous system. *JAMA*, 2015. 313(1): p. 54-61.
94. Gold MS, McIntyre P. Human papillomavirus vaccine safety in Australia: experience to date and issues for surveillance. *Sex Health*, 2010. 7(3): p. 320-4.
95. Kliwer EV, Demers AA, Brisson M, et al. The Manitoba human papillomavirus vaccine surveillance and evaluation system. *Health Reports*, 2010. 21(2): p. 37-42.
96. Nguyen M, Ball R, Midthun K, Lieu TA. The Food and Drug Administration's Post-Licensure Rapid Immunization Safety Monitoring program: strengthening the federal vaccine safety enterprise. *Pharmacoepidemiology and Drug Safety*, 2012. 21 Suppl 1(Suppl 1): p. 291-7.
97. World Health Organization. Global Advisory Committee on Vaccine Safety, 12–13 June 2013. *Weekly Epidemiological Record*, 2013. 88(29): p. 301–12.
98. World Health Organization. Global Advisory Committee on Vaccine Safety, 4–5 December 2019 *Weekly Epidemiological Record*, 2020. 95(4): p. 25-36.
99. World Health Organization. Meeting of the Strategic Advisory Group of Experts on Immunization, April 2016 – conclusions and recommendations. *Weekly Epidemiological Record* 2016. 91(21): p. 266–84.
100. Bonaldo G, Vaccheri A, D'Annibali O, Motola D. Safety profile of human papilloma virus vaccines: an analysis of the US Vaccine Adverse Event Reporting System from 2007 to 2017. *British Journal of Clinical Pharmacology*, 2019. 85(3): p. 634-643.
101. Klein NP, Hansen J, Chao C, et al. Safety of quadrivalent human papillomavirus vaccine administered routinely to females. *Arch Pediatr Adolesc Med*, 2012. 166(12): p. 1140-8.
102. World Health Organization. 2019. *Immunization Stress-related Response. A manual for program managers and health professionals to prevent, identify and respond to stress-related responses following immunization.* (ed.), Geneva: World Health Organization. URL: <https://www.who.int/publications-detail/978-92-4-151594-8> (accessed 07 May 2020)
103. Donahue JG, Kieke BA, Lewis EM, et al. Near Real-Time Surveillance to Assess the Safety of the 9-Valent Human Papillomavirus Vaccine. *Pediatrics*, 2019. 144(6).

104. Li Y, Zhu P, Wu M, et al. Immunogenicity and safety of human papillomavirus vaccine coadministered with other vaccines in individuals aged 9-25years: A systematic review and meta-analysis. *Vaccine*, 2020. 38(2): p. 119-134.

# 11 Influenza

## Key information

Mode of transmission	Spread by droplets generated by sneezing and coughing, by direct or indirect contact, or by the aerosol route.
Incubation period	Usually 1–3 days (range 1–7 days).
Period of communicability	From 1–2 days before symptoms start until about day 5 of illness; may be longer in young children and if immunocompromised. Asymptomatic spread is common.
Incidence and burden of disease	Influenza epidemics occur each year. The highest burden of disease is in the very young, the elderly, pregnant women, those with co-morbid conditions, people from low-income groups and Māori and Pacific ethnic groups.
Funded vaccines	<ul style="list-style-type: none"> <li>Quadrivalent inactivated split virion influenza vaccine for children age 6 months and over and adults: Influvac Tetra</li> </ul>
Dose, presentation, route	0.5 mL for adults and children 6 months of age and above. Pre-filled syringe, needled attached Intramuscular injection, or deep subcutaneous injection (if indicated)
Funded vaccine indications and recommended schedule	<p>1 dose is recommended and funded annually from 1 April for:</p> <ul style="list-style-type: none"> <li>people who are pregnant</li> <li>individuals aged 65 years and over</li> <li>individuals aged 6 months to under 65 years with eligible conditions (Table 11.2)</li> <li>children aged 6 months to under 5 years who have been hospitalised for respiratory illness (including measles) or have a history of significant respiratory illness</li> <li>individuals with serious mental health condition or addiction.</li> </ul> <p>Children aged under 9 years who have not previously received influenza vaccine require 2 doses 4 weeks apart (funded for children with eligible conditions).</p>
Recommended, unfunded	<p>Universally recommended for anyone age from 6 months, annually.</p> <ul style="list-style-type: none"> <li>Occupational: recommended for health care workers, teachers and support staff in schools and early childhood education and staff in long-term care and aged-care facilities. For individuals working with livestock, poultry and wild animals.</li> <li>Recommended particularly for all close contacts (eg, caregivers, family members) of those at high risk from influenza.</li> <li>Recommended for all adults of Māori and Pacific ethnicity aged from 55 years</li> </ul>
Vaccine effectiveness	Depends on the match of the strains in the vaccine with circulating strains, the age of the individual and whether they have any underlying medical conditions. Vaccination can prevent disease or reduce severity.

*Continued overleaf*



Precautions and special considerations	There may be a small increased risk of fever and febrile convulsions with concomitant delivery of PCV13 and influenza vaccine in children aged 6 months to under 5 years.
Potential response to vaccine	Mild fever, headache, muscle aches, local swelling and mild pain at injection site. Children aged under 5 years are more likely than older children or adults to have a febrile reaction to influenza vaccine.

## 11.1 Virology

Influenza viruses belong to the Orthomyxoviridae family, and are classified into influenza virus types A, B and C. Influenza A virus subtypes are classified based on two surface antigens:

- haemagglutinin (H), responsible for cell surface attachment during infection
- neuraminidase (N), which potentiates the release of new virions from the cell.

Subtypes which have in the past caused pandemics include the influenza A H1N1, H2N2, H3N2 and H1N1pdm09 viruses, while the H3N2 and H1N1pdm09 viruses continue to cause epidemics as seasonal influenza viruses. Prior to 2020, two lineages of influenza B, B/Victoria and B/Yamagata, were associated with outbreaks and epidemics, and accounted for a significant proportion of the overall burden of influenza.<sup>1</sup> Although B/Victoria continues contribute to the burden of influenza, with no detections since March 2020, it appears that the B/Yamagata strain is potentially, globally extinct.<sup>2</sup> Influenza C is associated with mild cases of upper respiratory infection.

### 11.1.1 Antigenic drift

Influenza A and B viruses undergo frequent small changes (mutations) in their segmented RNA genome over time. The mutations can occur in the coding regions responsible for H and N surface antigens. This 'antigenic drift' leads to the emergence of new antigenic variants or virus strains.

These new strains are described by the geographic site of isolation, laboratory number and year of isolation; for example, A/Hong Kong/4801/2014 (H3N2). Because of this ongoing antigenic drift, WHO reviews seasonal influenza virus vaccine formulations bi-annually.



## 11.1.2 Antigenic shift

New influenza A virus subtypes emerge periodically that have caused pandemics in humans. The new virus subtype has novel H and N surface antigens result from the mixing of genomic segments of two or more influenza A viruses. This is known as 'antigenic shift'. Other possible mechanisms for the emergence of new influenza viruses are through the adaptation of avian influenza viruses to infect humans and the re-assortment of the genomic segments of multiple viruses (ie, human, avian and pig influenza viruses).

## 11.2 Clinical features

Influenza is contagious, with a reproductive number (R0) estimated at 1.4–4 (see section 1.2.1).<sup>3</sup> The virus is transmitted by respiratory droplets generated by sneezing and coughing that land directly on respiratory mucous membranes by aerosolised droplets or by direct or indirect contact (via contaminated hands or fomites).<sup>3-5</sup> The incubation period can range from one to seven days (average one to three days), during which time the virus replicates in the ciliated columnar epithelial cells of the upper and lower respiratory tract. An infected person is contagious from one to two days before symptoms start until about day five of the illness. Peak viral shedding occurs one to three days after the development of symptoms, diminishing to low levels by five days. Children shed more virus and remain infectious for longer than adults.

There is a wide range of symptoms, from asymptomatic to severe disease. Mild influenza with non-specific symptoms is common, resulting in a large proportion of viral transmission and undetected infections.<sup>6</sup> In older children and adults, the illness characteristically begins abruptly with fever and a variety of clinical symptoms, including chills, malaise, headache, myalgia, non-productive cough, rhinitis, sore throat and mild conjunctivitis. Vomiting and diarrhoea may be present. While children aged under 5 years have fever, cough and rhinitis, infants may present with unexplained fever or sepsis-like syndrome only.<sup>4</sup> In the young, influenza virus may cause croup, bronchiolitis and pneumonia. Fever is often less evident in the elderly, who may present with other symptoms, such as anorexia, fatigue or confusion. Influenza typically resolves after several days in most people, although cough and malaise may persist for two or more weeks.

Infections due to pandemic influenza A strains are more likely to lead to severe morbidity and increased mortality than influenza B or seasonal influenza A strains.

Influenza B infections were previously thought to generally cause more mild illness, but numerous studies indicate that there is little difference between clinical symptoms and outcomes of influenza B compared to influenza A.<sup>1</sup> Influenza B-associated hospitalisations and mortality may have previously been underestimated; studies have reported higher mortality following influenza B infection than A in some years.<sup>1</sup> Influenza B infection is more common in children aged 5–17 years than in other age groups, and disease is likely to be more severe in children than in adults.<sup>7</sup>

Influenza can exacerbate underlying medical conditions, such as pulmonary, cardiac or metabolic disease. Some of the many reported complications associated with influenza include pneumonia, respiratory failure, myositis, encephalopathy, myocardial infarction, myocarditis and pericarditis, Reye syndrome (associated with aspirin use in children), bronchitis, otitis media and death. The risk of complications is increased in pregnancy.<sup>8</sup> Also associated with influenza infection is increased frailty and cognitive decline in older people and incidence of cardiovascular disease are also associated with influenza infection.<sup>9, 10</sup> Influenza during pregnancy can result in poorer outcomes for the mother and her fetus, including preterm birth and fetal loss.<sup>11, 12</sup>

## Asymptomatic influenza

The majority of influenza infections are asymptomatic, and most symptomatic cases self-manage without seeking medical help.<sup>13, 14</sup> Results from the 2015 New Zealand Southern Hemisphere Influenza and Vaccine Effectiveness, Research and Surveillance (SHIVERS) serosurvey showed that around 32 percent of people surveyed had serologically confirmed influenza over the 2015 season (adjusted for age and ethnicity).<sup>6, 15</sup> Overall only one-quarter of those reported influenza-like illness; three out of four people were asymptomatic; only 1 out of 47 visited their GP and 1 in 680 were hospitalised. Young children and Pacific people experienced the highest influenza infection attack rates.<sup>16</sup>

# 11.3 Epidemiology

## 11.3.1 Global epidemiology

Influenza is an important cause of disease worldwide. Annual epidemics are estimated to result in about 3 to 5 million cases of severe illness, and about 290,000 to 650,000 respiratory deaths globally.<sup>17, 18</sup> For example, it was estimated globally that 11.5 percent of lower respiratory tract infections (LRTI), 5.6 percent of LRTI deaths and 9.5 million LRTI hospitalisations were attributable to influenza in 2017.<sup>19</sup>

In temperate climates, seasonal epidemics occur mainly during winter, while in tropical regions, influenza occurs throughout the year causing outbreaks more irregularly.<sup>17</sup>

From time to time, pandemics occur when a new virus arises and spreads globally (see section 11.3.3). The last influenza pandemic was caused by the A(H1N1)pdm09 virus. More than 214 countries and overseas territories reported laboratory-confirmed influenza, including over 18,449 deaths.<sup>20</sup> Many more deaths were found to be associated with the pandemic due to respiratory and cardiovascular complications.<sup>21</sup>

## 11.3.2 New Zealand epidemiology

New Zealand experiences the typical temperate climate epidemiology of influenza, with the peak incidence occurring during the winter months, however, influenza activity occurs throughout the year.

The impact of influenza in New Zealand is substantial in terms of general practice consultations, hospitalisations and deaths. The highest burden of disease is in the very young, the elderly, pregnant women, those with co-morbid conditions, people from low-income groups, and Pacific and Māori ethnic groups.

### Influenza surveillance

The New Zealand influenza surveillance system compiles information from a variety of sources, including:

- national sentinel general practice-based influenza-like illness surveillance (part of the WHO's Global Influenza Programme)
- year-round laboratory-based surveillance by the regional virus diagnostic laboratories
- hospital-based severe acute respiratory infection surveillance in Auckland and Counties Manukau districts
- data from Healthline, HealthStat, publicly funded hospital discharges, and the AIR.

Influenza prevalence and circulating strains are monitored through general practice surveillance for influenza-like illness (ILI); hospitalisations are monitored for severe acute respiratory infection (SARI) admissions; and severity is determined by the proportion of hospitalisations requiring intensive care unit (ICU) admission.<sup>22</sup>

For example, during the 2019 season the levels of influenza-like illness and the overall impact were low and generally just above seasonal baseline.<sup>23</sup> However, SARI hospitalisation rates increased earlier than in previous years and, during the winter, a higher than usual proportion of viral respiratory illnesses were due to influenza. A(H3N2) and B/Victoria strains were co-circulating. Seriousness was similar to other A(H3N2) predominant years. Influenza A viruses were detected most frequently in hospitalised patients whereas influenza B was detected more in the community. In contrast, in 2018 the predominant strain was A(H1N1)pdm09 strain which is associated with high severity in those aged younger than 65 years.<sup>24</sup> Over one-half of those admitted to ICUs with influenza-associated SARI in 2018 did not report any pre-existing medical risk factors, consistent with being younger.<sup>24</sup>

In 2020 and 2021, due to COVID-19 pandemic restrictions, transmission of influenza in the community was interrupted: no cases with ILI symptoms and 0.6 percent of hospitalised SARI cases had detectable influenza virus in 2020 and no community influenza cases were detected during 2021.<sup>25, 26</sup> In 2022, there was very high incidence of influenza-associated acute respiratory infections in the community and a high influenza-associated hospitalisation burden, but the seriousness was low (as measured by the ratio of SARI-ICU to SARI case admissions).(SHIVERS data). A spike in influenza

was seen earlier than usual, coming in mid-June, with a very high rate of influenza-positive SARI hospitalisation activity (7.89 per 100,000 population).<sup>27</sup>

For detailed information, including influenza surveillance and influenza reports, see the ESR website (at [www.esr.cri.nz/expertise/public-health/infectious-disease-intelligence-surveillance/#Surveillancereports](http://www.esr.cri.nz/expertise/public-health/infectious-disease-intelligence-surveillance/#Surveillancereports) and [www.esr.cri.nz/digital-library/respiratory-illness-dashboard/](http://www.esr.cri.nz/digital-library/respiratory-illness-dashboard/)).

## Influenza immunisation uptake

Around 1.3 million doses of influenza vaccine were distributed to 25 November 2022.<sup>25</sup> This equated to around one third of the whole population (approximately 251 doses per 1,000 population).<sup>25</sup> According to Ministry of Health data, based on reporting from funding claims, publicly funded influenza vaccine uptake for individuals aged 65 years and older was around 71.2 percent in 2022; this is likely to be an underestimate of the coverage.

### 11.3.3 Pandemic influenza

The natural ecology of influenza type A viruses is among wild aquatic avian species, and from time to time, these viruses spill over into other species, including humans. These avian influenza virus infections are usually severe and associated with a high mortality; however, they are rarely transmitted from human to human. In the past, avian viruses have become transmissible either through adaptation or the acquisition of swine or human genomic material, and when natural immunity has been lacking in the population, have resulted in a pandemic with global spread. There have been four influenza pandemics recorded since 1918.

Pandemics have the potential to result in large numbers of severe infections, but the degree of severity is hard to predict and will depend upon many factors, including whether there is any previous community immunity. The most severe recorded influenza pandemic was the 'Spanish flu' A(H1N1) pandemic of 1918–1920, which caused an estimated 20–50 million deaths worldwide. The most recent pandemic was the 2009 A(H1N1)pdm09 strain. It was estimated that 18 percent (800,000) of the New Zealand population were infected with the virus during the first wave, including one in every three children.<sup>28</sup> Risk factors for severe outcomes included obesity, pregnancy,<sup>29</sup> diabetes mellitus and Pacific or Māori ethnicity.<sup>28</sup> This strain is now established as a circulating seasonal influenza strain.

Globally, in the first 16 months of the 2009 H1N1 influenza pandemic, 18,500 deaths were attributed to laboratory-confirmed influenza. When investigated further, it was estimated that over 201,000 respiratory deaths and an additional 83,300 cardiovascular deaths were associated with the pandemic – producing a rate 15 times higher than the laboratory-confirmed deaths. Of these deaths, 80 percent were younger than 65 years of age.<sup>21</sup>

Monitoring, surveillance and response for new pandemic strains are in place. See section 11.8.3.

## 11.4 Vaccines

Annual influenza vaccination is a most important measure for preventing influenza infection and mortality. New Zealand's annual National Influenza Immunisation Programme campaign includes an annual influenza kit for health care professionals (available from [influenza.org.nz](http://influenza.org.nz)) and a national education and communication programme.

### 11.4.1 Available vaccines

#### Funded vaccines

One quadrivalent inactivated, surface antigen influenza vaccine is funded.

**Influvac Tetra (Viatris) for adults and children aged 6 months and over**

Each 0.5 mL dose contains 15 µg haemagglutinin for each of the four recommended influenza virus strains; other components and excipients include potassium chloride, monobasic potassium phosphate, dibasic sodium phosphate dihydrate, sodium chloride, calcium chloride dihydrate, magnesium chloride hexahydrate and water for injections to 0.5 mL. Trace amounts of the following may also be present in each 0.5 mL dose: ovalbumin (<0.1 µg), formaldehyde, cetrimonium bromide, sodium citrate, sucrose, gentamicin sulphate, tylosine tartrate, hydrocortisone and polysorbate 80.

Availability of other influenza vaccines, particularly the unfunded vaccines, can vary between and during the season depending on demand and supply. Further details on other available vaccines [immune.org.nz](http://immune.org.nz).

#### Vaccine preparations and potential future options

Influenza vaccine preparations vary by their type, the number of influenza strains contained in the vaccine and their delivery systems. There are a range of delivery mechanisms available internationally, including intradermal injection and intranasal mists. Live attenuated influenza vaccines are delivered by intranasal spray. Some data suggest that intradermal vaccines may induce improved immune responses, particularly in older adults.<sup>30, 31</sup>

The seasonal influenza vaccine strains vary each year depending on the prevailing viruses. WHO conducts technical consultations in February/March and September each year to recommend viruses for inclusion in both trivalent and quadrivalent vaccines for the northern and southern hemisphere influenza seasons, respectively. In recent years, the southern hemisphere recommendations include the two influenza type A (H1N1pdm09 and H3N2) and two B (Victoria and Yamagata) strains likely to circulate in New Zealand over the coming influenza seasons.<sup>32</sup>

### Split virion influenza vaccines

Quadrivalent influenza vaccines (QIVs) contain two type A and two type B influenza strains. Some are split virion vaccines prepared from virus grown in embryonated hens' eggs. The virus is purified, disrupted and inactivated by splitting with beta-propiolactone or formaldehyde. QIVs offer broader protection against co-circulating B-strains and better effectiveness in seasons of B-strain mismatch than trivalent influenza vaccines (TIVs), which contain two influenza type A strains and one type B strain.<sup>1</sup>

### Cell-based influenza vaccine

For the 2024 influenza season, a cell-based QIV (QIVc; Flucelvax, Seqirus) is available (unfunded) to those aged 6 months and over.

Egg-based and cell-based influenza vaccines differ in their manufacturing processes. Traditional egg-based vaccines involve cultivating influenza viruses in embryonated chicken eggs, with harvested viral particles subsequently purified and inactivated for vaccine production. In contrast, the cell-based influenza vaccine uses mammalian cell cultures to rapidly propagate large volumes of the influenza virus, eliminating the need for chicken eggs and enabling more rapid manufacturing. Cell-based influenza vaccine manufacture offers advantages in situations where egg-based manufacture faces challenges, such as egg shortages and egg adaptation, or when there is antigenic mismatch due to mutations in the circulating season influenza virus.

Some studies comparing the relative efficacy of egg-based and cell-based influenza vaccines, show that a cell-based vaccine may have an advantage, particularly, during seasons when the variations between the egg-based vaccine strains and the influenza strains circulating in the population are substantial.<sup>33, 34</sup>

### Adjuvanted vaccines

Also for the 2024 influenza season, an adjuvanted QIV (aQIV; Fluad Quad, Seqirus) is available (unfunded) to those aged 65 years and over.

Adjuvants enhance the immune response to an antigen and enable the use of less antigen (antigen sparing). Internationally, there are three adjuvants licensed for use in influenza vaccines: two oil-in-water emulsions and a third that uses immunopotentiating reconstituted influenza virosomes.<sup>4</sup> Vaccines with these adjuvants show modestly improved immune responses, which may be particularly useful for the elderly and young children, but may also cause more local and systemic reactions than unadjuvanted vaccines.<sup>4, 35</sup>

The adjuvanted influenza vaccine available in New Zealand, FluAd Quad, contains a squalene-based oil-in-water emulsion adjuvant (designated MF-59). This adjuvant has



been used in influenza vaccines since 1997 and has a good safety record. Since there are limited head-to-head studies, a systematic review, comparing vaccine effectiveness of adjuvanted vaccine with the vaccine effectiveness of standard TIV or QIV or no vaccination found that adjuvanted TIV (aTIV) modestly improved vaccine effectiveness in adults aged 65 years or older.<sup>36</sup> During an A/H3N2 predominant season, a clinical trial comparing aTIV with standard TIV in nursing home settings in the US, with mean age of 79 years, reported that, while respiratory hospitalisation rates were similar in both groups, significant reductions in all-cause hospitalisations (unadjusted HR 0.94; 95% CI 0.87-1.0) and pneumonia/influenza hospitalisations (unadjusted HR 0.79; 0.65-0.96).<sup>37</sup> Over three influenza seasons (2017-2020) in the US, the use of aTIV in adults aged from 65 years was shown to improve vaccine effectiveness against influenza-related medical encounters compared with standard egg-based TIV (overall relative vaccine effectiveness point estimate range 20.8–27.5 percent).<sup>38</sup>

### High dose vaccines

As of 2024, high-dose influenza vaccine formulations are not available in New Zealand. High-dose influenza vaccines containing four times more haemagglutinin antigen than standard vaccines have been shown to be more effective against influenza-related death and all-cause hospitalisation in the elderly than standard-dose trivalent vaccines.<sup>39</sup> Evidence to compare high-dose and standard quadrivalent vaccines is currently limited and research is ongoing to evaluate their application. One meta-analysis in Europe found that either an adjuvanted or a high-dose influenza vaccine was preferred over standard TIV in older adults.<sup>40</sup> In the US over three influenza seasons, the relative effectiveness of high-dose TIV against influenza-related medical encounters compared with standard egg-based TIV increased by 13.0-16 percent in adults aged over 65 years.<sup>38</sup>

### Live attenuated influenza vaccines

At the time of writing, live attenuated influenza vaccines (LAIVs) are not approved for use in New Zealand.

LAIVs may induce stronger immune responses than TIV or QIVs, particularly in children, by mimicking natural influenza infection and evoking both mucosal and systemic immunity, including broader cellular immune responses.<sup>41</sup> Trivalent and quadrivalent LAIVs are licensed for use in North America for healthy non-pregnant individuals aged 2–49 years and in Europe for children aged 2–18 years.<sup>42</sup> LAIVs have been shown to be effective in children aged 6 months to 7 years.<sup>43</sup>

During the 2013/14 and 2015/16 influenza seasons, effectiveness of LAIV against the predominant A(H1N1) strain was lower in the US in children age 2–17 years than that observed in the UK during the same seasons, such that the US Advisory Committee on Immunization Practices (ACIP) temporarily withdrew its recommendations for LAIVs use during 2016/17 influenza season.<sup>42, 44</sup> LAIVs were reinstated during the 2019/2020 season.

UK data from the 2018/19 season showed that LAIV effectiveness in children aged 2–17 years was at least as good as QIV in children for whom LAIV is contraindicated, particularly against A(H1N1)pdm09.<sup>44, 45, 46</sup> It remains unclear why there were such significant differences in effectiveness for different regions, although variations in



circulating strain matches, the make-up of the LAIV itself and previous vaccination history may all have some effect.<sup>44</sup>

## 11.4.2 Efficacy and effectiveness

### International data

The efficacy (prevention of illness among vaccinated individuals in controlled trials) and effectiveness (prevention of illness in vaccinated populations) of influenza vaccine depends on several factors. The age and immune competence of the vaccine recipient are important factors, as well as the match between the virus strains in the vaccine and those in circulation each year. Mismatches can evolve during a season or due to mutations occurring during vaccine manufacture (egg adaptation).<sup>45</sup> Previous vaccination history has been suggested to reduce the vaccine effectiveness in some cases; possibly more so when the previous vaccination was mismatched with the circulating strains at the time.<sup>47</sup> More recently, prior-season vaccination history has not been associated with reduced vaccine effectiveness in children or adults, and findings support annual revaccination.<sup>45, 48-51</sup> With increasing complexity, this continues to be researched.

Prior to 2020, two influenza B strains have frequently co-circulated, and due to the challenges involved in predicting which B strains will circulate in the upcoming season, mismatches between the B strain selected for TIVs and the circulating B strains have occurred in up to one-half of influenza seasons. The capacity of QIVs (containing two B influenza strains) to provide broader immune responses against B strains and cross-protection during B-mismatched seasons was expected to prevent more influenza cases, hospitalisations and deaths than TIVs.<sup>1</sup> The composition of future vaccines will consider the status of influenza B virology.

Data for vaccine efficacy and effectiveness of TIVs is summarised in Table 11.1.

**Table 11.1: Current estimates of TIV influenza vaccine efficacy and effectiveness**

Population	Type of outcome	Level of protection (95% confidence intervals)	Ref
Pregnant women	Effectiveness		
	• against confirmed influenza	50% (15–71%)	52
	• against acute respiratory illness		53
	– requiring an ED visit	81% (31–95%)	
	– or hospitalisation	65% (3–87%)	
Infants aged under 6 months whose mothers received an influenza vaccination during pregnancy	Effectiveness		
	• against confirmed influenza	41% (7–63%) to 49% (12–70%)	54
	• against influenza-related hospitalisation	47% (12–68%)	55

*Continued overleaf*

Population	Type of outcome	Level of protection (95% confidence intervals)	Ref	
Healthy children <ul style="list-style-type: none"> <li>aged under 2 years</li> <li>aged 6–35 months</li> <li>aged 6 months to 17 years</li> <li>aged 2–15 years</li> </ul>	Effectiveness <ul style="list-style-type: none"> <li>against confirmed influenza</li> </ul>	Insufficient data under 2 years 66% (9–88%)	43, 56 57	
		66% (29–84%)	57	
		<ul style="list-style-type: none"> <li>against influenza-related death</li> </ul>	65% (47–78%)	58
		Efficacy against confirmed influenza	64% (52–72%)	56
		Effectiveness <ul style="list-style-type: none"> <li>against influenza-like illness</li> <li>against influenza-related hospitalisation</li> </ul>	28% (21–35%) to 47% (33–58%) 56% (12–78%)	56 59
Children with high-risk conditions aged 6 months to 17 years	Effectiveness against influenza-related death	51% (31–67%)	58	
Healthy adults (aged 18–64 years)	Effectiveness <ul style="list-style-type: none"> <li>against confirmed influenza</li> </ul>	59% (53–64%) to 66% (55–75%)	60	
		16% (5–25%) to 18% (2–31%)		
		61% (34–77%)	61	
		<ul style="list-style-type: none"> <li>against influenza-like illness general practice visit in New Zealand</li> </ul>	55% (24–73%)	
Adults with high-risk conditions: <ul style="list-style-type: none"> <li>heart failure</li> <li>diabetes (newly diagnosed, aged 65 years or older)</li> <li>chronic obstructive pulmonary disease</li> </ul>	Risk of: <ul style="list-style-type: none"> <li>all-cause mortality</li> <li>all-cause mortality</li> <li>influenza-related hospitalisation</li> </ul>	17% reduced risk 56% reduced risk 11% reduced risk	62 63	
		Effectiveness against influenza-related hospitalisation	22% (15–27%) to 43% (34–52%)	64
	Adults aged 40 years or older	Effectiveness against acute myocardial infarction	29% (9%–44%)	65
Adults aged 65 years or older	Effectiveness <ul style="list-style-type: none"> <li>against confirmed influenza</li> </ul>	49% (33–62%) 58% (34–73%)	66 67	
		39% (35–43%) 41% (27–53%)	66 67	
		<ul style="list-style-type: none"> <li>against non-fatal and fatal complications</li> </ul>	28% (26–30%)	67

## Vaccine effectiveness in New Zealand

New Zealand data is consistent with international data. While there is some variability from year to year and with different strains, the data overall show that the point estimate for influenza vaccine effectiveness is approximately 50 percent for preventing general practice visits, hospitalisations and for both influenza type A and B strains.<sup>61, 68-70</sup> Estimates for vaccine effectiveness tend to be higher in children and healthy midlife adults, and lower in the elderly. Influenza vaccination significantly reduces influenza-associated ICU admissions and attenuates disease severity in adults who were infected despite vaccination.<sup>71</sup>

Low influenza activity over recent years in New Zealand can cause imprecision in estimating annual vaccine effectiveness.<sup>24, 72</sup> According to the ESR for 2023, for influenza-confirmed ARI cases, the estimated crude vaccine effectiveness (VE) was 80.4 percent (95 percent CI: 72.7 to 86.1). For influenza-confirmed SARI cases, the estimated crude vaccine effectiveness (VE) was 58.6 percent (95 percent CI: 31.4 to 76.1). (Personal communication, January 2024).

## Pregnant women, the fetus and neonates

A pregnant woman and her fetus are at increased risk of influenza complications.<sup>8</sup> Physiological and immunological changes in pregnancy increase susceptibility to influenza.<sup>73</sup> Hospitalisation from influenza-related cardiorespiratory disorders during the second and third trimesters was especially apparent in the 2009 pandemic.<sup>74</sup> Influenza immunisation is therefore recommended during every pregnancy to reduce this risk, with similar effectiveness in healthy pregnant women as in other healthy adults against laboratory-confirmed influenza.<sup>75</sup> During the 2012–2013 seasons in Australia, women vaccinated in pregnancy were 81 percent less likely to attend emergency departments and 65 percent less likely to be hospitalised with acute respiratory illness than those unvaccinated.<sup>53</sup>

Influenza immunisation during pregnancy may reduce the incidence of stillbirth. Stillbirth was half as likely among vaccinated mothers compared to unvaccinated mothers in an Australian study.<sup>12</sup>

Maternal influenza immunisation offers protection to the newborn through maternal antibody transfer.<sup>41, 55, 74, 76</sup> Influenza vaccines are not registered and have not been shown to be effective in infants aged under 6 months: therefore, immunisation during pregnancy confers protection to newborns and infants who are too young to be vaccinated.<sup>11, 54</sup> Maternal influenza immunisation is significantly associated with reduced risk of influenza virus infection and influenza-related hospitalisation in infants up to 6 months of age and increased influenza antibody titres are maintained in infants through to age 2–3 months.<sup>54, 77</sup>

## Children

Influenza vaccination in children provides similar protection to that seen in healthy adults. Influenza infection rates are generally highest in children. Effectiveness against laboratory-confirmed influenza is around 65 percent in young children aged 6 months to 5 years when vaccine and circulating strains are well-matched.<sup>56-58</sup> Influenza

vaccination offers the greatest protection against influenza-related hospitalisation to children who are fully immunised with routine vaccines.<sup>78</sup> QIV vaccine effectiveness against influenza hospitalisation of children in the 2018 season in Australia was estimated to be 78.8 percent (95% CI 66.9–86.4); this was when Australia expanded the funded influenza vaccination programme to preschool children, those with comorbid medical conditions and all indigenous children.<sup>79</sup>

The additional benefit of vaccinating children is protection of those around them, including their peers, grandparents and infants.

## Healthy adults

Generally, randomised placebo-controlled trials of TIV in healthy adults support good protection against laboratory-confirmed influenza.<sup>60</sup> Effectiveness against laboratory-confirmed influenza is around 60 percent in adults, but varies with the match of vaccine with circulating strains (see Table 11.1).

Although currently available standard influenza vaccines are less effective at preventing clinical illness in older people,<sup>80</sup> influenza vaccination does reduce hospitalisation and deaths.

Effectiveness in community-dwelling adults aged over 60 years depends on how well the vaccine matches the circulating strains.<sup>4</sup> Influenza vaccine was moderately effective against laboratory-confirmed influenza during an epidemic season in community-dwelling adults age 65 year or older, irrespective of vaccine strain match. Significance was less during non-epidemic seasons and varied with virus type (the highest effectiveness was against A[H1N1] and the lowest against B).<sup>81</sup>

Vaccination has been demonstrated to prevent hospitalisation and death in older nursing home residents.<sup>82-85</sup> A meta-analysis across 11 studies estimated influenza vaccination effectiveness to 37 percent (95% CI: 18–53;  $p=0.001$ ) against pneumonia and 34 percent (95% CI: 10–53;  $p=0.01$ ) against death due to pneumonia or influenza in institutionalised older adults.<sup>86</sup> A 2010 Cochrane review concluded that there was insufficient evidence to support influenza vaccine effectiveness in the elderly;<sup>87</sup> however, reanalysis of that review and its methodology argued that there is substantial evidence for the ability of influenza vaccine to reduce the risk of influenza infection and influenza-related disease and death in the elderly.<sup>56, 66</sup>

Severity of influenza symptoms are modestly attenuated by influenza vaccination in the elderly.<sup>88</sup> Therefore, by reducing severity of disease, vaccination can reduce the risk or duration of hospitalisation. Hospitalisation and immobility in the elderly leads to physical and mental decline, increased frailty and loss of independence.<sup>9, 88-90</sup>

## Co-morbid conditions in adults and children

Influenza vaccination has been associated with reductions in hospitalisations and deaths among adults with risk factors for influenza complications, including diabetes,<sup>91, 92</sup> chronic obstructive pulmonary disease<sup>93, 94</sup> and heart failure.<sup>62</sup> Obese adults have a similar risk of influenza-associated hospitalisations as those with cardiovascular disease and diabetes.<sup>95</sup> Among Danish adults aged under 65 years with underlying medical

conditions, vaccination reduced all-cause deaths by 78 percent and hospitalisations attributable to respiratory infections or cardiopulmonary diseases by 87 percent.<sup>96</sup> An Australian study of adults aged 40 years and older showed that unvaccinated adults are almost twice as likely as vaccinated adults to have an acute myocardial infarct.<sup>97, 98</sup>

Influenza vaccination is as effective as other preventative coronary care therapies (eg, smoking cessation, statins and antihypertensives) in protection against cardiovascular events.<sup>98</sup>

During the 2018 season in Australia, QIV vaccine effectiveness against influenza-related hospitalisation for children with comorbidities was estimated to be 77.3 percent (95% CI 59.8–87.2%).<sup>79</sup>

This highlights the importance of vaccinating children, as well as adults, with comorbidities against influenza.

## Herd immunity

Influenza vaccination can provide indirect protection to those who are unimmunised or respond less well to the vaccine. This has been shown in certain settings, such as within schools and nursing homes.<sup>4</sup> There is evidence to suggest that herd immunity can be achieved, particularly by vaccinating children.<sup>99</sup>

The UK has progressively rolled-out a vaccination programme using LAIV and QIV, starting with children aged 2–3 years in 2013/14 and extended to children aged 4–7 years in 2015/16. As of the 2019/2020 season, influenza vaccine is offered in the UK to all children aged 2–10 years and up to 18 years for high risk groups. Early results from school-based pilot studies provided evidence of direct effect, indirect effects and overall impact, with decreases in disease incidence and influenza positivity in vaccinated and non-vaccinated groups.<sup>100</sup> A systematic review found that vaccination of children conferred indirect protection in some but not all settings.<sup>101</sup>

Some studies suggest that herd immunity may also be achieved in nursing homes if immunisation coverage of residents is greater than 80 percent.<sup>102</sup> Vaccinating health care workers is likely to be an effective strategy, particularly when in contact with high-risk patients.<sup>14</sup>

As shown by New Zealand SHIVERS data,<sup>6</sup> most people who catch the virus are asymptomatic or have very mild symptoms but are at risk of spreading it, such that increased vaccine uptake (funded and unfunded) across the whole population, from 6 months of age, is likely to achieve the greatest protection.

## Duration of immunity

Due to the continual drift of influenza viruses, duration of immunity provided by influenza vaccines is difficult to study. However, when the strains stay the same for consecutive years, vaccination in a previous year appears to confer immunity into the next year for healthy adults and children.<sup>4, 42</sup> However, shorter duration of immunity is likely in other groups, particularly the elderly.<sup>42</sup>

Protection due to LAIVs has been demonstrated to persist beyond a year.<sup>103, 104</sup>

### 11.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at [www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

Store in the dark at +2°C to +8°C. Do not freeze.

### 11.4.4 Dosage and administration

The funded quadrivalent influenza vaccine should be administered by intramuscular, or subcutaneous injection, if indicated (see section 2.2.3). The contents of the syringe must be shaken thoroughly before use.

#### Individuals aged 6 months and older

Individuals aged 6 months and older receive a single 0.5 mL intramuscular dose of a QIV vaccine.

Children aged under 9 years who have not previously received influenza vaccine require two doses of vaccine four weeks apart to produce a satisfactory immune response.

#### Immunocompromised individuals

Regardless of their age, previously unvaccinated immunocompromised individuals or those who have received a solid organ or haematopoietic stem cell transplant are recommended to receive two doses of influenza vaccine, four weeks apart (the second dose is unfunded).<sup>105</sup> One dose is then given in each subsequent year. (See section 4.3.)

#### Co-administration with other vaccines

Influenza vaccine can be coadministered with other vaccines, such as pneumococcal polysaccharide vaccine, tetanus diphtheria acellular pertussis (Tdap) vaccine, COVID-19 vaccines (mRNA-CV), and all the scheduled childhood vaccines, given at separate injection sites. Concurrent administration of influenza vaccine and 13-valent pneumococcal conjugate vaccine (PCV13) carries an increased risk of fever.<sup>106, 107</sup> Separation of the vaccines by two days can be offered, but is not essential. (See also section 17.6.2.)

## 11.5 Recommended immunisation schedule

The optimal time to vaccinate people against influenza, particularly those in high-risk groups, is generally recommended from 1 April, annually, in advance of the usual May to September period of influenza virus activity. The vaccine can be given even when influenza virus activity has been identified, because protective antibody levels develop from four days after immunisation, with full protection after two weeks.<sup>108</sup> The vaccine should be administered annually to maintain immunity and to provide protection against new strains.

Vaccine effectiveness may be reduced in those at highest risk from influenza. Influenza vaccine is therefore recommended annually for everyone from the age of 6 months to reduce the spread of influenza virus and to protect against influenza-related complications. It is particularly important to vaccinate contacts of high-risk individuals, such as family and caregivers, and those working in certain occupations. See Table 11.2 for a summary of the funded and unfunded recommendations for influenza immunisation.

See the national 2024 Influenza Immunisation Programme campaign website (at [immune.org.nz](https://immune.org.nz)) for further information.



**Table 11.2: Influenza vaccine recommendations**

Note: **Funded individuals are in the shaded rows.**

Refer to the Pharmaceutical Schedule ([pharmac.govt.nz](http://pharmac.govt.nz)) for any changes to the funding decisions.

<b>Recommended and funded</b>
All individuals aged 65 years and older.
Individuals aged 6 months to under 65 years who: <ul style="list-style-type: none"><li>• have cardiovascular disease (ischaemic heart disease, congestive heart failure, rheumatic heart disease, congenital heart disease or cerebrovascular disease)</li><li>• have chronic respiratory disease (asthma if on regular preventive therapy; other chronic respiratory disease with impaired lung function)</li><li>• have diabetes</li><li>• have chronic renal disease</li><li>• have any cancer, excluding basal and squamous skin cancers if not invasive</li><li>• have any of the following other conditions:<ul style="list-style-type: none"><li>– autoimmune disease</li><li>– immunosuppression or immune deficiency</li><li>– HIV infection</li><li>– Transplant recipients</li><li>– Neuromuscular and central nervous system diseases/disorders</li><li>– Haemoglobinopathies</li><li>– Is a child on long-term aspirin</li><li>– Has a cochlear implant</li><li>– Errors of the metabolism at risk of major metabolic decompensation</li><li>– Pre- or post-splenectomy</li><li>– Down syndrome</li></ul></li><li>• are pregnant, any trimester</li><li>• are children aged 4 years and under who have been hospitalised for respiratory illness or have a history of significant respiratory illness (see section 11.5.2)</li><li>• have serious mental health conditions (schizophrenia, major depressive disorder, bipolar disorder or schizoaffective disorder) and/or are currently accessing secondary or tertiary mental health and addiction services</li><li>•</li></ul>
<b>Recommended but not funded</b>
Generally, this vaccine is recommended annually for all individuals age from 6 months; it is particularly important for: <ul style="list-style-type: none"><li>• individuals with asthma not requiring regular preventive therapy</li><li>• individuals in essential positions, emergency responders and health care workers</li><li>• individuals with hypertension and/or dyslipidaemia without evidence of end-organ disease.</li><li>• individuals who may transmit influenza to persons at increased risk of complications from influenza infection, (eg, caregivers, family members, health care staff, child care staff and other close contacts)</li><li>• residents and staff of residential care facilities</li><li>• the homeless.</li><li>• livestock workers and those handling wild birds and marine mammals.</li></ul>

## 11.5.1 Pregnancy and breastfeeding

The influenza vaccine is strongly recommended, and funded, for people who will be pregnant while the vaccine is available. Pregnant women can receive influenza vaccination at any stage of pregnancy to protect themselves, their fetus and their newborn for each season they are pregnant. When pregnancy spans two influenza seasons, two vaccinations (one from each season) are recommended to protect against all the predicted strains.

Influenza vaccine is safe to administer during any stage of pregnancy or while lactating. There is no evidence that influenza vaccine prepared from inactivated split virus or subunits causes damage to the fetus or neonate<sup>109</sup> and there is some evidence it may be protective against stillbirth.<sup>12</sup>

Pregnant women are at greater risk from complications associated with influenza illness.<sup>8, 11</sup> When pregnancy is superimposed on high-risk conditions such as asthma or diabetes, influenza-related morbidity is three to four times greater than in non-pregnant women with similar high-risk conditions.

Globally, about one-quarter of influenza-associated hospital admissions and over one-third of in-hospital deaths are in infants under 6 months.<sup>110</sup> Because there is no registered or effective vaccine for children aged under 6 months, vaccination during pregnancy is highly recommended to improve maternal-fetal passive antibody transfer.<sup>11</sup> Influenza vaccination of pregnant women has been shown to significantly decrease influenza in their newborn babies.<sup>41, 55, 74, 76</sup> Breastfeeding is also recommended, to deliver passive immunity to the infant.<sup>41</sup> (See also section 4.1.2.)

## 11.5.2 Children at increased risk

Influenza vaccine is recommended and funded for children aged 6 months and over with certain chronic illnesses (see Table 11.2) and for children aged under 4 years a history of significant respiratory disease (including a history of measles). Children with the following conditions should be prioritised to receive influenza vaccine due to their increased risk, including:

- all asthmatics on regular preventive therapy
- other children with chronic respiratory disorders (eg, cystic fibrosis, non-cystic fibrosis bronchiectasis and chronic lung disease of infancy).

Special considerations apply to children, as follows (see also section 4.3):

- Immunisation is occasionally associated with fever between 6 and 24 hours after administration. In children aged 6–24 months with significant chronic medical conditions fever may cause an exacerbation of the underlying condition.
- Children receiving cancer chemotherapy may have a weaker response to influenza vaccine. Vaccination is recommended three to four weeks after the preceding dose of chemotherapy, when the neutrophil and lymphocyte counts are each  $\geq 1.0 \times 10^9/L$ . Children who are no longer receiving chemotherapy can be expected to show seroconversion to vaccine three months after the cessation of chemotherapy.

## 11.5.3 Adults at increased risk

### Adults aged 65 years and older

In adults aged 65 years and older, influenza vaccine has been shown to be effective against non-fatal and fatal influenza complications, influenza-like illness and laboratory-confirmed influenza (see Table 11.1). Influenza vaccination protects against loss of independence due to increasing levels of frailty associated with hospitalisation.<sup>9, 90, 111</sup>

### Adults with underlying medical conditions

Influenza has been associated with increased morbidity and mortality in adults with underlying medical conditions (see Table 11.2). Risk increases with multiple conditions. These also include those with serious mental health conditions and accessing mental health or addiction services. (See also Pregnancy and breastfeeding).

## 11.5.4 Recommended but not funded

Generally, influenza vaccination is recommended annually for all individuals aged from 6 months. It is particularly important for the groups listed in Table 11.2.

There are certain conditions that individually do not render a person eligible for funded influenza vaccine, but when combined, significantly increase the risk of influenza complications (this is described as 'risk stacking'). Such risks are further increased by smoking, alcohol dependency and obesity.

In order to optimise the protection of high-risk infants and toddlers, including those aged under 6 months, all household members and close contacts should receive influenza vaccine (not funded unless eligibility criteria are met).

### Adults of Māori or Pacific ethnicity aged 55 years and over

Māori and Pacific people are at greater risk of developing underlying health conditions, such as cardiovascular disease and chronic respiratory disease, at a younger age than other ethnicities,<sup>112</sup> which increases the risk of influenza severity and complications. Factors contributing to this risk an increased risk of respiratory virus transmission can included overcrowding due to lack of appropriate multigenerational housing and close-knit communities.

### Healthy individuals of any age from 6 months and older

Healthy individuals are encouraged to have an influenza vaccine, annually, especially if they are in close contact with individuals at high risk of complications. Employers are encouraged to provide influenza vaccine to avoid illness in their employees, especially

those engaged in health care and other essential community services (see Table 4.9). Immunising healthy individuals has been shown to be cost-effective.

To optimise the protection of high-risk infants and toddlers, including those aged under 6 months (see Table 11.2), all household members and close contacts are recommended to receive influenza vaccine (not funded for those aged under 65 years, unless eligibility criteria are met). Influenza vaccine is recommended and funded to be received at any stage of pregnancy, for those aged 65 years or over.

### Health care workers

Health New Zealand | Te Whatu Ora strongly recommends, and expects, that all health care workers will receive annual influenza vaccination for their own protection and the protection of those in their care.

### Travellers

Influenza vaccine is recommended for people travelling outside New Zealand, especially those who are in the at-risk groups who have not received vaccine during the previous autumn, depending on the season and their destination. In tropical countries, influenza activity can occur throughout the year but is more likely during the winter (wet) and summer seasons, while in the northern hemisphere activity is commonest between the months of December and March. Outbreaks of influenza among organised tourist groups (eg, on cruise ships) can occur throughout the year.

## 11.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

### 11.6.1 Contraindications

Influenza vaccine should not be administered to people with a history of an anaphylactic reaction to a prior dose of influenza vaccine or to a vaccine component. Egg allergy, including anaphylaxis, is **not** a contraindication or precaution: see section 11.6.3.

### 11.6.2 Precautions

#### History of Guillain–Barré syndrome

Influenza vaccination has been suggested to increase the risk of GBS. However, no association was found between administering 16 million doses of influenza vaccine and

GBS in adults aged from 65 years in the US.<sup>113</sup> Any potential risk increase would be less than one additional case per million doses administered.<sup>4, 42, 114</sup> The risk of developing GBS is increased following influenza infection, and the magnitude of the risk is several times greater than that possibly occurring following influenza vaccination.<sup>4, 114, 115</sup>

New Zealand hospitalisations for GBS showed no increase during the 1990s despite the marked increase in vaccine use during this period but apparent year-to-year variation was observed. In particular, the doubling of vaccine use (with the introduction of funded vaccine) in 1997 was not associated with any increase in GBS hospitalisations. No excess risk for GBS following influenza vaccine in children has been documented. No association between influenza vaccines and any other neurological disease has been substantiated.

The risks and benefits of withholding vaccination should be considered on an individual basis, based on the potential morbidity and mortality associated with influenza for that individual, including the potential risk of recurrent GBS following influenza infection.

### Co-administration with PCV13

Individuals (or their parents/guardians) who receive both influenza vaccine and 13-valent pneumococcal conjugate vaccine (PCV13) should be advised of the increased risk of fever following concomitant administration of these vaccines.<sup>106, 107, 116</sup> Separation of the vaccines by two days can be offered, but is not essential (see also section 17.6.2).

### 11.6.3 Egg allergy

Influenza vaccine can be safely administered to people with a history of egg allergy, including anaphylaxis, at general practices, pharmacies or at the workplace.<sup>117</sup>

Reported cases of anaphylaxis after influenza vaccination in egg-allergic individuals all occurred over 30 years ago, at a time when vaccine egg (ovalbumin) content was much higher than it is now. Recent studies have shown that influenza vaccines containing less than 1 µg of ovalbumin do not trigger anaphylaxis in sensitive individuals.<sup>117</sup>

## 11.7 Potential responses and AEFIs

Split virion or subunit influenza vaccines are generally well tolerated. The safety profile of quadrivalent vaccines is comparable to that of trivalent vaccines.<sup>42</sup>

Potential responses associated with these influenza vaccines in adults and children include pain, redness and/or swelling at the site of injection (10–64 percent of recipients, lasting less than two days).<sup>4</sup> These local inflammatory responses are almost always mild. Systemic events such as headache, muscle aches and fatigue may occur in adults. Passive reporting of local and systemic reactions to influenza vaccines is more

frequent for females (both young and older adults) than males.<sup>118</sup> Australian surveillance data (collected by AusVaxSafety) found that just over 6 percent of adults reported any adverse event following seasonal influenza vaccination, of which less than 1 percent were systemic responses (fever, rash and seizure).<sup>119</sup>

Systemic reactions are more likely in children not previously exposed to the vaccine or virus, these are generally self-limiting and resolve within one to two days.<sup>42</sup> A large post-licensure study in the US, which reviewed more than 250,000 children aged under 18 years given influenza vaccine, showed no increase in clinically important medically attended events for two weeks after vaccination compared to control periods.<sup>120</sup>

In early 2010, an increase in febrile seizures in children in both Australia and New Zealand were all linked to the Fluvax brand influenza vaccine. Active surveillance in Australia continues to monitor for potential safety signals.

Vaccinators need to emphasise to recipients that:

- the split virion vaccine contains components of the virus, not the intact virus, and cannot cause influenza
- local reaction and mild systemic symptoms may occur within a day or two of immunisation
- respiratory viral infections are common, and many individuals will develop one coincidentally following immunisation, and these should not be falsely attributed to the vaccine.

An association was found in 2010 between narcolepsy and one H1N1 pandemic vaccine (Pandemrix, an adjuvanted vaccine not licensed or used in New Zealand). Data from various European countries support a temporal link.<sup>121-123</sup> The onset of narcolepsy may be confounded by other factors, such as genetic predisposition, A(H1N1)pdm09 influenza and/or other environmental factors.<sup>124-126</sup> A 2018 systematic review found that although the risk of narcolepsy type 1 increased in association with this particular vaccine, it remains a rare disease and the benefit of the influenza vaccination outweighs the risk.<sup>127</sup>

## 11.8 Public health measures

### 11.8.1 Improving vaccine uptake

Studies in New Zealand and overseas have found that provider attitudes and provider recommendations are key to improving influenza vaccine uptake. Organised registers for recall and opportunistic immunisation are also likely to be important factors in achieving high uptake.

Every effort should be made during April to immunise all people at risk, particularly those aged 65 years and older, those aged under 65 years (including children) who have certain medical conditions, pregnant women and health care workers, and those of Māori or Pacific ethnicity aged 55 to 64 years. During an influenza outbreak,

recommend influenza vaccination to anyone at risk who was not immunised during the current season or to those who have not received an influenza vaccination for more than six months. Availability of an appropriate vaccine is the most pertinent of these factors.

Vaccination of all healthy adults and children from age 6 months is encouraged but not funded. Adult vaccination, especially for those in close contact with high-risk groups, may be funded by employers.

## 11.8.2 Antiviral drugs

Influenza antiviral drugs can be used to treat or to prevent influenza and can be adjuncts to influenza vaccination. Early use of antivirals, especially within the first 48 hours of illness, can reduce the duration of symptoms and the risk of complications from influenza. They are likely to be most effective against severe influenza and for those with high-risk comorbidities. Antivirals should be particularly considered for unimmunised or recently immunised contacts who are at high risk of severe disease to lower disease severity and improve recovery time.<sup>128, 129</sup>

## 11.8.3 Influenza pandemics

At the time of a pandemic, recommended public health advice, priority groups and the timing of vaccination may be quite different from those during inter-pandemic periods. The *New Zealand Pandemic Plan: A framework for action* (available at [www.health.govt.nz/publications/new-zealand-pandemic-plan-a-framework-for-action](http://www.health.govt.nz/publications/new-zealand-pandemic-plan-a-framework-for-action)) describes the key phases of a pandemic and the actions and responsibilities within each phase.

# 11.9 Variations from the vaccine data sheet

None.

## References

1. Ray R, Dos Santos G, Buck PO, et al. A review of the value of quadrivalent influenza vaccines and their potential contribution to influenza control. *Human Vaccines & Immunotherapeutics*, 2017. 13(7): p. 1640-1652.
2. Paget J, Caini S, Del Riccio M, et al. Has influenza B/Yamagata become extinct and what implications might this have for quadrivalent influenza vaccines? *Euro Surveillance*, 2022. 27(39).



3. Fine P, Mulholland K, Scott J, Edmunds W. 2018. Community Protection, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
4. Bresee JS. 2018. Inactivated influenza vaccines, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
5. Lowen AC, Mubareka S, Steel J, Palese P. Influenza virus transmission is dependent on relative humidity and temperature. *PLoS Pathogens*, 2007. 3(10): p. 1470-6.
6. Huang QS ,(on behalf of the SHIVERS Investigation team), Key Findings – SHIVERS (updated January 2017), in *Presented at the 2016 New Zealand Influenza Symposium*. 2016: Wellington
7. Caini S, Huang QS, Ciblak MA, et al. Epidemiological and virological characteristics of influenza B: results of the Global Influenza B Study. *Influenza Other Respir Viruses*, 2015. 9(Suppl 1): p. 3-12.
8. Prasad N, Huang QS, Wood T, et al. Influenza-associated outcomes among pregnant, postpartum, and nonpregnant women of reproductive age. *Journal of Infectious Diseases*, 2019. 219(12): p. 1893-1903.
9. Andrew MK, Shinde V, Ye L, et al. The importance of frailty in the assessment of influenza vaccine effectiveness against influenza-related hospitalization in elderly people. *Journal of Infectious Diseases*, 2017. 216(4): p. 405-414.
10. Warren-Gash C, Smeeth L, Hayward AC. Influenza as a trigger for acute myocardial infarction or death from cardiovascular disease: a systematic review. *Lancet Infectious Diseases*, 2009. 9(10): p. 601-10.
11. Marshall H, McMillan M, Andrews RM, et al. Vaccines in pregnancy: The dual benefit for pregnant women and infants. *Human Vaccines & Immunotherapeutics*, 2016. 12(4): p. 848-56.
12. Regan AK, Moore HC, de Klerk N, et al. Seasonal trivalent influenza vaccination during pregnancy and the incidence of stillbirth: population-based retrospective cohort study. *Clinical Infectious Diseases*, 2016. 62(10): p. 1221-7.
13. Fragaszy EB, Warren-Gash C, White PJ, et al. Effects of seasonal and pandemic influenza on health-related quality of life, work and school absence in England: Results from the Flu Watch cohort study. *Influenza Other Respir Viruses*, 2018. 12(1): p. 171-182.
14. Hayward AC, Harling R, Wetten S, et al. Effectiveness of an influenza vaccine programme for care home staff to prevent death, morbidity, and health service use among residents: cluster randomised controlled trial. *BMJ*, 2006. 333(7581): p. 1241.
15. Huang QS ,(on behalf of the SHIVERS Investigation team), Southern Hemisphere Influenza and Vaccine Effectiveness Research and Surveillance (SHIVERS) & beyond, in *Presented at the 4th New Zealand Influenza Symposium*. 2018: Wellington
16. Huang QS, Bandaranayake D, Wood T, et al. Risk factors and attack rates of seasonal influenza infection: Results of the Southern Hemisphere Influenza and Vaccine Effectiveness Research and Surveillance (SHIVERS) Seroepidemiologic Cohort Study. *Journal of Infectious Diseases*, 2019. 219(3): p. 347-357.
17. World Health Organization. 2018 *Influenza (Seasonal)*. 2018 [updated 6 November 2018]; URL: [https://www.who.int/en/news-room/fact-sheets/detail/influenza-\(seasonal\)](https://www.who.int/en/news-room/fact-sheets/detail/influenza-(seasonal)). (accessed 8 November 2019)
18. Iuliano AD, Roguski KM, Chang HH, et al. Estimates of global seasonal influenza-associated respiratory mortality: a modelling study. *Lancet*, 2018. 391(10127): p. 1285-1300.
19. GBD 2017 Influenza collaborators. Mortality, morbidity, and hospitalisations due to influenza lower respiratory tract infections, 2017: an analysis for the Global Burden of Disease Study 2017. *Lancet Respir Med*, 2019. 7(1): p. 69-89.

20. World Health Organization. 2010 *Pandemic (H1N1) 2009 – Update 112 (6 August 2010)*. Weekly update Weekly update; 2010; URL: [http://www.who.int/csr/don/2010\\_08\\_06/en/](http://www.who.int/csr/don/2010_08_06/en/). (accessed 3 July 2020)
21. Dawood FS, Iuliano AD, Reed C, et al. Estimated global mortality associated with the first 12 months of 2009 pandemic influenza A H1N1 virus circulation: a modelling study. *Lancet Infectious Diseases*, 2012. 12(9): p. 687-95.
22. Huang QS ,(on behalf of the SHIVERS Investigation team), Flu in NZ and SHIVERS II update, in *Presented at the 5th New Zealand Influenza Symposium*. 2019: Wellington
23. Institute of Environmental Science and Research (ESR). 2019 *2019 Annual Influenza Summary*. Porirua. URL: [https://surv.esr.cri.nz/PDF\\_surveillance/Virology/FluAnnRpt/InfluenzaAnn2019.pdf](https://surv.esr.cri.nz/PDF_surveillance/Virology/FluAnnRpt/InfluenzaAnn2019.pdf). (accessed 3 July 2020)
24. Institute of Environmental Science and Research (ESR). 2018 *2018 Annual Influenza Summary*. ESR; 2018; URL: [https://surv.esr.cri.nz/virology/influenza\\_annual\\_report.php](https://surv.esr.cri.nz/virology/influenza_annual_report.php). (accessed 3 July 2020)
25. Institute of Environmental Science and Research (ESR). 2020 *2020 Annual Influenza Summary*. Porirua. URL: [https://surv.esr.cri.nz/PDF\\_surveillance/Virology/FluAnnRpt/InfluenzaAnn2020.pdf](https://surv.esr.cri.nz/PDF_surveillance/Virology/FluAnnRpt/InfluenzaAnn2020.pdf). (accessed 28 March 2022)
26. Institute of Environmental Science and Research (ESR). 2021 *2021 Annual Influenza Summary*. Porirua. URL: [https://surv.esr.cri.nz/PDF\\_surveillance/Virology/FluAnnRpt/InfluenzaAnn2021.pdf](https://surv.esr.cri.nz/PDF_surveillance/Virology/FluAnnRpt/InfluenzaAnn2021.pdf). (accessed 28 March 2022)
27. Institute of Environmental Science and Research (ESR). 2023 *2022 Acute respiratory illness surveillance report*. URL: <https://www.esr.cri.nz/digital-library/influenza-annual-report-2022/>. (accessed 12 February 2024)
28. Institute of Environmental Science and Research Ltd. 2009. *Seroprevalence of the 2009 Influenza A (H1N1) Pandemic in New Zealand* (ed.), Porirua: Institute of Environmental Science and Research Ltd. URL: <https://www.health.govt.nz/publication/seroprevalence-2009-influenza-h1n1-pandemic-new-zealand> (accessed 19 March 2020)
29. Siston AM, Rasmussen SA, Honein MA, et al. Pandemic 2009 influenza A(H1N1) virus illness among pregnant women in the United States. *JAMA*, 2010. 303(15): p. 1517-25.
30. Marra F, Young F, Richardson K, Marra CA. A meta-analysis of intradermal versus intramuscular influenza vaccines: immunogenicity and adverse events. *Influenza Other Respir Viruses*, 2013. 7(4): p. 584-603.
31. Patel SM, Atmar RL, El Sahly HM, et al. Direct comparison of an inactivated subvirion influenza A virus subtype H5N1 vaccine administered by the intradermal and intramuscular routes. *Journal of Infectious Diseases*, 2012. 206(7): p. 1069-77.
32. World Health Organization. 2019 *Recommended composition of influenza virus vaccines for use in the 2020 southern hemisphere influenza season*. WHO; 2019 [updated 27 September 2019]; URL: [https://www.who.int/influenza/vaccines/virus/recommendations/2020\\_south/en/](https://www.who.int/influenza/vaccines/virus/recommendations/2020_south/en/). (accessed 8 November 2019)
33. Boikos C, McGovern I, Molrine D, et al. Review of Analyses Estimating Relative Vaccine Effectiveness of Cell-Based Quadrivalent Influenza Vaccine in Three Consecutive US Influenza Seasons. *Vaccines (Basel)*, 2022. 10(6).
34. Coleman BL, Gutmanis I, McGovern I, Haag M. Effectiveness of Cell-Based Quadrivalent Seasonal Influenza Vaccine: A Systematic Review and Meta-Analysis. *Vaccines (Basel)*, 2023. 11(10).

35. Tregoning JS, Russell RF, Kinnear E. Adjuvanted influenza vaccines. *Human Vaccines & Immunotherapeutics*, 2018. 14(3): p. 550-564.
36. Coleman BL, Sanderson R, Haag MDM, McGovern I. Effectiveness of the MF59-adjuvanted trivalent or quadrivalent seasonal influenza vaccine among adults 65 years of age or older, a systematic review and meta-analysis. *Influenza Other Respir Viruses*, 2021. 15(6): p. 813-823.
37. McConeghy KW, Davidson HE, Canaday DH, et al. Cluster-randomized trial of adjuvanted versus nonadjuvanted trivalent influenza vaccine in 823 US nursing homes. *Clinical Infectious Diseases*, 2021. 73(11): p. e4237-e4243.
38. Boikos C, McGovern I, Ortiz JR, et al. Relative vaccine effectiveness of adjuvanted trivalent influenza vaccine over three consecutive influenza seasons in the United States. *Vaccines (Basel)*, 2022. 10(9).
39. National Advisory Committee on Immunization (NACI), An Advisory Committee Review National Advisory Committee on Immunization (NACI): Literature Review Update on the Efficacy and Effectiveness of High-Dose (Fluzone® High-Dose) and MF59-Adjuvanted (Fluad®) Trivalent Inactivated Influenza Vaccines in Adults 65 Years of Age and Older. 2017, Public Health Agency of Canada.
40. Gartner BC, Weinke T, Wahle K, et al. Importance and value of adjuvanted influenza vaccine in the care of older adults from a European perspective - A systematic review of recently published literature on real-world data. *Vaccine*, 2022. 40(22): p. 2999-3008.
41. Esposito S, Tagliabue C, Tagliaferri L, et al. Preventing influenza in younger children. *Clinical Microbiology and Infection*, 2012. 18 Suppl 5(Suppl 5): p. 42-9.
42. Grohsköpf LA, Sokolow LZ, Broder KR, et al. 2016. Prevention and control of seasonal influenza with vaccines. *MMWR: Recommendations and Reports*. 65(5): p. 1-54. DOI: 10.15585/mmwr.rr6505a1 (accessed 9 March 2020)
43. Osterholm MT, Kelley NS, Sommer A, Belongia EA. Efficacy and effectiveness of influenza vaccines: a systematic review and meta-analysis. *Lancet Infectious Diseases*, 2012. 12(1): p. 36-44.
44. Pebody R, Warburton F, Ellis J, et al. Effectiveness of seasonal influenza vaccine for adults and children in preventing laboratory-confirmed influenza in primary care in the United Kingdom: 2015/16 end-of-season results. *Euro Surveillance*, 2016. 21(38): p. pii=30348.
45. Pebody R, Djennad A, Ellis J, et al. End of season influenza vaccine effectiveness in adults and children in the United Kingdom in 2017/18. *Euro Surveillance*, 2019. 24(31).
46. Pebody RG, Zhao H, Whitaker HJ, et al. Effectiveness of influenza vaccine in children in preventing influenza associated hospitalisation, 2018/19, England. *Vaccine*, 2019.
47. Skowronski DM, Chambers C, Sabaiduc S, et al. A perfect storm: Impact of genomic variation and serial vaccination on low influenza vaccine effectiveness during the 2014-2015 season. *Clinical Infectious Diseases*, 2016. 63(1): p. 21-32.
48. Bartoszko JJ, McNamara IF, Aras OAZ, et al. Does consecutive influenza vaccination reduce protection against influenza: A systematic review and meta-analysis. *Vaccine*, 2018. 36(24): p. 3434-3444.
49. Cheng AC, Macartney KK, Waterer GW, et al. Repeated vaccination does not appear to impact upon influenza vaccine effectiveness against hospitalization with confirmed influenza. *Clinical Infectious Diseases*, 2017. 64(11): p. 1564-1572.
50. McLean HQ, Caspard H, Griffin MR, et al. Association of prior vaccination with influenza vaccine effectiveness in children receiving live attenuated or inactivated vaccine. *JAMA Netw Open*, 2018. 1(6): p. e183742.
51. Ramsay LC, Buchan SA, Stirling RG, et al. The impact of repeated vaccination on influenza vaccine effectiveness: a systematic review and meta-analysis. *BMC Medicine*, 2017. 15(1): p. 159.

52. Madhi SA, Cutland CL, Kuwanda L, et al. Influenza vaccination of pregnant women and protection of their infants. *New England Journal of Medicine*, 2014. 371(10): p. 918-31.
53. Regan AK, Klerk N, Moore HC, et al. Effectiveness of seasonal trivalent influenza vaccination against hospital-attended acute respiratory infections in pregnant women: A retrospective cohort study. *Vaccine*, 2016. 34(32): p. 3649-56.
54. Eick AA, Uyeki TM, Klimov A, et al. Maternal influenza vaccination and effect on influenza virus infection in young infants. *Archives of Pediatrics and Adolescent Medicine*, 2011. 165(2): p. 104-11.
55. Poehling KA, Szilagyi PG, Staat MA, et al. Impact of maternal immunization on influenza hospitalizations in infants. *American Journal of Obstetrics and Gynecology*, 2011. 204(6 Suppl 1): p. S141-8.
56. Jefferson T, Rivetti A, Di Pietrantonj C, Demicheli V. Vaccines for preventing influenza in healthy children. *Cochrane Database Syst Rev*, 2018. 2: p. CD004879.
57. Heinonen S, Silvennoinen H, Lehtinen P, et al. Effectiveness of inactivated influenza vaccine in children aged 9 months to 3 years: an observational cohort study. *The Lancet Infectious Diseases*, 2011. 11(1): p. 23-9.
58. Flannery B, Reynolds SB, Blanton L, et al. Influenza vaccine effectiveness against pediatric deaths: 2010-2014. *Pediatrics*, 2017. 139(5).
59. Blyth CC, Macartney KK, Hewagama S, et al. Influenza epidemiology, vaccine coverage and vaccine effectiveness in children admitted to sentinel Australian hospitals in 2014: the Influenza Complications Alert Network (FluCAN). *Euro Surveillance*, 2016. 21(30).
60. Demicheli V, Jefferson T, Ferroni E, et al. Vaccines for preventing influenza in healthy adults. *Cochrane Database Syst Rev*, 2018. 2: p. CD001269.
61. Turner N, Pierse N, Bissielo A, et al. Effectiveness of seasonal trivalent inactivated influenza vaccine in preventing influenza hospitalisations and primary care visits in Auckland, New Zealand, in 2013. *Euro Surveillance*, 2014. 19(34).
62. Rodrigues BS, David C, Costa J, et al. Influenza vaccination in patients with heart failure: a systematic review and meta-analysis of observational studies. *Heart*, 2019.
63. Wang IK, Lin CL, Chang YC, et al. Effectiveness of influenza vaccination in elderly diabetic patients: a retrospective cohort study. *Vaccine*, 2013. 31(4): p. 718-24.
64. Gershon AS, Chung H, Porter J, et al. Influenza vaccine effectiveness in preventing hospitalizations in older patients with chronic obstructive pulmonary disease. *Journal of Infectious Diseases*, 2019.
65. Barnes M, Heywood AE, Mahimbo A, et al. Acute myocardial infarction and influenza: a meta-analysis of case-control studies. *Heart*, 2015. 101(21): p. 1738-47.
66. Beyer WE, McElhaney J, Smith DJ, et al. Cochrane re-arranged: support for policies to vaccinate elderly people against influenza. *Vaccine*, 2013. 31(50): p. 6030-3.
67. Demicheli V, Jefferson T, Di Pietrantonj C, et al. Vaccines for preventing influenza in the elderly. *Cochrane Database Syst Rev*, 2018. 2: p. CD004876.
68. Bissielo A, Pierse N, Huang QS, et al. Effectiveness of seasonal influenza vaccine in preventing influenza primary care visits and hospitalisation in Auckland, New Zealand in 2015: interim estimates. *Euro Surveillance*, 2016. 21(1).
69. Pierse N, Kelly H, Thompson MG, et al. Influenza vaccine effectiveness for hospital and community patients using control groups with and without non-influenza respiratory viruses detected, Auckland, New Zealand 2014. *Vaccine*, 2016. 34(4): p. 503-509.
70. Turner N, Pierse N, Bissielo A, et al. The effectiveness of seasonal trivalent inactivated influenza vaccine in preventing laboratory confirmed influenza hospitalisations in Auckland, New Zealand in 2012. *Vaccine*, 2014. 32(29): p. 3687-93.



71. Thompson MG, Pierse N, Sue Huang Q, et al. Influenza vaccine effectiveness in preventing influenza-associated intensive care admissions and attenuating severe disease among adults in New Zealand 2012-2015. *Vaccine*, 2018. 36(39): p. 5916-5925.
72. Huang QS, Jelley L, Bocacao J, et al., Recommendations for Season Influenza Vaccine Composition for New Zealand 2019. 2018, Institute of Environmental Science and Research: Wellington.
73. Sakala IG, Honda-Okubo Y, Fung J, Petrovsky N. Influenza immunization during pregnancy: Benefits for mother and infant. *Human Vaccines & Immunotherapeutics*, 2016. 12(12): p. 3065-3071.
74. Tamma PD, Ault KA, del Rio C, et al. Safety of influenza vaccination during pregnancy. *American Journal of Obstetrics and Gynecology*, 2009. 201(6): p. 547-52.
75. Quach THT, Mallis NA, Cordero JF. Influenza vaccine efficacy and effectiveness in pregnant women: systematic review and meta-analysis. *Matern Child Health J*, 2020. 24(2): p. 229-240.
76. Zaman K, Roy E, Arifeen SE, et al. Effectiveness of maternal influenza immunization in mothers and infants. *New England Journal of Medicine*, 2008. 359(15): p. 1555-64.
77. Dabrera G, Zhao H, Andrews N, et al. Effectiveness of seasonal influenza vaccination during pregnancy in preventing influenza infection in infants, England, 2013/14. *Euro Surveillance: Bulletin Europeen sur les Maladies Transmissibles = European Communicable Disease Bulletin*, 2014. 19(45): p. 20959.
78. Kalligeros M, Shehadeh F, Mylona EK, et al. Influenza vaccine effectiveness against influenza-associated hospitalization in children: A systematic review and meta-analysis. *Vaccine*, 2020. 38(14): p. 2893-2903.
79. Blyth CC, Cheng AC, Crawford NW, et al. The impact of new universal child influenza programs in Australia: Vaccine coverage, effectiveness and disease epidemiology in hospitalised children in 2018. *Vaccine*, 2020. 38(13): p. 2779-2787.
80. Govaert TM, Thijs CT, Masurel N, et al. The efficacy of influenza vaccination in elderly individuals. A randomized double-blind placebo-controlled trial. *JAMA*, 1994. 272(21): p. 1661-5.
81. Darvishian M, van den Heuvel ER, Bissielo A, et al. Effectiveness of seasonal influenza vaccination in community-dwelling elderly people: an individual participant data meta-analysis of test-negative design case-control studies. *Lancet Respir Med*, 2017. 5(3): p. 200-211.
82. Deguchi Y, Takasugi Y, Tatara K. Efficacy of influenza vaccine in the elderly in welfare nursing homes: reduction in risks of mortality and morbidity during an influenza A (H3N2) epidemic. *Journal of Medical Microbiology*, 2000. 49(6): p. 553-6.
83. Gross PA, Hermogenes AW, Sacks HS, et al. The efficacy of influenza vaccine in elderly persons. A meta-analysis and review of the literature. *Annals of Internal Medicine*, 1995. 123(7): p. 518-27.
84. Gross PA, Quinnan GV, Rodstein M, et al. Association of influenza immunization with reduction in mortality in an elderly population. A prospective study. *Archives of Internal Medicine*, 1988. 148(3): p. 562-5.
85. Saah AJ, Neufeld R, Rodstein M, et al. Influenza vaccine and pneumonia mortality in a nursing home population. *Archives of Internal Medicine*, 1986. 146(12): p. 2353-7.
86. Chan TC, Fan-Ngai Hung I, Ka-Hay Luk J, et al. Effectiveness of influenza vaccination in institutionalized older adults: a systematic review. *Journal of the American Medical Directors Association*, 2014. 15(3): p. 226 e1-226 e6.
87. Jefferson T, Di Pietrantonj C, Al-Ansary LA, et al. Vaccines for preventing influenza in the elderly. *Cochrane Database Syst Rev*, 2010(2): p. CD004876.
88. Mosnier A, Daviaud I, Caini S, et al. Does seasonal vaccination affect the clinical presentation of influenza among the elderly? A cross-sectional analysis in the outpatient setting in France, 2003-2014. *Vaccine*, 2017. 35(16): p. 2076-2083.

89. Brummel NE, Balas MC, Morandi A, et al. Understanding and reducing disability in older adults following critical illness. *Critical Care Medicine*, 2015. 43(6): p. 1265-75.
90. Gill TM, Allore HG, Holford TR, Guo Z. Hospitalization, restricted activity, and the development of disability among older persons. *JAMA*, 2004. 292(17): p. 2115-24.
91. Looijmans-Van den Akker I, Verheij TJ, Buskens E, et al. Clinical effectiveness of first and repeat influenza vaccination in adult and elderly diabetic patients. *Diabetes Care*, 2006. 29(8): p. 1771-6.
92. Vamos EP, Pape UJ, Curcin V, et al. Effectiveness of the influenza vaccine in preventing admission to hospital and death in people with type 2 diabetes. *CMAJ: Canadian Medical Association Journal*, 2016. 188(14): p. E342-E351.
93. Poole PJ, Chacko E, Wood-Baker RW, Cates CJ. Influenza vaccine for patients with chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*, 2006(1): p. CD002733.
94. Kopsaftis Z, Wood-Baker R, Poole P. Influenza vaccine for chronic obstructive pulmonary disease (COPD). *Cochrane Database Syst Rev*, 2018. 6: p. CD002733.
95. Karki S, Muscatello DJ, Banks E, et al. Association between body mass index and laboratory-confirmed influenza in middle aged and older adults: a prospective cohort study. *International Journal of Obesity (2005)*, 2018.
96. Hak E, Buskens E, van Essen GA, et al. Clinical effectiveness of influenza vaccination in persons younger than 65 years with high-risk medical conditions: the PRISMA study. *Archives of Internal Medicine*, 2005. 165(3): p. 274-80.
97. Macintyre CR, Heywood AE, Kovoov P, et al. Ischaemic heart disease, influenza and influenza vaccination: a prospective case control study. *Heart*, 2013. 99(24): p. 1843-8.
98. MacIntyre CR, Mahimbo A, Moa AM, Barnes M. Influenza vaccine as a coronary intervention for prevention of myocardial infarction. *Heart*, 2016. 102(24): p. 1953-1956.
99. Mertz D, Fadel SA, Lam PP, et al. Herd effect from influenza vaccination in non-healthcare settings: a systematic review of randomised controlled trials and observational studies. *Euro Surveillance*, 2016. 21(42): p. pii=30378.
100. Pebody R, UK Paediatric Influenza Vaccine Programme, in *3rd New Zealand Influenza Symposium*. 2016: Wellington.
101. Yin JK, Heywood AE, Georgousakis M, et al. Systematic review and meta-analysis of indirect protection afforded by vaccinating children against seasonal influenza: implications for policy. *Clinical Infectious Diseases*, 2017. 65(5): p. 719-728.
102. Oshitani H, Saito R, Seki N, et al. Influenza vaccination levels and influenza-like illness in long-term-care facilities for elderly people in Niigata, Japan, during an influenza A (H3N2) epidemic. *Infection Control and Hospital Epidemiology*, 2000. 21(11): p. 728-30.
103. Gaglani MJ, Piedra PA, Herschler GB, et al. Direct and total effectiveness of the intranasal, live-attenuated, trivalent cold-adapted influenza virus vaccine against the 2000-2001 influenza A(H1N1) and B epidemic in healthy children. *Archives of Pediatrics and Adolescent Medicine*, 2004. 158(1): p. 65-73.
104. Ambrose CS, Yi T, Walker RE, Connor EM. Duration of protection provided by live attenuated influenza vaccine in children. *Pediatric Infectious Disease Journal*, 2008. 27(8): p. 744-8.
105. Australian Technical Advisory Group on Immunisation. 2018. *Australian Immunisation Handbook* (ed.), Canberra: Australian Government Department of Health. URL: <https://immunisationhandbook.health.gov.au/> (accessed October 2019)
106. Tse A, Tseng HF, Greene SK, et al. Signal identification and evaluation for risk of febrile seizures in children following trivalent inactivated influenza vaccine in the Vaccine Safety Datalink Project, 2010-2011. *Vaccine*, 2012. 30(11): p. 2024-31.

107. Van Buynder PG, Frosst G, Van Buynder JL, et al. Increased reactions to pediatric influenza vaccination following concomitant pneumococcal vaccination. *Influenza Other Respir Viruses*, 2013. 7(2): p. 184-90.
108. Zuckerman M, Cox R, Taylor J, et al. Rapid immune response to influenza vaccination. *Lancet*, 1993. 342(8879): p. 1113.
109. Bednarczyk RA, Adjaye-Gbewonyo D, Omer SB. Safety of influenza immunization during pregnancy for the fetus and the neonate. *American Journal of Obstetrics and Gynecology*, 2012. 207(3 Suppl): p. S38-46.
110. Wang X, Li Y, O'Brien KL, et al. Global burden of respiratory infections associated with seasonal influenza in children under 5 years in 2018: a systematic review and modelling study. *Lancet Glob Health*, 2020.
111. Lee WJ, Chen LK, Tang GJ, Lan TY. The impact of influenza vaccination on hospitalizations and mortality among frail older people. *Journal of the American Medical Directors Association*, 2014. 15(4): p. 256-60.
112. Ministry of Health. 2018 *Ngā mana hauora tūtohu: Health status indicators*. Ministry of Health Manatū Hauora; 2018 [updated 02 August 2018]; URL: <https://www.health.govt.nz/our-work/populations/maori-health/tataukahukura-maori-health-statistics/nga-mana-hauora-tutohu-health-status-indicators>. (accessed 25 March 2022)
113. Perez-Vilar S, Wernecke M, Arya D, et al. Surveillance for Guillain-Barre syndrome after influenza vaccination among U.S. Medicare beneficiaries during the 2017-2018 season. *Vaccine*, 2019. 37(29): p. 3856-3865.
114. Jefferson T, Di Pietrantonj C, Rivetti A, et al. Vaccines for preventing influenza in healthy adults. *Cochrane Database Syst Rev*, 2010(7): p. CD001269.
115. Vellozzi C, Iqbal S, Broder K. Guillain-Barre syndrome, influenza, and influenza vaccination: the epidemiologic evidence. *Clinical Infectious Diseases*, 2014. 58(8): p. 1149-55.
116. Stockwell MS, Broder K, LaRussa P, et al. Risk of fever after pediatric trivalent inactivated influenza vaccine and 13-valent pneumococcal conjugate vaccine. *JAMA Pediatr*, 2014. 168(3): p. 211-9.
117. Australasian Society of Clinical Immunology and Allergy. 2017. Vaccination of the egg-allergic individual. *ASCI Guidelines*. [https://www.allergy.org.au/images/stories/pospapers/ASCI\\_Guidelines\\_vaccination\\_egg\\_allergic\\_individual\\_2017.pdf](https://www.allergy.org.au/images/stories/pospapers/ASCI_Guidelines_vaccination_egg_allergic_individual_2017.pdf) (accessed 6 November 2019)
118. Klein SL, Marriott I, Fish EN. Sex-based differences in immune function and responses to vaccination. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 2015. 109(1): p. 9-15.
119. AusVaxSafety. 2019 *Influenza vaccine safety surveillance 2019*. AusVaxSafety; 2019 [updated September 2019]; URL: <https://ausvaxsafety.org.au/influenza-vaccine/2019-influenza-data>. (accessed 10 May 2022)
120. France EK, Glanz JM, Xu S, et al. Safety of the trivalent inactivated influenza vaccine among children: a population-based study. *Archives of Pediatrics and Adolescent Medicine*, 2004. 158(11): p. 1031-6.
121. Kilpi T, Jokinen J, Nohynek H, et al. 2011. Reported incidence of narcolepsy in children and adolescents after Pandemrix/Arepanrix vaccination. [https://www.thl.fi/documents/10531/104009/Narkolepsia\\_posteri.pdf](https://www.thl.fi/documents/10531/104009/Narkolepsia_posteri.pdf) (accessed 20 June 2020)
122. Nohynek H, Jokinen J, Partinen M, et al. AS03 adjuvanted AH1N1 vaccine associated with an abrupt increase in the incidence of childhood narcolepsy in Finland. *PLoS One*, 2012. 7(3): p. e33536.
123. Vaarala O, Vuorela A, Partinen M, et al. Antigenic differences between AS03 adjuvanted influenza A (H1N1) pandemic vaccines: implications for pandemrix-associated narcolepsy risk. *PLoS One*, 2014. 9(12): p. e114361.



124. Dauvilliers Y, Montplaisir J, Cochen V, et al. Post-H1N1 narcolepsy-cataplexy. *Sleep*, 2010. 33(11): p. 1428-30.
125. European Centre for Disease Prevention and Control. 2012. *Narcolepsy in association with pandemic influenza vaccination (a multi-country European epidemiological investigation)* (ed.), Stockholm: ECDC. URL: <https://www.ecdc.europa.eu/en/publications-data/narcolepsy-association-pandemic-influenza-vaccination-multi-country-european> (accessed 8 November 2019)
126. Han F, Lin L, Warby SC, et al. Narcolepsy onset is seasonal and increased following the 2009 H1N1 pandemic in China. *Annals of Neurology*, 2011. 70(3): p. 410-7.
127. Sarkanen TO, Alakujala APE, Dauvilliers YA, Partinen MM. Incidence of narcolepsy after H1N1 influenza and vaccinations: Systematic review and meta-analysis. *Sleep Medicine Reviews*, 2018. 38: p. 177-186.
128. Butler CC, van der Velden AW, Bongard E, et al. Oseltamivir plus usual care versus usual care for influenza-like illness in primary care: an open-label, pragmatic, randomised controlled trial. *Lancet*, 2020. 395(10217): p. 42-52.
129. Jefferson T, Jones M, Doshi P, et al. Oseltamivir for influenza in adults and children: systematic review of clinical study reports and summary of regulatory comments. *BMJ*, 2014. 348(9 April): p. g2545.

# 12 Measles

## Key information

Mode of transmission	By direct contact with infectious droplets or by airborne spread. Measles is one of the most highly communicable of all infectious diseases (R0=12–18).
Incubation period	About 10 days but may be 7–18 days from exposure to onset of fever. The incubation period may be longer in those given IG after exposure.
Period of communicability	From 4 days before to 4 days after rash onset, counting the day of rash onset as day 0.
Incidence and burden of disease	New Zealand was declared free of endemic measles in 2017. Outbreaks continue to occur through imported cases, as occurred in 2019. To prevent recurrent outbreaks of measles, 95 percent of the population must be immune.
Funded vaccine	MMR (Priorix) is a live attenuated vaccine.
Dose, presentation, route	0.5 mL per dose after reconstitution. Pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. Intramuscular or subcutaneous injection.
Funded vaccine indications and schedule	Children at ages 12 months and 15 months. Adults who are susceptible to one or more of measles, mumps and rubella. This includes all adults born in New Zealand from 1 January 1969 without two documented doses of measles-containing vaccine received after age 12 months. For (re)vaccination following immunosuppression (if the individual is immunocompetent enough to safely receive the vaccine).
Recommended	All adults born since January 1969 should be up to date with two doses of MMR or have evidence of immunity to all three vaccine components. It is particularly important for health care workers, individuals who work with children, armed forces personnel, staff of correctional facilities, long-term care facilities and immigration/refugee centres and laboratory staff. All vaccine-eligible travellers, particularly to high risk countries. Some adults born overseas before 1969 may also be susceptible to measles, mumps or rubella.
Vaccine effectiveness	Measles vaccines are around 95 percent effective after 1 dose and 99 percent effective after two doses.
Duration of protection	Two doses are anticipated to provide lifelong protection. Protection is best achieved through herd immunity from high immunisation coverage.
Contraindications	MMR is contraindicated for immunocompromised individuals and in pregnancy. Priorix is contraindicated for anaphylaxis to neomycin.

*Continued overleaf*

Precautions and special considerations	See section 12.6 for cautions around receipt of blood products and other live vaccines, and other precautions.
Potential responses to vaccine	MMR is generally well tolerated. Fever and rash 6–12 days after vaccination. Salivary gland swelling and joint pain is possible due to mumps and rubella components.
Public health measures	Notify the local medical officer of health immediately on suspicion of wild-type measles. Promote immunisation to susceptible individuals.
Post-exposure prophylaxis	Management of contacts of measles cases should be discussed with the medical officer of health. (see section 12.8)

## 12.1 Virology

The measles virus is an RNA virus, from the genus *Morbillivirus*, in the family Paramyxoviridae. Humans are the only natural host for the measles virus. The virus has a survival time of around two hours and is rapidly inactivated by sunlight, heat and extremes of pH.<sup>1</sup>

## 12.2 Clinical features

Measles is transmitted by airborne spread as well as direct contact with infectious droplets. It is one of the most highly communicable of all infectious diseases, with an approximate basic reproductive number of 12–18 in high-income countries<sup>2</sup> (see section 1.2.1). There is a prodromal phase of two to four days with fever, conjunctivitis, coryza and Koplik's spots on the buccal mucosa. The characteristic maculopapular rash classically appears first behind the ears on the third to seventh day, spreads over three to four days from the head and face, over the trunk to the extremities. It lasts for up to one week. The patient is most unwell during the first day or two after the appearance of the rash.

The incubation period is about 10 days, but may be 7–18 days, from exposure to onset of fever, and about 14 days, but may be 7–21 days, from exposure to onset of rash. Measles is highly infectious from four days before to four days after rash onset, counting the day of rash onset as day zero. Incubation may be longer in those given IG after exposure or in infants with residual maternal antibody and can present as a modified, attenuated measles with a mild prodrome and a sparse discrete rash of short duration.<sup>3</sup>

Complications are common, occurring in 10 percent of cases, and include otitis media, pneumonia, croup and diarrhoea. Encephalitis has been reported in 1 in every 1,000 cases, of whom some 15 percent die and a further 25–35 percent are left with permanent neurological damage. Other complications of measles include bronchiolitis, sinusitis, myocarditis, corneal ulceration, mesenteric adenitis, hepatitis and idiopathic thrombocytopenic purpura (ITP or immune thrombocytopenia).

Measles infection causes acute immune suppression of the cellular and humoral immunity that leads to the depletion of immunological memory and antibody repertoire. This loss in immunity increases the long-term risk of further infections requiring medical treatment.<sup>4-8</sup> Although there are potential implications for long term effects on immune memory of individuals who have had measles, currently, there is no evidence to recommend reimmunisation.

Sub-acute sclerosing panencephalitis (SSPE) is a rare but fatal degenerative central nervous system disease resulting from persistent measles virus infection. It typically occurs 7–11 years after wild-type measles infection, at an estimated rate of 4–11 per 100,000 measles cases with higher incidence if measles occurs before 2 years of age.<sup>9</sup> Recent literature shows that SSPE is under-reported or under-diagnosed in the US.<sup>10</sup> Cases have occurred following undiagnosed measles or clinically mild disease, particularly when immunisation coverage has been low or where infants too young to have been immunised have acquired the infection while travelling to endemic regions.<sup>11, 12</sup>

The case-fatality rate for reported cases of measles in the US is 1–3 per 1,000.<sup>9</sup> Pneumonia is responsible for approximately 60 percent of deaths, more commonly in young patients. Measles is particularly severe and has a much higher case-fatality rate in the malnourished children with vitamin A deficiency, which is further exacerbated by diarrhoea; in patients with defective cell-mediated immunity, who may develop giant cell pneumonia or encephalitis without evidence of rash;<sup>9</sup> and in pregnant women.<sup>9</sup> Measles during pregnancy can cause miscarriage, stillbirth and preterm delivery.<sup>1</sup>

Measles is also serious in healthy children: over half of all the children who died from measles in the UK between 1970 and 1983 were previously healthy.<sup>13</sup> No other conditions were reported as contributing to the death of seven people who died from measles in the 1991 New Zealand epidemic.

## 12.3 Epidemiology

### 12.3.1 Global burden of disease

#### Mortality and morbidity

From 2000 to 2016, the annual reported measles incidence decreased by 75 percent worldwide, from 146 to 35 cases per million population, due to increased vaccine coverage.<sup>14</sup> Annual worldwide estimated measles deaths was 89,780 in 2016, representing an 84 percent decline since 2000.<sup>15</sup>

However, there was a worldwide increase in disease during 2019. Over 1.3 million confirmed and suspected cases of measles were reported to WHO from 187/194 member states, resulting from multiple outbreaks, including in the previously measles-free Americas.<sup>16</sup>

Although measles mortality rates have fallen significantly,<sup>17</sup> measles remains an important vaccine-preventable cause of death among children throughout the world, particularly in low-income countries in Africa and Asia. The disease is highly infectious in non-immune communities, with epidemics occurring approximately every second year. During 2019, the countries with the highest number of cases were Philippines, Madagascar, India, Ukraine, the Nigeria and Brazil.<sup>16</sup> The incidence rate in Samoa was almost 10 times that observed in New Zealand (4525 versus 476 per million population). In Samoa, around 1.5 percent of cases died and one-third were hospitalised (there were 83 deaths, 5,707 cases and 1,868 hospitalised as of 20 January 2020).<sup>18</sup>

## Measles elimination

When a country is verified by the Measles Regional Verification Commission as having eliminated measles, it means that the country interrupted transmission of the endemic strain of circulating measles virus for a period of 36 months. Importations of measles virus may have occurred during this period, but circulation of the imported strains of measles virus was interrupted within 12 months of the importation.<sup>19</sup>

In May 2012 the 194 member states of the World Health Assembly endorsed the *Global Vaccine Action Plan 2011–2020*,<sup>20</sup> which aimed to eliminate measles in at least four WHO regions by 2015 and in five WHO regions by 2020. In September 2016, the Region of the Americas was the first WHO region to be declared free of endemic measles and New Zealand was verified as having eliminated measles in 2017.

Disappointingly, no region has sustained measles elimination. Measles cases were reported to have climbed by 300 percent globally in the first three months of 2019.<sup>21</sup> For example, four European countries (Albania, Czechia, Greece and the UK) lost measles elimination status and the US reported it highest number of cases in 25 years.<sup>22</sup> Global coverage for the first measles vaccine dose has stalled at 85 percent and for the second doses at 67 percent, falling short of the 95 percent required to prevent outbreaks.<sup>21</sup>

## 12.3.2 New Zealand epidemiology

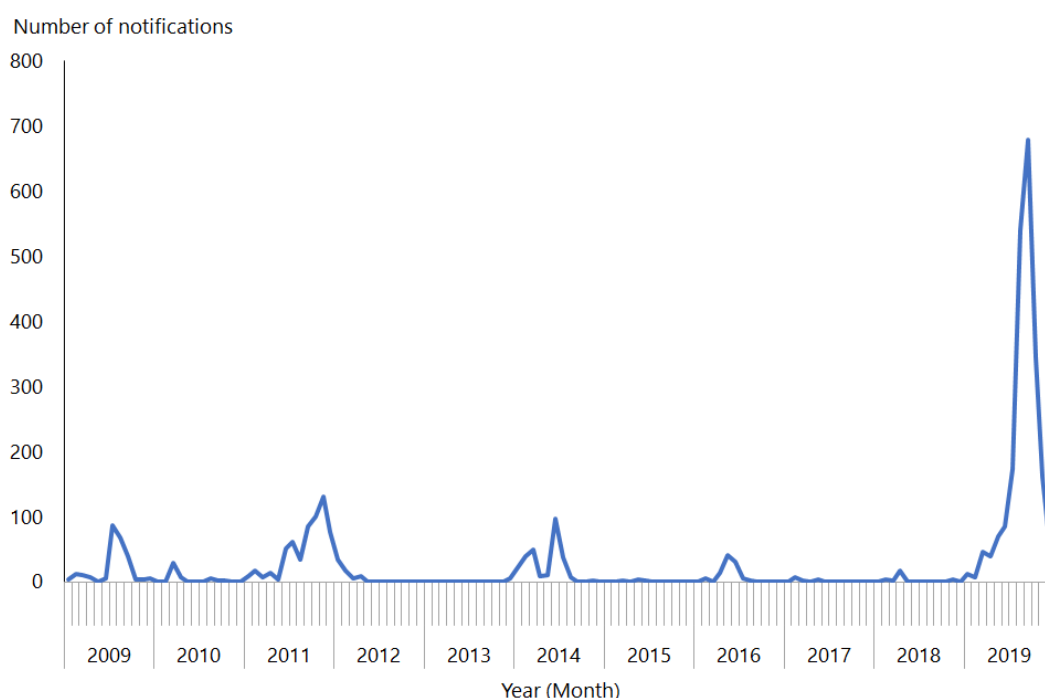
Measles vaccine was introduced in New Zealand in 1969 and moved to a two-dose schedule (as a combined MMR vaccine) in 1992. Measles became a notifiable disease in 1996. The two-dose schedule at ages 15 months and 4 years was introduced in 2001 (see Appendix 1 for more information about the history of the Schedule) and was changed in 2020 to 12 months and 15 months following the 2019 outbreaks.

Historical holes in coverage, due to a combination of issues including historically low immunisation coverage in the childhood programme, unfounded vaccine safety concerns at the turn of the 21st century, changes to the schedule for MMR dose 2 from age 11 years to 4 years and compromised vaccine due to lack of adequate cold chain processes prior to 2004 have meant that young adults and adolescents (ages 15–30 years), in particular, are under immunised against measles.<sup>23</sup>

Prior to the introduction of two-dose MMR schedule, measles epidemics occurred in 1991 (the number of cases was estimated to be in the tens of thousands) and 1997 (when 2,169 cases were identified). In 2019, nine outbreaks occurred, six were linked to imported cases from the Philippines, Japan, Thailand, Australia and Singapore. In 2019, 2,213 cases were notified, of which 775 were hospitalised (ESR, 8 June 2020). The worst affected district was Counties Manukau, which had 1,174 cases, many of whom were of Māori and Pacific ethnicity, children too young to be immunised and unimmunised young adults.<sup>24</sup>

Importation of measles by non-immune people who had travelled overseas was also linked to the smaller measles outbreaks in New Zealand in 2009, 2011, 2014 and 2016 (see Figure 12.1; see also section 12.5.5).

**Figure 12.1: Number of measles notifications by month reported, January 2009 to December 2019**



Source: ESR

To eliminate measles epidemics, modelling suggests that New Zealand needs to achieve a coverage level of 90 percent or greater for both doses of MMR.<sup>25</sup> If this coverage level is achieved and maintained in those aged 12 months to 50 years, elimination of measles can be maintained. In quarter ending 31 December 2019, the 5-year-old immunisation coverage rate (ie, fully immunised with two doses of MMR) was 89 percent – nearing a target of 95 percent.

For details of measles notifications, refer to the most recent measles and notifiable disease reports from ESR (available at [www.esr.cri.nz/digital-library/notifiable-disease-dashboard/](http://www.esr.cri.nz/digital-library/notifiable-disease-dashboard/)).

## 12.4 Vaccines

### 12.4.1 Available vaccines

The measles vaccine is only available as one of the components of MMR. This vaccine is a freeze-dried preparation containing live attenuated measles, mumps and rubella viruses.

#### Funded vaccine

Each 0.5 mL dose of the reconstituted MMR (Priorix, GSK) contains:

- not less than 103.0 CCID50 of the attenuated line of Schwarz strain measles, propagated in chick embryo tissue culture
- not less than 103.7 CCID50 of RIT 4385 mumps strain, derived from the Jeryl Lynn strain and propagated in chick embryo tissue culture
- not less than 103.0 CCID50 of the Wistar RA 27/3 rubella strains, propagated in MRC5 human diploid cells
- lactose, amino acids supplement, mannitol, sorbitol and neomycin sulphate as excipients, and water for injection.

#### Other vaccines

M-M-R II (MSD) was the funded vaccine prior to the 1 July 2017 Schedule change. It contains an attenuated line of measles virus derived from Enders' attenuated Edmonston strain; the Jeryl Lynn (B level) strain of mumps virus; and the Wistar RA 27/3 strain of live attenuated rubella virus.

Two quadrivalent measles, mumps, rubella and varicella vaccines (MMRV: see chapter 24) are also registered but not currently available in New Zealand:

- Priorix-Tetra (GSK) contains the Schwarz measles, RIT 4385 mumps, Wistar RA 27/3 rubella and Oka/Merck varicella-zoster virus strains.
- ProQuad (MSD) contains Enders' attenuated Edmonston (Moraten) measles virus strain, Wistar RA 27/3 rubella virus, Jeryl Lynn mumps virus and live varicella virus vaccines (Oka/Merck).



## 12.4.2 Efficacy and effectiveness

Measles vaccines are highly efficacious, and immunisation programmes have controlled measles to the point of elimination in many populations.<sup>26</sup> Outbreaks and epidemics continue to occur where low immunisation rates and/or sufficient numbers of susceptible members of communities are present. A 2012 Cochrane review of the safety and effectiveness of MMR concluded that a single dose of MMR is at least 95 percent effective in preventing clinical measles and 92 percent effective in preventing secondary cases among household contacts aged 6 months and older.<sup>27</sup> This was a systematic review of clinical trials and studies, which involved approximately 14.7 million children.

Seroconversion to all three viruses of MMR occurs in 85–100 percent of recipients. 'Primary vaccine failure' refers to the lack of protective immunity despite vaccination. It is due to failure of the vaccine to stimulate an immune response. This occurs in 5–10 percent of recipients after the first dose and is rare after a second dose. More than 99 percent of people who receive two MMR doses (given at least four weeks apart, with the first dose given after age 12 months) develop serologic evidence of immunity to measles.<sup>9</sup> Two doses are required for measles control and elimination in populations.<sup>9</sup> The second MMR dose is not a booster: it is given to increase vaccine efficacy to 98 percent and address primary vaccine failure.

Measles vaccination may have nonspecific effects, reducing mortality from other infectious diseases. Infection with the measles virus causes immune memory loss and predispose people to opportunistic infections for more than three years.<sup>5, 7, 8</sup> Population-level data from the UK, US and Denmark indicates that when measles was common, measles virus infections could have been implicated in as many as half of all childhood deaths from infectious disease.<sup>8</sup> The reduction in measles infections is suggested to be the main factor in reducing overall childhood infectious disease mortality after the introduction of vaccination.

### Duration of immunity

Even though antibody levels decline over time, secondary vaccine failure (ie, vaccine failure due to waning of protective immunity) has been documented for measles but remains rare.<sup>28</sup> There were three cases in the recent New Zealand outbreak with documented secondary vaccine failure but no transmission was recorded from these cases. Breakthrough cases, as a result of secondary vaccine failure, appear to be attenuated and less likely to be hospitalised.<sup>29</sup>

In Finland in 1982 a cohort was recruited at the start of the national MMR vaccination programme to study the persistence of vaccine-induced antibodies. By the mid-1990s Finland had eliminated measles, mumps and rubella, and there was little opportunity for natural boosting to occur. The follow-up of this cohort has shown that while antibodies wane over time, 20 years after the second MMR dose, 95 percent of people remained seropositive for measles.<sup>30</sup> The antibody avidity also decreased by 8 percent for measles.<sup>31</sup> Waning of both the concentration and the avidity of antibodies might contribute to measles infections occurring in individuals who have received two doses of MMR. Waning in immunity was suggested in a small proportion of vaccinated cases (less than 1 percent) in the 31–42 year age group reported in an outbreak in Berlin.<sup>32</sup>

## 12.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at [www.tewhaturora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhaturora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

Store at +2°C to +8°C. Do not freeze.

MMR must be reconstituted only with the diluents supplied by the manufacturer. Use MMR as soon as possible after reconstitution. If storage is necessary, reconstituted vaccine can be stored at +2°C to +8°C for up to eight hours.

## 12.4.4 Dosage and administration

The dose of MMR is all of the reconstituted vaccine (approximately 0.5 mL) administered by intramuscular injection, or subcutaneous injection if indicated (see section 2.2.3).

### Co-administration with other vaccines

MMR can be given concurrently with other vaccines, as long as separate syringes are used, and the injections are given at different sites. If not given concurrently, live vaccines should be given at least four weeks apart. (See also section 2.2.7 for information about multiple injections at the same visit.) Note that TST/Mantoux testing for tuberculosis must be deferred by at least four weeks after MMR if not given concurrently (see section 12.6.2).

### Interchangeability

The two brands of MMR (Priorix and M-M-RII) may be used interchangeably for completion of a course.<sup>33</sup>

## 12.5 Recommended immunisation schedule

**Table 12.1: Recommended MMR vaccination schedule**

	Schedule
Usual childhood schedule <sup>a</sup>	2 doses: at ages 12 months and 15 months
Catch-up <sup>b</sup> for children, adolescents and adults	2 doses: at least 4 weeks apart

- If MMR is given to children aged under 12 months, 2 further MMR doses are still required at age 12 months (given at least 4 weeks since the previous dose) and 15 months.
- For those born from 1 January 1969 who do not have documented evidence of two doses of a MMR-containing vaccine given after age 1 year, or who do not have serological evidence of protection for measles, mumps and rubella. See section 12.5.2.

### 12.5.1 Usual childhood schedule

A two-dose MMR vaccination schedule (with appropriate documentation) is recommended irrespective of a history of measles, mumps or rubella infection or measles immunisation. A clinical history does not reliably indicate immunity. Positive serology for measles cannot be used as a proxy for mumps or rubella immunity. There are no known ill effects from vaccinating children, even if they have had serologically confirmed infection with any of the viruses.

Measles vaccine is recommended as MMR at age 12 and 15 months. Two doses of measles vaccine are recommended because nearly all the approximately 5 percent who fail to be protected by the first dose will be protected by the second.<sup>9</sup> The second dose of measles vaccine can be given as soon as four weeks after the first dose.

#### MMR vaccination when aged under 12 months

A dose of MMR (called MMR0 [zero]) may be recommended for infants aged 4 months to under 12 months during measles outbreaks for pre-exposure prophylaxis (for post-exposure prophylaxis and HNIG use see section 12.8). These children still require a further two doses of MMR at ages 12 months (given at least four weeks after previous dose) and 15 months because their immune response and long-term protection from measles is less when the vaccine is given at a younger age.<sup>34, 35</sup> Any recommendations in this regard will be made by the local medical officer of health and Health New Zealand | Te Whatu Ora based on local epidemiology.

The first dose of MMR is scheduled and recommended at age 12 months, if infants are given MMR from age 11 months in other circumstances, they are considered to have been given MMR1 and therefore only need one further dose, ideally given at age 15 months. To optimise early protection, dose two can be given from age 12 months, **at least four weeks later**. For toddlers and children older than 15 months, give both doses of MMR four weeks apart.

Note:

- For infants born to mothers who received immunomodulatory biologic agents in pregnancy, see precautions section 12.6.2 and section 4.2.5.
- Some immigrant children may have received a measles-containing vaccine when aged under 12 months.

## 12.5.2 Catch-up

Two doses of documented MMR (at least four weeks apart) are recommended and funded for any child, adolescent or adult who is known to be susceptible to one or more of the three diseases.

A second dose of MMR should be given at least four weeks after MMR1 to all children who are older than 15 months but have not yet received their second MMR dose (ie, those who would have been due their second dose at age 4 years).

### Adults born from 1 January 1969

All individuals born in 1969 or later who have documented evidence of two doses of MMR given after age 12 months or who have serological evidence of protection for measles are considered immune to measles.

Some adults may have received one dose of measles-containing vaccine and one dose of MMR or MR during one of the catch-up campaigns (eg, the 1997 campaign, when all those aged up to 10 years were offered MMR, or from international schedules). They will have therefore received the recommended two doses of measles vaccine, but only one of mumps and rubella vaccines. While the main reason for a two-dose MMR schedule is to protect against measles, two doses of all three antigens is recommended and funded. These individuals can receive a second dose of MMR (ie, a third dose of measles vaccine) without any concerns. It is important that women of childbearing age are immune to rubella (see chapter 21).

All persons born from 1 January 1969 with only one documented dose of prior MMR should receive a further dose of MMR; if there are no documented doses of prior MMR or documented evidence of immunity, then two doses should be administered, at least four weeks apart.

### Occupational risk groups

Certain occupational groups are at increased risk of exposure to measles; particularly those who travel frequently, such as military personnel and cruise ship staff and aircrew (in this case MMR is funded for those eligible for New Zealand health services). See Table 4.9 for details of relevant occupational groups.

## 12.5.3 Immunocompromise

### Contacts of immunocompromised individuals

In general, MMR is contraindicated in immunocompromised individuals (see section 4.3). These people can be partially protected from exposure to infection by ensuring that all their close contacts, including hospital staff and family members, are fully immunised (this is funded), including hospital staff and family members, through cocoon strategies. There is no risk of transmission of MMR vaccine viruses from a vaccine recipient to an immunocompromised individual. See section 12.7.2.

See also '*Vaccination of close contacts of immunocompromised individuals*' in section 4.3.1 for general vaccination information for contacts of immunocompromised individuals.

### (Re)vaccination before or following immunosuppression

MMR is funded to be given at least 28 days before planned immunosuppression.

For vaccination or revaccination following immunosuppression (funded), it is important to be sure that the individual is immunocompetent enough to safely receive the vaccine.

### HIV infection

Discuss vaccination of individuals with HIV infection with their specialist (see 'HIV infection' in section 4.3.12).

Receipt of MMR, on time at age 12 and 15 months, is recommended for asymptomatic children who are not severely immunocompromised. MMR is recommended for all HIV-positive individuals aged from 12 months, whether they are symptomatic or asymptomatic, if their CD4+ lymphocyte level is over 15 percent or CD4+ lymphocyte count is at least 200 cells/mm<sup>3</sup>. Administration of MMR with CD4+ counts below these recommended levels has been associated with vaccine-related pneumonitis (from the measles component).<sup>9</sup>

## 12.5.4 Pregnancy and breastfeeding

MMR is contraindicated during pregnancy. Pregnancy should be avoided for four weeks after MMR vaccination.<sup>1,9</sup>

### After delivery

If MMR and Rhesus anti-D IG are required after delivery, both the vaccine and anti-D IG may be given at the same time, in separate sites with separate syringes. The vaccine may be given at any time after the delivery. Anti-D IG does not interfere with the antibody response to the vaccine, but whole blood transfusion does inhibit the response in up to 50 percent of vaccine recipients (see section A6.4.1).

MMR can be given to breastfeeding women.

(See also sections 4.1.3, 12.6.1 and 21.5.3.)

## 12.5.5 Travel

International travel is an important factor in reintroducing measles into New Zealand. To avoid importing measles to New Zealand, vaccination with MMR is recommended for all children aged 12 months and older and adults travelling overseas if they have not previously been adequately vaccinated (see Appendix 2 for planning catch-up immunisations). Infants aged from 4 months can receive a dose of MMR if they are travelling to a country with an active measles outbreak. These children will still require two doses from age 12 months to be fully immunised.

Measles remains endemic in many countries, including areas in Europe, Asia, the Pacific and Africa, and outbreaks are ongoing worldwide. A high rate of measles incidence was reported in the Philippines during 2019 and early 2020.<sup>36</sup> During January to October 2019, 52 (64 percent) out of 81 imported measles cases in the US were residents returning from travel abroad and 73 (90 percent) were unvaccinated or had unknown vaccination status. Eight outbreaks (85 percent of cases of the resulting 1,259 cases) were associated with unvaccinated close-knit populations, such as the Orthodox Jewish community in New York; these began from two single imported cases.<sup>37</sup> Travel was also linked to the measles outbreaks in New Zealand in 2011, 2014, 2016 and 2019.

## 12.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general vaccine contraindications.

### 12.6.1 Contraindications

The general contraindications that apply to all immunisations are relevant to MMR (eg, children with an acute febrile illness should have their immunisation deferred).

Anaphylaxis following a previous dose of MMR or any of the vaccine components is a contraindication to a further dose of MMR. Individuals who have anaphylaxis after receiving MMR should be serologically tested for immunity and referred to, or discussed with, a specialist if they are non-immune to rubella or measles.

MMR is contraindicated for:

- those with proven anaphylaxis to the vaccine or vaccine component (eg, neomycin)
- immunocompromised individuals (ie, those with significantly impaired cell-mediated immunity, such as those with untreated malignancy, type 1 interferon receptor (IFNAR) signalling pathway defects, or altered immunity as a result of drug therapy, including high-dose steroids, or receiving high-dose radiotherapy) (see section 4.3)
- individuals who have received another live vaccine, including BCG, within the previous 4 weeks unless given concurrently (for BCG, see chapter 23)
- pregnant women – pregnancy should be avoided for four weeks after immunisation<sup>1, 9</sup> (see section 21.5.3)
- individuals who have received IG or a blood transfusion during the preceding 11 months (see Table A6.1 in Appendix 6 for the length of time to defer measles vaccine after specific blood products)
- those with severe immune deficiency from HIV, because vaccine-related pneumonitis (from the measles component) has been reported<sup>9</sup> – discuss vaccination of individuals with HIV infection with their specialists.

Note: Inadvertent immunisation with a rubella-containing vaccine in early pregnancy is no longer considered an indication for termination of pregnancy. There have been no cases of teratogenic damage from vaccine virus despite intensive surveillance in the US, the UK and Germany.<sup>38</sup>

## 12.6.2 Precautions

Children with a history of seizures should be given MMR, but the parents/guardians should be warned that there may be a febrile response. In the case of children with current ITP, the timing of vaccination should be discussed with their specialist.

Women of childbearing age should be advised to avoid pregnancy for the next four weeks after MMR vaccination (see section 21.5.3).<sup>1, 9</sup>

Measles vaccination may temporarily suppress tuberculin skin test (TST/Mantoux) reactivity, so if required, a TST should be placed on the same day as MMR vaccination or be postponed for four to six weeks after vaccination.<sup>9</sup> TST is not a prerequisite for measles vaccination. An individual with active TB should be established on treatment before administering MMR.

For infants aged under 12 months, please discuss immunomodulatory therapies taken during pregnancy with infant's mother or specialist, or contact IMAC before administration of MMR0. See section 4.2.5.

### Interferon alpha receptor deficiencies

IFNAR deficiencies can increase the risk of severe reaction to some live viral vaccines, such as MMR. These are extremely rare immune disorders that can result in a defective



response to certain viruses, including measles and COVID-19.<sup>39</sup> If an older sibling or relative had a severe illness following MMR this should be discussed with immunisation specialists. If a child did not develop a serious illness in response to their first dose of MMR, it appears unlikely that they will have a serious reaction to their second MMR vaccine due to undiagnosed IFNAR1 deficiency. For more information see section 4.3.2.

### 12.6.3 Egg allergy

The measles and mumps components of the MMR are manufactured in chick embryo cell culture, so there may be trace amounts of egg protein in the vaccine. Egg allergy, including anaphylaxis, is **not** a contraindication to measles-containing vaccines. Various studies have confirmed that children with egg allergy can be vaccinated safely.<sup>9, 40, 41</sup> Other components of the vaccine may be responsible for allergic reactions.<sup>42</sup> Individuals with egg allergy may therefore be safely vaccinated in primary care.<sup>43</sup>

## 12.7 Potential responses and AEFIs

### 12.7.1 Potential responses

Some children, around 5–15 percent, may experience fever of 39.4°C or more between 6 and 12 days after immunisation that generally lasts one to two days and is associated with a strong measles antibody response.<sup>9, 44</sup> Rash, often with atypical distribution, can occur in approximately 5 percent of vaccine recipients at the same interval post-vaccination: these individuals are not infectious to others.<sup>9</sup> Fevers, rashes and other systemic symptoms can occur coincidentally after vaccination due to common childhood infections and are not caused by the vaccine.<sup>45</sup>

Serological tests or PCR can be expected to be positive if performed during this time, so testing should not be routinely performed. During an outbreak, genotyping the sample can help to identify vaccine strain versus wild type disease.

The mumps vaccine may produce parotid and/or submaxillary swelling in about 1 percent of vaccine recipients, most often 10–14 days after immunisation.<sup>46</sup> The rubella vaccine can cause a mild rash, fever, joint pain and lymphadenopathy between one and three weeks after immunisation.<sup>9, 47</sup> There were no persisting sequelae associated with the administration of 3 million doses of MMR to 1.5 million children in Finland.<sup>45, 48</sup>

### 12.7.2 AEFIs

Temporally related reactions, including febrile seizures, nerve deafness, aseptic meningitis, encephalitis, rash, pruritus and purpura, may follow immunisation rarely; however, causality has not been established.<sup>49</sup>

## Vaccine virus transmission

MMR vaccine viruses are regarded as being non-transmissible from vaccine recipients. Two historical, poorly documented case of transmission (of a rubella and a mumps vaccine strain) were reported from a vaccine that is no longer in production.<sup>50</sup> Following immunisation with both measles and rubella vaccines, live virus has been isolated rarely from pharyngeal secretions.<sup>38, 51</sup> There have been no confirmed cases of disease transmission from MMR vaccine viruses.

## Idiopathic thrombocytopenic purpura

MMR is the only childhood vaccine with an elevated risk of ITP, which occurs in 1 in 25,000 to 40,000 people, 15 days to six weeks after immunisation.<sup>9</sup> ITP is mild and transient, resolving within six months in 93 percent of cases.<sup>1, 52</sup> If ITP occurs, measles, mumps and rubella serology should be measured, and if the individual is immune to all three infections, a second dose is not required. However, if the individual is susceptible to any of the three infections, a second dose should be administered.<sup>53-55</sup> The risk of thrombocytopenia is higher after the first dose of vaccine than after the second dose and is much rarer after vaccination than after wild-type infection.<sup>9</sup>

### 12.7.3 Adverse outcomes not linked to MMR

Over three decades, multiple published epidemiological studies in the UK,<sup>56</sup> Finland<sup>57</sup> and elsewhere<sup>27</sup> have confirmed that there is no link between MMR and the development of autism in young children (see section 3.2.4 for further discussion on this issue).

## 12.8 Public health measures

It is a legal requirement that all cases of measles be notified immediately on suspicion to the local medical officer of health – do not wait for a laboratory confirmation as this can delay contact tracing and allow outbreaks to become established if disease is confirmed.

For details of public health control measures, see the measles chapter in the *Communicable Disease Control Manual* at [www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/measles/](http://www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/measles/)

### 12.8.1 Diagnosis

A single case of measles should be considered an outbreak and result in an appropriate outbreak response. Practitioners should have a low index of suspicion for notification, and all suspected clinical cases should be self-isolated immediately and notified to the medical officer of health.

The standard clinical case definition for measles is 'an illness characterised by all of the following: generalised maculopapular rash, starting on the head and neck then spreading down and out and fading; fever (at least 38°C if measured) present at the time of rash onset; and cough and/or coryza and/or conjunctivitis and/or Koplik's spots present at the time of rash onset'.

It is important that the diagnosis be laboratory confirmed, as many viral infections can mimic measles.

For more details on case definition, diagnosis and management, refer to the 'Measles' chapter of the online *Communicable Disease Control Manual* (available at [www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/measles/](http://www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/measles/) )

## 12.8.2 Post-exposure prophylaxis

Management of contacts of a measles case should be discussed with the local medical officer of health.

### MMR vaccination

A single dose of MMR when given to an unvaccinated person, from age 6 months, within 72 hours of first contact with an infectious person may reduce the risk of developing disease as post exposure prophylaxis.<sup>1</sup> If there is doubt about vaccination status, MMR should still be given. MMR will not exacerbate the symptoms of measles if a person is already incubating the disease, but in these situations, any measles-like illness occurring shortly after vaccination is likely to be due to infection. Note, for post-exposure prophylaxis of infants aged under 6 months, give HNIG (see below) as a priority, not MMR0. (Table A6.1 for spacing of MMR after HNIG). Pre-exposure MMR vaccination can be given from age 4 months.

If MMR is not given within 72 hours of first exposure, it should still be offered at any later interval to provide protection from future exposures, unless the vaccine is contraindicated.

Most individuals born prior to 1969 will have measles immunity, either through wild-type infection or measles vaccination. Individuals who were born in countries with limited circulating measles prior to 1969 can be considered for post-exposure prophylactic MMR vaccination in the case of a community outbreak. Seek advice from IMAC prior to vaccinating adults born prior to 1960.

## Human normal immunoglobulin prophylaxis for contacts

Human normal immunoglobulin (HNIG; Normal Immunoglobulin-VF) is recommended for measles-susceptible individuals in whom the vaccine is contraindicated (see section 12.6) and susceptible pregnant contacts. For these individuals, HNIG is given to attenuate disease and should be given as soon as possible, up to a maximum of six days after exposure. All other susceptible contacts should be offered MMR as post-exposure prophylaxis (as described above).

HNIG provides no benefit to those who are already exhibiting symptoms of measles.

HNIG may be recommended for the following contacts of measles cases as soon as possible and up to six days after exposure:

- immunocompromised or immune-deficient people
- susceptible pregnant women (if no evidence of two measles-containing vaccine doses, give HNIG or check serology)
- immune-competent infants aged under 6 months: because maternal antibody wanes in the first six months of life, evidence of maternal vaccination status or serology tests may not predict protection for these infants. Maternal serology may be helpful for neonates. The role of an infant measles IgG test is unclear but may be helpful if available rapidly. Discuss use of HNIG for these infants with a paediatrician
- immune-competent children aged between 6 and 12 months, who are outside the 72-hour exposure window for MMR vaccination
- infants born prematurely <28 weeks' gestation are considered non-immune irrespective of maternal immune status
- infants aged under 12 months born to mothers who received immunomodulatory biologic agents in pregnancy, unable to receive MMR0.

For further details for infants under 6 months and immunocompromised children refer to the Starship Child Health guidelines (available at [starship.org.nz/guidelines/measles](http://starship.org.nz/guidelines/measles)).

The recommended dose for pregnant women and immunocompromised or immunodeficient people is 0.6 mL/kg intramuscularly, to a maximum dose of 15 mL, usually administered as three 5 mL injections.

## Prophylaxis with intravenous immunoglobulin

IVIg can be considered for: immunosuppressed and immune-deficient measles contacts (who may, for example, have a central venous catheter); individuals with reduced muscle bulk; those whom intramuscular injection is contraindicated; or in individuals for whom large doses are required (see Appendix 6 for more information about passive immunisation). IVIg is not given if a person is already symptomatic.

See the guidance from the Public Health England for further information (available at [www.gov.uk/government/publications/measles-post-exposure-prophylaxis](http://www.gov.uk/government/publications/measles-post-exposure-prophylaxis)).<sup>58</sup>

Queries regarding usage and dosage of IVIG for measles prophylaxis can be directed to the New Zealand Blood Service transfusion medicine specialists via the district blood bank and refer to the Immunoglobulin Preparations section in the **Transfusion Medicine Handbook** (available at [nzblood.co.nz](http://nzblood.co.nz)).

### 12.8.3 Restriction

Restriction of measles cases or contacts should be discussed with the local medical officer of health.

For further information see the 'Measles' chapter of the *Communicable Disease Control Manual* (available at [www.tewhaturora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/measles/](http://www.tewhaturora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/measles/) )

## 12.9 Variations from the vaccine data sheet

The vaccine data sheet recommends a single dose of MMR. However, as 2–5 percent of recipients fail to seroconvert after the first dose (see section 12.4.2), Health New Zealand | Te Whatu Ora recommends and funds a second dose of MMR. Two doses are required for measles control and elimination;<sup>9</sup> the second MMR dose is not a booster.

The vaccine data sheet states that individuals who have experienced anaphylaxis after egg ingestion should be vaccinated with extreme caution, with adequate treatment for anaphylaxis on hand should such a reaction occur. However, various studies have confirmed that egg-allergic children can be vaccinated safely.<sup>9, 40, 41</sup> Health New Zealand | Te Whatu Ora recommends that individuals with egg allergy, including anaphylaxis, may be safely vaccinated in primary care (see section 12.6.3).

## References

1. Strebel P, Papania M, Gastañaduy P, Goodson J. 2018. Measles Vaccine, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
2. Fine P, Mulholland K, Scott J, Edmunds W. 2018. Community Protection, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
3. Centers for Disease Control and Prevention. 2019. Measles. in *Epidemiology and Prevention of Vaccine-Preventable Diseases. The Pink Book 13th edition*. URL: <https://www.cdc.gov/vaccines/pubs/pinkbook/meas.html>. (accessed 6 April 2020)

4. Laksono BM, de Vries RD, Verburgh RJ, et al. Studies into the mechanism of measles-associated immune suppression during a measles outbreak in the Netherlands. *Nat Commun*, 2018. 9(1): p. 4944.
5. Mina MJ, Kula T, Leng Y, et al. Measles virus infection diminishes preexisting antibodies that offer protection from other pathogens. *Science*, 2019. 366(6465): p. 599-606.
6. Petrova VN, Sawatsky B, Han AX, et al. Incomplete genetic reconstitution of B cell pools contributes to prolonged immunosuppression after measles. *Sci Immunol*, 2019. 4(41).
7. Gadroen K, Dodd CN, Masclee GMC, et al. Impact and longevity of measles-associated immune suppression: a matched cohort study using data from the THIN general practice database in the UK. *BMJ Open*, 2018. 8(11): p. e021465.
8. Mina MJ, Metcalf CJ, de Swart RL, et al. Long-term measles-induced immunomodulation increases overall childhood infectious disease mortality. *Science*, 2015. 348(6235): p. 694-9.
9. American Academy of Pediatrics. 2018. Measles. in *Red Book: 2018 Report of the Committee on Infectious Diseases*, Kimberlin D, Brady M, Jackson M, and Long S (eds). Elk Grove Village, IL. p. 537-550. URL: <https://redbook.solutions.aap.org/redbook.aspx>. (accessed 3 July 2020)
10. Wendorf KA, Winter K, Zipprich J, et al. Subacute sclerosing panencephalitis: the devastating measles complication that might be more common than previously estimated. *Clinical Infectious Diseases*, 2017. 65(2): p. 226-232.
11. Bellini WJ, Rota JS, Lowe LE, et al. Subacute sclerosing panencephalitis: more cases of this fatal disease are prevented by measles immunization than was previously recognized. *Journal of Infectious Diseases*, 2005. 192(10): p. 1686-93.
12. Pittet LF, Posfay-Barbe KM. Increasing incidence of subacute sclerosing panencephalitis in infants: a collateral effect of under-vaccination. *Clinical Microbiology and Infection*, 2020. (pre-print).
13. Miller C. Deaths from measles in England and Wales, 1970–83. *British Medical Journal*, 1985. 290(6466): p. 443–4.
14. World Health Organization. Measles vaccines: WHO position paper, April 2017 - Recommendations. *Vaccine*, 2019. 37(2): p. 219-222.
15. World Health Organization. 2018 *Measles*. WHO; 2018 [updated April 2018 ]; URL: <https://www.who.int/immunization/diseases/measles/en/>. (accessed November 2019)
16. World Health Organization. *Measles and Rubella Surveillance Data*.: WHO; [updated 13 March 2020]; URL: [https://www.who.int/immunization/monitoring\\_surveillance/burden/vpd/surveillance\\_type/active/measles\\_monthlydata/en/](https://www.who.int/immunization/monitoring_surveillance/burden/vpd/surveillance_type/active/measles_monthlydata/en/) (accessed 25 April 2020)
17. GBD 2015 Child Mortality Collaborators. Global, regional, national, and selected subnational levels of stillbirths, neonatal, infant, and under-5 mortality, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*, 2016. 388(10053): p. 1725–74.
18. World Health Organization, UNICEF. 2020 *Measles outbreak in the Pacific - Situation report no. 11*. URL: [https://www.who.int/docs/default-source/wpro---documents/dps/outbreaks-and-emergencies/measles-2019/20200122-measles-pacific-who-unicef-sitrep-11.pdf?sfvrsn=9e1851f5\\_2](https://www.who.int/docs/default-source/wpro---documents/dps/outbreaks-and-emergencies/measles-2019/20200122-measles-pacific-who-unicef-sitrep-11.pdf?sfvrsn=9e1851f5_2). (accessed 3 July 2020)
19. World Health Organization. Framework for verifying elimination of measles and rubella. *Weekly Epidemiological Record*, 2013. 88(9): p. 89-99.
20. World Health Organization. 2013. *Global Vaccine Action Plan 2011–2020* (ed.), Geneva: World Health Organization. URL:



- [https://www.who.int/immunization/global\\_vaccine\\_action\\_plan/GVAP\\_doc\\_2011\\_2020/en/](https://www.who.int/immunization/global_vaccine_action_plan/GVAP_doc_2011_2020/en/) (accessed 6 November 2019)
21. World Health Organization. 2019 *New measles surveillance data for 2019*: WHO; 2019 [updated April 2019]; URL: <https://www.who.int/immunization/newsroom/measles-data-2019/en/>. (accessed 3 July 2020)
  22. World Health Organization. 2019 *More than 140,000 die from measles as cases surge worldwide (Press release)*. World Health Organization: Joint News Release. 5 December 2019 URL: <https://www.who.int/news-room/detail/05-12-2019-more-than-140-000-die-from-measles-as-cases-surge-worldwide>. (accessed 3 July 2020)
  23. Reynolds G, Dias C, Thornley S, et al. Analysis of the Auckland 2014 measles outbreak indicates that adolescents and young adults could benefit from catch-up vaccination. *New Zealand Medical Journal*, 2015. 128(1422): p. 53-62.
  24. Institute of Environmental Science and Research. 2020 *Measles report*. Public Health Surveillance: ESR; Public Health Surveillance; 2020; URL: <https://surv.esr.cri.nz/surveillance/WeeklyMeaslesRpt.php>. (accessed 10 February 2020)
  25. Roberts M, A Mathematical Model for Measles Vaccination. 2004: Unpublished report to the Ministry of Health, New Zealand.
  26. Zahraei SM, Gouya MM, Azad TM, et al. Successful control and impending elimination of measles in the Islamic Republic of Iran. *Journal of Infectious Diseases*, 2011. 204 Suppl 1(Suppl 1): p. S305-11.
  27. Demicheli V, Rivetti A, Debalini MG, Di Pietrantonj C. Vaccines for measles, mumps and rubella in children. *Cochrane Database Syst Rev*, 2012(2): p. CD004407.
  28. Albertson JP, Clegg WJ, Reid HD, et al. Mumps Outbreak at a University and Recommendation for a Third Dose of Measles-Mumps-Rubella Vaccine - Illinois, 2015-2016. *MMWR: Morbidity and Mortality Weekly Report*, 2016. 65(29): p. 731-4.
  29. Gibney KB, Attwood LO, Nicholson S, et al. Emergence of attenuated measles illness among IgG positive/IgM negative measles cases, Victoria, Australia 2008-2017. *Clinical Infectious Diseases*, 2019.
  30. Davidkin I, Jokinen S, Broman M, et al. Persistence of measles, mumps, and rubella antibodies in an MMR-vaccinated cohort: a 20-year follow-up. *Journal of Infectious Diseases*, 2008. 197(7): p. 950-6.
  31. Kontio M, Jokinen S, Paunio M, et al. Waning antibody levels and avidity: implications for MMR vaccine-induced protection. *Journal of Infectious Diseases*, 2012. 206(10): p. 1542-8.
  32. Bitzegeio J, Majowicz S, Matysiak-Klose D, et al. Estimating age-specific vaccine effectiveness using data from a large measles outbreak in Berlin, Germany, 2014/15: evidence for waning immunity. *Euro Surveill*, 2019. 24(17).
  33. Australian Technical Advisory Group on Immunisation (ATAGI). 2018. Measles. in *Australian Immunisation Handbook*. Canberra. URL: <https://immunisationhandbook.health.gov.au/vaccine-preventable-diseases/measles>. (accessed 25 April 2020)
  34. Nic Lochlainn LM, de Gier B, van der Maas N, et al. Immunogenicity, effectiveness, and safety of measles vaccination in infants younger than 9 months: a systematic review and meta-analysis. *Lancet Infectious Diseases*, 2019. 19(11): p. 1235-1245.
  35. Nic Lochlainn LM, de Gier B, van der Maas N, et al. Effect of measles vaccination in infants younger than 9 months on the immune response to subsequent measles vaccine doses: a systematic review and meta-analysis. *Lancet Infectious Diseases*, 2019. 19(11): p. 1246-1254.



36. Regional Office for the Western Pacific Region. 2019 *Measles-Rubella Bulletin 2020*. World Health Organization; 2019 [updated 20 May 2020]; URL: <https://apps.who.int/iris/handle/10665/331240>. (accessed 10 May 2022)
37. Patel M, Lee AD, Clemmons NS, et al. National Update on Measles Cases and Outbreaks - United States, January 1-October 1, 2019. *MMWR: Morbidity and Mortality Weekly Report*, 2019. 68(40): p. 893-896.
38. Reef SE, Plotkin S. 2018. Rubella Vaccines, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
39. Bastard P, Hsiao K-C, Zhang Q, et al. A loss-of-function *IFNAR1* allele in Polynesia underlies severe viral diseases in homozygotes. *J. Exp. Med*, 2022. 219(6).
40. James JM, Burks AW, Roberson PK, Sampson HA. Safe administration of the measles vaccine to children allergic to eggs. *New England Journal of Medicine*, 1995. 332(19): p. 1262-6.
41. Khakoo G, Lack G. Recommendations for using MMR vaccine in children allergic to eggs. *British Medical Journal*, 2000. 320(7239): p. 929-32.
42. Fox A, Lack G. Egg allergy and MMR vaccination. *British Journal of General Practice*, 2003. 53(495): p. 801-2.
43. Clark AT, Skypala I, Leech SC, et al. British Society for Allergy and Clinical Immunology guidelines for the management of egg allergy. *Clinical and Experimental Allergy*, 2010. 40(8): p. 1116-29.
44. Carazo Perez S, Bureau A, De Serres G. Post-immunisation fever and the antibody response to measles-containing vaccines. *Epidemiology and Infection*, 2018. 146(12): p. 1584-1592.
45. Peltola H, Heinonen OP. Frequency of true adverse reactions to measles-mumps-rubella vaccine. A double-blind placebo-controlled trial in twins. *Lancet*, 1986. 1(8487): p. 939-42.
46. Rubin S. 2018. Mumps Vaccines, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
47. American Academy of Pediatrics. 2018. Rubella. in *Red Book: 2018 Report of the Committee on Infectious Diseases*, Kimberlin D, Brady M, Jackson M, and Long S (eds). Elk Grove Village, IL. URL: <https://redbook.solutions.aap.org/redbook.aspx>. (accessed 3 July 2020)
48. Peltola H, Patja A, Leinikki P, et al. No evidence for measles, mumps, and rubella vaccine-associated inflammatory bowel disease or autism in a 14-year prospective study. *Lancet*, 1998. 351(9112): p. 1327-8.
49. American Academy of Pediatrics. 2018. Mumps. in *Red Book: 2018 Report of the Committee on Infectious Diseases*, Kimberlin D, Brady M, Jackson M, and Long S (eds). Elk Grove Village, IL. URL: <https://redbook.solutions.aap.org/book.aspx?bookid=2205>. (accessed 3 July 2020)
50. Wolf JE, Eisen JE, Fraimow HS. Symptomatic rubella reinfection in an immune contact of a rubella vaccine recipient. *Southern Medical Journal*, 1993. 86(1): p. 91-3.
51. Morfin F, Beguin A, Lina B, Thouvenot D. Detection of measles vaccine in the throat of a vaccinated child. *Vaccine*, 2002. 20(11-12): p. 1541-3.
52. O'Leary ST, Glanz JM, McClure DL, et al. The risk of immune thrombocytopenic purpura after vaccination in children and adolescents. *Pediatrics*, 2012. 129(2): p. 248-55.
53. Beeler J, Varricchio F, Wise R. Thrombocytopenia after immunisation with measles vaccines: review of the vaccine adverse events reporting system (1990 to 1994). *Pediatric Infectious Disease Journal*, 1996. 15(1): p. 88-90.
54. Miller E, Waight P, Farrington CP, et al. Idiopathic thrombocytopenic purpura and MMR vaccine. *Archives of Disease in Childhood*, 2001. 84(3): p. 227-9.

55. Stowe J, Kafatos G, Andrews N, Miller E. Idiopathic thrombocytopenic purpura and the second dose of MMR. *Archives of Disease in Childhood*, 2008. 93(2): p. 182-3.
56. Miller E. MMR vaccine: review of benefits and risks. *Journal of Infection*, 2002. 44(1): p. 1-6.
57. Makela A, Nuorti JP, Peltola H. Neurologic disorders after measles-mumps-rubella vaccination. *Pediatrics*, 2002. 110(5): p. 957-63.
58. Public Health England. 2019. *Guidelines on Post-Exposure Prophylaxis for measles*. (ed.): Crown Copyright. URL: <https://www.gov.uk/government/publications/measles-post-exposure-prophylaxis> (accessed 21 October 2019)

# 13 Meningococcal disease

## Key information

Mode of transmission	By respiratory droplets or direct contact with nasopharyngeal secretions from a carrier or case.
Incubation period	2–10 days, commonly 3–4 days.
Period of communicability	Commonly 3–4 days without treatment, range 2–10 days. Certain antibiotic therapy eradicates <i>N. meningitidis</i> from mucosal surfaces within 24 hours, and the case is no longer considered infectious.
Funded vaccines	<ul style="list-style-type: none"><li>• Meningococcal B recombinant (MenB): Bexsero</li><li>• Quadrivalent meningococcal conjugate (MenACWY): MenQuadfi and Nimenrix</li></ul>
Dose, presentation, route	0.5 mL per dose. Presentation: <ul style="list-style-type: none"><li>• MenB: pre-filled syringe</li><li>• MenACWY:<ul style="list-style-type: none"><li>– MenQuadfi - vial</li><li>– Nimenrix - vial and pre-filled syringe, must be reconstituted before use</li></ul></li></ul> Intramuscular injection.

*Continued overleaf*

Funded vaccine indications	<p>MenB (Bexsero)</p> <ul style="list-style-type: none"> <li>• All infants aged 3 months and 5 months, and booster given age 12 months.</li> <li>• Alternative approved schedule: ages 8 weeks and 4 months, plus booster at age 12 months.</li> <li>• If offered at age 6 weeks, this is off-label and requires prescription.</li> <li>• Catch-up is available from age 13 to 59 months.</li> </ul> <p>MenB (Bexsero) and MenACWY (Nimenrix, from age 6 weeks to under 12 months; MenQuadfi from age 12 months) for:</p> <ul style="list-style-type: none"> <li>• patients pre- or post-splenectomy or with functional or anatomical asplenia</li> <li>• patients with HIV, complement deficiency (acquired, including monoclonal antibody therapy against C5, or inherited)</li> <li>• pre- or post-solid organ transplant</li> <li>• HSCT (bone marrow transplant) patients</li> <li>• patients prior to planned and following immunosuppression</li> <li>• close contacts of meningococcal cases (any group)</li> <li>• patients with prior meningococcal disease of any group.</li> </ul> <p>MenB and MenACWY (MenQuadfi) for:</p> <ul style="list-style-type: none"> <li>• adolescents and young adults aged 13–25 years inclusive who will be living or are currently living in a boarding school hostel or university hall of residence, military barracks, youth justice residences or prison, including those who turn 13 years of age while living in a boarding school hostel.</li> </ul>
Recommended, unfunded	<p>Laboratory workers handling bacterial cultures</p> <p>Health care professionals in very close contact with cases.</p>
Vaccine effectiveness	<p>MenB: 75% reduction in group B cases in infants over a 3-year period in the UK and cross-protection against group W observed; 71% reduction in group B disease in adolescents.</p> <p>MenACWY: 80–85%; effectiveness wanes to 50–60% within 2–5 years after vaccination.</p> <p>MenC: effectiveness of 83–100%; antibody wanes within 2–3 years.</p>
Potential responses to vaccines	<p>MenB: increased risk of fever and fever-related events in children &lt;2 years (prophylactic antipyretic advised). Older age groups: localised pain, nausea, myalgia, malaise, mild fever and headache.</p> <p>MenC and MenACWY: localised pain, irritability, headache and fatigue, mild fever.</p>
Contraindications	<p>No specific contraindications or precautions, except prior anaphylaxis to vaccine components.</p>
Public health measures	<p>All cases must be notified if clinically suspected.</p> <p>Parenteral antibiotics should be administered as soon as possible in hospital or before admission to hospital if delays of longer than 30 minutes are likely.</p>
Post-exposure prophylaxis	<p>For vaccination of contacts see section 13.8.</p>

# 13.1 Bacteriology

Meningococcal disease is caused by *Neisseria meningitidis*, a gram-negative bacterium, causing sepsis, meningitis and some less common clinical syndromes. Groups B and W are currently the most important types in New Zealand. Increasingly, group W and Y organisms are the cause of bacteraemia and pneumonia in the elderly. Predominant groups differ between countries; group A is an important epidemic strain, particularly in Africa and the Middle East. Meningococci are spread from person to person by respiratory droplets or direct contact with nasopharyngeal secretions from a carrier or case.

# 13.2 Clinical features

Table 13.1 below describes the symptoms and signs of meningococcal disease – individuals may present with some or all of these. Meningococcal septicaemia is more common than meningitis, and presentation varies from a mild non-specific illness to rapid progression with fatal outcome. Symptoms and signs in infants are frequently non-specific. The classical rapidly progressing petechial or purpuric rash may not be present or may initially appear maculopapular. Atypical initial presentations, including gastrointestinal symptoms, septic arthritis and epiglottitis, are more frequently reported with meningococcal W disease, and may contribute to delayed diagnosis and increased case-fatality.<sup>1, 2</sup> Pneumonia is more frequently reported with group Y.

**Table 13.1: Symptoms and signs of meningococcal disease**

Adolescents and adults	Young infants and children
<ul style="list-style-type: none"><li>• Sepsis syndrome, including poor peripheral perfusion and tachycardia</li><li>• Nausea/vomiting</li><li>• Meningeal signs</li><li>• Rash – petechial/purpuric, but may be maculopapular; rash may not be present early and absent in about one-third of cases</li><li>• Sleepy, difficult to rouse</li><li>• Occasionally in young adults, irrational behaviour</li><li>• Arthralgia, myalgia, leg pain</li><li>• Atypical presentation (particularly group W) may include pneumonia, septic arthritis, myocarditis or diarrhoea</li></ul>	<p>As for adolescents and adults, plus the following:</p> <ul style="list-style-type: none"><li>• bulging fontanelle</li><li>• tachycardia</li><li>• altered responsiveness</li><li>• irritability and/or floppiness</li><li>• refusing drinks or feeds</li><li>• poor peripheral perfusion</li><li>• atypical presentation may include epiglottitis, diarrhoea or septic arthritis</li></ul>

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Notify all suspected cases urgently to local medical officer of health, including out-of-hours.

Meningococcal disease covers a spectrum, from persistent fever with or without rash and arthritis to rapidly progressive purpuric rash and shock. Meningitis can occur with and without signs of sepsis. In fulminant cases, coma and death can occur within a few hours despite appropriate treatment.

Because of the potential for rapid progression, antibiotics should be administered (Table 13.2) as soon as possible, even before hospital admission. Antibiotics given prior to transfer should be clearly noted on information accompanying the patient to hospital.

**Table 13.2: Recommended antibiotics for suspected cases**

Check The New Zealand Formulary ([nzformulary.org](http://nzformulary.org)) for up to date dosing details, as well as the Starship guidelines ([starship.org.nz/guidelines/meningococcaemia/](http://starship.org.nz/guidelines/meningococcaemia/)).

Antibiotic	Children <30kg	Children >30kg and Adults (max dose)
Ceftriaxone <sup>a</sup> (first line treatment)	50 mg/kg when given by GP/primary care 100 mg/kg IV (or IM) up to 2g when given in ED	2 g IV (or IM)
Benzylpenicillin <sup>b</sup> (second choice)	50 mg/kg IV (or IM)	2.4 g IV (or IM)

- Patients allergic to penicillin who do not have a documented history of anaphylaxis to penicillin can be given ceftriaxone.
- Patients with a documented history of anaphylaxis to penicillin and who are suspected of suffering from meningococcal disease should be sent immediately to hospital without pre-admission antibiotics.

## 13.3 Epidemiology

### 13.3.1 Global burden of disease

#### Incidence and serotypes

The prevalence of meningococcal groups varies geographically. The highest burden of disease occurs in sub-Saharan Africa, where despite a dramatic fall in Group A disease following introduction of a Group A conjugate vaccine, in this 'meningitis belt' epidemics continue with around 30,000 cases reported annually, now including Group W.

The incidence in Canada, the US and Europe varies substantially from 0.2 to 3 per 100,000 persons per year.<sup>3</sup> Group B has become the predominant capsular group in Europe, Americas and Australia, with incidence typically highest in children aged under 2 years.<sup>4</sup> Group C disease has almost disappeared in countries with universal immunisation programmes, but outbreaks have been observed in men who have sex with men in the US and Europe.

Since 2009 there has been an emerging global incidence of Group W disease, initially in the United Kingdom and South America. Australia has experienced a rapid increase in Group W cases since 2013 with New Zealand also seeing a rapid increase in cases since 2017. Like group C clonal complex ST11 strains, group W ST11 strains have enhanced virulence. Higher rates of carriage of these ST11 strains has been noted within age groups where invasive group W disease is more prevalent (infants and the elderly).<sup>5</sup>

Some parts of the world, particularly Scandinavia, have reported an increase in group Y disease. In other regions, there is evidence of colonisation, but disease caused by group Y is rare. Patients with group Y strain disease are more likely to develop pneumonia and to be elderly.<sup>3, 4</sup>

This emergence of group W and Y strains has led to meningococcal C vaccines being replaced by quadrivalent (group A, C, W, Y) meningococcal conjugate vaccines (MenACWY).

## Risk groups

The highest incidence of meningococcal disease occurs in children aged under 5 years (especially under 2 years) with a secondary peak in older adolescents (15–19 years). The age distribution for groups W and Y is more likely to include older people than for B and C. A pooled overall case-fatality rate of 8.3 percent (range 4.1–20 percent) is reported internationally, varying by group and age.<sup>6</sup>

Most infection occurs in healthy people, but those with certain rare immune deficiencies (of terminal components of complement (C5–9) or properdin) or asplenia are at much higher risk, particularly of recurrent meningococcal disease. Individuals with infection caused by groups other than A, B, C, W, Y and untypeable strains or who experience recurrent disease should be investigated.

Close contacts of primary cases of meningococcal infection are at increased risk of developing infection, such as the case's household,<sup>7</sup> early childhood education services, semi-closed communities, schools, correctional facilities and military recruit camps. Students living in hostel accommodation may also be at higher risk.<sup>8–10</sup> In health care settings, only those with close exposure to oropharyngeal secretions of patients with meningococcal disease (as may occur during intubation or resuscitation) and microbiology laboratory workers are considered to be at increased risk.

It is not possible to calculate the incubation period for meningococcal disease for sporadic cases. Secondary cases (ie, in contacts of known cases of meningococcal disease) usually occur within four days, but it can be up to 10 days. The infectivity of patients with meningococcal disease is markedly reduced after 24 hours of antibiotic therapy, although treatment with cefotaxime, ceftriaxone, rifampicin or ciprofloxacin is necessary to reliably eradicate nasopharyngeal carriage.

In high-income countries in the absence of immunisation, nasopharyngeal carriage of *N. meningitidis* occurs in approximately 10 percent of the overall population, rising from 2 percent in children aged under 4 years to a peak of 24.5 percent to 32 percent among 15–24-year-olds, then declining with increasing age.<sup>3, 11</sup> In adolescents and young adults, the overall and capsular group carriage vary between regions and age groups.<sup>12</sup> The relationship between risk factors for disease and those associated with carriage is incompletely understood.<sup>3</sup> Carriage prevalence does not predict the disease incidence nor the occurrence or severity of outbreaks, as most of the carried strains are non-encapsulated and do not cause disease.<sup>3</sup> Smoking, passive smoking, household crowding and upper respiratory tract infections increase carriage.



## 13.3.2 New Zealand epidemiology

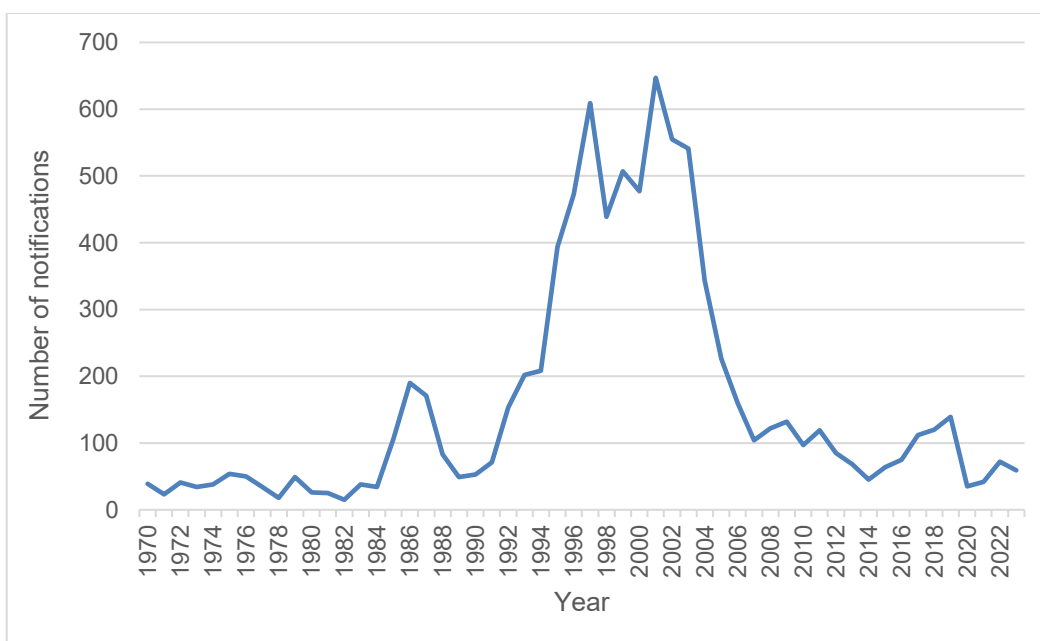
### Incidence and mortality

From 1 January to 31 December 2023, there were 59 cases of meningococcal disease (52 confirmed cases), which was an increase from the same period in 2020 and 2021 but lower than in 2017, 2018, 2019 and 2022. Of the 15 cases aged under 5 years, 87 percent were of Māori and/or Pacific ethnicity. There was one death in an adult aged 20–29 years.<sup>13</sup>

For 2023, the notification rate for meningococcal disease was 1.1 cases per 100,000 population, with a total of 59 cases notified (52 laboratory confirmed; ESR, 12 July 2024). Cases remained significantly lower than the peak annual incidence rate of 16.7 per 100,000 for all ages and 200 per 100,000 in children under 12 months as experienced in 2001 during the meningococcal epidemic from 1991 to 2007. The epidemic was largely due to a single group B subtype (B:P1.7-2,4). The annual number of notified cases of meningococcal disease in New Zealand since 1970 is shown in Figure 13.1.<sup>13</sup>

For further details and reports of meningococcal disease in New Zealand refer to the ESR surveillance reports (available at [www.esr.cri.nz/meningococcal-reports](http://www.esr.cri.nz/meningococcal-reports))

**Figure 13.1: Notified cases of meningococcal disease, 1970–2023**



Source: ESR

Meningococcal disease incidence is highest in Pacific peoples (3.1 per 100,000, 11 cases in 2023) and Māori (2.1 per 100,000, 18 cases in 2023) compared with the total population. Household crowding is an important risk factor for meningococcal disease, independent of ethnicity. For 2023, the highest age-specific disease rates were among those aged under 1 year (12.2 per 100,000, seven cases) decreasing in ages 1–4 years

(3.3 per 100,000, eight cases). One death occurred in 2023, giving a case fatality rate of 1.7 percent (ESR, 12 July 2024).

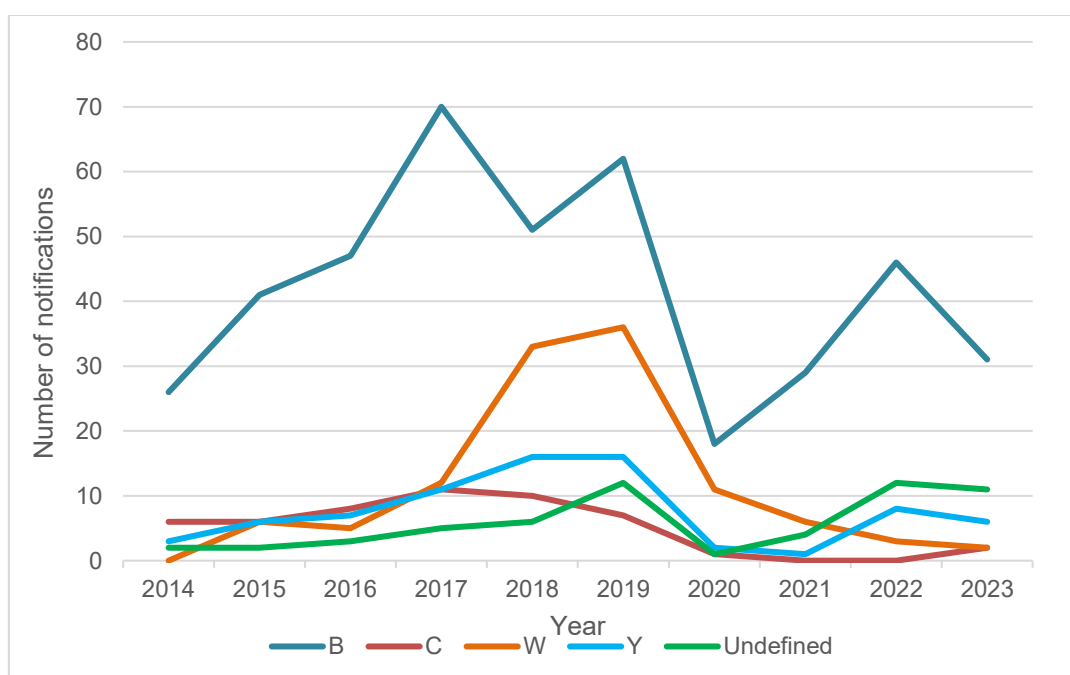
## Strain types

Strain type was determined for 41 of the 52 confirmed cases in 2023. In 2023, group B strains were the most prevalent (Figure 13.2). Out of 41 cases with the group identified, 31 (76 percent) were group B, six (15 percent) were group Y, two (5 percent) group W, and two (5 percent) group C.<sup>13</sup>

Within the group B cases, there were nine different PorA types identified. The most common were B:P1.7-12, 14 (11/31 cases, 35 percent) and the former epidemic strain B:P1.7-2,4 (8/31 cases, 26 percent).<sup>13</sup>

Cases of meningococcal disease caused by group C strains decreased since 2017 (Figure 13.2), while group W decreased from six cases in 2021 to three in 2022 and two in 2023. Cases in groups C, W and Y decreased in 2021, likely in part, due to the public health measures implemented to control the COVID-19 pandemic.

**Figure 13.2: Meningococcal disease notifications by group, 2014–2023**



Source: ESR

## 13.4 Vaccines

### 13.4.1 Available vaccines

Internationally, meningococcal vaccination programmes were revolutionised by the development of conjugate vaccines, which allow vaccination in younger children and induced herd immunity when used in population-wide programmes due to reduced nasopharyngeal carriage (see section 1.4.3).

The quadrivalent (ACWY) conjugate vaccines contain group A, C, W, Y polysaccharides conjugated to tetanus toxoid protein. Previously used, polysaccharide-only vaccines provided three to five years' protection in adults, but they are generally regarded as inferior to conjugate vaccines and are no longer approved for use in New Zealand. Those travelling to Africa, the Middle East and other areas with wide serogroup prevalence, including group A, require MenACWY vaccine for broad protection. In 2018, a multicomponent meningococcal group B recombinant vaccine (MenB, formerly abbreviated 4CMenB) was registered in New Zealand to protect against group B disease.

With the current New Zealand epidemiology, neither MenACWY nor MenB give protection across all prevailing meningococcal groups and both types of vaccine are recommended. The meningococcal vaccines registered and available are summarised in Table 13.3 below.

**Table 13.3: Meningococcal vaccines registered and available in New Zealand**

Name (manufacturer)	Vaccine type
Bexsero (GSK)	Meningococcal group B four-component recombinant (MenB)
MenQuadfi (sanofi-aventis)	Quadrivalent meningococcal conjugate (MenACWY): contains group A, C, W and Y polysaccharides conjugated to tetanus toxoid
Nimenrix (Pfizer NZ)	Quadrivalent meningococcal conjugate (MenACWY): contains group A, C, W and Y polysaccharides conjugated to tetanus toxoid

### Funded vaccines

Meningococcal B vaccine (Bexsero) is funded as part of the routine childhood Schedule for all infants. No meningococcal ACWY vaccines are currently on the routine Schedule. See section 13.5 for funded vaccines for special groups.

Three meningococcal vaccines are funded for certain groups (see section 13.5).

- Recombinant meningococcal B vaccine, MenB (Bexsero, GSK) contains four components from the group B meningococcus: three recombinant N. meningitidis group B surface proteins associated with bacterial adhesion and survival (*Neisseria* heparin binding antigen fusion protein, adhesin A protein, and factor H binding protein) plus detoxified outer membrane vesicles containing antigen as used in the MenNZB epidemic vaccine. Other components include aluminium hydroxide, sodium chloride, histidine and sucrose.
- Quadrivalent meningococcal conjugate vaccine MenACWY (MenQuadfi, sanofi-aventis). Each 0.5 mL dose contains 10 µg of each capsular polysaccharide, conjugated to 55 µg tetanus toxoid for each of the *N. meningitidis* group A, C, W and Y strains. Also contains sodium chloride, sodium acetate and water for injection. There is no preservative or adjuvant.
- Quadrivalent meningococcal conjugate vaccine, MenACWY (Nimenrix, Pfizer NZ). Each 0.5 mL contains 5 µg of each polysaccharide derived from the capsules of group A, C, W and Y *N. meningitidis* strains, conjugated to 44 µg of tetanus toxoid carrier protein. Other components and excipients include sodium chloride, trometamol and sucrose.

The tetanus toxoid-conjugated meningococcal MenACWY vaccine (MenQuadfi) replaced Menactra as the funded vaccine in mid-2023, for use in individuals aged 12 months and over. In July 2024, the monovalent MenC vaccine (NeisVac-C) was replaced by a tetanus toxoid-conjugated quadrivalent MenACWY vaccine, Nimenrix, funded for use in infants aged from 6 weeks to under 12 months with increased risk of meningococcal disease.

## Other vaccines

A two-component meningococcal group B recombinant vaccine (MenB-fHbp; Trumenba, Pfizer) is licensed from 10 years of age, including in the US, Europe and Australia. A pentavalent meningococcal vaccine, MenACWY/MenB-fHbp (Penbraya, Pfizer), is also approved for use in those aged 10-25 years in the US (which contains the same components as Nimenrix and Trumenba). Neither vaccine is available in New Zealand.

## Historic MeNZB vaccine

A strain-specific group B meningococcal vaccine (MeNZB, Chiron/Novartis) containing outer membrane vesicles derived from the epidemic strain B:4:P1.7b,4 (NZ 98/254) was developed for epidemic control in New Zealand and used between 2004 and 2008. The programme ceased in 2008 because of a decline in incidence of epidemic strain group B disease (see previous editions of the *Handbook*).

Since the immune response to MenNZB was short-lived, previous recipients who wish to be protected against meningococcal B disease will need to be fully immunised with MenB.

## 13.4.2 Efficacy and effectiveness

### Meningococcal group B recombinant vaccine

Three years after initiation of the introduction of MenB to the national immunisation schedule in the UK, a 75 percent reduction in group B disease was reported in the vaccine-eligible age groups compared with a historical cohort.<sup>14</sup> With 88 percent coverage but a low number of cases (25), adjusted vaccine effectiveness for all group B strains was 59.1 percent (95% CI: -31.1–87.2) following two primary doses and one booster dose, with an estimated 277 cases prevented.<sup>14</sup> This research is ongoing.

Following MenB vaccination of adolescents aged 15–16 years in South Australian schools, there was an overall reduction of 71 percent (95% CI 15–90;  $p=0.02$ ) in group B meningococcal disease cases aged 16–19 years: five cases in 2017–2018 (predicted 9.9 [95% predicted interval 3.9–17.5]) and one case in 2018–2019 (predicted 10.9 [4.4–19.1]).<sup>15</sup>

As was observed during college outbreaks in the US,<sup>16, 17</sup> in South Australia where MenB is administered in a school-based programme at age 15–18 years, MenB had no effect on disease-causing meningococcal carriage suggesting that vaccination of adolescents is unlikely to generate herd immunity.<sup>18</sup> A MenB vaccination campaign used during an isolated outbreak in a region of Québec, Canada outbreak demonstrated direct protection of 79 percent against outbreak strain group B disease and an overall impact of 86 percent in target groups with no herd effects.<sup>19</sup>

Cross-protection against meningococcal group W has been observed following vaccination of infants with MenB in the UK. Among age-cohorts that were fully and partially eligible to receive MenB, respectively, it was estimated that there were 69 percent (adjusted incidence rate ratio 0.31; 95% CI 0.2–0.67) and 52 percent (0.48; 0.28–0.81) fewer cases of group W disease than predicted in 2018/2019; this included direct and indirect protection over four years. An estimated 98 cases (95% CI 34–201) of group W disease were directly prevented in children aged under 5 years.<sup>20</sup> The researchers state that MenACWY conjugate vaccines would still be required for direct and indirect protection against those groups, since the degree of cross-protection is dependent on the expression of vaccine antigens on the meningococcal surface.<sup>20</sup>

There is limited data on its use in patients with chronic medical conditions and those immunocompromised by medication or disease, such as HIV infection or hereditary immune system defects. In a phase 3 clinical trial, children aged 2–17 years showed good but reduced immunogenicity in those with immunocompromise.<sup>21</sup> Immunogenicity in children with asplenia and splenic dysfunction was similar to healthy children but reduced in children with complement deficiencies.<sup>22</sup>

The safety and efficacy of MenB in adults above 50 years of age have not been established.

## Quadrivalent meningococcal conjugate vaccines

Clinical trial data use immunogenicity and bactericidal antibody titres as a proxy for efficacy. Effectiveness of conjugate meningococcal vaccination against laboratory-confirmed disease is difficult to assess due to the low incidence of cases, even during localised epidemics, such that data is limited around the effectiveness of the MenACWY vaccines. With the emergence of group W and Y strains, more countries have implemented mass campaigns and routine immunisation programmes to control outbreaks with MenACWY vaccines and can assess impact through disease incidence and carriage studies. The current evidence indicates that MenACWY (MenQuadfi) has similar or superior immunogenicity to other MenACWY vaccines; real-world effectiveness data is limited to date as it was first licensed in 2020.

Several phase II and III clinical trials have assessed the immunogenicity of the MenACWY vaccine, MenQuadfi. These studies have included healthy vaccine-naïve toddlers aged from 12 months; vaccine-naïve older children and adolescents; booster doses in toddlers, children and adolescents following prior MenACWY or MenC vaccination; given concurrently with routine vaccines (DTaP-IPV-HepB/Hib, MMR, VV, PCV13, Tdap and HPV); and in adults aged over 56 years.<sup>23</sup> In all studies, robust antibody responses were observed in all groups, immunogenicity was non-inferior to comparator vaccines and booster responses were observed.

Bactericidal antibody responses in adults (aged 18-55 years) were two to six times greater in those vaccinated with MenQuadfi, compared those vaccinated with diphtheria-toxoid conjugated MenACWY (Menactra), and a higher proportion of participants had a positive seroresponse.<sup>24</sup>

One clinical trial observed lower antibody responses to FHA, PRN and FIM2/3 pertussis antigens but not pertussis toxin, when MenACWY was given concurrently with Tdap and HPV in adolescents compared with without MenACWY.<sup>25</sup> The clinical relevance is unknown and has been observed with other MenACWY vaccines.<sup>23</sup> No interference was documented with other vaccines. There is no published data to date on effectiveness or use in immunocompromised individuals.

The other MenACWY vaccine (Nimenrix) is registered in New Zealand for individuals from aged 6 weeks. Clinical trials showed that the vaccine elicited bactericidal antibodies against all four groups from age 2 months with acceptable reactogenicity and safety profile.<sup>26</sup>

There is no published data on effectiveness in older adults for these vaccines.

### 13.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at [www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

Store at +2°C to +8°C. MenACWY vaccines and MenB should be protected from light. Do not freeze.

## Reconstitution

The MenACWY vaccine, Nimenrix, must be reconstituted with the supplied diluent and used as soon as possible. The other meningococcal vaccines are fully liquid formulations and do not require reconstitution.

## 13.4.4 Dosage and administration

### Meningococcal group B recombinant vaccine (MenB)

Each MenB (Bexsero) dose is 0.5 ml, administered by intramuscular injection (see section 2.2.3).

- For infants aged 8 weeks to 11 months, two doses are given with a minimum of eight weeks between doses, with a booster given at least six months after the second dose, from age 12 months.
- For toddlers aged 12–23 months (at time of first dose) a primary course of two doses is given at least eight weeks apart. A booster dose is recommended from 12 to 23 months after dose two.
- For children aged from 2 years (at time of first dose) and adults, two doses are given at least eight weeks apart (see section 13.5.1 for reduced spacing). (Note: the safety and efficacy in individuals aged over 50 years have not been established, but no safety concerns are expected.)

Generally, the need for booster doses from the age 2 years or older at the time of their first dose has not been established. A booster dose can be considered for individuals at continued risk of exposure to meningococcal disease. Booster doses are funded five-yearly for some high-risk individuals (see Table 13.6).

MenB can be administered concurrently with other scheduled vaccines, in separate syringes and at separate sites (see section 2.2.7).

See section 13.5.1 for recommendations around antipyretic prophylaxis use with delivery in children aged under 2 years.

### Quadrivalent meningococcal conjugate vaccines (MenACWY)

Each MenACWY dose is 0.5 mL, administered by intramuscular injection (see section 2.2.3).

MenACWY and MenC vaccines can be concurrently administered with other vaccines in separate syringes and at separate sites.

### MenQuadfi

MenQuadfi is given as a single dose to individuals aged 12 months and over. See Table 13.6 for schedules and dosing for certain special groups.



A single booster dose may be given to adolescent and adults who have been primed with another MenACWY vaccine at least 4 years previously. There is currently no data available to indicate the need for or timing of a booster dose.

### Nimenrix

Nimenrix is approved for use in New Zealand for individuals from age 6 weeks.

- For infants aged under 12 months, two doses are given eight weeks apart, plus a booster at least six months after second dose, from age 12 months. Primary doses are funded for certain infants aged 6 weeks to under 12 months (see Table 13.6).
- Healthy infants aged 6 months to under 12 months, who are not immunocompromised, can be given one dose (unfunded) instead of two primary doses, plus a booster from age 12 months, at least eight weeks later.
- For adults and children from age 12 months, one dose is given (unfunded).
- Booster doses may be indicated in some individuals.

## 13.5 Recommended immunisation schedule

### 13.5.1 Usual childhood schedule

A primary course of MenB is recommended and funded for all children at ages 3 months, 5 months and a booster given at age 12 months. In an alternative approved schedule, MenB can be given at ages 2 months (ie, approved from 8 weeks) and 4 months with a booster at age 12 months; this would be outside the standard scheduled immunisation visits. **Do not delay** the 6-week vaccination event for the other Schedule vaccines.

For children at high risk of meningococcal disease aged younger than 8 weeks, to align with the routine schedule visit, MenB can be given at ages 6 weeks and 3 months. This is off-label use and requires a prescription for both events. No prescription is required if given as per the alternative schedule at ages 2 and 4 months.

A catch-up programme of MenB is funded for children aged 13 months to 59 months from 1 March 2023 until 31 August 2025. All children eligible for meningococcal B catch-up should be vaccinated at the earliest opportunity. Give two doses 8 weeks apart. For children aged 12 to under 24 months at time of their first dose, a further dose can be given from 12 to 24 months after second dose. If MenB is started before the age 5 years, then the funded course can be completed.

As an antipyretic, prophylactic paracetamol is recommended to be given up to 30 minutes prior to or immediately after MenB vaccination and give up to two further doses four to six hours apart for children aged under 2 years. Ibuprofen may be given as an alternative to paracetamol six to eight hourly (see section 13.7.1).

**Table 13.4: Recommended MenB immunisation schedule for children aged under 5 years**

Age	Dose	Comment
<b>National Immunisation Schedule</b>		
3 months <sup>a</sup>	Dose 1	Given together with routine vaccinations
5 months	Dose 2	
12 months	Dose 3 (booster)	
<b>Approved alternative schedule</b>		
8 weeks <sup>a</sup>	Dose 1	Additional visit
4 months	Dose 2	Additional visit if dose one received at age 2 months
12 months	Dose 3 (booster)	Given together with routine vaccinations
<b>Catch-up for those aged 12–59 months at time of first dose</b>		
Age 12–23 months	Give 2 doses at least 8 weeks apart <sup>b</sup> . Give a booster dose 12–24 months after dose two.	
Age 24–59 months	Give 2 doses at least 8 weeks <sup>c</sup> apart, no booster.	

- For children at high risk of meningococcal disease aged younger than 8 weeks, to align with the routine schedule visit, MenB can be given at ages 6 weeks and 3 months. This is off-label use and requires a prescription for both doses. No prescription is required if given as per the alternative schedule at ages 2 months (ie, 8 weeks) and 4 months. See Table 13.6 for high-risk infants.
- For children aged 8 weeks to under 24 months, spacing between dose one and two can be reduced to 6 weeks, if indicated with a prescription.
- For children aged 2 years and over, spacing between doses can be reduced to four weeks, if indicated. No prescription required.

## 13.5.2 Individuals at increased risk

Meningococcal vaccines are funded in special circumstances, as described in the shaded section of Table 13.5; Table 13.6 shows the recommended dosing schedules.

See sections 4.3, 4.4 and 4.5 for more information about vaccination of special groups, including recommended immunisation schedules for high-risk individuals with certain medical conditions.

The meningococcal vaccines are recommended (but not funded) for other individuals at risk, as described in non-shaded rows in Table 13.5.

### Before travel

There are areas of the world where the risk of meningococcal disease is increased. Nevertheless, the risk to travellers to the developing world has been estimated as being less than one in a million per month. Recurrent epidemics of meningococcal disease occur in the sub-Saharan 'meningitis belt', from Senegal in the west to Ethiopia in the east, usually during the dry season (December to June). Epidemics are occasionally identified in other parts of the world, including in Europe and the

Americas. Generally, countries outside of Africa experience smaller outbreaks, but case-fatality rates can be high.

The preferred vaccines (MenACWY and/or MenB) for travel would be based on the epidemiology of the country. For website sources for information about meningococcal vaccines for travellers, see the WHO website ([who.int/travel-advice](https://www.who.int/travel-advice)). Quadrivalent meningococcal vaccine is a requirement for pilgrims to the Hajj.

### Before moving into communal living situations

MenACWY and MenB are recommended and funded from age 13–25 years inclusively for individuals who will be living in communal accommodation within the next three months, or who are in their first year of living in communal accommodation (specifically, boarding school hostels, tertiary education halls of residence, military barracks, youth justice residences or prisons) as they are likely to be at higher risk of acquiring meningococcal infection. This includes children who turn 13 years of age while living in boarding school hostels.

**Table 13.5: Meningococcal vaccine recommendations**

Note: **Funded circumstances are in the shaded rows.**

See the Pharmaceutical Schedule ([pharmac.govt.nz](http://pharmac.govt.nz)) for any changes to the funding decisions.

<b>Recommended and funded</b>
MenB is recommended and funded for: <ul style="list-style-type: none"><li>• all infants at ages 3<sup>a</sup> months, 5 months and 12 months</li><li>• an alternative primary schedule, at ages 8 weeks and 4 months, can be used, requiring additional visits<sup>a</sup></li><li>• catch-up is available to those aged 13 months to &lt;5 years (until 31 August 2025).</li></ul> MenB and MenACWY <sup>b</sup> are recommended and funded for: <ul style="list-style-type: none"><li>• patients pre- or post-splenectomy or with functional or anatomical asplenia<sup>c,d</sup></li><li>• patients with HIV, complement deficiency (acquired, including monoclonal antibody therapy against C5, or inherited)</li><li>• patients who are pre- or post-solid organ transplant<sup>d</sup></li><li>• HSCT (bone marrow transplant) patients<sup>d</sup></li><li>• patients prior to planned immunosuppression<sup>d,e</sup></li><li>• patients following immunosuppression<sup>d,e</sup></li><li>• close contacts of meningococcal cases of any group<sup>f</sup></li><li>• individuals who have previously had meningococcal disease of any group<sup>f,g</sup></li></ul> MenB and MenACWY are recommended and funded for: <ul style="list-style-type: none"><li>• individuals aged 13–25 years inclusively who are entering within three months or are in their first year of living in boarding school hostels, tertiary education halls of residence, military barracks, prisons or youth justice residences. This includes those who turn 13 years of age while living in boarding school hostels.</li></ul>
<b>Recommended but not funded</b>
<b>Priority groups</b> <p>MenACWY and MenB are recommended, but not funded, for:</p> <ul style="list-style-type: none"><li>• individuals are laboratory workers regularly handling meningococcal cultures</li><li>• adolescents and young adults living in communal or overcrowded accommodation not covered by funded vaccine</li><li>• individuals who are travelling to high-risk countries (see <a href="http://who.int/travel-advice">who.int/travel-advice</a>) or before the Hajj.</li></ul>
<b>Other groups</b> <p>MenACWY and MenB are recommended but not funded for all infants,<sup>h</sup> young children, adolescents and young adults (see Table 13.7).</p>

- For children at high risk of meningococcal disease aged younger than 8 weeks, to align with the routine schedule visit, MenB can be given at ages 6 weeks and 3 months. This is off-label use and requires a prescription for both doses. No prescription is required if given as per the alternative schedule at ages 8 weeks and 4 months.
- For these groups, Nimenrix is funded from age 6 weeks to <12 months; MenQuadfi at age 12 months and over. MenB is routinely funded for infants and catch-up is available for children aged 13 months to <5 years (until 31 August 2025).
- Pneumococcal, Hib, influenza and varicella vaccines are also recommended for individuals pre- or post-splenectomy or with functional asplenia. See section 4.3.3.
- See section 4.3.3 for more information.
- The period of immunosuppression due to steroid or other immunosuppressive therapy must be longer than 28 days.
- For close contacts and individuals who have had previous meningococcal disease, given as per the routine dosage schedule (see section 13.4.4)
- Regardless of time elapsed since disease. Vaccination can commence at any time from when the person is no longer acutely unwell.

**Table 13.6: Recommended meningococcal vaccine schedule for high-risk individuals (funded)**

Note: See the Pharmaceutical Schedule ([pharmac.govt.nz](http://pharmac.govt.nz)) for any changes to funding decisions.

Age at diagnosis	Vaccine (trade name)	Recommended vaccine schedule
Infants aged 6 weeks <sup>a,b</sup> to under 12 months	MenACWY (Nimenrix)	<ul style="list-style-type: none"> <li>Give 2 doses 8 weeks apart.</li> <li>When infant reaches age 12 months, then give one dose of MenACWY (MenQuadfi) at least 6 months after the second Nimenrix dose.<sup>c</sup> Give a further MenACWY (MenQuadfi) dose<sup>d</sup> after 3 years then 5 yearly if risk persists</li> </ul>
	MenB (Bexsero) <sup>a</sup>	<ul style="list-style-type: none"> <li>Give 2 doses 8 weeks apart<sup>b</sup>, plus booster given at least 6 months after second dose, from age 12 months and then 5-yearly<sup>d</sup>.</li> </ul>
Children aged 12 months to under 18 years	MenACWY (MenQuadfi)	<ul style="list-style-type: none"> <li>If aged 12 months<sup>c</sup> to under 7 years at diagnosis, give 2 doses of MenACWY<sup>e</sup> 8–12 weeks apart followed by a booster dose after 3 years, then 5yearly.<sup>d</sup></li> <li>If aged 7 years or older give 2 doses of MenACWY<sup>e</sup> 8 weeks apart followed by a booster dose 5-yearly.<sup>d</sup></li> </ul>
	MenB (Bexsero)	<ul style="list-style-type: none"> <li>For toddlers aged 12–23 months (at time of first dose), give 2 doses 8 weeks apart and a booster dose 12–23 months after second primary dose</li> <li>From age 2 years (at time of first dose), give 2 doses 8 weeks apart<sup>f</sup>.</li> <li>Give booster dose 5-yearly from age 2 years<sup>d</sup></li> </ul>
Adults aged 18 years and older	MenACWY (MenQuadfi)	Give 2 doses 8 weeks apart, then 1 dose every 5 years. <sup>d</sup>
	MenB <sup>g</sup> (Bexsero)	Give 2 doses 8 weeks apart <sup>e</sup> , then booster 5 yearly. <sup>d</sup>
Individuals aged between 13 and 25 years, in certain communal living situations <sup>h</sup>	MenACWY (MenQuadfi)	1 dose, no booster required <sup>h,i</sup>
	MenB	Give 2 doses 8 weeks apart <sup>f</sup>

a. Nimenrix is approved for use from age 6 weeks.

b. For children at high risk of meningococcal disease aged younger than 8 weeks, to align with the routine schedule visit, MenB can be given at ages 6 weeks and 3 months. This is off-label use and requires a prescription for both doses. No prescription is required if given as per the alternative approved schedule at ages 8 weeks and 4 months.

c. For children given MenC prior to 1 July 2024, give two doses Nimenrix or MenQuadfi as age appropriate. If an infant has received two doses of Nimenrix before age 12 months (previously unfunded) instead of MenC prior to 1 July 2024, give just one dose of MenQuadfi at least 6 months after the MenACWY second dose, from age 12 months.

d. MenACWY and MenB boosters are funded for individuals pre- and post-splenectomy and for patients with functional or anatomic asplenia, HIV, complement deficiency (acquired or inherited), or pre- or post-solid organ transplant.

e. A second primary dose of MenACWY (MenQuadfi) from age 12 months is off-label and requires a prescription from an authorised prescriber under section 25 of the Medicines Act.

f. From age 2 years, MenB can be given 4 weeks apart if there is a clinical need.

- g. MenB is licensed up to age 50 years, but no safety concerns are expected when given to adults aged over 50 years.
- h. Funded for individuals aged 13–25 years inclusively who either: are entering within three months or who are in their first year of living in boarding school hostels, tertiary education halls of residence, military barracks, youth justice residences or prisons. This includes those who turn 13 years of age while living in boarding school hostels.
- i. A single booster dose can be given to adolescents and young adults who were primed at least 4 years previously with any MenACWY vaccine.

### 13.5.3 Recommendations for children and adolescents

Non-high-risk children and adolescents may be offered meningococcal vaccines. These vaccines are only funded for certain groups (see Table 13.4). Table 13.7 suggests the most appropriate ages for this, reflecting the known ages of increased risk. The predominant meningococcal strains in New Zealand in childhood are B, W and Y. With the current New Zealand epidemiology, neither MenACWY nor MenB give protection across all prevailing meningococcal groups and both types of vaccine are recommended. For those who are likely to travel, the broadest protection is preferable because of the differing serotype patterns between countries.

**Table 13.7: Recommended schedule for non-funded meningococcal vaccines in children and adolescents**

Note: Vaccine immunity is not long-lasting. The suggested ages of vaccination are not expected to protect individuals through all of childhood but focused on protection during the ages of highest risk. Due to being at lowest risk, healthy children aged 5–11 years are not specifically recommended meningococcal vaccination in this table. This does not apply to epidemic situations.

Age at time of consultation	Vaccine options (trade name)	Number of doses <sup>a</sup>
6 weeks to <12 months	MenACWY (Nimenrix)	ages 6 weeks–5 months give 2 doses or if aged from 6 to <12 months <sup>b</sup> give 1 dose plus a booster from age 12 months
12 months to <5 years	MenACWY (MenQuadfi or Nimenrix)	1 dose MenACWY
Early adolescence (12 to <16 years) <sup>c,d</sup>	MenB (Bexsero)	2 doses <sup>d</sup>
	MenACWY (MenQuadfi or Nimenrix)	1 dose plus a booster 5 years later <sup>d</sup>
Late adolescence ≥16 years <sup>c,d</sup>	MenB (Bexsero)	2 doses
	MenACWY (MenQuadfi or Nimenrix)	1 dose, no booster required

- Refer to section 13.4.4 for the intervals between doses.
- Infants aged from 6 months to ≤12 months who are not immunocompromised, can instead be given one dose plus booster from age 12 months at least two months later.
- For individuals aged 13–25 years not eligible for funded vaccine, particularly living in crowded private homes, other hostels or private student accommodation, or planning overseas travel.
- A booster dose of MenACWY and MenB can be given if it is at least 5 years since primary dose of these vaccines. The need for MenB vaccination is not established for this group but can be considered if at continued risk.

## 13.5.4 Pregnancy and breastfeeding

There are no reports of any adverse effects among pregnant women who have been vaccinated during pregnancy.<sup>27</sup> Meningococcal vaccines may be given in pregnancy and to those who are lactating, if indicated.<sup>28, 29</sup>

## 13.5.5 (Re)vaccination

Meningococcal conjugate vaccines, MenC, MenACWY and MenB are funded for vaccination or re-vaccination of eligible individuals, as follows. See also section 4.3.

### Quadrivalent meningococcal conjugate vaccines, MenACWY

- Age under 12 months – up to three doses (Nimenrix), plus booster (MenQuadfi) after age 12 months and every five years (as appropriate)



- Age from 12 months – up to two doses (MenQuadfi) plus booster every five years (as appropriate)

Primary vaccination plus booster doses of MenACWY (as age appropriate) are funded for individuals:

- pre- or post-splenectomy
- with functional or anatomic asplenia
- pre- or post-solid organ transplantation
- with complement deficiency (acquired or inherited)
- who are HIV-positive.

A maximum of two (MenQuadfi) or three (Nimenrix, depending on age of first dose) doses are funded for individuals:

- post-haematopoietic stem cell transplantation
- prior to planned and following immunosuppression for longer than 28 days.

### Recombinant meningococcal B vaccine, MenB

- Age under 12 months – up to three doses, plus booster after age 12 months and every five years (as appropriate)
- Age from 12 – 23 months – up to two doses plus booster given 12 to 23 months after second dose, and booster every five years (as appropriate)
- Age from 2 years – up to two doses plus a booster every five years (as appropriate)

Primary vaccination plus booster doses funded individuals:

- pre- or post-splenectomy
- with functional or anatomic asplenia
- pre- or post-solid organ transplantation
- with complement deficiency (acquired or inherited)
- who are HIV-positive.

Two primary doses are funded for individuals aged from 12 months:

- post-haematopoietic stem cell transplantation
- prior to planned and following immunosuppression for longer than 28 days.

## 13.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

There are no specific contraindications for meningococcal vaccines, except for anaphylaxis to a previous dose or any component of the vaccine.

## 13.7 Potential responses and AEFIs

### 13.7.1 Meningococcal B recombinant vaccine

There is an increased risk of fever and medically attended fever-related events, such as sepsis screening and febrile seizures associated with MenB in some children age under 2 years.<sup>4, 30-33</sup> These events peaked at six hours post-vaccination and generally subsided by day 3. Fever of at least 38°C was observed in 80 percent of infants who received MenB and routine vaccines concomitantly, and 71 percent who had MenB and routine vaccines separately, compared with 51 percent who receive routine vaccines only.<sup>34, 35</sup> Paracetamol was shown to reduce the incidence of fever. Prophylactic paracetamol is recommended from 30 minutes prior to or immediately after vaccination, then two further doses can be given four to six hours apart for children aged under 2 years. Some infants will still develop a fever and/or injection-site pain even though they have received paracetamol doses.<sup>36</sup>

In clinical trials, most infants and young children had at least one solicited adverse reaction (84–97 percent)<sup>35</sup>, including injection-site tenderness and irritability. Adolescents and adults may experience localised pain, nausea, myalgia, malaise, mild fever and headache.

### 13.7.2 Quadrivalent meningococcal conjugate vaccine

Potential adverse reactions after meningococcal conjugate vaccines include localised injection-site pain, irritability, headache, malaise and fatigue.<sup>26, 37</sup> The safety profile of all the MenACWY vaccines are very similar.<sup>26, 27, 38</sup> In infants, unusual crying, irritability, drowsiness and vomiting have been reported in clinical trials.<sup>24, 39</sup> Fever is reported by 2–5 percent of adolescents and less than 10 percent of infants who receive MenACWY. Concurrent administration with routine vaccines did not increase solicited systemic responses in young children (when given with PCV13) but was slightly increased in adolescents (with Tdap and HPV) during clinical trials of MenQuadfi.<sup>24, 38, 39</sup>

#### Guillain–Barré syndrome

There is no evidence of an association between meningococcal conjugate vaccines and GBS. An early report in the US of a suspected temporal association between MenACWY (Menactra) and GBS was followed by a large retrospective cohort study in the US that found no evidence of an increased risk of GBS following administration of MenACWY.<sup>28, 40</sup> If indicated, meningococcal conjugate vaccines may be administered to individuals with a history of GBS.<sup>41</sup>

## 13.8 Public health measures

Invasive meningococcal disease must be notified on suspicion to the local medical officer of health.

For details of public health control measures see the Communicable Disease Control Manual at [www.tewhātuora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/neisseria-meningitidis-invasive-disease-meningococcal-disease/](http://www.tewhātuora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/neisseria-meningitidis-invasive-disease-meningococcal-disease/)

The overall rate of secondary cases in untreated adults is around 1 per 300. Adults and children in close contact with primary cases of invasive meningococcal infection are recommended to receive antibiotic prophylaxis, preferably within 24 hours of the initial diagnosis, but prophylaxis is recommended up to 14 days after diagnosis of illness.

### 13.8.1 Use of meningococcal vaccines for close contacts

Close contacts of cases of any group (including group A, B, C, W or Y) meningococcal disease may be offered both MenB and MenACWY meningococcal vaccines (see section 13.5).

See below for the use of the vaccines for the control of outbreaks, as initiated by the local public health service.

### 13.8.2 Outbreak control

When there is an outbreak of meningococcal disease of a specific vaccine group, an immunisation programme may be recommended and funded for a defined population. The local medical officer of health will determine the necessary action in discussion with Health New Zealand.

For more details on control measures, refer to the '*Neisseria meningitidis* invasive disease' chapter of the *Communicable Disease Control Manual* (available at [www.tewhātuora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/neisseria-meningitidis-invasive-disease-meningococcal-disease/](http://www.tewhātuora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/neisseria-meningitidis-invasive-disease-meningococcal-disease/)).

## 13.9 Variations from the vaccine data sheets

The MenQuadfi data sheet states to give a single dose for individuals from age 12 months. Health New Zealand | Te Whatu Ora recommends that two doses are given to individuals at high risk of meningococcal disease (see Table 13.6 and section 4.3), with booster doses every five years. If the child is still under the age of 7 years, give a booster after three years then five-yearly.<sup>37</sup> The second primary dose of MenQuadfi requires a prescription from an authorised prescriber.

The MenB data sheet states that the vaccine is indicated from age 8 weeks or older. However, Health New Zealand recommends that MenB can be given from age 6 weeks to infants at high risk of meningococcal disease (see Table 13.6). This is an off-label use and requires a prescription from an authorised prescriber. The datasheet states that infants who received their primary course from ages 6 to 11 months can receive a booster in the second year of life at least 2 months later. The Ministry recommends that all infants aged 11 months or less receive a booster dose at least 6 months after the primary doses, from the age of 12 months.

The data sheet recommends two doses of MenB to be given eight weeks apart between ages 12 and 23 months and not less than one month apart from the age of 2 years. Health New Zealand recommends two doses of MenB be given at least eight weeks apart for those aged 12 months or older at the time of the first dose, this may be reduced to at least 4 weeks if required.

## References

1. Campbell H, Parikh SR, Borrow R, et al. Presentation with gastrointestinal symptoms and high case fatality associated with group W meningococcal disease (MenW) in teenagers, England, July 2015 to January 2016. *Euro Surveillance*, 2016. 21(12).
2. Ladhani SN, Beebeejaun K, Lucidarme J, et al. Increase in endemic Neisseria meningitidis capsular group W sequence type 11 complex associated with severe invasive disease in England and Wales. *Clinical Infectious Diseases*, 2015. 60(4): p. 578-85.
3. Cohn A, MacNeil J. The Changing Epidemiology of Meningococcal Disease. *Infectious Disease Clinics of North America*, 2015. 29(4): p. 667-77.
4. Harrison LH, Granoff DM, Pollard AJ. 2018. Meningococcal Capsular Group A, C, W and Y conjugate vaccines, in *Plotkin's Vaccines (7th edition)*, Plotkin SA, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
5. Rubilar PS, Barra GN, Gabastou JM, et al. Increase of Neisseria meningitidis W:cc11 invasive disease in Chile has no correlation with carriage in adolescents. *PLoS One*, 2018. 13(3): p. e0193572.
6. Wang B, Santoreneos R, Giles L, et al. Case fatality rates of invasive meningococcal disease by serogroup and age: A systematic review and meta-analysis. *Vaccine*, 2019. 37(21): p. 2768-2782.
7. Meningococcal Disease Surveillance Group. Analysis of endemic meningococcal disease by serogroup and evaluation of chemoprophylaxis. *Journal of Infectious Diseases*, 1976. 134(2): p. 201-4.

8. Neal KR, Nguyen-Van-Tam JS, Jeffrey N, et al. Changing carriage rate of *Neisseria meningitidis* among university students during the first week of term: cross sectional study. *BMJ*, 2000. 320(7238): p. 846-9.
9. Bruce MG, Rosenstein NE, Capparella JM, et al. Risk factors for meningococcal disease in college students. *JAMA*, 2001. 286(6): p. 688-93.
10. Nelson SJ, Charlett A, Orr HJ, et al. Risk factors for meningococcal disease in university halls of residence. *Epidemiology and Infection*, 2001. 126(2): p. 211-7.
11. Christensen H, May M, Bowen L, et al. Meningococcal carriage by age: a systematic review and meta-analysis. *Lancet Infectious Diseases*, 2010. 10(12): p. 853-61.
12. Peterson ME, Li Y, Shanks H, et al. Serogroup-specific meningococcal carriage by age group: a systematic review and meta-analysis. *BMJ Open*, 2019. 9(4): p. e024343.
13. Institute of Environmental Science and Research (ESR). 2024 *Invasive meningococcal disease report, January - December 2023*. ESR: Porirua, New Zealand. URL: (accessed
14. Ladhani SN, Andrews N, Parikh SR, et al. Vaccination of Infants with Meningococcal Group B Vaccine (4CMenB) in England. *New England Journal of Medicine*, 2020. 382(4): p. 309-317.
15. McMillan M, Wang B, Koehler AP, et al. Impact of Meningococcal B Vaccine on Invasive Meningococcal Disease in Adolescents. *Clinical Infectious Diseases*, 2021.
16. McNamara LA, Thomas JD, MacNeil J, et al. Meningococcal Carriage Following a Vaccination Campaign With MenB-4C and MenB-FHbp in Response to a University Serogroup B Meningococcal Disease Outbreak-Oregon, 2015-2016. *Journal of Infectious Diseases*, 2017. 216(9): p. 1130-1140.
17. Soeters HM, Whaley M, Alexander-Scott N, et al. Meningococcal carriage evaluation in response to a serogroup B meningococcal disease outbreak and mass vaccination campaign at a college – Rhode Island, 2015 – 2016. *Clinical Infectious Diseases*, 2017. 64(8): p. 1115-1122.
18. Marshall HS, Lally N, Flood L, Phillips P. First statewide meningococcal B vaccine program in infants, children and adolescents: evidence for implementation in South Australia. *Medical Journal of Australia*, 2020.
19. Deceuninck G, Lefebvre B, Tsang R, et al. Impact of a mass vaccination campaign against Serogroup B meningococcal disease in the Saguenay-Lac-Saint-Jean region of Quebec four years after its launch. *Vaccine*, 2019. 37(31): p. 4243-4245.
20. Ladhani SN, Campbell H, Andrews N, et al. First real world evidence of meningococcal group B vaccine, 4CMenB, protection against meningococcal group W disease; prospective enhanced national surveillance, England. *Clinical Infectious Diseases*, 2020.
21. GlaxoSmithKline NZ Ltd, New Zealand Data sheet: Bexsero multicomponent meningococcal group B vaccine (recombinant, adsorbed). 2020, Medsafe.
22. Martín-Torres F, Bernatowska E, Shcherbina A, et al. Meningococcal B vaccine immunogenicity in children with defects in complement and splenic function. *Pediatrics*, 2018. 142(3).
23. Martín-Torres F, Bertrand-Gerentes I, Oster P. A novel vaccine to prevent meningococcal disease beyond the first year of life: an early review of MenACYW-TT. *Expert Rev Vaccines*, 2021. 20(9): p. 1123-1146.
24. sanofi-aventis New Zealand. *New Zealand datasheet: MenQuadfi*. Medsafe; [updated 22 September 2022]; URL: <https://www.medsafe.govt.nz/Profs/Datasheet/m/Menquadfiinj.pdf>. (accessed 1 December 2022)
25. Chang LJ, Hedrick J, Christensen S, et al. A Phase II, randomized, immunogenicity and safety study of a quadrivalent meningococcal conjugate vaccine, MenACYW-TT, in healthy adolescents in the United States. *Vaccine*, 2020. 38(19): p. 3560-3569.

26. Hedari CP, Khinkarly RW, Dbaibo GS. Meningococcal serogroups A, C, W-135, and Y tetanus toxoid conjugate vaccine: a new conjugate vaccine against invasive meningococcal disease. *Infect Drug Resist*, 2014. 7(3 April): p. 85-99.
27. Mbaeyi SA, Bozio CH, Duffy J, et al. Meningococcal Vaccination: Recommendations of the Advisory Committee on Immunization Practices, United States, 2020. *MMWR: Recommendations and Reports*, 2020. 69(9): p. 1-41.
28. Centers for Disease Control and Prevention. 2013. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morbidity and Mortality Weekly Report: Recommendations and Reports*. 62(2): p. 1-28.  
<https://www.cdc.gov/mmwr/pdf/rr/rr6202.pdf> (accessed 27 February 2020)
29. Drugs and Lactation Database (LactMed). 2006-. Meningococcal Vaccines. in *Drugs and Lactation Database (LactMed)*. Bethesda MD. URL: <https://www-ncbi-nlm-nih-gov.ezproxy.auckland.ac.nz/books/NBK501014/>. (accessed 1 December 2022)
30. Vesikari T, Esposito S, Prymula R, et al. Immunogenicity and safety of an investigational multicomponent, recombinant, meningococcal serogroup B vaccine (4CMenB) administered concomitantly with routine infant and child vaccinations: results of two randomised trials. *Lancet*, 2013. 381(9869): p. 825-35.
31. Vesikari T, Prymula R, Merrall E, et al. Meningococcal serogroup B vaccine (4CMenB): Booster dose in previously vaccinated infants and primary vaccination in toddlers and two-year-old children. *Vaccine*, 2015. 33(32): p. 3850-8.
32. Harcourt S, Morbey RA, Bates C, et al. Estimating primary care attendance rates for fever in infants after meningococcal B vaccination in England using national syndromic surveillance data. *Vaccine*, 2018. 36(4): p. 565-571.
33. Zafack JG, Bureau A, Skowronski DM, De Serres G. Adverse events following immunisation with four-component meningococcal serogroup B vaccine (4CMenB): interaction with co-administration of routine infant vaccines and risk of recurrence in European randomised controlled trials. *BMJ Open*, 2019. 9(5): p. e026953.
34. Gossger N, Snape MD, Yu L-M, et al. Immunogenicity and tolerability of recombinant serogroup B meningococcal vaccine administered with or without routine infant vaccinations according to different immunization schedules. *JAMA*, 2012. 307(6).
35. Martín-Torres F, Safadi MAP, Martínez AC, et al. Reduced schedules of 4CMenB vaccine in infants and catch-up series in children: Immunogenicity and safety results from a randomised open-label phase 3b trial. *Vaccine*, 2017. 35(28): p. 3548-3557.
36. De Serres G, Billard MN, Gariépy MC, et al. Short-term safety of 4CMenB vaccine during a mass meningococcal B vaccination campaign in Quebec, Canada. *Vaccine*, 2018. 36(52): p. 8039-8046.
37. American Academy of Pediatrics. 2018. Meningococcal disease. in *Red Book: 2018 Report of the Committee on Infectious Diseases*, Kimberlin D, Brady M, Jackson M, and Long S (eds). Elk Grove Village, IL. p. 551-561. URL: <https://redbook.solutions.aap.org/redbook.aspx>. (accessed 15 April 2020)
38. Pina LM, Bassily E, Machmer A, et al. Safety and immunogenicity of a quadrivalent meningococcal polysaccharide diphtheria toxoid conjugate vaccine in infants and toddlers: three multicenter phase III studies. *Pediatric Infectious Disease Journal*, 2012. 31(11): p. 1173-83.
39. Marshall GS, Pelton SI, Robertson CA, Oster P. Immunogenicity and safety of MenACWY-TT, a quadrivalent meningococcal tetanus toxoid conjugate vaccine recently licensed in the United States for individuals  $\geq 2$  years of age. *Human Vaccines & Immunotherapeutics*, 2022: p. 2099142.



40. Velentgas P, Amato AA, Bohn RL, et al. Risk of Guillain-Barré syndrome after meningococcal conjugate vaccination. *Pharmacoepidemiology and Drug Safety*, 2012. 21(12): p. 1350-8.
41. Australian Technical Advisory Group on Immunisation. 2018. *Australian Immunisation Handbook* (ed.), Canberra: Australian Government Department of Health. URL: <https://immunisationhandbook.health.gov.au/> (accessed October 2019)



# 14 Mpox (orthopoxvirus)

## Key information

Mode of transmission	Close physical contact, including intimate household and sexual contact, with bodily fluids or internal mucosal surfaces, direct contact with skin lesions and contaminated objects, such as bedding, or prolonged exposure to respiratory droplets
Incubation period	Average 6 to 13 days, range of 2 to 21 days.
Period of communicability	Self-limiting, usually 2 to 4 weeks.
Funded and available vaccine	Mpox (orthopoxvirus) vaccine (MPV): Jynneos (Bavarian Nordic) Live non-replicating vaccine
Dose, presentation, route	0.5 mL per dose, two doses given at least four weeks apart single dose vial Subcutaneous injection.
Funded vaccine indications and schedule (section 14.5.1)	Funded vaccination of those aged 18 or over who are at high risk of mpox. This includes those at risk or who anticipate being: <ul style="list-style-type: none"> <li>• at risk of occupational exposure to mpox</li> <li>• at risk of mpox infection during a local mpox outbreak</li> <li>• at risk of mpox infection because they are: <ul style="list-style-type: none"> <li>○ gay, bisexual and other men who have sex with men (GBMSM), transgender or non-binary people with certain high-risk indications</li> <li>○ people living with HIV, if at risk of mpox exposure</li> </ul> </li> <li>• sexual partners of those at increased risk of mpox infection.</li> <li>• People who anticipate experiencing any of the above</li> </ul>
Contraindications (section 14.6.1)	Anaphylaxis (severe systemic allergy) to a previous dose of the vaccine or any component of the vaccine, including chicken protein. History of myocarditis or pericarditis associated with a previous dose of MPV.
Precautions and other considerations	Those with a history of severe allergy to the trace components of the vaccine should weigh the risk with the risk of mpox infection. (section 14.6.2) Written informed consent is required for those who are pregnant or breastfeeding (section 14.5.3).
Potential vaccine response	Mild to moderate, local injection-site pain, redness, swelling and itching and systemic muscle aches, fatigue, headache, nausea, and less commonly, fever and lymphadenopathy.

*Continued overleaf*

Vaccine effectiveness	Efficacy based on immunogenicity – seroconversion rates of 99.8 percent observed two weeks after second dose in healthy adults. Effectiveness against clade IIb mpox – pre-exposure effectiveness of 76 percent after one dose and 82 percent after two doses. Effectiveness predicted to be similar for other clades.
Public health measures (section 14.8)	All cases of mpox must be notified immediately on suspicion. Vaccine can be used for post-exposure prophylaxis; optimally one dose is given within 4 days but can be given up to 14 days post exposure.

## 14.1 Virology

Monkeypox virus is a rare double-stranded DNA zoonotic orthopoxvirus from the same Poxviridae family as the variola virus (smallpox virus), the vaccinia virus (in the vaccine for the smallpox eradication programme) and the cowpox virus (used in first generation smallpox vaccines). There are two clades of the monkeypox virus: clade I (formerly the Congo Basin clade) and clade II (formerly the West African clade).<sup>1</sup> Subclades have emerged that have caused large rapidly spreading outbreaks of mpox disease in humans, notably subclade IIa and IIb. In 2024, subclade Ib was identified and found to have spread beyond the Congo. Available data suggest human mpox with clade I is more severe than clade II with an almost ten-times higher case-fatality rate (in endemic areas up to 10 percent versus 1 percent). No natural reservoir species has been identified to date, but zoonotic spread has been observed from animal hosts including forest-dwelling rodents, particularly rats, and non-human primates.

## 14.2 Clinical features

Mpox is an infectious disease caused by the monkeypox virus. It classically presents with a prodrome of fever, aches and lymphadenopathy followed by a characteristic centrifugal rash. Systemic prodromal symptoms may also include intense fatigue, headache, muscle pain, backache, chills and sore throat, and last for one to three days before rash onset. The rash lesions first appear on the face and in the mouth and move to distal extremities. These lesions usually progress through four stages: macules, papules, fluid-filled vesicles and pustular pustules, eventually forming scabs. The mpox rash resembles that of other common infections such as foot-and-mouth disease, varicella (chickenpox), herpes simplex, syphilis and molluscum contagiosum. Coinfections can occur, particularly with other sexually transmitted infections. Monkeypox virus can be detected by PCR testing from swabs of lesions.

The typical incubation period is seven to 14 days, with a range of two to 21 days or longer.<sup>1</sup> This period can be shorter with invasive exposure, such as through broken skin or mucosal surfaces. An infected individual is infectious from onset of the first symptoms (usually fever but occasionally a rash) and until all the rash lesions crust and fall off over a period of two to three weeks. Scabs may still contain infectious virus. Mpox subclade IIb is generally mild and self-limiting, lasting two to four weeks. Severe illness, which can be fatal, is more common in children, and in pregnant or

immunocompromised individuals, such as those living with advanced HIV infection. Clade I infections are associated with more severe disease and death. The mortality rate of the subclade Ib outbreak in Africa is around 4 percent.

Mpox virus does not spread easily between individuals. Human to human transmission occurs primarily through close, direct physical contact with infected skin, mucosal lesions and body fluids. It can also be spread by respiratory droplets during prolonged face-to-face contact. Infrequent transmission has been reported through contaminated materials like clothing, towels or bedding. Viral shedding has been reported in semen and saliva, notably for longer duration in people who are immunocompromised due to HIV infection.<sup>2,3</sup> Mpox can also be transmitted through close contact with infected animals.<sup>1</sup>

During the 2022-23 outbreak of subclade IIb, presentations were often atypical. Prodromal systemic symptoms may have been absent, blunted or develop after the onset of rash. Frequently, rash lesions were confined to anogenital skin, oropharynx or rectal mucosa, at various stages of evolution and atypical progression, or with only a single lesion. Most cases were mild and presented to sexual health services. Spontaneous and complete recovery typically occurred within three weeks. Complications included secondary cellulitis (reported in around 11 percent of cases), severe proctitis, odynophagia, tonsillitis, epiglottitis, pneumonia, sepsis, encephalitis, and keratitis that could lead to vision loss.

Data is limited around mpox infection in pregnancy, but case reports from DRC associated vertical transmission with miscarriage and fetal infection resulting in stillbirth.<sup>4,5</sup>

See the Mpox chapter of *Communicable Disease Control Manual* for further information, available at [www.tewhaturora.govt.nz/for-health-professionals/clinical-guidance/communicable-disease-control-manual/mpox](http://www.tewhaturora.govt.nz/for-health-professionals/clinical-guidance/communicable-disease-control-manual/mpox).

## 14.3 Epidemiology

### 14.3.1 Global burden of disease

The first human monkeypox (renamed mpox) case was reported in 1970. Cases and occasional outbreaks were successively reported in 11 countries of Central and West Africa. Occasional travel-associated cases and small clusters have occurred in nonendemic countries over the past decades. An increase in cases has been seen in Nigeria since 2017.

In May 2022, three separate incidents of clade IIb mpox were identified in the UK. The first case was a recognised travel-associated case from Nigeria and did not lead to further spread. The second case was not related to travel and indicated local transmission. With over 15,000 confirmed cases of clade IIb reported in 74 non-endemic countries across the six WHO regions, including New Zealand and Australia, WHO declared the outbreak a Public Health Emergency of International Concern

(PHEIC) on the 23 July 2022.<sup>1</sup>This PHEIC was declared over in May 2023, but clade II infections continue to be notified globally, including in the Western Pacific region and in particular, with an increase in cases in Australia in July 2024.

During 2022-2023, the ten most affected countries were in the Americas, Europe and the UK accounting for 86 percent of the global clade IIb cases. Transmission was mainly among young males who identify as gay, bisexual and other men-who-have-sex-with-men (GBMSM) through sexual encounters (96.4 percent of cases with known sexual orientation and 86.9 percent sexual encounters, median age 34 years).<sup>6</sup> Sporadic cases were also reported among household members, nonsexual, heterosexual and pregnant contacts, and children (1.3 percent of cases were children).<sup>7</sup> Most infections in health workers occurred in the community through sexual encounters, but approximately 10 percent reported transmission through occupational exposure.<sup>6</sup>

On 14 August 2024, WHO declared second mpox PHEIC in response to rising cases and deaths, predominantly due to the new clade Ib subvariant. Subclades Ia and Ib had spread from the Democratic Republic of Congo (DRC), where 96.3 percent of cases and 96.3 percent of deaths had occurred in 2024. Fifteen African Union member states reported cases, including Burundi, Cameroon, the Central African Republic, Egypt, Morocco, Rwanda, South Africa, Sudan and Uganda. By 28 July 2024, reported cases had increased by 160 percent and mpox deaths by 19 percent compared with the same period in 2023. Active outbreaks of clade Ia, Ib and II mpox were reported in additional African countries in differing contexts. An outbreak of subclade IIb infections emerged in May 2024 in South Africa causing high mortality in immunocompromised individuals.<sup>1</sup> Subclade Ia mpox is endemic in DRC and primarily affects children aged under 15 years through non-sexual contact with infected household members or animals. Cases of subclade Ib are predominantly adults presumed to be transmitted via sexual contact, but cases have been reported children aged under 5 years. The first case of clade Ib outside of Africa was detected in Sweden in an individual who had travelled from central Africa in August 2024. Since clade Ib risk is in different age groups in Africa, it may not confer the same epidemiological risk in New Zealand as the clade IIb outbreak.

For status of current cases see WHO 2022-2024 Mpox (Monkeypox) Outbreak: Global trends website [https://worldhealthorg.shinyapps.io/mpx\\_global/](https://worldhealthorg.shinyapps.io/mpx_global/)

### 14.3.2 New Zealand epidemiology

The first confirmed case of mpox during the 2022-2023 clade II outbreak was reported in New Zealand on 7 July 2022 and a second unrelated confirmed case was reported on 12 July 2022. By 15 December 2022, 40 cases had been reported to WHO. Nine cases were acquired overseas and 31 were identified as community transmission associated with attendance at sex-on-site venues. By 15 August 2024, 53 cases had been notified in total. An increase in cases was linked with the Queenstown Winter Pride festival, and as of 20 September 2024, a further 11 cases had been reported. No clade Ib cases have been reported to date in New Zealand.

## 14.4 Vaccines

The mpox vaccine (MPV) is a smallpox vaccine with cross-protection against monkeypox (orthopoxvirus vaccine). First- and second- generation smallpox vaccines utilised live attenuated vaccinia virus, which despite being highly effective and lead to the eradication of smallpox, were associated with serious adverse events. To address this issue, a modified replication-deficient virus known as modified vaccinia virus Ankara (MVA) was developed as a third-generation vaccine.<sup>8</sup> This virus was created through over 570 passages in chick fibroblast cell culture, resulting in loss of 12 percent of the viral genome rendering it unable to replicate in mammalian cells. Additionally, MVA also lost genes that would otherwise interfere with the host immune response, reducing its reactogenicity. Although MVA is a considered a live virus, its inability to replicate means that it cannot cause disseminated disease in severely immunocompromised people, but it can still induce a robust humoral (antibody) response. As well as use as a third-generation orthopoxvirus vaccine (MVA-BN), this non-replicating, attenuated virus has also been used as a viral vector to express recombinant antigens for other infectious disease vaccines and cancer vaccines in children and adults (fourth generation vaccines).

### 14.4.1 Available vaccines

#### Funded mpox vaccine

The mpox (orthopoxvirus) vaccine (MPV) is available in New Zealand for prevention of mpox infection. Initially from late 2022, it was accessed as part of the National Immunisation Programme under section 29 of the Medicine Act 1981. Provisional approval for use in adults was granted by Medsafe in September 2024.

Orthopoxvirus (smallpox and mpox) vaccine, Jynneos, is a live non-replicating vaccine (also known elsewhere as Imvanex or Imvamune, manufactured by Bavarian Nordic).

Each 0.5 mL dose contains:

- $0.5 \times 10^8$  to  $3.95 \times 10^8$  infectious units of non-replicating, live modified vaccinia virus Ankara – Bavarian Nordic (MVA-BN) with Tris (tromethamine) and sodium chloride.
- May also contain trace residues of host cell DNA, chicken protein, benzonase, gentamicin and ciprofloxacin.

This vaccine does not contain preservatives, and the vial stopper (bromobutyl rubber) does not contain natural rubber latex.

#### Other vaccines

A live attenuated replicating smallpox and mpox vaccine (ACAM2000) is available in other countries, including Australia, and a minimally replicating modified-vaccinia

vaccine (LC16m8) is available in Japan. These vaccines are not available in New Zealand.<sup>1</sup>

## 14.4.2 Efficacy and effectiveness

Data on the efficacy of MPV against smallpox or mpox in humans is limited. Due to the eradication of smallpox and the rarity of mpox—previously seen only in West and Central Africa—immunogenicity has been used as a proxy for efficacy in clinical trials in humans. Preclinical studies were used to demonstrate that the vaccine protects against lethal mpox challenges in primates<sup>9</sup> and related viruses in other animals.

Another challenge is that the transmission patterns in the 2022 subclade IIb outbreak, which primarily affected GBMSM including those living with HIV, differed from earlier African outbreaks that predominantly involved children through household and zoonotic transmission.<sup>10</sup> While more data has become available from the subclade IIb outbreak, information on the vaccine's efficacy against clade I remains limited, but WHO anticipates that MPV will demonstrate effectiveness against both clade I and II infections (although the demographics differ with more children affected by clade I and subclade Ib).<sup>1</sup>

### Immunogenicity

Most of the existing immunogenicity data has primarily concentrated on neutralizing antibody activity. There is no defined correlate of protection but antibody levels appear to correlate well with effectiveness.<sup>1</sup> Significant correlation between vaccinia-binding antibody titres and vaccine effectiveness was shown by a meta-analysis.<sup>11</sup> Additionally, T cell cross-protection between mpox clades is possible. Mpox virus clade I and the 2022 outbreak clade IIb share 71 percent of the T cell epitopes with the vaccinia virus used in the live smallpox vaccine and modified in the MVA-BN vaccine.<sup>12</sup>

A phase 3 placebo-controlled trial showed seroconversion rates of 99.8 percent at two weeks after dose two of MPV. Just over 4,000 healthy male and female recipients aged 18–40 years received two doses of MPV subcutaneously (SC) four weeks apart.<sup>13</sup>

### HIV infection and prior smallpox vaccination

Comparable antibody responses to two doses of MPV, with no significant differences in neutralising antibody titres, were shown between 91 HIV-infected (CD4 cell count  $\geq 350$  cells/mm<sup>3</sup>) and 60 HIV-uninfected clinical trial participants.<sup>14</sup> A study (in preprint) in New York found that HIV status with CD4 cell counts over 250 cells/mm<sup>3</sup> did not affect the response to MPV and that immunity was comparable between those with and without HIV when one-fifth dose was given intradermally.<sup>15</sup>

There is evidence in humans of cross-protection between smallpox vaccination and mpox. Surveillance data in DRC found that people born prior to 1980 who were vaccinated with live vaccinia-based smallpox vaccine had greater than five-fold reduction in mpox risk than those not previously vaccinated (VE against mpox of 68–88



percent).<sup>1</sup> But it is unclear what protection historical smallpox vaccination affords in those living with HIV.

In those with a history of vaccination with vaccinia (smallpox) vaccine, one dose of MPV induces a rapid antibody response and have comparable seroconversion rates whether given one or two doses of MPV.<sup>14, 16</sup> A small study in New York (in preprint) found that the initial response to MPV induced comparable and robust antibody responses in those with or without prior smallpox (vaccinia) vaccination. But in vaccinia-naïve individuals, antibody levels after one dose waned to baseline within one year and had lower avidity than in those previously vaccinated.<sup>15</sup>

An Italian prospective cohort study in 164 adults found that two doses were preferable to maximise the neutralising antibody response, regardless of prior smallpox (vaccinia) vaccination, and particularly in those living with HIV.<sup>17</sup> Two doses of MPV in smallpox-naïve individuals induced a stronger cellular response than one dose in smallpox-primed individuals, but with no evidence of a difference in IgG and neutralising antibody responses. In participants living with well-controlled HIV infection, a neutralising antibody response was detected in fewer than half of the participants after one dose in those who had previously had smallpox vaccination than those who were smallpox-naïve after two doses of MPV. In this study, approximately half of the first doses were given subcutaneously, and all the second doses were given intradermally.<sup>17</sup>

## Effectiveness

### Pre-exposure vaccination

Much of the recently published data on pre-exposure vaccinations investigated vaccine effectiveness after only one dose of MPV during the clade IIb outbreak due to limited vaccine availability to complete course. Further studies are needed in other populations with different modes of transmission, particularly in children, and to investigate the duration of protection.

A systematic review reported vaccine effectiveness of 76 percent (95% CI 64-88 percent; 12 studies) after one dose of MPV and after two doses to be 82 percent (72-92 percent; six studies).<sup>18</sup> The 33 studies included in the review predominantly vaccinated GBMSM between ages of 18-49 years during mid-2022.<sup>18</sup> Due to a shortage of vaccine doses, intradermal (ID) vaccination and a mix of SC and ID administration was used. One case-control study reported comparable vaccine effectiveness between SC, ID or a heterologous administration, with overall effectiveness of 85.9 percent (73.8-92.4 percent) after two doses.<sup>18, 19</sup>

### Breakthrough infection

Breakthrough infections, including asymptomatic and subclinical infections, have been reported following mpox vaccination.<sup>20</sup> In some cases, symptoms have arisen because the individual was unknowingly infected less than 21 days prior to vaccination.<sup>21</sup> Other cases occur several weeks after vaccination. For example, an mpox case in New Zealand occurred in an HIV-negative man 13 weeks after two subcutaneous doses of MPV. This case underscores the need for ongoing surveillance of individuals presenting with mpox-like symptoms, even if when fully vaccinated.<sup>22</sup>



Given the broad confidence intervals for effectiveness data, a Canadian observational study examined whether MPV reduced disease severity in breakthrough cases that occurred after one dose of MPV, where pre-exposure vaccination was received at least 14 days prior to symptom onset.<sup>23</sup> The study found that one dose of MPV was around 60 percent effective in mitigating the extent of clinical manifestations (eg, number of lesions and sites affected and other symptoms) in breakthrough mpox cases, regardless of HIV status.<sup>23</sup> Milder reinfections following wild-type mpox was also reported during the global outbreak.<sup>1</sup>

### Post-exposure vaccination

Further research is needed to better understand the efficacy of MPV for post-exposure prophylaxis with vaccination. A systematic review and meta-analysis found that vaccine effectiveness of a single dose of MPV given for post-exposure prophylaxis against clade IIb was 20 percent (95% CI -24 to 65 percent) and lower than when given pre-exposure.<sup>18</sup> The wide confidence intervals were attributed to the fact that many studies included cases that occurred within the 14-day period after vaccination and due to immortal time biases in the unvaccinated group.<sup>18</sup> A Spanish study reported a vaccine effectiveness of 65 percent (22.9–88.0 percent) at seven or more days after vaccination, and 79.3 percent (33.3–100 percent) at 14 or more days post-vaccination, though it did not specify the time between exposure and vaccination.<sup>18, 24</sup> When adjusting for immortal time bias, the vaccine effectiveness at less than 14 days post-exposure decreased from 78 percent to 19 percent.<sup>25</sup>

Nonetheless, post-exposure vaccination seems to offer some protection against mpox. An observational study in the US found that the incidence of mpox was significantly lower among individuals with known exposure or presumed exposure to mpox who received a single dose of MPV, given SC or ID, compared with those exposed and unvaccinated.<sup>26</sup> Of the 5,402 cases of mpox in males aged 18–49 years reported from 31 July to 3 September 2022, 4,606 cases (85.3 percent) were unvaccinated. The average incidence rate (cases per 100,000) was 14.3 times (95% CI 5.0–41.0) higher among unvaccinated individuals than for those who had received at least one dose of MPV at least 14 days prior to illness. Those who were vaccinated less than 13 days before illness or with an unknown vaccination date were excluded from the analysis.<sup>26</sup>

A small retrospective cohort study in France, of 108 participants given one dose of MPV post-exposure, found around 10 percent developed symptomatic breakthrough mpox within 21 days of mpox exposure.<sup>27</sup> In these cases, the clinical course was mild and none were hospitalised. Breakthrough infection was associated with sexual exposure (OR 12.5, 2.3–235,  $p = 0.018$ ), to some extent immunosuppression, and to earlier vaccination post-exposure, potentially due to increased risk awareness or more intense mpox exposure.<sup>27</sup>

## 14.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at

[www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

Store unopened vials at +2 to +8°C for maximum of 24 weeks (if within approved shelf-life, dependent on prior storage at -50°C ± -10°C). Protect from light. Do not refreeze once thawed. Allow vaccine to reach room temperature (maximum +25°C) and swirl the vial gently for at least 30 seconds before use.

When used for intradermal administration, store opened vials at +2 to +8°C for a maximum of 8 hours from the first vial puncture.

## 14.4.4 Dosage and administration

Each dose of mpox vaccine (MPV) is 0.5 mL, administered by subcutaneous injection (see section 2.2.3). Two doses are given at least four weeks apart.

In circumstances where dose sparing is required (in the case of vaccine supply shortage), intradermal (ID) administration of 0.1 mL of MPV can be given as pre-exposure prophylaxis (see section 14.5 for criteria, this is off-label use requires a prescription from an authorised prescriber and preferably written consent). MPV can be administered intradermally in the volar aspect of the forearm, the upper arm or scapular. Depending on availability of vaccine, up to two doses are given from four weeks to 2 years apart.

The need for booster doses has not been established and are not recommended currently for those who have received two doses.

### Co-administration with other vaccines

No studies to date have reported on coadministration of MPV (Jynneos) with other vaccines. Based on first principles, there is minimal risk of interference between MPV and other vaccines if given concurrently. Although the datasheet says to avoid concomitant administration with other vaccines and the attribution of adverse events is likely to be more difficult if given concurrently, this needs to be balanced with the risk of the individual not returning for other vaccinations. Concomitant administration of more than one vaccine can be considered at the same vaccination event alongside the delivery of MPV, with written consent.

# 14.5 Recommended immunisation schedule

## 14.5.1 Recommended groups

MPV is recommended and funded for individuals aged 18 years or over who are at high risk for mpox infection. (See section 14.5.5 for children and adolescents). As it is a non-replicating viral, MPV can be given to individuals with immunocompromising medical conditions or therapy, including those living with HIV infection or receiving immunosuppressive medications (see section 14.5.4).

Adolescents aged under 18 years who meet the criteria for being at high risk of mpox exposure (as listed below) are highly recommended MPV vaccination, to be given under a prescription with consent.

Pre-exposure vaccination is recommended for individuals at high risk of being exposed to mpox virus, includes those who are:

- at risk of occupational exposure to mpox
  - Laboratory staff working with orthopoxviruses
  - Health workers at risk of repeated exposures to patients with mpox.
  - Sex workers, particularly for those with clients who are risk of exposure to mpox
- at risk of mpox infection during a local mpox outbreak, as determined by a medical officer of health
- at risk of mpox infection because they are:
  - gay, bisexual or other men who have sex with men (GBMSM), transgender or non-binary people who in the past 6 months have had one of the following:
    - A new diagnosis of a sexually transmitted disease
    - More than one sex partner
    - Sex at a commercial venue
    - Sex in association with a large public event in an area where mpox transmission is likely to occur
  - people living with HIV, if at risk of mpox exposure
  - sexual partners of those at increased risk of mpox infection.
- People who anticipate experiencing any of the above.

Post-exposure vaccination is recommended to be given within 4 days preferably (no later than 14 days) of exposure to a confirmed mpox case (see 14.8.1).

This vaccine is not available for travel purposes, to areas with an active outbreak, unless the individuals meet the criteria for being at high risk of infection, as listed above.

## 14.5.2 Intradermal or subcutaneous administration

ID administration is only recommended for pre-exposure vaccination when vaccine supply is limited. If the SC route was used for the first dose, the vaccination course can be completed by ID injection for the second dose, and vice versa. This use is off-label and requires a prescription from an authorised prescriber and informed consent.

SC administration of the complete two-dose course is specifically recommended for:

- all individuals who are severely immunocompromised (see section 14.5.4)
- individuals with a history of keloid scarring
- children aged under 18 years (see section 14.5.5)

MPV should not be given ID to those specifically recommended SC administration.

## 14.5.3 Pregnancy and breastfeeding

Mpox can be severe in pregnant people and have adverse effects on the fetus.<sup>4,5</sup> There is limited data on the use of MPV in human pregnancy or assessing the effects in breastfed infants. As a non-replicating virus vaccine, no theoretical concerns related to pregnancy contraindicate the use of MPV in pregnancy or while lactating. The adverse event profile is expected to be similar to that seen in non-pregnant recipients. No pregnancy-related adverse events were reported when MPV was used in fewer than 300 pregnancies and no safety concerns were raised when an MVA-vectored Ebola vaccine has been given inadvertently in pregnancy.<sup>28</sup> Animal studies did not identify any evidence of harm to the fetus when given during or prior to gestation.

It is unknown whether the vaccine virus, MVA-BN, is excreted in human milk but it is considered unlikely to infect the infant since it is unable to replicate in human cells.

It is preferable to avoid the use of MPV in pregnancy or while breastfeeding, however, pregnant or lactating individuals at high risk of exposure to mpox are recommended to discuss vaccination with health professionals. In these situations, the risk from exposure to mpox infection in pregnancy, such as risk of fetal loss, severe disease and peripartum transmission, should be discussed and written informed consent acquired. For individuals aged under 18 years who are pregnant or breastfeeding, a prescription from an authorised prescriber is also required.

## 14.5.4 Immunocompromised individuals

Individuals with severe immunocompromise are recommended and prioritised to receive both MPV doses subcutaneously, given 4 weeks apart, for protection against potentially fatal disseminated mpox.

If indicated, MPV can be given to individuals with immunocompromising medical conditions or therapy, including those living with HIV infection or receiving immunosuppressive medications, because it contains a non-replicating virus. The immune response could be reduced in those who are severely immunosuppressed, it is

important to reduce the risk of exposure and ensure close contacts are vaccinated if at risk.

### 14.5.5 Children and adolescents

Although MPV is not approved for use in infants and children aged under 18 years, several paediatric clinical studies using MVA-BN as a viral vector (including Ebola, TB and malaria vaccine candidates) have demonstrated an acceptable safety profile.<sup>1</sup> Small studies where children were administered MPV pre or post-mpox exposure also reported no serious adverse events and a favourable safety profile.<sup>1</sup> Children and adolescents exposed to mpox are at high risk of severe mpox infection<sup>5</sup> and hence MPV is recommended for children at high risk of being infected. Give two doses subcutaneously at least four weeks apart. This is an off-label use and requires a prescription from an authorised prescriber.

Adolescents aged under 18 years who meet the criteria for being at high risk of mpox exposure (as listed in section 14.5.1) are highly recommended MPV vaccination, to be given with a prescription and consent.

### 14.5.6 Individuals who have had mpox infection

Individuals who have either been diagnosed with laboratory-confirmed mpox prior to vaccination or after the first dose are not recommended vaccination or further doses. This is because mpox infection likely confers adequate immune protection or boosts immunity in those recently vaccinated. For those with immunocompromise and diagnosed with mpox after their first dose of MPV, a second dose of MPV can be considered based on clinical judgement.

### 14.5.7 Individuals with a known history of smallpox vaccination

Two doses of MPV are recommended, particularly for individuals with immunocompromise including well-controlled HIV infection, regardless of smallpox (vaccinia) vaccination history.

## 14.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

### 14.6.1 Contraindications

MPV is contraindicated for anyone with a severe systemic allergic reaction (anaphylaxis) to a previous dose or any component of the vaccine, including a history of anaphylaxis to chicken protein.

MPV is contraindicated for anyone who has been diagnosed with myocarditis or pericarditis following a previous dose of this vaccine.

### 14.6.2 Precautions

Individuals with a history of severe allergy to any excipient or trace residual of the vaccine, including chicken or egg protein, benzonase, gentamicin and ciprofloxacin, can receive MPV following discussion with vaccinator to weigh the risk of severe allergy with the risk of mpox infection. In these cases, observe for 30 minutes following vaccination and give post-vaccine advice.

It is unknown whether MPV (Jynneos) is associated with an increased risk for myocarditis or pericarditis, however, there is a theoretical risk (see section 14.7.1). Those with previous myocarditis or pericarditis should have a risk-benefit discussion.

Subcutaneous, not intradermal, administration is preferred for individuals with a history of severe keloid scarring.

## 14.7 Potential responses and AEFIs

Immunisation-stress related responses, including palpitation, syncope and tachycardia, have been reported following administration of this vaccine.

Potential responses to this vaccine include injection-site pain, redness, swelling, itching at injection site and influenza-like symptoms such as muscle pain, headache, fatigue, nausea, chills and less commonly, fever and lymphadenopathy.<sup>29</sup> These are usually mild to moderate and short-lived for less than seven days. Local and more widespread rashes (non-vesicular) can occur within a few days of vaccination, which tend to be mild to moderate and resolve without sequelae. Responses are similar after dose two as observed after dose one.

Local reactions are more common after intradermal administered MPV and can last for a few weeks, longer than after subcutaneous injection. ID administration can result in more frequent and severe redness and itching at the injection site. Skin discolouration and/or nodules may persist for at least 30 days and remain after six months after ID administration.

### 14.7.1 AEFI

Although mild to moderate AEFI have occurred following vaccination with mpox, no serious adverse events have been reported to be causally associated with the vaccine. Adverse events were reported at similar rates for doses received by intradermal and subcutaneous administration.<sup>30</sup>

Active surveillance in Aotearoa New Zealand from the Post Vaccine Symptom Check (PVSC) survey of the MPV (Jynneos; administered via both ID and SC during the survey period from 26 January to June 2023) was in line with expected adverse events reported during clinical trials. Of those that reported experiencing a reaction, the most common were local reactions, fatigue, head/muscle and body aches, dizziness, chills and fever (unpublished data, Health New Zealand).

**Table 14.1: Active surveillance of adverse events following mpox vaccination from Post Vaccine Symptom Check survey, January to June 2023 (source: Health New Zealand)**

Adverse events	Survey Responses (%)		
	Days 1-7 (n=181)	Days 8-14 (n=128)	Days 1-14* (n=309)
Local reaction	62%	33%	50%
Fatigue or tiredness	23%	9%	17%
Headache, muscle or body aches or pain	16%	8%	13%
Dizziness or feeling lightheaded	7%	3%	5%
Chills	5%	2%	4%
Fever	4%	2%	3%

The day 42 survey included a question on whether consumers had been diagnosed with any rare medical conditions since receiving the vaccine. From the responses received, no one reported that they were diagnosed with Guillain-Barré syndrome (GBS), myocarditis, or pericarditis.

Based on the older replication-competent smallpox (vaccinia) vaccines, there is a theoretical risk of myocarditis and pericarditis with MPV. Clinical trials of MPV found no signal for myocarditis or pericarditis. Two cases were reported to the VAERS in the US after approximately 652,641 first doses and 334,568 second doses (incidence <3 per



million doses).<sup>30</sup> As the incidence of these adverse events is very rare, it is important to remain vigilant for potential symptoms in young men following MPV vaccination.

Bavarian Nordics' global safety database contained 9,585 AEFI from 3,363 individual case safety reports following approximately 1.7 million doses of MPV up to 31 July 2023 (1.2 million doses given in the US). The majority were general local and systemic inflammatory reactions. Many of the reports were either 'incorrect route of product administration' errors or immunisation-stress related responses following the change to ID injections. The passive reporting frequency of myocarditis (9 cases) or pericarditis (4 cases) was less than 1 per 100,000 doses.<sup>31</sup>

Clinical trials of MPV found that individuals with atopic dermatitis reported a higher frequency of adverse reactions than healthy individuals. Higher rates of injection site erythema and swelling, and slightly higher rates of systemic reactions were observed. Although around 7 percent experienced a flare-up or worsening of their skin condition during the clinical trials, this may have been in line with the underlying relapsing-remitting nature of the disease rather than in response to vaccination.<sup>32</sup>

## 14.8 Public health measures

It is a legal requirement that all cases be notified immediately on suspicion of mpox to the local medical officer of health.

Mpox should be considered a possible diagnosis for patients with rash that could be consistent with mpox, especially those with a history of travel endemic areas or countries experiencing cases in the past 21 days. Information about all recent travel, and sexual history should be collected.

PCR testing of samples vesicle/pustule fluid can be performed after communication with the local Medical Officer of Health and clinical microbiologist.

For further information see [www.tewhaturora.govt.nz/for-health-professionals/clinical-guidance/diseases-and-conditions/mpox/](http://www.tewhaturora.govt.nz/for-health-professionals/clinical-guidance/diseases-and-conditions/mpox/) and the mpox chapter of the *Communicable Disease Control Manual* available at [www.tewhaturora.govt.nz/for-health-professionals/clinical-guidance/communicable-disease-control-manual/mpox/](http://www.tewhaturora.govt.nz/for-health-professionals/clinical-guidance/communicable-disease-control-manual/mpox/)

### 14.8.1 Post exposure vaccination

Give one 0.5 mL dose of MPV subcutaneously, preferably within four days of exposure to mpox virus. Asymptomatic individuals can be offered vaccination up to 14 days after exposure with the aim of reducing severity of symptoms. A high-risk close contact can include:

- Direct physical contact with skin or mucous membranes of a case. (i.e., skin to skin, skin to mucous membranes, mucous membrane to mucous membrane).
- People whose occupation might put them at increased risk where there is a breach of protective personal equipment (PPE) (i.e., healthcare workers caring for those infected with mpox and laboratory workers handling mpox swabs).
- Direct contact with potentially contaminated materials (bed linens, healthcare equipment), crusts from lesions or with bodily fluids from a case.
- It also includes any household member who has had close physical contact with the mpox case or close contact with bedding, towels or clothing used by an individual with mpox.
- Those recommended to have the vaccine by their doctor.

If the individual remains mpox symptom-free for up to 4 weeks after exposure, give a second dose to provide longer lasting, particularly for those at risk of future exposures (ie would be considered the same as a pre-exposure vaccination).

## 14.9 Variations from the vaccine data sheet

Due to a lack of experience, the datasheet states concomitant administration with other vaccines should be avoided. However, in situations where there is a risk that the individual may not return for further vaccinations, thereby putting them at risk of other diseases, then coadministration, in separate limbs, can be considered.

The data sheet indicates the use of MPV for the prevention of mpox in adults aged from 18 years. Health New Zealand | Te Whatu Ora recommends the vaccination of children and adolescents if at risk of mpox infection (see section 14.5.5). A prescription and written informed consent are required.

Intradermal administration or mixed routes of administration (ID and SC) of MPV is advised at times of shortage of supply. This is not the approved route of administration on the vaccine datasheet and require would a prescription and written consent. Subcutaneous administration is recommended for certain groups, regardless of vaccine supply (see section 14.5.2).

## References

1. World Health Organization. Smallpox and mpox (orthopoxviruses) vaccine position paper. *Weekly Epidemiological Record*, 2024. 99(34): p. 429-456.
2. Lapa D, Carletti F, Mazzotta V, et al. Monkeypox virus isolation from a semen sample collected in the early phase of infection in a patient with prolonged seminal viral shedding. *Lancet Infectious Diseases*, 2022. 22(9): p. 1267-1269.

3. Peiro-Mestres A, Fuertes I, Camprubi-Ferrer D, et al. Frequent detection of monkeypox virus DNA in saliva, semen, and other clinical samples from 12 patients, Barcelona, Spain, May to June 2022. *Euro Surveill*, 2022. 27(28).
4. Mbala PK, Huggins JW, Riu-Rovira T, et al. Maternal and fetal outcomes among pregnant women with human monkeypox infection in the Democratic Republic of Congo. *Journal of Infectious Diseases*, 2017. 216(7): p. 824-828.
5. Sanchez Clemente N, Coles C, Paixao ES, et al. Paediatric, maternal, and congenital mpox: a systematic review and meta-analysis. *Lancet Glob Health*, 2024. 12(4): p. e572-e588.
6. Laurenson-Schafer H, Sklenovska N, Hoxha A, et al. Description of the first global outbreak of mpox: an analysis of global surveillance data. *Lancet Glob Health*, 2023. 11(7): p. e1012-e1023.
7. Hoxha A, Kerr SM, Laurenson-Schafer H, et al. Mpox in children and adolescents during multicountry outbreak, 2022-2023. *Emerging Infectious Diseases*, 2023. 29(10): p. 2125-2129.
8. Gilbert SC. Clinical development of Modified Vaccinia virus Ankara vaccines. *Vaccine*, 2013. 31(39): p. 4241-6.
9. Stittelaar KJ, van Amerongen G, Kondova I, et al. Modified vaccinia virus Ankara protects macaques against respiratory challenge with monkeypox virus. *Journal of Virology*, 2005. 79(12): p. 7845-51.
10. Poland GA, Kennedy RB, Tosh PK. Prevention of monkeypox with vaccines: a rapid review. *Lancet Infectious Diseases*, 2022. 22(12): p. e349-e358.
11. Berry MT, Khan SR, Schlub TE, et al. Predicting vaccine effectiveness for mpox. *Nat Commun*, 2024. 15(1): p. 3856.
12. Ghazy RM, Elrewany E, Gebreal A, et al. Systematic review on the efficacy, effectiveness, safety, and immunogenicity of monkeypox vaccine. *Vaccines (Basel)*, 2023. 11(11).
13. Overton ET, Lawrence SJ, Wagner E, et al. Immunogenicity and safety of three consecutive production lots of the non replicating smallpox vaccine MVA: A randomised, double blind, placebo controlled phase III trial. *PLoS One*, 2018. 13(4): p. e0195897.
14. Greenberg RN, Overton ET, Haas DW, et al. Safety, immunogenicity, and surrogate markers of clinical efficacy for modified vaccinia Ankara as a smallpox vaccine in HIV-infected subjects. *Journal of Infectious Diseases*, 2013. 207(5): p. 749-58.
15. Oom AL, Kottkamp AC, Wilson KK, et al. 2024 (preprint). The durability and avidity of MPXV-specific antibodies induced by the two-dose MVA-BN mpox vaccine. DOI: 10.1101/2024.01.28.24301893 (accessed 19 September 2024)
16. Greenberg RN, Hay CM, Stapleton JT, et al. A randomized, double-blind, placebo-controlled phase II trial investigating the safety and immunogenicity of Modified Vaccinia Ankara smallpox vaccine (MVA-BN®) in 56-80-year-old subjects. *PLoS One*, 2016. 11(6): p. e0157335.
17. Mazzotta V, Lepri AC, Matusali G, et al. Immunogenicity and reactogenicity of modified vaccinia Ankara pre-exposure vaccination against mpox according to previous smallpox vaccine exposure and HIV infection: prospective cohort study. *EClinicalMedicine*, 2024. 68: p. 102420.
18. Pischel L, Martini BA, Yu N, et al. Vaccine effectiveness of 3rd generation mpox vaccines against mpox and disease severity: A systematic review and meta-analysis. *Vaccine*, 2024. 42(25): p. 126053.
19. Dalton AF, Diallo AO, Chard AN, et al. Estimated effectiveness of JYNNEOS vaccine in preventing mpox: A multijurisdictional case-control study - United States, August 19, 2022-March 31, 2023. *MMWR: Morbidity and Mortality Weekly Report*, 2023. 72(20): p. 553-558.

20. Golden MR, Soge OO, Mills M, et al. Asymptomatic and subclinical mpox: An association with Modified Vaccinia Ankara vaccine. *Sexually Transmitted Diseases*, 2024. 51(5): p. 342-347.
21. Thy M, Peiffer-Smadja N, Mailhe M, et al. Breakthrough infections after postexposure vaccination against mpox. *New England Journal of Medicine*, 2022. 387(26): p. 2477-2479.
22. Cornelisse VJ, Kearley JJM, Vargas Castillo J, et al. Case study: breakthrough mpox infection in Aotearoa New Zealand and Australia after completed two-dose course of subcutaneous modified vaccinia Ankara (MVA-BN) vaccines. *Sex Health*, 2023. 20(6): p. 585-587.
23. Allard R, Leclerc P, Bergeron G, Cadieux G. Breakthrough cases of mpox: One-dose vaccination is associated with milder clinical manifestations. *J Infect Public Health*, 2024. 17(4): p. 676-680.
24. Fontán-Vela M, Hernando V, Olmedo C, et al. Effectiveness of modified Vaccinia Ankara-Bavaria Nordic vaccination in a population at high risk of mpox: A Spanish cohort study. *Clinical Infectious Diseases*, 2024. 78(2): p. 476-483.
25. Rosen JB, Arciuolo RJ, Pathela P, et al. JYNNEOS effectiveness as post-exposure prophylaxis against mpox: Challenges using real-world outbreak data. *Vaccine*, 2024. 42(3): p. 548-555.
26. Payne AB, Ray LC, Kugeler KJ, et al. Incidence of monkeypox among unvaccinated persons compared with persons receiving  $\geq 1$  JYNNEOS vaccine dose - 32 U.S. jurisdictions, July 31-September 3, 2022. *MMWR: Morbidity and Mortality Weekly Report*, 2022. 71(40): p. 1278-1282.
27. Merad Y, Gaymard A, Cotte L, et al. Outcomes of post-exposure vaccination by modified vaccinia Ankara to prevent mpox (formerly monkeypox): a retrospective observational study in Lyon, France, June to August 2022. *Euro Surveillance*, 2022. 27(50).
28. Khalil A, Samara A, O'Brien P, et al. Monkeypox vaccines in pregnancy: lessons must be learned from COVID-19. *Lancet Glob Health*, 2022. 10(9): p. e1230-e1231.
29. Jackson LA, Frey SE, El Sahly HM, et al. Safety and immunogenicity of a modified vaccinia Ankara vaccine using three immunization schedules and two modes of delivery: A randomized clinical non-inferiority trial. *Vaccine*, 2017. 35(13): p. 1675-1682.
30. Duffy J, Marquez P, Moro P, et al. Safety monitoring of JYNNEOS vaccine during the 2022 mpox outbreak - United States, May 22-October 21, 2022. *MMWR: Morbidity and Mortality Weekly Report*, 2022. 71(49): p. 1555-1559.
31. Weidenthaler H, Vidojkovic S, Martin BK, De Moerlooze L. Real-world safety data for MVA-BN: Increased frequency of syncope following intradermal administration for immunization against mpox disease. *Vaccine*, 2024. 42(22): p. 126024.
32. Greenberg RN, Hurley MY, Dinh DV, et al. A multicenter, open-label, controlled phase II study to evaluate safety and immunogenicity of MVA smallpox vaccine (IMVAMUNE) in 18-40-year-old subjects with diagnosed atopic dermatitis. *PLoS One*, 2015. 10(10): p. e0138348.

# 15 Mumps

## Key information

Mode of transmission	Airborne droplets or by direct contact with saliva or urine from an infected person.
Incubation period	About 16 to 18 days, ranging from 12 to 25 days.
Period of communicability	For contact tracing purposes, the recommended period of communicability is from 2 days before to 5 days after the onset of parotitis. The virus is also transmitted by asymptomatic infections.
Incidence and burden of disease	Outbreaks are continuing to occur in New Zealand.
Funded vaccine	MMR (Priorix) is a live attenuated vaccine.
Dose, presentation, route	0.5 mL per dose after reconstitution. Pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. Intramuscular or subcutaneous injection.
Funded vaccine indications and schedule	Children at ages 12 months and 15 months. Adults who are susceptible to one or more of measles, mumps and rubella. For (re)vaccination following immunosuppression (if the individual is immunocompetent enough to safely receive the vaccine).
Recommended	All adults born since January 1969 should be up to date with two doses of MMR or have evidence of immunity to all three vaccine components. It is particularly important for health care workers, individuals who work with children, armed forces personnel, staff of correctional facilities, long-term care facilities and immigration/refugee centres and laboratory staff. All vaccine-eligible travellers, particularly to high-risk countries
Vaccine effectiveness	After one dose, MMR is 64–66 percent effective against laboratory-confirmed mumps and 83–88 percent after two vaccine doses.
Duration of protection	At least 10 years; protection is best achieved via herd immunity from high immunisation coverage.
Contraindication and precautions	MMR is contraindicated for anaphylaxis to neomycin, immunocompromise and in pregnancy. See section 12.6 for cautions around receipt of blood products and other live vaccines, and other precautions. MMR may temporarily suppress tuberculin skin test reactivity.

*Continued overleaf*

Potential responses to vaccine	MMR is generally well tolerated. There can be mild salivary gland swelling after 10–14 days. If there is fever and rash 6–12 days after vaccination this is due to measles and rubella components. Alert parents of possible febrile seizure risk, particularly for those with a history of seizure.
Public health measures	Notify the local medical officer of health immediately on suspicion of wild-type mumps. (see section 15.8)

## 15.1 Virology

Mumps is a paramyxovirus, genus *Rubulavirus*, with a single-stranded RNA genome. It is rapidly inactivated by heat, formalin, ether, chloroform and light.

## 15.2 Clinical features

Mumps is transmitted by airborne droplets or direct contact with infected respiratory tract secretions or urine. Humans are the only known host of the virus.

People with mumps are most infectious from two days before to five days after the onset of parotitis;<sup>1</sup> therefore, this is the recommended period of communicability for contact tracing purposes.<sup>1</sup> However, mumps virus has been isolated in saliva from seven days before to nine days after the onset of parotitis. Asymptomatic cases also can be infectious.<sup>1</sup>

Classic mumps, an acute viral illness, is characterised by fever, headache, and swelling and tenderness of one or more parotid (salivary) glands. Mumps starts as an upper respiratory tract infection that disseminates via plasma viremia to glandular tissue, kidneys and central nervous system. Some patients may experience involvement of other organs (eg, orchitis or meningitis) without salivary gland involvement. At least 30 percent of mumps infections in children are asymptomatic.<sup>2</sup>

The complications of symptomatic mumps include clinically evident aseptic meningitis in 5–10 percent (almost always without sequelae), orchitis (usually unilateral) in up to one-third of post-pubertal males, and oophoritis and mastitis in 5–30 percent of post-pubertal females. Sterility is exceedingly rare in males and unconfirmed in females.<sup>2</sup> Profound sudden onset unilateral nerve deafness occurs in 1 in 15,000–20,000 cases. Pancreatitis, neuritis, arthritis, myelitis, nephritis, thyroiditis and pericarditis may also occur.<sup>3</sup>

Encephalitis has been reported to occur at a frequency of between 1 in 400 and 1 in 6,000, the latter being a more realistic estimate. The case fatality rate for mumps encephalitis is 1.4 percent, while the overall mumps case fatality rate is reported as 1.8 per 10,000 cases. Mumps in the first trimester of pregnancy may increase the rate of spontaneous abortion, but there is no evidence that it causes fetal abnormalities.



## 15.3 Epidemiology

### 15.3.1 Global burden of disease

Prior to the introduction of immunisation, approximately 85 percent of adults had evidence of past mumps infection. Most infections in those aged under 2 years are subclinical, while those affected in adulthood are more likely to experience severe disease. The peak incidence was in late winter and spring.

More recently, there have been numerous reports of increasing numbers of mumps cases in the US, the UK and elsewhere, thought to be due to a waning of vaccine-induced immunity.<sup>4</sup> Many cases are reported in 18–30-year olds.<sup>5</sup> Outbreaks appear to occur mainly in those in crowded situations, such as university students and other close-knit communities, and have been associated with international travel.<sup>6</sup>

### 15.3.2 New Zealand epidemiology

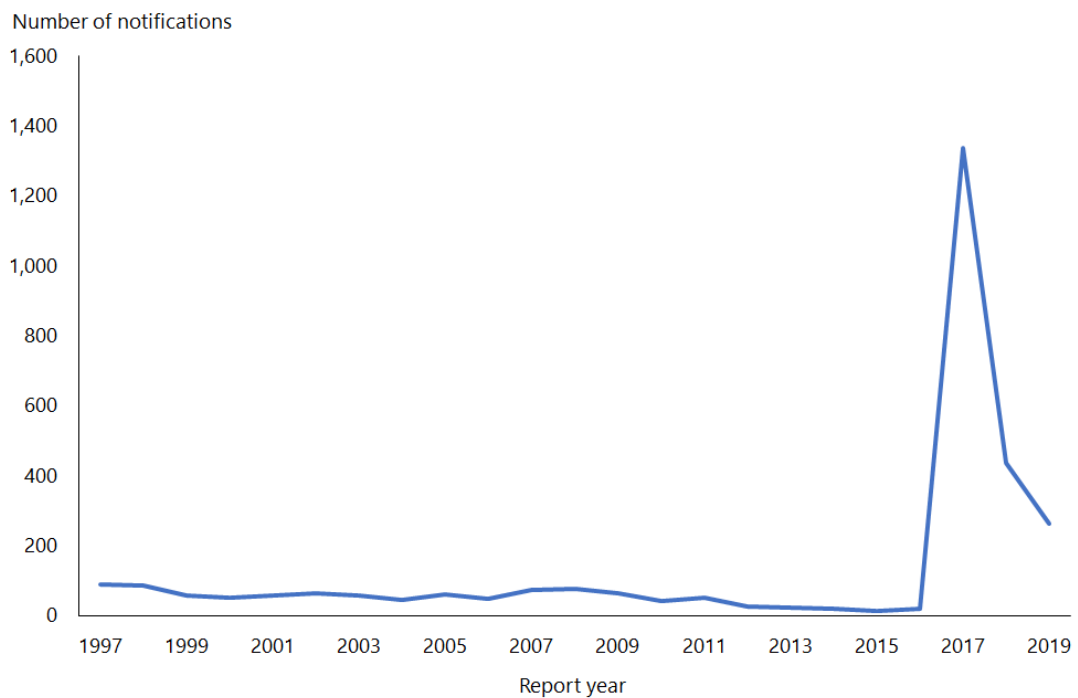
Mumps vaccine (as MMR) was introduced to the Schedule in 1990 for children aged 12 to 15 months, with a second dose introduced in 1992 for children aged 11 years. A two-dose schedule at ages 15 months and 4 years was introduced in 2001 (see Appendix 1 for more information). Prior to 2017, the last mumps epidemic had occurred in 1994. The current two-dose schedule was introduced in 2020 at age 12 months and 15 months.

People aged 12–29 years are at the greatest risk of catching mumps, as they are the group least likely to have been fully immunised as children. Those born in Fiji, Tonga, Kiribati, Nauru, Papua New Guinea, Solomon Islands, Tuvalu and Vanuatu as well as many mainland nations in Asia may not have been offered mumps immunisation as children.

From 1 January 2017 to 31 December 2019, 1,773 cases of mumps were notified (ESR, 8 June 2020). During 2019, the notification rate was 5.4 per 100,000 (264 cases) compared with 9.0 per 100,000 (435 cases) in 2018. In 2019, the highest notification rates were seen in young adults aged 15 to 29 years. Cases were predominantly in the Auckland region, with the highest notification rates in the Middle Eastern/Latin American/African (MELAA) ethnic group (19.9 per 100,000) and Pacific people (15.2 cases per 100,000; ESR, 8 June 2020).



**Figure 15.1: Notified cases of mumps, 1997–2019**



Source: ESR

Outbreaks continue to occur throughout New Zealand. For further details refer to the ESR surveillance reports for notifiable diseases (available at [www.esr.cri.nz/digital-library/notifiable-disease-dashboard/](http://www.esr.cri.nz/digital-library/notifiable-disease-dashboard/)).

## 15.4 Vaccines

### 15.4.1 Available vaccines

Mumps vaccine is one of the components of the live attenuated MMR, considered in section 12.4 (and MMRV mentioned in section 24.4). There are no single antigen mumps vaccines available.

#### Funded vaccine

MMR vaccine funded as part of the Schedule is Priorix (GSK), which contains attenuated Schwarz strain measles, RA 27/3 rubella and Jeryl Lynn mumps. See section 12.4.1 for more information.

## Other vaccines

M-M-R II (MSD) was the funded vaccine prior to the 1 July 2017 Schedule change (see section 12.4.1).

### 15.4.2 Efficacy and effectiveness

A 2012 Cochrane review of the safety and effectiveness of MMR estimated that a single dose of MMR was 69–81 percent effective in preventing clinical mumps. Effectiveness of MMR in preventing laboratory-confirmed mumps cases in children and adolescents was estimated to be between 64 and 66 percent for one dose and between 83 and 88 percent for two vaccine doses.<sup>7</sup>

A two-dose vaccination schedule and high immunisation coverage has been very successful in controlling disease. However, outbreaks can still occur in highly immunised populations, because two doses of vaccine are not 100 percent effective. Community coverage needs to be 85–90 percent by 2 years of age to prevent outbreaks from asymptomatic cases.<sup>2</sup> Declining vaccine-induced mumps immunity may also contribute to outbreaks.<sup>4</sup> Data from Finland shows that 20 years after the second MMR dose, immunity to mumps declined with just under 75 percent being seropositive.<sup>8</sup> The antibody avidity also decreased over time, by 24 percent for mumps.<sup>9</sup>

Two doses of MMR are required to ensure a high rate of seroprotection against mumps and induce antibody responses that persist for at least 10 years post-vaccination.<sup>10, 11</sup> However, waning in immunity has been observed in young adults and a third dose of MMR has been used safely and effectively during mumps outbreaks in highly immunised populations.<sup>12, 13</sup> Although the mumps vaccine is not quite as effective as measles and rubella vaccines, cases that have been vaccinated are significantly less likely to experience complications from disease such as orchitis, meningitis and hospitalisation.<sup>14</sup>

### 15.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at [www.tewhaturora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhaturora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

Store at +2°C to +8°C. Do not freeze.

MMR must be reconstituted only with the diluents supplied by the manufacturer. Use MMR as soon as possible after reconstitution. If storage is necessary, reconstituted vaccine can be stored at +2°C to +8°C for up to eight hours.

## 15.4.4 Dosage and administration

The dose of MMR is all of the reconstituted vaccine (approximately 0.5 mL) administered by intramuscular injection, or subcutaneous injection if indicated (see section 2.2.3).

### Co-administration with other vaccines

MMR can be given concurrently with other vaccines, by using separate syringes and giving the injections at different sites. If not given concurrently, live vaccines should be given at least four weeks apart. (See also section 2.2.7 for information about multiple injections at the same visit.)

### Interchangeability

The two brands of MMR available in New Zealand (Priorix and M-M-R II) may be used interchangeably for completion of a course.<sup>15</sup>

## 15.5 Recommended immunisation schedule

**Table 15.1: Recommended MMR vaccination schedule**

	Schedule
Usual childhood schedule <sup>a</sup>	2 doses: at ages 12 months and 15 months
Catch-up <sup>b</sup> for children, adolescents and adults	2 doses: at least 4 weeks apart

- If MMR is given to children aged under 12 months for outbreak control, 2 further MMR doses are still required at ages 12 months (at least 4 weeks after previous dose) and 15 months.
- MMR is funded for those who are susceptible to one or more of the three diseases.

### 15.5.1 Usual childhood schedule

Two doses of mumps-containing vaccine as MMR are recommended at age 12 months and 15 months (Table 15.1).

The second dose can be given as soon as four weeks after the first dose.

Children who receive MMR when aged under 11 months (MMR0) during an outbreak require two further doses administered after age 12 months. No opportunity should be missed to achieve immunity.

## 15.5.2 Catch-up

MMR is recommended and funded for children, adolescents and adults (especially those born since 1 January 1969) who are known to be susceptible to one or more of the three diseases (two doses, four weeks apart). See sections 12.5.2 and 21.5.2.

## 15.5.3 Immunocompromise

### Contacts of immunocompromised individuals

In general, MMR is contraindicated in immunocompromised individuals (see section 4.3). These individuals can be partially protected from exposure to infection by ensuring that all contacts are fully immunised (funded), including hospital staff and family members. There is no risk of transmission of MMR vaccine viruses from a vaccine recipient to the immunocompromised individual (see section 12.7.2).

See also in section 4.3.1.

### (Re)vaccination following immunosuppression

MMR is funded for (re)vaccination following immunosuppression. However, it is important to be sure that the individual is immunocompetent enough to safely receive the vaccine.

### HIV infection

Discuss vaccination of individuals with HIV infection with their specialist (see 'HIV infection' in section 4.3.12).

MMR is recommended for all HIV-positive children, whether they are symptomatic or asymptomatic, if their CD4+ lymphocyte percentage is 15 percent or greater. Asymptomatic children who are not severely immunocompromised are recommended to receive MMR from age 12 months to provide early protection against the three diseases. Susceptible HIV-positive children and adults aged 14 years and older may receive MMR if their CD4+ lymphocyte count is at least 200 cells/mm<sup>3</sup>. Administration of MMR with CD4+ counts below these recommended levels has been associated with vaccine-related pneumonitis (from the measles component).<sup>16</sup>

## 15.5.4 Pregnancy and breastfeeding

MMR is contraindicated during pregnancy. Pregnancy should be avoided for four weeks after MMR vaccination.<sup>16, 17</sup> (see section 15.6.1).

## After delivery

If MMR and Rhesus anti-D IG are required after delivery, both the vaccine and anti-D IG may be given at the same time, in separate sites with separate syringes. The vaccine may be given at any time after the delivery. Anti-D IG does not interfere with the antibody response to the vaccine, but whole blood transfusion does inhibit the response in up to 50 percent of vaccines recipients (see section A6.4.1). MMR can safely be given to breastfeeding women.

# 15.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general vaccine contraindications.

## 15.6.1 Contraindications

See section 12.6.1 for specific MMR contraindications.

Anaphylaxis to a previous dose of MMR or any of the vaccine components (including neomycin) is a contraindication to a further dose of MMR.

MMR should not be given to women who are pregnant, and pregnancy should be avoided for four weeks after immunisation.<sup>16, 17</sup> However, inadvertent immunisation with a rubella-containing vaccine in early pregnancy is no longer considered an indication for termination of pregnancy. There have been no cases of teratogenic damage from vaccine virus despite intensive surveillance in the US, the UK and Germany.<sup>18</sup>

## 15.6.2 Precautions

Egg allergy, including anaphylaxis, is **not** a contraindication to MMR. See section 12.6.3 for more information, and section 12.6.2 for further precautions.

For infants aged under 12 months, please discuss immunomodulatory therapies taken during pregnancy with infant's mother or specialist, or contact IMAC before administration of MMR0 in an outbreak situation. See section 4.2.5.

## 15.7 Potential responses and AEFIs

See sections 12.7 and 21.7.

## 15.8 Public health measures

It is a legal requirement that all cases of mumps be notified immediately on suspicion to the local medical officer of health.

For details on control measures and notification, refer to the latest version of the 'Mumps' chapter of the *Communicable Disease Control Manual* (available at [www.tewhatoruora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/mumps/](http://www.tewhatoruora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/mumps/)).

### 15.8.1 Diagnosis

All suspected mumps cases should have diagnostic testing (eg, by buccal swab detection of wild-type mumps virus by PCR or culture) as there are other causes of parotitis other than the mumps virus. See the latest version of the 'Mumps' chapter of the *Communicable Disease Control Manual* for the specimens required for laboratory confirmation of mumps, or discuss these with the local laboratory (See case definition at [www.tewhatoruora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/mumps/](http://www.tewhatoruora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/mumps/)).

### 15.8.2 Susceptible contacts

A susceptible contact is anyone born after 1981 who has not had mumps infection or has not been fully vaccinated for their age.

All susceptible contacts should be offered MMR vaccinations. (All vaccinations given should be recorded on the AIR.) There is no increased risk of adverse events after immunisation during the incubation period of mumps or if the recipient is already immune. Immunoglobulin is ineffective after exposure to mumps.

### 15.8.3 Post-exposure prophylaxis

Passive immunisation is not effective against mumps. Active immunisation with MMR is not considered effective against incubating infection, but MMR should be offered to susceptible contacts for protection against future exposure.

For detailed information see *Management of Cases and Management of Contacts* in the mumps chapter of the *Communicable Disease Control Manual* at [www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/mumps/](http://www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/mumps/)

## 15.9 Variations from the vaccine data sheet

See section 12.9 for variations from the MMR (Priorix) data sheet.

### References

1. Ministry of Health. 2012. Mumps in *Communicable Disease Control Manual*. Wellington. URL: <https://www.health.govt.nz/publication/communicable-disease-control-manual>. (accessed 10 May 2022)
2. Rubin S. 2018. Mumps Vaccines, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
3. American Academy of Pediatrics. 2018. Mumps. in *Red Book: 2018 Report of the Committee on Infectious Diseases*, Kimberlin D, Brady M, Jackson M, and Long S (eds). Elk Grove Village, IL. URL: <https://redbook.solutions.aap.org/book.aspx?bookid=2205>. (accessed 3 July 2020)
4. Albertson JP, Clegg WJ, Reid HD, et al. Mumps Outbreak at a University and Recommendation for a Third Dose of Measles-Mumps-Rubella Vaccine - Illinois, 2015-2016. *MMWR: Morbidity and Mortality Weekly Report*, 2016. 65(29): p. 731-4.
5. Public Health England. 2017. Laboratory-confirmed cases of measles, mumps and rubella, England: October to December 2016. *Infection Report*. 11(8): p. 1-5. URL: [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/594801/hpr0817\\_mmr.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/594801/hpr0817_mmr.pdf) (accessed 11 March 2020)
6. Centers for Disease Control and Prevention. 2019 *Measles Cases and Outbreaks*. CDC; 2019 [updated 17 September 2019]; URL: <https://www.cdc.gov/mumps/outbreaks.html>. (accessed 06 November 2019)
7. Demicheli V, Rivetti A, Debalini MG, Di Pietrantonj C. Vaccines for measles, mumps and rubella in children. *Cochrane Database Syst Rev*, 2012(2): p. CD004407.
8. Davidkin I, Jokinen S, Broman M, et al. Persistence of measles, mumps, and rubella antibodies in an MMR-vaccinated cohort: a 20-year follow-up. *Journal of Infectious Diseases*, 2008. 197(7): p. 950-6.
9. Kontio M, Jokinen S, Paunio M, et al. Waning antibody levels and avidity: implications for MMR vaccine-induced protection. *Journal of Infectious Diseases*, 2012. 206(10): p. 1542-8.
10. Santos EM, Silva e Sa GR, Siqueira MM, et al. Immune response to the mumps component of the MMR vaccine in the routine of immunisation services in the Brazilian National Immunisation Program. *Memorias do Instituto Oswaldo Cruz*, 2014. 109(3): p. 335-9.



11. Carryn S, Feysaguet M, Povey M, Di Paolo E. Long-term immunogenicity of measles, mumps and rubella-containing vaccines in healthy young children: A 10-year follow-up. *Vaccine*, 2019. 37(36): p. 5323-5331.
12. Cardemil CV, Dahl RM, James L, et al. Effectiveness of a Third Dose of MMR Vaccine for Mumps Outbreak Control. *New England Journal of Medicine*, 2017. 377(10): p. 947-956.
13. Ogbuanu IU, Kutty PK, Hudson JM, et al. Impact of a third dose of measles-mumps-rubella vaccine on a mumps outbreak. *Pediatrics*, 2012. 130(6): p. e1567-74.
14. Hahné S, Whelan J, van Binnendijk R, et al. Mumps vaccine effectiveness against orchitis. *Emerging Infectious Diseases*, 2012. 18(1): p. 191-3.
15. Australian Technical Advisory Group on Immunisation (ATAGI). 2018. Mumps. in *Australian Immunisation Handbook*. Canberra. URL: <https://immunisationhandbook.health.gov.au/vaccine-preventable-diseases/mumps>. (accessed 20 October 2019)
16. American Academy of Pediatrics. 2018. Measles. in *Red Book: 2018 Report of the Committee on Infectious Diseases*, Kimberlin D, Brady M, Jackson M, and Long S (eds). Elk Grove Village, IL. p. 537-550. URL: <https://redbook.solutions.aap.org/redbook.aspx>. (accessed 3 July 2020)
17. Strebel P, Papania M, Gastañaduy P, Goodson J. 2018. Measles Vaccine, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
18. Reef SE, Plotkin S. 2018. Rubella Vaccines, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.

# 16 Pertussis (whooping cough)

## Key information

Mode of transmission	By aerosolised droplets.	
Incubation period	7–10 days (range 5–21 days).	
Period of communicability	For control purposes, in untreated cases the communicable stage lasts from the catarrhal stage to 3 weeks after the onset of paroxysmal cough. When treated communicability lasts approximately 2–5 days from the first dose.	
Incidence and burden of disease	Widespread outbreaks occur every 3–5 years. Infants aged under 12 months are at highest risk from pertussis, particularly those who have received fewer than two doses of vaccine and if the mother did not receive vaccine in pregnancy.	
Funded vaccines	DTaP-IPV-HepB/Hib (Infanrix-hexa). DTaP-IPV (Infanrix-IPV). Tdap (Boostrix).	
Dose, presentation, route	0.5 mL per dose. DTaP-IPV-HepB/Hib: pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. DTaP-IPV, Tdap: pre-filled syringe. Intramuscular injection.	
Funded vaccine indications and schedule	During each pregnancy (recommended from 16 weeks' gestation)	Tdap
	6 weeks, 3 months and 5 months	DTaP-IPV-HepB/Hib
	4 years	DTaP-IPV
	11 years	Tdap
	45 years (catch-up, if individual has not received 4 previous tetanus doses)	Tdap
	65 years	Tdap
	Parents or primary caregivers of infants admitted to neonatal intensive or special care baby units for more than 3 days and whose mothers had not received Tdap at least 14 days prior to birth	Tdap
	For vaccination of previously unimmunised or partially immunised patients	DTaP-IPV-HepB/Hib, DTaP-IPV or Tdap
	For (re)vaccination of eligible patients	

*Continued overleaf*

Vaccine effectiveness	Vaccination in pregnancy is over 90 percent effective in preventing pertussis in infants up to age 3 months. A 3-dose primary course in infants has 84 percent efficacy against hospitalisation for pertussis.
Contraindications	Contraindicated where anaphylaxis to vaccine or vaccine components is proven.
Potential responses to vaccine	Extensive limb swelling occurs more commonly after increasing number of doses of DTaP. Affecting less than in 2 percent of children, this is typically painless and resolves spontaneously.
Public health measures	Notify the local medical officer of health immediately on suspicion of wild-type pertussis. (see section 16.8)
Post-exposure prophylaxis	For management of contacts, see section 16.8

## 16.1 Bacteriology

Pertussis (whooping cough) is a bacterial respiratory infection caused by *Bordetella pertussis*, an exotoxin-producing gram-negative bacillus. The bacillus is fastidious (requires special techniques to grow in culture) and will often have decreased in numbers by the time the typical cough develops, making laboratory confirmation by culture difficult. The availability of sensitive and specific PCR and serological assays has improved laboratory confirmation of suspected *B. pertussis* infection (see section 16.8).

## 16.2 Clinical features

Pertussis is highly transmissible. It is one of the most infectious vaccine-preventable diseases in humans. The rate of transmission is several-fold greater than most respiratory pathogens, including influenza, such that in a non-immune population, approximately 5–17 secondary pertussis cases are expected from one case (see section 1.2.1).<sup>1</sup> Transmission occurs by aerosolised droplets, and the incubation period is 7–10 days (range 5–21 days).

There are three stages of typical pertussis infection:

1. Catarrhal stage – rhinorrhoea and irritating mild cough (typically lasting 7–10 days).
2. Paroxysmal stage – paroxysms (bursts) of coughing; in children, these may end in vomiting, cyanosis or apnoea and inspiratory gasp or whoop (1–6 weeks). Usually afebrile.
3. Convalescent stage – less persistent cough, gradual recovery (up to 10 weeks).

The communicable period lasts from the onset of symptoms to three weeks after the start of the paroxysmal stage.

Clinical presentation varies with age, immunisation status and previous infection. Pertussis must be considered in infants presenting with apnoea, since apnoea and/or cyanosis may precede paroxysmal cough.<sup>2</sup> In school-aged children, inspiratory whoop, post-tussive vomiting and the absence of wheezing and fever distinguish pertussis from other causes of coughing illnesses.<sup>3,4</sup> Almost all pertussis infections in adolescents and adults occur in the context of previous infection and/or immunisation. Persistent cough for more than 14 days is the cardinal feature in adults.<sup>4-6</sup> Coughing is often paroxysmal and worsens at night, with the patient waking with a choking sensation, but post-tussive vomiting and whoop are infrequent.

Studies performed in several countries during both epidemic and non-epidemic periods have shown that between 12 and 37 percent of school-aged children, adolescents and adults with persistent cough (lasting 14 days or more) have evidence of recent *B. pertussis* infection.<sup>3,5,7-9</sup> A primary care-based study in New Zealand performed during the early phase of the 2011–2013 epidemic showed recent *B. pertussis* infection in 17 percent of children aged 5–16 years and 7 percent of adults aged 17–49 years presenting to primary care with a persistent cough of two or more weeks' duration.<sup>10</sup>

The disease is most often severe in infants in the first few months of life. One in six infants with pertussis sufficiently severe to require intensive care admission will either die or be left with brain or lung damage.<sup>11</sup> The most common complications of pertussis are secondary infections, such as otitis media and pneumonia, and the physical sequelae of paroxysmal coughing, (eg, petechiae and other haemorrhages within subconjunctiva, nasopharynx and central nervous system; pneumothorax; hernia; and urinary incontinence). At the peak of the paroxysmal phase, vomiting can lead to weight loss especially in infants and young children.

## 16.3 Epidemiology

The epidemiology of *B. pertussis* infection and pertussis disease differ. Infection occurs across the age spectrum, and repeated infection without disease is common.<sup>12</sup> The endemic circulation of *B. pertussis* in older children and adults provides a reservoir for spread of the infection and the development of severe disease in incompletely vaccinated infants. The high prevalence of subclinical infections in household contacts of pertussis cases indicates a significant role in disease transmission to young infants.<sup>13</sup> <sup>14</sup> As observed in Australia, seasonal peaks in incidence in children aged less than 5 years occurred 1–2 months later than for the general population, supporting the theory that older household members are sources of infection to younger children.<sup>15</sup>

## 16.3.1 Global burden of disease

Pertussis mortality and morbidity rates continue to be highest in the first year of life.<sup>13</sup> In the US during the 1940s pertussis resulted in more infant deaths than measles, diphtheria, poliomyelitis and scarlet fever combined.<sup>16</sup> Beyond age 3 years mortality rates have always been relatively low. In immunised populations virtually all deaths occur in the first two months of life, and deaths in toddlers and preschool-aged children have largely disappeared. Among infants, younger age, lack of immunisation, low socioeconomic status, premature gestation, low birthweight and female gender are associated with an increased risk of fatal pertussis.<sup>17</sup>

Pertussis mortality and morbidity is under-reported.<sup>18, 19</sup> It is estimated that there are three times more deaths due to pertussis than are reported in high-income countries.<sup>18, 20, 21</sup> The burden of pertussis in older adults is underestimated, particularly for those with chronic respiratory conditions, and increases with age.<sup>22, 23</sup> Infants continue to die from pertussis despite advances in intensive care.<sup>11, 24-26</sup>

Following the introduction of mass immunisation, countries with consistently high immunisation coverage rates have achieved consistently low pertussis incidence rates.<sup>27</sup> The most pronounced decrease in incidence was seen in those aged under 10 years. Although primarily associated with low immunisation coverage, in some instances higher pertussis incidence rates are due to lower or waning vaccine efficacy or less-than-optimal immunisation schedules.<sup>28-30</sup> The burden of severe disease, particularly since the introduction of acellular vaccines, is highest in infants and unvaccinated young children.<sup>31</sup> However, less severe pertussis cases are also seen in vaccinated children who are further away from the last DTaP and, in some countries, adolescents.<sup>32-34</sup> Infants too young to have received more than one dose of pertussis vaccine (age 3 months or less) have the highest rate of notification, hospitalisation and death.<sup>35, 36</sup>

Epidemic peaks of pertussis occur every 2–5 years without the consistent seasonal pattern that is typical of most respiratory infections, although evidence from Australia suggests increased incidence (by 15 percent compared with annual average) during spring to summer months.<sup>15</sup> Epidemics are frequently sustained over 18 months or more, during which there are dramatic increases in hospital admission rates. Lack of change in the pertussis epidemic cycle with mass immunisation suggests minimal impact on the circulation of *B. pertussis* in the population, unlike other epidemic vaccine-preventable diseases, such as measles.<sup>12, 19, 37</sup>

## 16.3.2 New Zealand epidemiology

### Pertussis mortality in New Zealand

On average, zero to one deaths are associated with pertussis each year in New Zealand. During the 2011–2013 pertussis epidemic there were three deaths in children: two in infants aged under 6 weeks and one in an unimmunised pre-schooler.<sup>38</sup> No deaths from pertussis (as recorded in EpiSurv) occurred during the latest epidemic from October 2017 to May 2019.<sup>38, 39</sup>

## Pertussis morbidity in New Zealand

Pertussis morbidity in New Zealand has usually been described using hospital discharge data. National passive surveillance data has been available since 1996, when pertussis became a notifiable disease.

Outbreaks continue to occur throughout New Zealand. For further details refer to the ESR surveillance reports for notifiable diseases and pertussis dashboard (available at [esr.cri.nz/digital-library/www.esr.cri.nz/digital-library/pertussis-dashboard/](http://esr.cri.nz/digital-library/www.esr.cri.nz/digital-library/pertussis-dashboard/)).

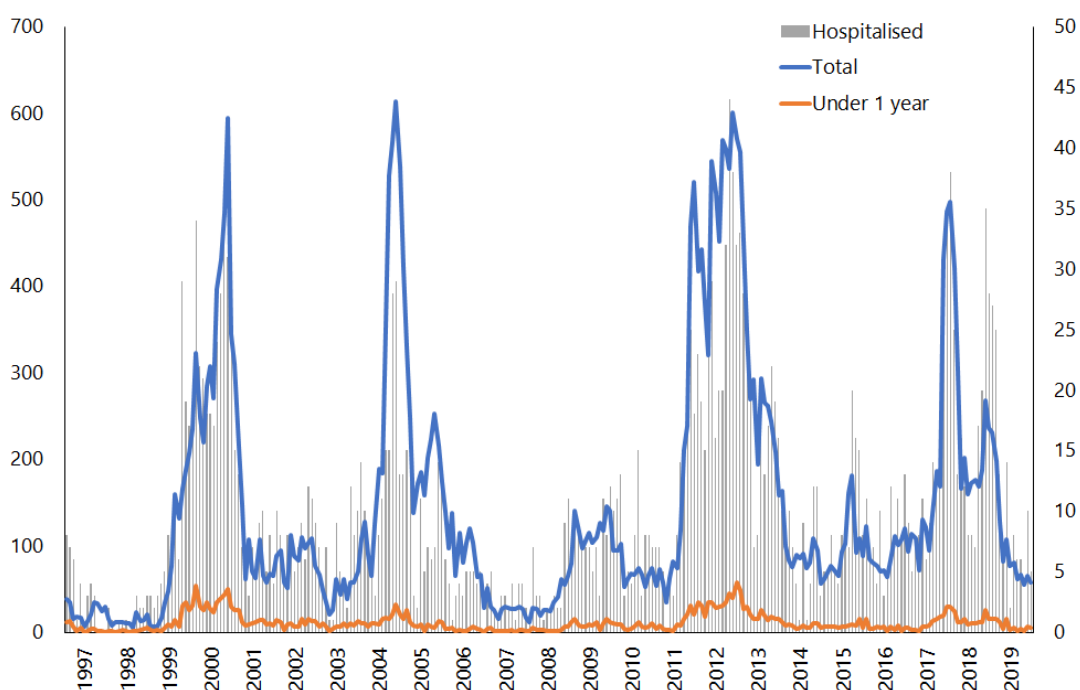
### Pertussis morbidity in New Zealand as described by notification data

Four epidemics have occurred since pertussis became a notifiable disease, with an epidemic peak annual number of notified cases of 4,140 in 2000, 3,485 in 2004, 5,897 in 2012 and 2956 in 2018 (see Figure 16.1).

The most recent outbreak commenced in October 2017; by the end of May 2019, there were 4,697 cases notified (2,939 laboratory-confirmed).<sup>39</sup> During 2019, 1206 cases were notified, an overall notification rate of 24.5 cases per 100,000 population. Of these cases, 88 (7.3 percent, incidence 148 cases per 100,000) were aged under 1 year and half of these were hospitalised. The youngest infants were at highest risk of hospitalisation with 85 percent of cases age under 2 months, 80 percent age under 3 months and 66 percent aged under 6 months hospitalised (ESR, 8 June 2020). The next highest incidence rate occurred in children aged 1–4 years (68 per 100,000). Pacific and Māori infants had the highest notification rates (300 and 177 per 100,000 respectively), and in children aged 1–4 years, MELAA ethnic group had the highest notification rate (175 per 100,000) followed by European/Other (77 per 100,000).

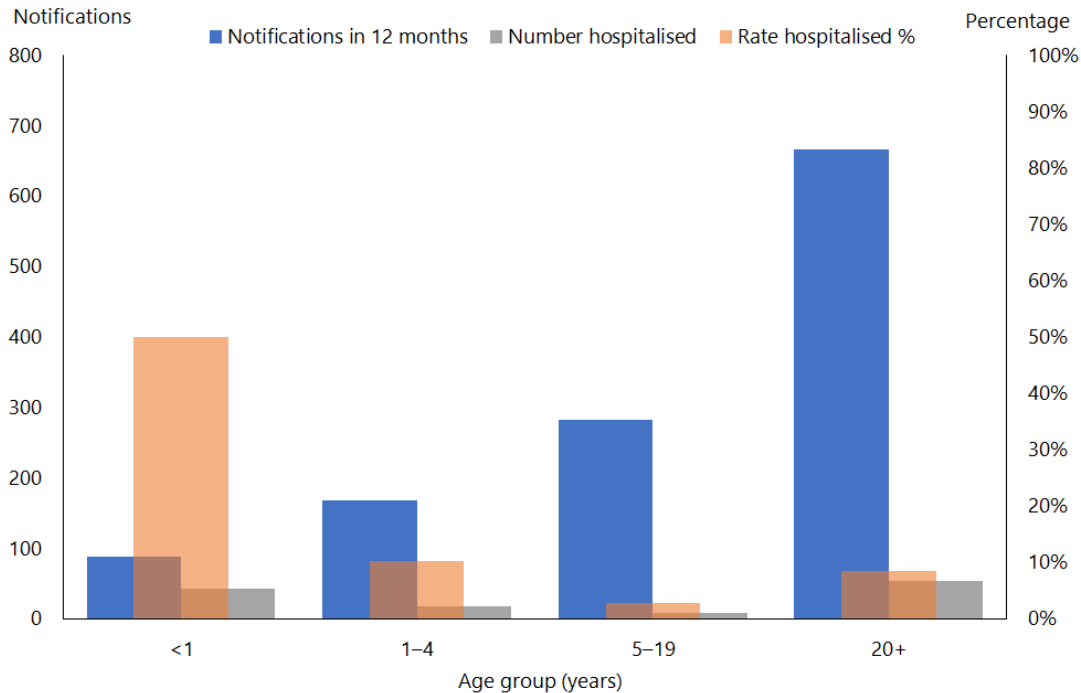
**Figure 16.1: Pertussis notifications and hospitalisations, 1997–2019**

Note: Includes confirmed, probable and suspect cases, and notifications still under investigation.



Since pertussis became notifiable, the annual proportion of notified cases aged 30 years or older has increased from 23 percent in 1997 to 48 percent in 2019 (ESR, 8 June 2020).<sup>38</sup> However, the highest proportion of hospitalised cases continues to be in infants. From 2010 to 2019 there were 1,544 notified cases in infants with 769 (53 percent) recorded as hospitalised (Figure 16.2).

**Figure 16.2: Age distribution of notified and hospitalised pertussis cases, 2019**



Source: ESR

### Pertussis morbidity in New Zealand, as described by hospital discharge data

Infants aged under 1 year with pertussis are more likely (nearly 80 percent) to be admitted to hospital than older children and account for almost all the pertussis cases admitted to the paediatric intensive care unit.<sup>40</sup>

Hospitalisation rates for pertussis, as measured by ICD discharge diagnostic codes, provide a measure of severe pertussis disease. The discharge rate in the 2000s was lower than it was in the 1990s (2000s versus 1990s, relative risk 0.8 [95% CI: 0.7–0.8]). Despite this decrease, the infant hospitalisation rate for pertussis in New Zealand in the 2000s (at nearly 200 per 100,000) remained three times higher than contemporary rates in Australia (2001 infant rate: 56 per 100,000) and the US (2003 infant rate: 65 per 100,000).<sup>41-43</sup>

Pertussis hospital admission rates vary with ethnicity and household deprivation. From 2000–2014 the infant (under 1 year old) hospitalisation rates for pertussis fluctuated but were consistently higher for Pacific and Māori than European/Other prioritised ethnicities. Between 2010 and 2014, the hospitalisation rate was over 2.5 times higher for Pacific (4.4 per 1,000) and over 2 times higher for Māori (3.6 per 1,000) than it was for European/Other ethnicities (1.7 per 1,000).<sup>44</sup>



From 2010 to 2014 an infant living in a household in the most deprived quintile was at a five-fold increased risk of being hospitalised with pertussis compared with an infant in the least deprived quintile (4.0 versus 0.8 per 1,000).<sup>44</sup>

## 16.4 Vaccines

Whole-cell pertussis vaccine for routine use was introduced in 1960 and was replaced with acellular pertussis vaccine in 2000. The current schedule of three acellular pertussis-containing vaccines in the first year of life plus booster doses at ages 4 and 11 years has been in effect since 2006. See Appendix 1 for more information about the history of pertussis-containing vaccines in New Zealand.

### 16.4.1 Available vaccines

#### Funded pertussis vaccines

The acellular pertussis-containing vaccines funded as part of the Schedule are:

- DTaP-IPV-HepB/Hib (Infanrix-hexa, GSK): diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and *Haemophilus influenzae* type b vaccine
- DTaP-IPV (Infanrix-IPV, GSK): diphtheria, tetanus, acellular pertussis and inactivated polio vaccine
- Tdap (Boostrix, GSK): a smaller adult dose of diphtheria and pertussis vaccine, together with tetanus vaccine.

See section 6.4.1 for more details.

#### Other vaccines

Other acellular pertussis-containing vaccines registered (approved for use) and available (marketed) in New Zealand include:

- Tdap: Adacel (Sanofi)
- Tdap-IPV: Adacel Polio (Sanofi).

## 16.4.2 Efficacy and effectiveness

### Immunogenicity

A review of published data on DTaP-IPV-HepB/Hib found it to be highly immunogenic in infants aged under 2 years for primary and booster vaccination.<sup>45</sup> In clinical studies there was a strong immune response against the vaccine antigens, which persisted for up to approximately six years after vaccination. A review of published clinical trial and post-marketing surveillance data supported the immunogenicity of DTaP-IPV-HepB/Hib across a range of schedules and when administered concurrently with other vaccines.<sup>46</sup>

### Efficacy and effectiveness

#### Vaccination in pregnancy

Maternal vaccination, given more than seven days before delivery, was estimated to be 91 percent (95% CI: 88–94) effective against laboratory-confirmed pertussis in infants younger than 3 months of age.<sup>47</sup> Protection of infants is achieved both by passive antibody transfer and reduced exposure to maternal disease.<sup>48</sup> Tdap given in pregnancy was shown to be 85 percent more effective than post-partum vaccination in preventing pertussis in infants younger than 8 weeks of age.<sup>49</sup>

Timing is important because protection is not as good if the mother is vaccinated less than two weeks prior to birth.<sup>50</sup> Vaccinating from 16 weeks' gestation allows time for passive transfer and accumulation of antibody in the fetus, such that by 40 weeks' gestation, infant antibody levels at birth are higher than those in the mother.<sup>51</sup> Giving maternal vaccination during the second trimester rather than later provides more preterm infants with pertussis protection.<sup>52, 53</sup>

See section 16.5.2 for information about maternal pertussis vaccine safety.

#### Direct protection

The acellular pertussis vaccines approved for use in New Zealand have been shown to provide around 81–85 percent efficacy (95% CI: 51–100) against confirmed pertussis after three infant doses, with follow-up studies suggesting sustained efficacy to age 6 years.<sup>13, 54, 55</sup> In a Swiss study, effectiveness against pertussis hospitalisation increased with each consecutive primary dose in infants from age 2.5 months to 2 years from 42.1 percent (95% CI: 11.3–62.6) after the first dose, 83.9 percent (70.2–92.1) after the second then 98.2 percent (96.1–99.3) to 100 percent (97.9–100) after the third and fourth doses.<sup>56</sup>

While effective, observational data from Australia found that acellular pertussis vaccines may be less effective than the best-performing whole-cell vaccines in preventing whooping cough.<sup>57, 58</sup> However, the quality of the whole cell vaccine varied between countries and a Canadian study found it to be less effective than the acellular vaccine.<sup>59</sup>

Age-appropriate pertussis vaccination in the US was shown to reduce the severity of symptoms and complications of the disease, including 60 percent reduction in the odds of severe disease (seizure, encephalopathy, pneumonia and/or hospitalisation) in children aged 7 months to 6 years, and 30 percent reduction in post-tussive vomiting in those aged 19 months to 64 years.<sup>60</sup>

### Duration of protection

Protection against pertussis begins to wane within several years of completion of a three-dose primary and two-dose booster immunisation series. The US has a pertussis immunisation schedule that includes three doses of acellular vaccine during infancy and booster doses at 15 to 18 months and 4 to 6 years.<sup>61</sup> The risk of pertussis increases in the six years after receipt of the fifth dose of this series, indicating a waning in vaccine-induced immunity over this time interval.

A decline in effectiveness was seen in children more distant from the last DTaP dose, by 27 percent per year on average.<sup>62</sup> Waning effectiveness is more rapid following the adolescent booster at around 35 percent per year.<sup>63</sup> In children, vaccine was 80 percent (95% CI: 71–86) effective against pertussis from two weeks to a year following vaccination, 84 percent (77–89) after 1–3 years, declining to 62 percent (42–75) after 4–7 years and to 41 percent (0–66) at eight or more years after vaccination.<sup>64</sup> A meta-analysis estimated that only 10 percent of those vaccinated with five doses of DTaP would be immune to pertussis 8.5 years after their last DTaP dose.<sup>65</sup>

Antibodies to pertussis toxoid, filamentous hemagglutinin and pertactin have been shown to persist five years after receipt of Tdap (Boostrix) in a study of Australian adults aged 18 years and older.<sup>66</sup> However, the duration of protection is unknown.

## 16.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at [www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

Store at +2°C to +8°C. Do not freeze. DTaP-IPV-HepB/Hib should be stored in the dark.

DTaP-IPV-HepB/Hib (Infanrix-hexa) must be reconstituted by adding the entire contents of the supplied container of the DTaP-IPV-HepB vaccine to the vial containing the Hib-PRP pellet. After adding the vaccine to the pellet, the mixture should be shaken until the pellet is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.

## 16.4.4 Dosage and administration

The dose of DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap is 0.5 mL, administered by intramuscular injection (see section 2.2.3).

### Co-administration with other vaccines

DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap can be administered simultaneously (at separate sites) with other vaccines or IGs.

## 16.5 Recommended immunisation schedule

**Table 16.1: Immunisation schedule for pertussis-containing vaccines (excluding catch-up)**

Age	Vaccine	Comment
Pregnant women: recommended from 16 weeks' gestation of every pregnancy, preferably in the second trimester (funded when given any time in second or third trimester)	Tdap	Booster for mother Passive immunity for infant
6 weeks	DTaP-IPV-HepB/Hib	Primary series
3 months	DTaP-IPV-HepB/Hib	Primary series
5 months	DTaP-IPV-HepB/Hib	Primary series
4 years	DTaP-IPV	Booster
11 years	Tdap	Booster
45 years (individuals who have not received 4 tetanus vaccinations in their lifetime)	Tdap	Booster
From 65 years	Tdap	Booster

### 16.5.1 Children

A primary course of pertussis vaccine is given as DTaP-IPV-HepB/Hib (Infanrix-hexa) at ages 6 weeks, 3 months and 5 months, followed by a dose of DTaP-IPV (Infanrix-IPV) at age 4 years (Table 16.1). A further booster is given at age 11 years (school year 7) as Tdap (Boostrix).

It is important to administer all vaccinations on time. Delays in receipt of infant immunisations significantly increase the risk of infants being hospitalised for severe pertussis.<sup>67</sup>

If a course of immunisation is late or interrupted for any reason, it may be resumed without repeating prior doses (see Appendix 2). The minimum interval between doses is four weeks. A booster dose should be given no earlier than six months after the primary series.

## Catch-up immunisation

See Appendix 2 for detailed catch-up immunisation information.

- DTaP-IPV-HepB/Hib or DTaP-IPV may be used for primary immunisation and boosting of children aged under 10 years.
- Tdap may be used for primary immunisation and boosting of children aged 7 to under 18 years.

Tdap is also funded:

- as a single dose for vaccination of patients from aged 65 years old (if not previously received 65-year-old Td dose, within the last 10 years)
- as single dose for vaccination of patients aged 45 years old who have not had 4 previous tetanus doses
- for vaccination of previously unimmunised or partially immunised patients
- for vaccination prior to planned or revaccination following immunosuppression (see section 16.5.3)
- for boosting of patients with tetanus-prone wounds (see section 22.5.5).

## 16.5.2 Pregnancy and breastfeeding

Pregnant women should receive a dose of Tdap in every pregnancy so that antibodies can pass to the fetus to provide protection from birth (funded when given any time in second or third trimester). It is recommended to be given from 16 weeks' gestation of every pregnancy, preferably in the second trimester to protect both the mother and her infant from pertussis.<sup>47, 51</sup> Post-partum maternal vaccination may reduce the risk of a mother infecting her baby but does not have the added benefit of providing the baby with passive antibodies (see section 16.4.2 for details of effectiveness).

Maternal Tdap vaccination has been shown to prevent pertussis disease or reduce severity of the disease and risk of pertussis-related death in very young infants.<sup>68</sup> There is no evidence that Tdap vaccination affects pregnancy outcomes<sup>68-70</sup> or causes harm to the fetus or neonate.<sup>68, 71</sup>

Tdap vaccines can be given to breastfeeding women, if not given during pregnancy.<sup>72</sup>

## 16.5.3 (Re)vaccination

Pertussis-containing vaccines are funded for vaccination or re-vaccination of eligible patients who have become immunocompromised, as follows. See also sections 4.2 and 4.3.

## DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV)

An additional four doses (as appropriate) of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for (re)vaccination of patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- prior to planned or following other severely immunosuppressive regimens.

Up to an additional four doses (as appropriate) of DTaP-IPV-HepB/Hib are funded for children aged 10 years to under 18 years for (re)vaccination of patients post HSCT. This is an off-label use of this vaccine which requires a prescription from an authorised prescriber or the patient's specialist. In this group, all prior immunity will have been lost and revaccination is equivalent to a primary immunisation schedule. DTaP-IPV-HepB/Hib not recommended for other severely immunocompromised individuals aged 10-18 years that require revaccination as they may have residual immune memory.

## Tdap (Boostrix)

An additional four doses (as appropriate) of Tdap (Boostrix) are funded for patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- prior to planned or following other severely immunosuppressive regimens.

A single dose of Tdap is funded for parents or primary caregivers of infants admitted to a neonatal intensive care unit or special care baby unit for more than three days and whose mothers had not received Tdap at least 14 days prior to baby's birth.

## 16.5.4 Recommended but not funded

Tdap is recommended but not funded, unless given as prophylaxis for a tetanus-prone wound, for protection against pertussis for:

- professions and students of professions in contact with infants, a booster dose given 5- to 10-year intervals (depending on employer requirements), for example, lead maternity carers and other health care personnel who work in neonatal units, other clinical settings (such as GPs and practice nurses) and early childhood education services staff (see Table 4.9). Infants with respiratory, cardiac, neurological or other co-morbid conditions are particularly at risk from pertussis.
- household members and other who have regular close contact with a newborn, is recommended to have a booster dose of Tdap if they have not had a dose in the previous 10 years. Household members aged under 18 years who are unimmunised or incompletely immunised for their age can receive funded pertussis vaccine; see Appendix 2 for catch-up schedules)

- regardless of maternal vaccination history, all caregivers of infants born at less than 32 weeks' gestation are recommended to receive a single dose of Tdap (see section 4.2.2)
- early childhood workers and students are recommended a Tdap booster dose at 10-year intervals, although the priority is to ensure all children attending childcare have received age-appropriate vaccination
- adults with a medical condition, not eligible for funded vaccine, who are at increased risk of severe consequences of pertussis (eg, those with chronic respiratory disease).

## 16.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

### 16.6.1 Contraindications

The only contraindication is an immediate severe anaphylactic reaction to the vaccine, or any component of the vaccine, following a previous dose.

### 16.6.2 Precautions

A history of well-controlled seizures in the vaccine recipient or a family history of seizures (febrile or afebrile) or other neurologic disorder is not a contraindication to vaccination against pertussis.<sup>50</sup>

Although previously been considered a precaution, vaccination is recommended for infants with an unstable neurological disorder (eg, poorly controlled epilepsy or deteriorating neurological state) as they may be at high risk of severe pertussis complications.<sup>50</sup>

## 16.7 Potential responses and AEFIs

Unless the specific contraindications and precautions outlined in section 16.6 above are present, practitioners should have no hesitation in advising the administration of acellular pertussis vaccine. Acellular pertussis vaccine has been used in New Zealand since 2000 and is significantly less reactogenic than the whole-cell pertussis vaccine.



## 16.7.1 DTaP-containing vaccines

DTaP-containing vaccines (eg, DTaP-IPV-HepB/Hib and DTaP-IPV) are generally well tolerated in children,<sup>73</sup> including preterm (24 to 36 weeks' gestation) and/or low birthweight (820–2,020 g) infants.<sup>74, 75</sup>

Local reactions commonly include pain, redness, swelling and induration at the injection site. Less common reactions include fretfulness, anorexia, vomiting, crying and slight to moderate fever. These local and systemic reactions usually occur within several hours of pertussis immunisation and spontaneously resolve within 48 hours without sequelae.<sup>73</sup>

Local reactions increase with age and additional doses of vaccine. The reaction may be due to some of the other vaccine components, such as aluminium. These reactions are usually minor and only last a day or so.

## 16.7.2 Tdap vaccine

The adult reduced-concentration Tdap (Boostrix) vaccines have been found to have no safety concerns in those aged 10–64 years and those aged over 65 years.<sup>76-79</sup> Studies of Tdap in pregnant women have not identified any increased risk of adverse maternal, infant or fetal outcomes.<sup>12, 71, 80-82</sup>

Local reactions following immunisation of adolescents with Tdap are common but usually mild. They include pain (in 75 percent of recipients), swelling (21 percent) and redness (23 percent) at the injection site.<sup>83</sup> Potential systemic reactions following immunisation of adolescents with Tdap include fever >38°C (5 percent), headache (16 percent), fatigue (14 percent) and gastrointestinal symptoms (10 percent).<sup>83</sup>

## 16.7.3 Major adverse events associated with pertussis-containing vaccines

The incidence of major adverse events following primary pertussis immunisation is summarised in Table 16.2.

**Table 16.2: Incidence of major adverse reactions following acellular pertussis vaccines (based on clinical trial data for DTaP vaccines)**

Event following immunisation	Timing post-vaccination	Incidence per 100,000 doses
High fever >38°C	0–2 days	36
Persistent (>3 hours) inconsolable screaming	0–24 hours	44
Seizures	0–2 days	7
Hypotonic-hyporesponsive episode	0–2 days	0–47 <sup>a</sup>
Anaphylaxis	0–1 hour	Very rare

a. Across clinical trials of multiple licensed DTaP formulations

Source: Edwards KM, Decker MD. 2018. Pertussis vaccines. In: Plotkin S, Orenstein W, Offit P, et al (eds) *Plotkin's Vaccines (7th edition)*. Elsevier.

Parents should be alerted to the small but defined risk of extensive limb swelling to the injected thigh or upper arm, particularly following the fourth and fifth DTaP dose. This transient, usually painless and benign swelling occurs in 2–3 percent of children.<sup>73</sup> Resolution occurs without sequelae and it is not a contraindication for further pertussis vaccine doses.<sup>72, 84</sup>

Neither a hypotonic-hyporesponsive episode nor seizures are associated with long-term consequences for the child (see section 2.3.3).<sup>85–87</sup> Children who have febrile seizures after pertussis immunisation do not have an increased risk of subsequent seizures or neurodevelopmental disability.<sup>88</sup> It is safe to give acellular pertussis vaccine after a hypotonic-hyporesponsive episode has occurred following a previous dose.<sup>89</sup> A significant decrease of 60–67 percent in hypotonic-hyporesponsive episodes was observed in Canada following the switch from whole cell to acellular pertussis vaccines.<sup>90</sup>

## 16.8 Public health measures

### 16.8.1 Notification

It is a legal requirement that all cases of pertussis be notified immediately on suspicion to the local medical officer of health.

For detailed information about public health control measures, see the Communicable Disease Control Manual pertussis chapter at [www.tewhaturora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/pertussis/](http://www.tewhaturora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/pertussis/)

A suspected pertussis case can be confirmed if a clinically compatible illness is laboratory-confirmed or is epidemiologically linked to a confirmed case. Because

transmission is by aerosolised droplets, health care personnel looking after pertussis cases should be vaccinated and wear a mask.

## 16.8.2 Management of contacts

The local medical officer of health will advise on the management of contacts. For more details on control measures, see the Communicable Disease Control Manual pertussis chapter at [www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/pertussis/](http://www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/pertussis/)

## 16.8.3 Improving pertussis control

The goal of the pertussis immunisation programme is to protect those most at risk of developing severe disease; that is, infants in the first year of life. Two key strategies for reducing the burden of disease in infants are the administration of Tdap vaccination during pregnancy and on-time infant immunisation. Vaccination during pregnancy is recommended and funded for women from the second trimester, preferably from 16 weeks' gestation (see section 16.5.2). This is the most effective way to protect young infants. More complete and timely delivery of the current infant immunisation schedule would reduce the infant pertussis disease burden in older infants.<sup>67</sup> It is important that all children attending early childhood services are fully vaccinated for their age.

Data on the protective effects of indirect strategies is currently incomplete. 'Cocoon strategy' is the term used to describe the protection of infants by immunising those who are potential sources of *B. pertussis*.<sup>91</sup> Three identified target groups who have the most contact with young and vulnerable infants are (1) new mothers who have not had recent immunisation, family and close contacts of newborns; (2) health care workers; and (3) early childhood workers. Some protection may be provided to infants by cocoon immunisation of parents and other potential household members post-partum, may be pertinent in some circumstances where maternal vaccination did not occur, such as preterm birth, and infants in neonatal intensive care.<sup>92</sup>

Health care workers in particular are at increased risk of pertussis and can transmit pertussis to other health care workers and to patients.<sup>93</sup> Outbreaks in maternity wards, neonatal units and outpatient settings have been described.<sup>94</sup> Fatalities occur as a result of such nosocomial spread.<sup>95</sup>

Mass immunisation cannot be used to control an established community outbreak, although action to update age-appropriate vaccination in institutional settings (schools and early childhood services for staff and students) is appropriate. When an outbreak occurs, individual immunisation status should be checked, and any missing doses given. Vaccination in pregnancy is particularly important to protect the most vulnerable, young infants.

## 16.9 Variations from the vaccine data sheets

The DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV) data sheets state that these vaccines are indicated for primary immunisation of infants and as a booster dose for children. Health New Zealand | Te Whatu Ora recommends that DTaP-IPV-HepB/Hib and DTaP-IPV vaccines may also be used for catch-up of the primary schedule in children aged under 10 years (see Appendix 2).

To reduce the number of injections required and to provide a higher antigen dose than Tdap, DTaP-IPV-HepB/Hib is recommended and funded for the revaccination of children aged 10 to <18 years post-haematopoietic stem cell transplantation. This use requires a prescription from an authorised prescriber.

The data sheets for DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap (Boostrix) state that these vaccines are contraindicated in children with encephalopathy of unknown aetiology or with neurologic complications occurring within seven days following a vaccine dose. Health New Zealand recommends that the only contraindication is a history of anaphylaxis to a previous dose or to any of the vaccine components (see section 16.6.1). The risks and benefits of withholding vaccination until the clinical situation has stabilised should be considered on an individual basis (see section 16.6.2).

Tdap is not approved for use (registered) for primary immunisation. However, Health New Zealand recommends that children aged from 7 years and adults may receive Tdap for catch-up of the primary schedule (see Appendix 2).

The Tdap data sheet states that the vaccine may be used during pregnancy when the possible advantages outweigh the possible risks for the fetus. However, Health New Zealand recommends Tdap vaccine for all pregnant women from 16 weeks' gestation of every pregnancy, preferably in the second trimester, but at least two weeks before birth. It is funded when given any time in second or third trimester (see section 16.5.2).

## References

1. Fine P, Mulholland K, Scott J, Edmunds W. 2018. Community Protection, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
2. McGovern MC, Smith MB. Causes of apparent life threatening events in infants: a systematic review. *Archives of Disease in Childhood*, 2004. 89(11): p. 1043-8.
3. Harnden A, Grant C, Harrison T, et al. Whooping cough in school age children with persistent cough: prospective cohort study in primary care. *BMJ*, 2006. 333(7560): p. 174-7.
4. Moore A, Ashdown HF, Shinkins B, et al. Clinical characteristics of pertussis-associated cough in adults and children: A diagnostic systematic review and meta-analysis. *Chest*, 2017. 152(2): p. 353-367.

5. Wirsing von König C-H, Halperin S, Riffelmann M, Guiso N. Pertussis of adults and infants. *Lancet Infectious Diseases*, 2002. 2(12): p. 744-50.
6. Ebell MH, Marchello C, Callahan M. Clinical diagnosis of *Bordetella pertussis* infection: a systematic review. *Journal of the American Board of Family Medicine*, 2017. 30(3): p. 308-319.
7. Robertson PW, Goldberg H, Jarvie BH, et al. *Bordetella pertussis* infection: a cause of persistent cough in adults. *Medical Journal of Australia*, 1987. 146(10): p. 522-5.
8. Senzilet LD, Halperin SA, Spika JS, et al. Pertussis is a frequent cause of prolonged cough illness in adults and adolescents. *Clinical Infectious Diseases*, 2001. 32(12): p. 1691-7.
9. Gilberg S, Njamkepo E, Du Chatelet IP, et al. Evidence of *Bordetella pertussis* infection in adults presenting with persistent cough in a french area with very high whole-cell vaccine coverage. *Journal of Infectious Diseases*, 2002. 186(3): p. 415-8.
10. Philipson K, Goodyear-Smith F, Grant CC, et al. When is acute persistent cough in school-age children and adults whooping cough? A prospective case series study. *British Journal of General Practice*, 2013. 63(613): p. e573-9.
11. Surridge J, Segedin ER, Grant CC. Pertussis requiring intensive care. *Archives of Disease in Childhood*, 2007. 92(11): p. 970-5.
12. Cherry JD. The epidemiology of pertussis: a comparison of the epidemiology of the disease pertussis with the epidemiology of *Bordetella pertussis* infection. *Pediatrics*, 2005. 115(5): p. 1422-7.
13. Edwards KM, Decker MD. 2018. Pertussis vaccines, in *Vaccines 7th Edition*, Plotkin S, Orenstein W, Offit P (eds). Elsevier
14. Craig R, Kunkel E, Crowcroft NS, et al. Asymptomatic infection and transmission of pertussis in households: a systematic review. *Clinical Infectious Diseases*, 2019.
15. Leong RNF, Wood JG, Turner RM, Newall AT. Estimating seasonal variation in Australian pertussis notifications from 1991 to 2016: evidence of spring to summer peaks. *Epidemiology and Infection*, 2019. 147: p. e155.
16. Gordon JE, Hood RI. Whooping cough and its epidemiological anomalies. *American Journal of the Medical Sciences*, 1951. 222(3): p. 333-61.
17. Haberling DL, Holman RC, Paddock CD, Murphy TV. Infant and maternal risk factors for pertussis-related infant mortality in the United States, 1999 to 2004. *Pediatric Infectious Disease Journal*, 2009. 28(3): p. 194-8.
18. Sutter RW, Cochi SL. Pertussis hospitalizations and mortality in the United States, 1985-1988. Evaluation of the completeness of national reporting. *JAMA*, 1992. 267(3): p. 386-91.
19. Crowcroft NS, Pebody RG. Recent developments in pertussis. *Lancet*, 2006. 367(9526): p. 1926-36.
20. Shaikh R, Guris D, Strebel PM, Wharton M. Underreporting of pertussis deaths in the United States: need for improved surveillance. *Pediatrics*, 1998. 101(2): p. 323.
21. Crowcroft NS, Andrews N, Rooney C, et al. Deaths from pertussis are underestimated in England. *Archives of Disease in Childhood*, 2002. 86(5): p. 336-8.
22. Kandeil W, Atanasov P, Avramioti D, et al. The burden of pertussis in older adults: what is the role of vaccination? A systematic literature review. *Expert Rev Vaccines*, 2019. 18(5): p. 439-455.
23. Karki S, McIntyre P, Newall AT, et al. Risk factors for pertussis hospitalizations in Australians aged 45 years and over: A population based nested case-control study. *Vaccine*, 2015. 33(42): p. 5647-5653.
24. Mikelova LK, Halperin SA, Scheifele D, et al. Predictors of death in infants hospitalized with pertussis: a case-control study of 16 pertussis deaths in Canada. *Journal of Pediatrics*, 2003. 143(5): p. 576-81.

25. Winter K, Zipprich J, Harriman K, et al. Risk factors associated with infant deaths from pertussis: a case-control study. *Clinical Infectious Diseases*, 2015. 61(7): p. 1099-106.
26. Cherry JD. The prevention of severe pertussis and pertussis deaths in young infants. *Expert Rev Vaccines*, 2019. 18(3): p. 205-208.
27. Joo I, Epidemiology of pertussis in Hungary, in *Developments in Biological Standardization*. 1991. p. 357-9.
28. Kimura M ,Kuno-Sakai H. Developments in pertussis immunisation in Japan. *Lancet*, 1990. 336(8706): p. 30-2.
29. Miller E, Vurdien JE ,White JM. The epidemiology of pertussis in England and Wales. *Communicable Disease Report. CDR Review*, 1992. 2(13): p. R152-4.
30. Domenech de Celles M, Magpantay FMG, King AA,Rohani P. The impact of past vaccination coverage and immunity on pertussis resurgence. *Science Translational Medicine*, 2018. 10(434).
31. Farizo KM, Cochi SL, Zell ER, et al. Epidemiological features of pertussis in the United States, 1980-1989. *Clinical Infectious Diseases*, 1992. 14(3): p. 708-19.
32. Provenzano RW, Wetterlow LH ,Ipsen J. Pertussis immunization in pediatric practice and in public health. *New England Journal of Medicine*, 1959. 261(10): p. 473-8.
33. Guris D, Strebel PM, Bardenheier B, et al. Changing epidemiology of pertussis in the United States: increasing reported incidence among adolescents and adults, 1990-1996. *Clinical Infectious Diseases*, 1999. 28(6): p. 1230-7.
34. Zerbo O, Bartlett J, Goddard K, et al. Acellular Pertussis Vaccine Effectiveness Over Time. *Pediatrics*, 2019. 144(1).
35. Ranganathan S, Tasker R, Booy R, et al. Pertussis is increasing in unimmunized infants: is a change in policy needed? *Archives of Disease in Childhood*, 1999. 80(3): p. 297-9.
36. Tanaka M, Vitek CR, Pascual FB, et al. Trends in pertussis among infants in the United States, 1980-1999. *JAMA*, 2003. 290(22): p. 2968-75.
37. Broutin H, Guegan JF, Elguero E, et al. Large-scale comparative analysis of pertussis population dynamics: periodicity, synchrony, and impact of vaccination. *American Journal of Epidemiology*, 2005. 161(12): p. 1159-67.
38. Institute of Environmental Science and Research Ltd. 2016. *Notifiable Diseases in New Zealand: Annual Report 2015* (ed.), Porirua, New Zealand: The Institute of Science and Environmental Research Ltd. URL: [https://surv.esr.cri.nz/PDF\\_surveillance/AnnualRpt/AnnualSurv/2015/2015AnnualReportFinal.pdf](https://surv.esr.cri.nz/PDF_surveillance/AnnualRpt/AnnualSurv/2015/2015AnnualReportFinal.pdf) (accessed 3 July 2020)
39. Institute of Environmental Science and Research. 2019 *Pertussis Report May 2019*. Porirua, Wellington. URL: [https://surv.esr.cri.nz/PDF\\_surveillance/PertussisRpt/2019/PertussisReportMay2019.pdf](https://surv.esr.cri.nz/PDF_surveillance/PertussisRpt/2019/PertussisReportMay2019.pdf). (accessed 3 July 2020)
40. Ganeshalingham A, Reed P, Grant C, et al. Hospital costs of Bordetella pertussis in New Zealand children. *New Zealand Medical Journal*, 2016. 129(1445): p. 75-82.
41. Elliott E, McIntyre P, Ridley G, et al. National study of infants hospitalized with pertussis in the acellular vaccine era. *Pediatric Infectious Disease Journal*, 2004. 23(3): p. 246-52.
42. Cortese MM, Baughman AL, Zhang R, et al. Pertussis hospitalizations among infants in the United States, 1993 to 2004. *Pediatrics*, 2008. 121(3): p. 484-92.
43. Grant CC. Recent indication of progress in pertussis hospitalisation rates in NZ. *Australian and New Zealand Journal of Public Health*, 2012. 36(4): p. 398-398.
44. Simpson J, Duncanson M, Oben G, et al. 2016 *The Health Status of Children and Young People in New Zealand 2015*.: Dunedin. URL: <https://www.otago.ac.nz/nzcyes/reports-by-category/reports-by-year/index.html>. (accessed 3 July 2020)



45. Dhillon S. DTPa-HBV-IPV/Hib vaccine (Infanrix hexa): a review of its use as primary and booster vaccination. *Drugs*, 2010. 70(8): p. 1021-58.
46. Zepp F, Schmitt HJ, Cleerbout J, et al. Review of 8 years of experience with Infanrix hexa (DTPa-HBV-IPV/Hib hexavalent vaccine). *Expert Rev Vaccines*, 2009. 8(6): p. 663-78.
47. Amirthalingam G, Campbell H, Ribeiro S, et al. Sustained effectiveness of the maternal pertussis immunization program in England 3 years following introduction. *Clinical Infectious Diseases*, 2016. 63(suppl 4): p. S236-S243.
48. Amirthalingam G, Andrews N, Campbell H, et al. Effectiveness of maternal pertussis vaccination in England: an observational study. *Lancet*, 2014. 384(9953): p. 1521-8.
49. Winter K, Nickell S, Powell M, Harriman K. Effectiveness of prenatal versus postpartum tetanus, diphtheria, and acellular pertussis vaccination in preventing infant pertussis. *Clinical Infectious Diseases*, 2017. 64(1): p. 3-8.
50. Liang JL, Tiwari T, Moro P, et al. Prevention of pertussis, tetanus, and diphtheria with vaccines in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR: Recommendations and Reports*, 2018. 67(2): p. 1-44.
51. Eberhardt CS, Blanchard-Rohner G, Lemaitre B, et al. Maternal immunization earlier in pregnancy maximizes antibody transfer and expected infant seropositivity against pertussis. *Clinical Infectious Diseases*, 2016. 62(7): p. 829-836.
52. Eberhardt CS, Blanchard-Rohner G, Lemaitre B, et al. Pertussis antibody transfer to preterm neonates after second- versus third-trimester maternal immunization. *Clinical Infectious Diseases*, 2017. 64(8): p. 1129-1132.
53. Kent A, Ladhani SN, Andrews NJ, et al. Pertussis antibody concentrations in infants born prematurely to mothers vaccinated in pregnancy. *Pediatrics*, 2016. 138(1): p. 07.
54. Greco D, Salmaso S, Mastrantonio P, et al. A controlled trial of two acellular vaccines and one whole-cell vaccine against pertussis. Progetto Pertosse Working Group. *New England Journal of Medicine*, 1996. 334(6): p. 341-8.
55. Gustafsson L, Hessel L, Storsaeter J, Olin P. Long-term follow-up of Swedish children vaccinated with acellular pertussis vaccines at 3, 5, and 12 months of age indicates the need for a booster dose at 5 to 7 years of age. *Pediatrics*, 2006. 118(3): p. 978-84.
56. Mack I, Erlanger TE, Lang P, et al. Dose-dependent effectiveness of acellular pertussis vaccine in infants: A population-based case-control study. *Vaccine*, 2019.
57. Sheridan SL, Ware RS, Grimwood K, Lambert SB. Number and order of whole cell pertussis vaccines in infancy and disease protection. *JAMA*, 2012. 308(5): p. 454-6.
58. Sheridan SL, Ware RS, Grimwood K, Lambert SB. Reduced risk of pertussis in whole-cell compared to acellular vaccine recipients is not confounded by age or receipt of booster-doses. *Vaccine*, 2015. 33(39): p. 5027-30.
59. Wilkinson K, Righolt CH, Kwong JC, et al. A nested case-control study measuring pertussis vaccine effectiveness and duration of protection in Manitoba, Canada, 1992-2015: A Canadian Immunization Research Network Study. *Vaccine*, 2019. 37(48): p. 7132-7137.
60. McNamara LA, Skoff T, Faulkner A, et al. Reduced severity of pertussis in persons with age-appropriate pertussis vaccination – United States, 2010–2012. *Clinical Infectious Diseases*, 2017. 65(5): p. 811-818.
61. Tartof SY, Lewis M, Kenyon C, et al. Waning immunity to pertussis following 5 doses of DTaP. *Pediatrics*, 2013. 131(4): p. e1047-52.
62. Klein NP, Bartlett J, Fireman B, et al. Waning protection following 5 doses of a 3-component diphtheria, tetanus, and acellular pertussis vaccine. *Vaccine*, 2017. 35(26): p. 3395-3400.



63. Klein NP, Bartlett J, Fireman B, Baxter R. Waning Tdap Effectiveness in Adolescents. *Pediatrics*, 2016. 137(3): p. e20153326.
64. Schwartz KL, Kwong JC, Deeks SL, et al. Effectiveness of pertussis vaccination and duration of immunity. *CMAJ: Canadian Medical Association Journal*, 2016. 188(16): p. E399-E406.
65. McGirr A, Fisman DN. Duration of pertussis immunity after DTaP immunization: a meta-analysis. *Pediatrics*, 2015. 135(2): p. 331-43.
66. McIntyre PB, Burgess MA, Egan A, et al. Booster vaccination of adults with reduced-antigen-content diphtheria, Tetanus and pertussis vaccine: immunogenicity 5 years post-vaccination. *Vaccine*, 2009. 27(7): p. 1062-6.
67. Grant CC, Roberts M, Scragg R, et al. Delayed immunisation and risk of pertussis in infants: unmatched case-control study. *BMJ*, 2003. 326(7394): p. 852-3.
68. Campbell H, Gupta S, Dolan GP, et al. Review of vaccination in pregnancy to prevent pertussis in early infancy. *Journal of Medical Microbiology*, 2018. 67(10): p. 1426-1456.
69. Griffin JB, Yu L, Watson D, et al. Pertussis Immunisation in Pregnancy Safety (PIPS) Study: A retrospective cohort study of safety outcomes in pregnant women vaccinated with Tdap vaccine. *Vaccine*, 2018. 36(34): p. 5173-5179.
70. McHugh L, Marshall HS, Perrett KP, et al. The safety of influenza and pertussis vaccination in pregnancy in a cohort of Australian mother-infant pairs, 2012-2015: The FluMum Study. *Clinical Infectious Diseases*, 2019. 68(3): p. 402-408.
71. Petousis-Harris H, Jiang Y, Yu L, et al. A retrospective cohort study of safety outcomes in New Zealand infants exposed to Tdap vaccine in utero. *Vaccines (Basel)*, 2019. 7(4).
72. Australian Technical Advisory Group on Immunisation. 2018. *Australian Immunisation Handbook* (ed.), Canberra: Australian Government Department of Health. URL: <https://immunisationhandbook.health.gov.au/> (accessed October 2019)
73. American Academy of Pediatrics. 2018. Pertussis (Whooping Cough). in *Red Book: 2018 Report of the Committee on Infectious Diseases*, Committee on Infectious Diseases, Kimberlin D, Brady M, et al. (eds). Elk Grove Village, IL. URL: <https://redbook.solutions.aap.org/redbook.aspx>. (accessed 3 July 2020)
74. Omeñaca F, Garcia-Sicilia J, Garcia-Corbeira P, et al. Response of preterm newborns to immunization with a hexavalent diphtheria-tetanus-acellular pertussis-hepatitis B virus-inactivated polio and *Haemophilus influenzae* type b vaccine: first experiences and solutions to a serious and sensitive issue. *Pediatrics*, 2005. 116(6): p. 1292-8.
75. Lyseng-Williamson KA, Dhillon S. DTPa-HBV-IPV/Hib vaccine (Infanrix hexa): a guide to its use in infants. *Paediatric Drugs*, 2012. 14(5): p. 337-43.
76. Jackson LA, Yu O, Belongia EA, et al. Frequency of medically attended adverse events following tetanus and diphtheria toxoid vaccine in adolescents and young adults: a Vaccine Safety Datalink study. *BMC Infectious Diseases*, 2009. 9(165): p. 165.
77. Yih WK, Nordin JD, Kulldorff M, et al. An assessment of the safety of adolescent and adult tetanus-diphtheria-acellular pertussis (Tdap) vaccine, using active surveillance for adverse events in the Vaccine Safety Datalink. *Vaccine*, 2009. 27(32): p. 4257-62.
78. Moro PL, Yue X, Lewis P, et al. Adverse events after tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccine administered to adults 65 years of age and older reported to the Vaccine Adverse Event Reporting System (VAERS), 2005-2010. *Vaccine*, 2011. 29(50): p. 9404-8.
79. Baxter R, Hansen J, Timbol J, et al. Post-licensure safety surveillance study of routine use of tetanus toxoid, reduced diphtheria toxoid and 5-component

- acellular pertussis vaccine. *Human Vaccines & Immunotherapeutics*, 2016. 12(11): p. 2742-2748.
80. Zheteyeva YA, Moro PL, Tepper NK, et al. Adverse event reports after tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccines in pregnant women. *American Journal of Obstetrics and Gynecology*, 2012. 207(1): p. 59 e1-7.
  81. Donegan K, King B, Bryan P. Safety of pertussis vaccination in pregnant women in UK: observational study. *BMJ*, 2014. 349(11 July): p. g4219.
  82. Petousis-Harris H, Walls T, Watson D, et al. Safety of Tdap vaccine in pregnant women: an observational study. *BMJ Open*, 2016. 6(4): p. e010911.
  83. Centers for Disease Control and Prevention. 2006. Preventing tetanus, diphtheria, and pertussis among adolescents: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morbidity and Mortality Weekly Report*. 55(RR-3): p. 1-44. <https://www.cdc.gov/mmwr/pdf/rr/rr5503.pdf> (accessed 3 July 2020)
  84. Southern J, Waight PA, Andrews N, Miller E. Extensive swelling of the limb and systemic symptoms after a fourth dose of acellular pertussis containing vaccines in England in children aged 3-6 years. *Vaccine*, 2017. 35(4): p. 619-625.
  85. Hirtz DG, Nelson KB, Ellenberg JH. Seizures following childhood immunizations. *Journal of Pediatrics*, 1983. 102(1): p. 14-8.
  86. Baraff LJ, Shields WD, Beckwith L, et al. Infants and children with convulsions and hypotonic-hyporesponsive episodes following diphtheria-tetanus-pertussis immunization: follow-up evaluation. *Pediatrics*, 1988. 81(6): p. 789-94.
  87. Braun MM, Terracciano G, Salive ME, et al. Report of a US public health service workshop on hypotonic-hyporesponsive episode (HHE) after pertussis immunization. *Pediatrics*, 1998. 102(5): p. E52.
  88. Barlow WE, Davis RL, Glasser JW, et al. The risk of seizures after receipt of whole-cell pertussis or measles, mumps, and rubella vaccine. *New England Journal of Medicine*, 2001. 345(9): p. 656-61.
  89. Goodwin H, Nash M, Gold M, et al. Vaccination of children following a previous hypotonic-hyporesponsive episode. *Journal of Paediatrics and Child Health*, 1999. 35(6): p. 549-52.
  90. Le Saux N, Barrowman NJ, Moore DL, et al. Decrease in hospital admissions for febrile seizures and reports of hypotonic-hyporesponsive episodes presenting to hospital emergency departments since switching to acellular pertussis vaccine in Canada: a report from IMPACT. *Pediatrics*, 2003. 112(5): p. e348-e348.
  91. McIntyre P, Wood N. Pertussis in early infancy: disease burden and preventive strategies. *Current Opinion in Infectious Diseases*, 2009. 22(3): p. 215-23.
  92. Rowe SL, Tay EL, Franklin LJ, et al. Effectiveness of parental cocooning as a vaccination strategy to prevent pertussis infection in infants: A case-control study. *Vaccine*, 2018. 36(15): p. 2012-2019.
  93. De Serres G, Shadmani R, Duval B, et al. Morbidity of pertussis in adolescents and adults. *Journal of Infectious Diseases*, 2000. 182(1): p. 174-9.
  94. Centers for Disease Control and Prevention. 2008. Prevention of pertussis, tetanus, and diphtheria among pregnant and postpartum women and their infants: recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morbidity and Mortality Weekly Report: Recommendations and Reports*. 57(RR-4): p. 1-51. <https://www.cdc.gov/mmwr/PDF/rr/rr5704.pdf> (accessed 3 July 2020)
  95. Bonacorsi S, Farnoux C, Bidet P, et al. Treatment failure of nosocomial pertussis infection in a very-low-birth-weight neonate. *J Clin Microbiol*, 2006. 44(10): p. 3830-2.

# 17 Pneumococcal disease

## Key information

Mode of transmission	Contact with respiratory droplets.
Incubation period	Asymptomatic nasopharyngeal carriage is common. The incubation period is variable and may be as short as 1–3 days.
Incidence and burden of disease	Highest at extremes of age (<2 years and >75 years), Māori and Pacific people, those with multiple comorbidities and with immunocompromise.
Funded vaccines	All children aged under 5 years: PCV13 (Prevenar 13). Children and adults with eligible conditions: <ul style="list-style-type: none"><li>• PCV13 (Prevenar 13)</li><li>• 23PPV (Pneumovax 23).</li></ul>
Dose, presentation and route	All vaccines: <ul style="list-style-type: none"><li>• 0.5 mL per dose</li><li>• pre-filled syringe</li><li>• intramuscular injection (23PPV can also be given subcutaneously).</li></ul>
Funded vaccine indications and schedule	PCV13 at ages 6 weeks, 5 months and 12 months, and age-appropriate catch-up for children <5 years; an additional dose is given at age 3 months for those with eligible conditions. PCV13 and 23PPV: <ul style="list-style-type: none"><li>• vaccination or re-vaccination at any age with eligible conditions</li><li>• testing for primary immune deficiencies.</li></ul>
Vaccine efficacy	For pneumococcal conjugate vaccines: reductions in pneumococcal disease and carriage of vaccine serotypes in vaccinated populations, plus herd immunity effects reducing pneumococcal disease in other age groups; some increases in disease caused by non-vaccine serotypes.
Precautions and special considerations	Concomitant PCV13 and influenza vaccine may increase risk of fever and febrile convulsions in children aged 6 months to <5 years. 23PPV should not be given to children aged under 2 years as polysaccharide vaccines are poorly immunogenic in this age group.
Public health measures	Notify the local medical officer of health immediately on suspicion of invasive pneumococcal disease (see section 17.8)
Post-exposure prophylaxis	Antimicrobial prophylaxis is not indicated.

## 17.1 Bacteriology

*Streptococcus pneumoniae* is a gram-positive diplococcus. It is ubiquitous, and many individuals carry the organism asymptotically in their upper respiratory tract.<sup>1</sup> There are over 90 identifiable serotypes of *S. pneumoniae*. Certain serotypes are more invasive or more associated with antibiotic resistance, and dominant serotypes vary by age and geographical distribution.

See section 17.4.1 and Table 17.1 for the serotypes contained in the pneumococcal conjugate vaccines (PCV) and pneumococcal polysaccharide vaccine (PPV).

## 17.2 Clinical features

*Streptococcus pneumoniae* causes a wide variety of clinical illnesses from common but troublesome otitis media to life-threatening invasive pneumococcal disease (IPD). IPD is defined by isolation of *S. pneumoniae* from a usually sterile site, such as blood, pleural fluid or cerebrospinal fluid, and represents the most severe end of the disease spectrum. The most common clinical syndromes in IPD are bacteraemic pneumonia, non-localised bacteraemia and meningitis. Older adults generally have bacteraemic pneumonia, while young children may have any of the three, with meningitis being the most severe.

Pneumonia without bacteraemia is up to five times more common than bacteraemic pneumonia, especially in older adults, where it also has high mortality. Non-invasive infections include acute otitis media (predominantly in children) and sinusitis (predominantly older children and adults).

## 17.3 Epidemiology

### 17.3.1 Global burden of disease

The human nasopharynx is the only natural reservoir of *S. pneumoniae*. Transmission is by contact with respiratory droplets. Carriage rates in young children range from 21 percent in high-income settings to more than 90 percent in resource-limited countries.<sup>1</sup> Although nasopharyngeal colonisation precedes disease, most who are colonised do not develop disease. The period between colonisation with *S. pneumoniae* and infection is variable but may be as short as one day. Transmission and invasive potential are increased by concomitant viral upper respiratory tract infection, especially influenza.

Pneumococcal disease is a common cause of morbidity and mortality worldwide. Rates of disease and death are highest in low-income countries with the majority of deaths occurring in sub-Saharan Africa and Asia.<sup>2</sup> Along with the very old and very young, patients with underlying cardiorespiratory disease and congenital or acquired immunosuppression have the highest rates of disease.

Risk of disease increases with multiple comorbidities and lifestyle factors (this is described as risk-stacking, see section 17.5.4).<sup>3</sup> The risk of IPD in children and adults with two or more comorbid conditions can be as high as in those with a recognised 'high-risk' condition.<sup>4</sup> Lifestyle factors, such as passive smoking, environmental and workplace pollutions, smoking and alcohol dependency, can increase the risk of severe pneumococcal disease, especially in those with chronic illnesses that predispose them to infection, such as asthma, diabetes, dementia and mental illness.<sup>5,6</sup> Socioeconomic deprivation, homelessness and overcrowding have also been associated with increased risk of IPD.<sup>7</sup>

The WHO estimates that 300,000 (range 200–370,000) children aged under 5 years died from pneumococcal infections, representing around 5 percent of all-cause mortality in this age group, in 2015.<sup>8</sup> An additional 23,000 (15–40,000) deaths were estimated to occur in children co-infected with HIV. On average 75 percent of IPD and 83 percent of pneumococcal meningitis cases are aged under 2 years but the incidence and age distribution vary by country and socioeconomic status.<sup>8</sup> Importantly, at least one quarter of survivors of pneumococcal meningitis experience long-term sequelae such as hearing loss, seizures, mental and motor abnormalities.

In each geographical region globally, PCV10 and PCV13 were shown to cover more than 70 percent of the serotypes causing IPD under 5 years of age during 1980–2007 prior to PCV introduction (PCV10 range 70–94 percent and 74–88 percent for PCV13).<sup>8</sup>

## 17.3.2 Global epidemiology since the introduction of pneumococcal conjugate vaccines

### Direct impact of PCV programmes on IPD in children

Reductions in IPD among target cohorts of children in high income countries have been similar for PCV10 and PCV7/13 in reported studies. Québec (PCV10 and 13) and Finland (PCV10) both used 2+1 schedules and observed 83 percent and 79 percent reductions in IPD in vaccine-eligible children, respectively.<sup>9,10</sup> In England, using PCV7 then PCV13 in a 2+1 schedule, there was an estimated 5,000 (54 percent) fewer hospital admissions for bacteraemia, meningitis and pneumonia in children aged under 5 years over 12 years after the introduction of PCV7 and PCV13. The greatest reductions were seen in meningitis (by 71 percent) in children under 2 years age.<sup>11</sup>

### Direct impact of vaccination on non-invasive pneumococcal disease

The impact of pneumococcal conjugate vaccination on the large burden of non-invasive pneumococcal disease has been clearly demonstrated internationally in countries that have introduced these vaccines, particularly through reductions in

childhood hospitalisations due to pneumonia.<sup>12, 13</sup> Other impacts, such as on acute otitis media, are less clear and more difficult to measure accurately.<sup>14</sup> However, a systematic review found PCVs were associated with large reductions in risk of pneumococcal acute otitis media, but there was no evidence of benefit against all-cause otitis media in high-risk children over 1 year of age or older children with a history of respiratory illness.<sup>15</sup>

## Herd immunity

The extent to which childhood PCV immunisation programmes provide indirect reductions in IPD among high-risk children and older adults varies between reports, settings and vaccine serotype (notably serotypes 3 and 19A). There is some good evidence for the indirect (herd) effects of infant PCV immunisation on vaccine serotype pneumococcal disease in the non-vaccinated population, especially in adults aged 65 years and older, and an all age-effect on non-bacteraemic pneumonia.<sup>16</sup> This includes data showing reductions in the rates of IPD due to PCV7 and, more recently, PCV13 serotypes in non-vaccinated groups in many countries (for both pneumonia and IPD in adults) in North America and Europe,<sup>11, 17-26</sup> Reductions in adult pneumococcal pneumonia have also been observed in Western Kenya following the introduction of PCV10 in children<sup>27</sup> and in Japanese community-dwelling older adults following the introduction of PCV13.<sup>28</sup> These herd effects are predominantly due to decreased nasopharyngeal carriage of vaccine types in immunised children lowering transmission to unimmunised older children and adults.

Although many countries have reported significant decreases in vaccine-type IPD among children and the wider population following the introduction of PCVs to the childhood schedules, IPD due to non-PCV serotypes has increased in some, particularly in older adults.<sup>29, 30</sup> Therefore, for direct protection against a broad range of serotypes 23PPV continues to be necessary for those at highest risk of IPD.

## 17.3.3 New Zealand epidemiology

Pneumococcal disease occurs throughout the year, but is more common in the autumn and winter months.<sup>31, 32</sup> Incidence of IPD is highest in infants and the elderly, especially among Māori and Pacific peoples.<sup>31, 33-35</sup>

Isolates from cases of IPD are serotyped at ESR and detailed information by age group is regularly updated on the ESR Public Health Surveillance website (available at [www.esr.cri.nz/digital-library/notifiable-disease-dashboard/](http://www.esr.cri.nz/digital-library/notifiable-disease-dashboard/)).

### Incidence and mortality

In 2021, there were 468 notified IPD cases and the overall notification rate was 9.2 cases per 100,000 population (ESR, 3 May 2022). The highest rates of IPD were in adults aged 85 years and older (47.5 per 100,000) and in children aged under 1 year (46.0 per 100,000), followed by adults aged 75–84 years (24.3 per 100,000) and 65–74 years (17.8 per 100,000). The age-standardised rates of IPD were highest for the Pacific peoples (31.0 per 100,000, 64 cases) and Māori (26.5 per 100,000, 149 cases) ethnic



groups. These rates were 4.9 and 4.2 times higher than the age-standardised rate for the European/Other ethnic group (6.3 per 100,000, 217 cases). The incidence of IPD was 12.5-fold higher for those living in areas with the highest levels of deprivation than those living in low deprivation areas across all age groups (60.9 vs 4.9 per 100,000). IPD was recorded as the primary cause of death for 16 cases in 2022, including 5 children aged under 5 years (the most since IPD became notifiable in late 2008). In 2021, the most reported risk factor in cases aged under 5 years were children who were born premature (7.6 percent) and children who were immunocompromised (4.5 percent) (ESR, 3 May 2022).

## New Zealand epidemiology since the introduction of PCV

PCV7 was introduced in June 2008, PCV10 in July 2011 and PCV13 in July 2014, PCV10 replaced PCV13 in July 2017 on the routine Schedule (see Appendix 1). From October 2020, the number of primary doses of PCV10 were reduced to two (at age 6 weeks and 5 months) and the booster dose was brought forward from 15 months to 12 months. In December 2022, PCV13 replaced PCV10, given as a two-primary plus booster schedule routinely, and with an additional three-month dose of PCV13 for those with high-risk medical conditions as part of the extended immunisation programme.

## IPD incidence

There have been dramatic reductions in the incidence of IPD in the vaccine-eligible age groups in New Zealand following the introduction of PCV to the Schedule in 2008 (see Figure 17.1).

In children under 2 years of age, the total rate of IPD decreased by 74.3 percent since the introduction of PCV to the Schedule in late 2008: from 46.0 per 100,000 in 2009 to 11.8 per 100,000 in 2015. However, the rate has steadily increased since 2015 and in 2021 the rate of 35.7 per 100,000 was the highest since 2009.

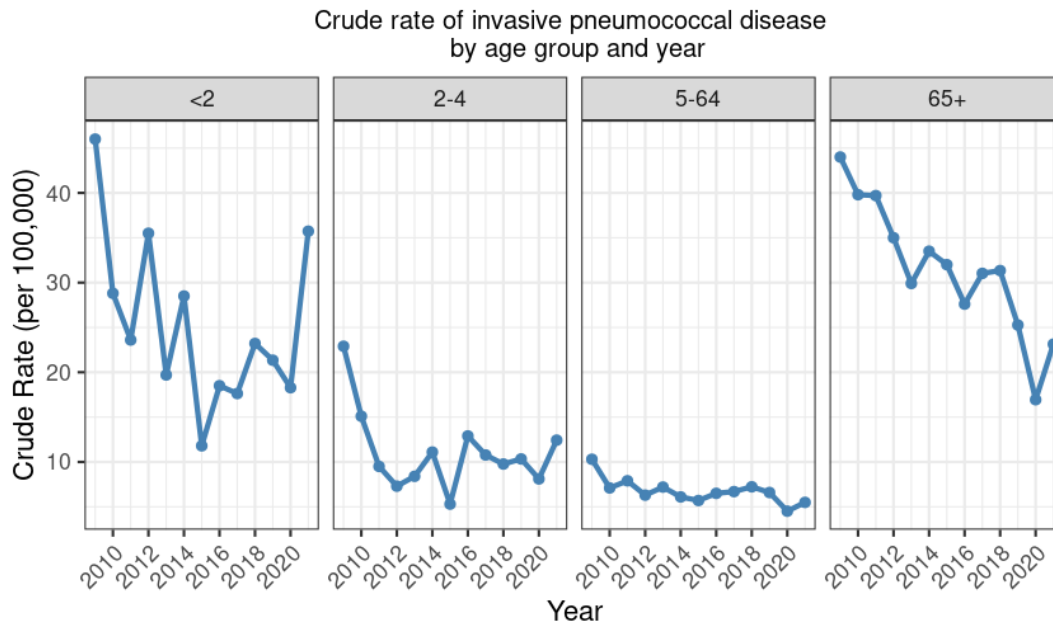
There has been a sustained reduction in PCV7 serotypes (see Figure 17.2), with few cases of PCV7 serotype IPD detected in children aged under 2 years since 2015 (ESR, 3 May 2022).

Similar reductions were seen for IPD caused by PCV10 serotypes under 2 years (see Figure 17.2). The incidence of all-cause IPD decreased in children aged 2–4 years from 2009 (by 45.9 percent; Figure 17.1), but have been rising again. Further, the rate of IPD due to PCV13-specific serotypes has been increasing since 2018 among children aged 2–4 years, though the rates are still lower than pre-2009 (Figure 17.2) (ESR, 3 May 2022). Serotype 19A has become an increasing problem, despite the theoretical cross-protection from 19F in the PCV10 vaccine.<sup>36</sup>

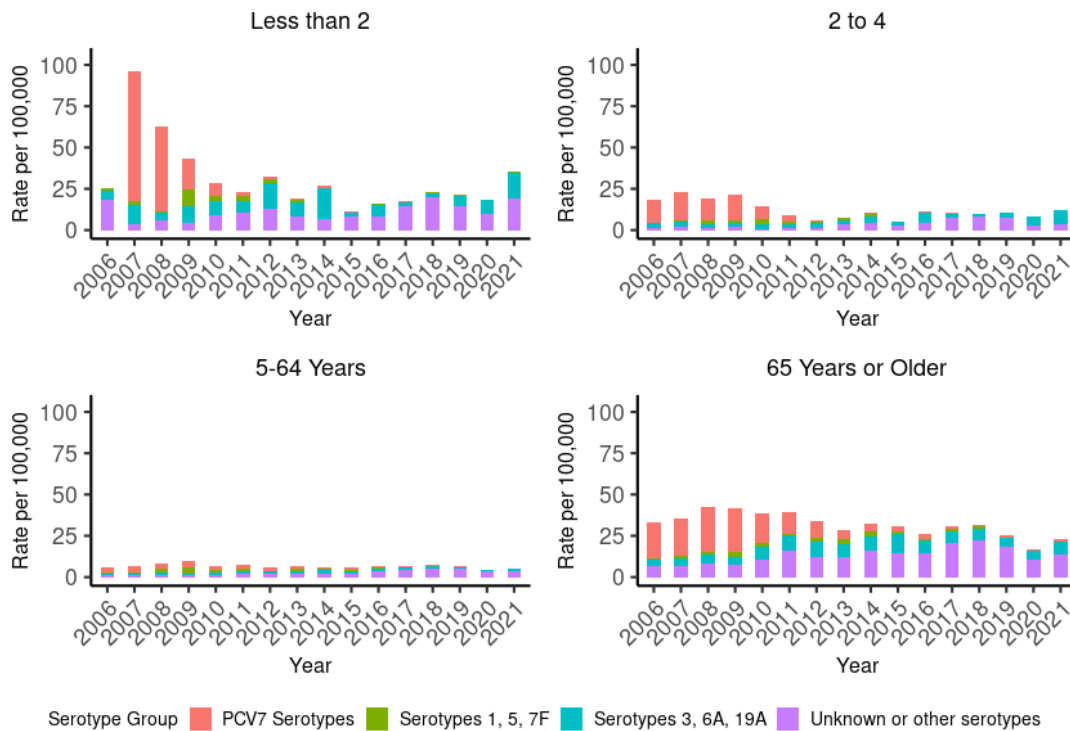
In 2021, 41.0 percent of cases in adults aged 65 years and over were PCV13 serotypes, and 73.8 percent were due to 23PPV serotypes. Of these, 37.0 percent (50/135 cases) were due to serotype 19A, and 44.4 percent were due to 23PPV-non-PCV13 serotypes (ESR, 3 May 2022).



**Figure 17.1: Rate per 100,000 of invasive pneumococcal disease by age group and year, 2009-2021**



**Figure 17.2: Rate per 100,000 population of invasive pneumococcal disease due to PCV7 serotypes, additional PCV10 types, additional PCV13 types and non-PCV types, by age group and year, 2006–2021**



**Notes:**

PCV7 was introduced in 2008, PCV10 in 2011, PCV13 in 2014 and PCV10 reintroduced in 2017.

'PCV7 serotypes' are cases due to serotypes covered by PCV7 (4, 6B, 9V, 14, 18C, 19F and 23F); 'Serotypes 1, 5, 7F' are cases due to the additional serotypes covered by PCV10; 'Serotypes 3, 6A, 19A' are cases due to the additional serotypes covered by PCV13; and 'Unknown or Other serotypes' are all other culture-positive IPD cases.

IPD became a notifiable disease in 2008. Data presented from 2009 onwards is based on IPD notifications, and data prior to 2009 is from ESR's national laboratory-based surveillance of IPD.

## Pneumococcal serotypes

Of the 468 IPD cases notified in 2021, 448 isolates were referred to ESR for serotyping. In children aged under 5 years, 49.2 percent (30/61) of cases were due to serotypes not covered by PCV, compared with 65.1 percent (136/209) and 57.9 percent (103/178) in the 5–64 years and 65 years and older age groups (ESR, 3 May 2022). In adults aged 65 years or older, serotype 23B and 16F were the most prevalent non-vaccine serotypes (PCV13 or 23PPV) in 2021 (ESR, 3 May 2022).

The number of IPD cases (246 cases) reported during July to September 2022 (Q3) was the highest of any year since IPD became a notifiable disease in 2008. In the 12 months to September 2022, the rate of 19A cases reached a record high of 23.3 cases per 100,000 in children aged under 2 years and 96 percent of PCV13-serotype cases in children under 5 years were 19A. The annualised rate was three times higher than the highest peak since IPD was notifiable: in children under 2 years the rate of 19A incidence is estimated to be 31 cases per 100,000 and 15 per 100,000 in 2–4-year-olds; and highest on record in those aged 65 years and older (10 cases per 100,000).<sup>37</sup>

## Herd immunity

The addition of PCV to the New Zealand schedule in 2008 was followed by significant reductions in IPD due to PCV7 serotypes in age groups not eligible for routine infant immunisation (Figure 17.2). Since notification-based surveillance began in late 2008, the rate of IPD due to PCV7 serotypes in the 5–64-year age group decreased 96 percent from 3.8 per 100,000 to 0.2 per 100,000 in 2021, and the rate in cases aged 65 years and over decreased 94.3 percent from 26.6 to 1.5 per 100,000 (ESR, 3 May 2022). Though not as much of a decrease, the total rate of IPD in adults decreased by approximately 50 percent from 2009 to 2021 (rate for age 5–64 years: 10.3 to 5.5 per 100,000; age 65 years and over: 44.0 to 23.1 per 100,000).

## Impact of vaccination on non-invasive pneumococcal disease

While hospitalisations for respiratory infections in children aged 5 years and under have been increasing in New Zealand, hospitalisations for all-cause pneumonia have declined significantly since the implementation of the pneumococcal conjugate vaccine programme in 2008. The largest reductions in all-cause pneumonia hospitalisations between 2006 and 2015 were in Māori (a 12 percent reduction) and Pacific children (a 21 percent reduction) and those living in areas of high deprivation.<sup>38</sup> A 51 percent decline in otitis media hospitalisations was observed for Māori children aged under 6 years following PCV immunisation, compared with 8 percent decline in otitis media across all ethnicities.<sup>38</sup>

## Antimicrobial resistance

Introduction of pneumococcal conjugate vaccination reduced the circulation of resistant pneumococcal serotypes in the US,<sup>39</sup> but little change has been seen in

New Zealand since PCV introduction. *S. pneumoniae* resistance to penicillin (14.1–23.5 percent) and cefotaxime resistance (0.4–2.1 percent) has varied year-to-year over the last decade with no significant trend.<sup>40</sup> A systematic review found that in countries with relatively high levels of pneumococcal antimicrobial resistance, the introduction of PCV13 was associated with reduction in antimicrobial resistance likely due to a reduction in serotype 19A.<sup>41</sup> However, heterogeneity between studies reflects the multiple drivers of antimicrobial resistance between countries and over time.<sup>42</sup>

In 2020, PCV7 serotypes accounted for 7 percent of the penicillin-resistant isolates compared with 92.8 percent in 2006/07, prior to vaccine introduction, but the prevalence of penicillin resistance among serotype 19A isolates increased just over four-fold from 15.8 percent in 2006/07 to 72.2 percent in 2020. The relative contribution of serotype 19A to penicillin-resistant invasive pneumococci had decreased, from a high of 52.1 percent in 2015 to 28.1 percent in 2019. In 2020, serotype 19A accounted for 44.8 percent of the penicillin-resistant isolates (ESR, 3 May 2022).

## 17.4 Vaccines

### 17.4.1 Available vaccines

There are two types of pneumococcal vaccine approved for use in New Zealand for use against *S. pneumoniae*: pneumococcal conjugate vaccine (PCV) with ten or 13 serotypes and a plain polysaccharide pneumococcal vaccine (PPV) containing 23 serotypes. In PCVs, the pneumococcal surface polysaccharide is coupled to a carrier protein that induces increased production of type-specific antibodies, particularly in children aged under 2 years, and immunological memory enabling booster responses with subsequent doses (see section 1.4.3). Table 17.1 presents the polysaccharide serotypes contained within each vaccine.

**Table 17.1: Pneumococcal vaccine serotype content**

PCV7			4			6B				9V			14		18C	19F		23F					
PCV10	1		4	5		6B	7F			9V			14		18C	19F		23F					
PCV13	1		3	4	5	6A	6B	7F		9V			14		18C	19A	19F		23F				
23PPV	1	2	3	4	5	6B	7F	8	9N	9V	10A	11A	12F	14	15B	17F	18C	19A	19F	20	22F	23F	33F

Note: PCV10 contained serotype 6B and 19F, which elicit cross-reactive opsonophagocytic antibodies against serotype 6A and 19A, respectively, but at a lower level than PCV13.<sup>8</sup> The use of this vaccine has discontinued in New Zealand.

## Funded vaccines

### **PCV13 (Prevenar 13, Pfizer)**

Each 0.5 mL dose of PCV13 contains:

- 2.2 µg of pneumococcal purified capsular polysaccharides for serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F and 23F, and 4.4 µg of serotype 6B, conjugated to non-toxic diphtheria CRM197 protein and adsorbed onto aluminium phosphate (0.565 mg)
- succinic acid, polysorbate 80, aluminium phosphate, phosphate, and sodium chloride in water for injection.

### **23PPV (Pneumovax 23, MSD)**

Each 0.5 mL dose of 23PPV contains:

- 25 µg of each capsular polysaccharide antigen (serotypes: 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F and 33F)
- sodium chloride, water for injection, and phenol (0.25 percent) added as a preservative.

## Other vaccine

A ten-valent pneumococcal conjugate vaccine, PCV10 (Synflorix, GSK), was used as part of the Schedule from 2017 to 2022, and previously from 2010 to 2014, with a 2+1 schedule (at ages 6 weeks, 5 months and 12 months) implemented routinely in 2020. This vaccine contains polysaccharides from pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14 and 23F conjugated to non-typeable *Haemophilus influenzae* (NTHi) protein D, serotype 18C conjugated to tetanus toxoid, and serotype 19F conjugated to diphtheria toxoid, adsorbed onto aluminium phosphate. The use of this vaccine was discontinued in New Zealand in December 2022.

## 17.4.2 Efficacy and effectiveness

### 13-valent pneumococcal conjugate vaccine

#### Childhood schedule

The immunogenicity of PCV13 in a 2+1 schedule (two primary plus booster) was found to be non-inferior to a PCV10 3+1 schedule (three primary doses plus booster) in Vietnam. In a clinical trial, 250 infants received PCV13 at ages 2, 4 and 9.5 months and were compared with 152 infants given PCV10 at ages 2, 3, 4 and 9.5 months or PCV10 as 2+1 schedule, and given concomitantly with DTaP-IPV-HepB/Hib. In the PCV13 group, more than 95 percent of infants responded to most serotypes after the primary doses (except for serotypes 6B and 23F). The magnitude of the response was greater for eight of the shared serotypes in the PCV13 group than the PCV10 groups. At 9 months (pre-booster), 75.4 percent to 100 percent of PCV10 groups and 68.9 percent

to 99.1 percent of the PCV13 group had seroprotective antibody levels to most of the ten shared serotypes. Post-booster more than 97 percent of participants had IgG concentrations  $\geq 0.35$   $\mu\text{g/ml}$  for all ten shared serotypes. Geometric mean concentrations followed a similar pattern post-booster to that seen post-primary for most serotypes. Only modest responses were seen against serotype 3 in the PCV13 group. For non-PCV10 serotypes, 94 percent of infants who received PCV13 had seroprotective levels of IgG against serotypes 3, 6A and 19A post primary and 99 percent post booster. At age 18 months, at least 95 percent of participants had seroprotective IgG levels for serotypes 14 and 19F, and for 6B (in PCV10 group), and more than 59 percent for all other shared serotypes.<sup>43</sup>

When breakthrough cases of IPD caused by serotype 19A were investigated in Québec, 19 of 31 cases (61 percent) occurred between ages 8 and 14 months, following two primary doses of PCV13 and prior to the toddler dose. Although PCV10-serotype 19F showed direct cross-protection against 19A in infants, there was no evidence of reduction in 19A carriage or indirect (herd) reductions in adults, whereas PCV13 did reduce 19A carriage and induce herd effects. It was proposed that a recent upswing in 19A may be due to a window of susceptibility in infants under a 2+1 schedule for PCV13 as 19A continues to circulate, but this was anticipated to decrease with stronger herd effects over time.<sup>9</sup>

### Individuals at increased risk of IPD

Few studies have investigated the immunogenicity and effectiveness of PCV13 in individuals at increased risk of IPD. Studies using pneumococcal vaccines with similar but fewer antigens have demonstrated vaccine efficacy in individuals with immunocompromising conditions (eg, HIV, sickle cell disease), but the duration of protection against IPD remains unknown.<sup>44</sup> High IgG titres have been demonstrated following PCV13 vaccination of children with sickle cell disease,<sup>45</sup> HIV infection<sup>46</sup> and nephrotic syndrome.<sup>47</sup>

WHO recommends that children with medical conditions that reduce humoral immune response to vaccines, such as HIV, sickle cell disease and primary immune deficiencies, to have a 3+1 schedule of PCV13.<sup>8</sup> In children and adolescents with underlying medical conditions, such as type-1 diabetes, cancer, cystic fibrosis or asthma, the broader serotype protection provided by PCV13 can reduce nasopharyngeal carriage and the associated risk of IPD.<sup>48-51</sup>

### Use of pneumococcal conjugate vaccines in adults

PCV13 induces robust immune responses in adults,<sup>52-55</sup> including elderly adults.<sup>56</sup> Although the antibody titres vary with serotype and between age groups, particularly for those aged over 65 years, the clinical significance of this variation is unclear.<sup>53</sup> PCV13 is at least as immunogenic as 23PPV in adults. Some studies suggest that prior 23PPV attenuates the immune response to PCV13, an effect not seen if PCV13 is given before 23PPV; conversely given first, PCV13 may augment the response to subsequent 23PPV vaccination.<sup>56-58</sup>

With respect to clinical outcomes, the Community-Acquired Pneumonia Immunization Trial in Adults (CAPITA) was a large, randomised, placebo-controlled trial conducted in the Netherlands that assessed efficacy of PCV13 against pneumococcal community-

acquired pneumonia (CAP) with and without IPD in adults aged 65 years and older. The efficacy of PCV13 against vaccine-type IPD was 75 percent (95% CI: 41.4–90.8) and 45.6 percent (95% CI: 21.8–62.5) against vaccine-type pneumococcal CAP; 45.0 percent (95% CI: 14.2–65.3) for both combined.<sup>59</sup> Although this study showed individual protection for vaccine-type CAP, there was no significant reduction in all-cause pneumonia.<sup>59</sup>

An important uncertainty is the extent of indirect protection against vaccine-type IPD cases stemming from childhood immunisation programmes, which varies between countries. Where vaccine serotypes are sufficiently prevalent, PCV13 would provide some protection against all-cause CAP and lobar pneumonia.<sup>60</sup> Some of the non-PCV13 vaccine serotypes more likely to cause disease in adults are covered by 23PPV.

Data is limited for younger adults and specific at-risk adult populations.

## 23-valent vaccine pneumococcal polysaccharide

The polysaccharide vaccine (23PPV, Pneumovax 23) is made from the purified capsular polysaccharides of 23 serotypes of *S. pneumoniae*. It is available in New Zealand for adults and children from age 2 years. The 23 serotypes included in 23PPV (see Table 17.1) are responsible for about 90 percent or more of IPD in high-income countries.

See recent IPD surveillance reports from ESR for prevalence of serotypes covered by 23PPV in New Zealand (available at [hwww.esr.cri.nz/digital-library/notifiable-disease-dashboard/surv.esr.cri.nz/surveillance/IPD.php](http://hwww.esr.cri.nz/digital-library/notifiable-disease-dashboard/surv.esr.cri.nz/surveillance/IPD.php)).

A meta-analysis of IPD in adults aged from 65 years in 10 European countries showed that incidence of PCV7 serotypes had declined by 77 percent and for additional PCV13 serotypes by 38 percent after 5 years of PCV13/PCV10 immunisation programmes. The incidence rate of 23PPV-non-PCV13 serotypes had increased by around 50 percent with these 11 serotypes causing 22–54 percent of IPD.<sup>61</sup> In 2016, more than two-thirds of IPD cases in adults age 65 years or older were 23PPV-non-PCV13 serotypes.<sup>40</sup>

The efficacy of 23PPV varies depending on whether immune-competent or immunocompromised patients are studied, and whether the end point is pneumococcal pneumonia or bacteraemia.

The limitations of the polysaccharide vaccine have been summarised as:

- reduced efficacy in high-risk individuals
- uncertain efficacy against pneumonia
- it is only suitable for children aged 2 years and older.
- waning protection 2.5 to 5 years after vaccination.

A 2017 meta-analysis from Germany found pooled VE for 23PPV against any serotype IPD of 45 percent (95% CI: 15–65), 59 percent (95% CI: 35–74) or 73 percent (95% CI: 10–92) across cohort, case-control or clinical trial data; and pooled VE against any serotype pneumococcal pneumonia of 48 percent (95% CI: 25–63) and 64 percent (95% CI: 35–80) in cohort studies and clinical trials.<sup>62</sup> For both outcomes, waning of



protection was found between 2.5 years and 5 years of follow-up after 23PPV.<sup>62</sup> Other systematic reviews, with differing eligibility criteria, found lower pooled VE estimates against IPD or pneumococcal pneumonia for 23PPV.<sup>63-65</sup> A Japanese prospective study found 23PPV to have moderate but variable effectiveness against vaccine-type pneumococcal pneumonia in adults aged 65 years or older.<sup>66</sup> Hence, questions remain around the clinical effectiveness and intervals between repeat doses of 23PPV that provide continued protection.

### 17.4.3 Dosage and administration

The dose of PCV13 and 23PPV is 0.5 mL, administered by intramuscular injection (see section 2.2.3). 23PPV can also be administered by subcutaneous injection (see section 2.2.3), but there is an increased likelihood of injection-site reactions.<sup>67</sup>

#### Co-administration with other vaccines

PCV13 or 23PPV may be administered at the same time as other routine childhood vaccinations, in a separate syringe at a separate injection site (see section 2.2.7 for information about multiple injections at the same visit).

PCV13 has been associated with increased risk of fever over 39°C and febrile convulsions when co-administered with inactivated influenza vaccine in children aged 6 months to under 5 years. Separation of the vaccines by two days can be offered but is not essential (see section 17.6.2). Systemic reactions have been noted in adults aged over 65 years.

### 17.4.4 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at [www.tewhātuora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhātuora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

Store at +2°C to +8°C. Do not freeze.



## 17.5 Recommended immunisation schedule

### 17.5.1 Usual childhood schedule

#### Children aged under 5 years

PCV13 (Prevenar 13) vaccine is funded for all children aged under 5 years. Two doses of PCV13 are given as the primary course, with a booster at age 12 months (Table 17.2). Children who started their immunisation course with PCV10 can complete it with PCV13.

**Table 17.2: Usual childhood PCV schedule**

Age	Vaccine	Comment
6 weeks	PCV13	Primary series
5 months	PCV13	Primary series
12 months	PCV13	Booster

Where a previously unimmunised child aged under 5 years presents late for pneumococcal vaccination, the age-appropriate catch-up schedules in Appendix 2 should be followed.

### 17.5.2 Extended pneumococcal immunisation for high-risk groups

As part of the extended immunisation programme for high-risk groups, PCV13 and 23PPV are funded for eligible individuals, as shown in Table 17.3, Table 17.4 and Table 17.5. Because the recommended schedule depends on the age of the individual at diagnosis, the tables have been organised into age groups (under 5 years, 5–18 years and 18 years and older).

The PCV13 and 23PPV funding restrictions are as follows. See Table 17.3, Table 17.4 and Table 17.5 for the eligible conditions and dosing requirements.

#### PCV13

All high-risk infants (aged under 12 months) are recommended to receive three doses of a PCV vaccine, with at least one booster dose at or after 12 months of age. Change to the PCV13 extended schedule as soon as the infant is diagnosed as being at high risk (a dose is given at age 3 months in addition to the usual schedule).

- Two doses of PCV13 are funded for high-risk children aged from 12 months and under 18 years irrespective of previous doses of any non-PCV13 vaccine (PCV10 or PCV7); or,
- Up to an additional four doses of PCV13 are funded for vaccination or re-vaccination of high-risk children aged under 5 years.
- Up to an additional four doses of PCV13 are funded for vaccination or re-vaccination of eligible individuals aged 5 years and older.

## 23PPV

- Up to three doses of 23PPV are funded for individuals with eligible conditions.
- Up to two doses of 23PPV are funded for high-risk children aged under 18 years.

See also section 17.5.3 '(Re)vaccination'. See sections 4.2 and 4.3 for more information about immunocompromised infants, children and adults, including additional vaccine recommendations and schedule tables for certain conditions.

**Table 17.3: Extended pneumococcal immunisation for children aged under 5 years – funded PCV13 and 23PPV indications and schedules**

See the Pharmaceutical Schedule ([pharmac.govt.nz](http://pharmac.govt.nz)) for any changes to funding decisions.

**PCV13 (Prevenar 13) and 23PPV (Pneumovax 23) are funded for children aged under 5 years with any of the following:**

- prior to planned immunosuppressive therapy or radiotherapy, including prior to solid organ transplantation
- on immunosuppressive therapy or radiotherapy (vaccinate when there is expected to be a sufficient immune response)
- primary immune deficiencies
- HIV infection
- renal failure or nephrotic syndrome
- who are immunosuppressed following organ transplantation (including HSCT)
- cochlear implants or intracranial shunts
- cerebrospinal fluid leaks
- receiving corticosteroid therapy for more than 2 weeks, and who are on an equivalent daily dosage of prednisone of 2 mg/kg per day or greater, or children who weigh more than 10 kg on a total daily dosage of 20 mg or greater
- with chronic pulmonary disease (including asthma treated with high-dose corticosteroid therapy)
- who were preterm infants, born before 28 weeks' gestation<sup>a</sup>
- cardiac disease, with cyanosis or failure
- diabetes
- Down syndrome
- who are pre- or post-splenectomy, or with functional asplenia.

Age at diagnosis	Vaccine	Recommended vaccine schedule
<12 months	PCV13	PCV13 at ages 6 weeks, 3, 5 <sup>b</sup> and 12 months or an age-appropriate catch-up schedule.  For those who have not been immunised at age 7–11 months – give 2 doses of PCV13 (8 weeks apart) and a further dose 8 weeks later, from age 12 months.  For children aged 7–11 months who have completed a 2-dose primary course with PCV10, give 1 dose of PCV13 as soon as possible and another dose (of PCV13) 8 weeks later, from age 12 months.
	23PPV	Following the completion of the PCV course, give 1 dose of 23PPV at age ≥2 years. There must be at least 8 weeks between the last PCV dose and the 23PPV dose.  If risk persists, revaccinate once with 23PPV, 5 years after the first 23PPV.
12 months to <5 years	PCV13	For children who have not yet received any PCV13, give 2 doses of PCV13 at least 8 weeks apart. <sup>c,d</sup>
	23PPV	Give 1 dose at least 8 weeks after the last PCV13 dose, from age 2 years.  If risk persists, revaccinate once with 23PPV, 5 years after the first 23PPV.

- a. Children aged from 2 years who were born prematurely <28 weeks can benefit from 23PPV if they have ongoing lung disease
- b. A dose of PCV13 is given at 3 months, in addition to the usual Schedule.
- c. If 23PPV has already been given (prior to any doses of PCV13) to children aged under 5 years, wait at least 8 weeks before administering PCV13 (note: this timing differs in adults, see footnote in Table 17.5).

- d. There are no safety concerns, regardless of the interval between the last dose of PCV10 and the first dose of PCV13.

**Table 17.4: Extended pneumococcal immunisation for children aged from 5 to under 18 years – funded PCV13 and 23PPV indications and schedules**

**PCV13 (Prevenar 13) and 23PPV (Pneumovax 23) are funded for children aged 5 to under 18 years:**

- with HIV infection
- who are pre- or post-HSCT<sup>a</sup> or chemotherapy<sup>a</sup>
- who are pre- or post-splenectomy or with functional asplenia
- who are pre- or post-solid organ transplant
- undergoing renal dialysis
- with complement deficiency (acquired or inherited)
- with cochlear implants or intracranial shunts
- with cerebrospinal fluid leaks
- with primary immunodeficiency<sup>d</sup>

**Additionally, 23PPV (Pneumovax 23) is funded for children aged 5 to under 18 years:**

- prior to planned immunosuppressive therapy or radiotherapy, including prior to solid organ transplantation
- on immunosuppressive therapy or radiotherapy (vaccinate when there is expected to be a sufficient immune response)
- with renal failure or nephrotic syndrome
- who are immunosuppressed following organ transplantation (including HSCT)
- who are receiving corticosteroid therapy for more than 2 weeks, and who are on an equivalent daily dosage of prednisone of 2 mg/kg per day or greater, or children who weigh more than 10 kg on a total daily dosage of 20 mg or greater
- with chronic pulmonary disease (including asthma treated with high-dose corticosteroid therapy)
- who were preterm infants, born before 28 weeks' gestation<sup>e</sup>
- with cardiac disease, with cyanosis or failure
- with diabetes
- with Down syndrome

Age at diagnosis	Vaccine	Recommended vaccine schedule
5 years to <18 years	PCV13	For children who have not previously received PCV13 – give 1 dose of PCV13, even if fully vaccinated <sup>b,c</sup>
	23PPV	1 dose of 23PPV at least 8 weeks after the PCV13 dose. If risk persists, revaccinate once with 23PPV, 5 years after the first 23PPV.

- a. PCV13 is funded pre- or post-HSCT or chemotherapy. 23PPV is only funded post-HSCT or chemotherapy.
- b. If 23PPV has already been given (prior to any doses of PCV13) to children aged under 18 years, wait at least 8 weeks before administering PCV13.
- c. There are no safety concerns, regardless of the interval between the last dose of PCV10 and the first dose of PCV13.
- d. See section 4.3.2 for children with Down syndrome
- e. Children aged from 2 years who were born prematurely <28 weeks can benefit from 23PPV if they have ongoing lung disease. If lung disease persists, a further dose may be required to be given after 5 years.

**Table 17.5: Extended pneumococcal immunisation for adults aged 18 years and older – funded PCV13 and 23PPV indications and schedules**

<b>PCV13 (Prevenar 13) and 23PPV (Pneumovax 23) are funded for (re)vaccination of patients:</b>		
<ul style="list-style-type: none"> <li>• with HIV infection</li> <li>• who are pre- or post-HSCT<sup>a</sup> or chemotherapy<sup>a</sup></li> <li>• who are pre- or post-splenectomy or with functional asplenia</li> <li>• who are pre- or post-solid organ transplant</li> <li>• undergoing renal dialysis</li> <li>• with complement deficiency (acquired or inherited)</li> <li>• with cochlear implants, intracranial shunts<sup>b</sup> or cerebrospinal fluid leaks<sup>b</sup></li> <li>• with primary immunodeficiency.</li> </ul>		
<b>Age at diagnosis</b>	<b>Vaccine</b>	<b>Recommended vaccine schedule</b>
≥18 years	PCV13	Give one dose of PCV13 <sup>c</sup>
	23PPV	Give a maximum of 3 doses of 23PPV in a lifetime, a minimum of 5 years apart. The first 23PPV dose is given at least 8 weeks after PCV13, the 2nd a minimum of 5 years later, and the 3rd dose at age ≥65 years.

- a. PCV13 is funded pre- or post-HSCT or chemotherapy. 23PPV is only funded post HSCT or chemotherapy.
- b. Only PCV13 is funded for these indications; 23PPV is recommended but not funded.
- c. If 23PPV has already been given (prior to any doses of PCV13) to adults aged 18 years and older, wait at least 1 year before administering PCV13.

### 17.5.3 (Re)vaccination

Up to an additional four doses of PCV13 and up to additional three doses of 23PPV are funded for vaccination or re-vaccination of high-risk individuals (as listed in Table 17.3, Table 17.4 and Table 17.5).

See also sections 4.3 and 4.6.

### 17.5.4 Recommended but not funded

#### Risk stacking

Two classifications of IPD risk are recognised: ‘high-risk’ conditions for which there is significant risk of IPD and ‘at-risk’ conditions, which on their own may not significantly increase risk, but when combined or with added lifestyle risk factors increase an individual’s risk of IPD. This is described as ‘risk stacking’ – IPD incidence substantially increases with the accumulation of concurrent risk factors or conditions.<sup>3, 4</sup> The risk of pneumococcal infections in those with two or more at-risk conditions may be as high as the risk for those with a recognised high-risk condition.<sup>68-70</sup>

## Recommendations

PCV13 and 23PPV are recommended but not funded for the following individuals:

- immune-competent adults (aged 18 years and older) at increased risk of pneumococcal disease or its complications because of chronic illness (eg, chronic heart, renal, liver or pulmonary disease, diabetes or alcohol dependency)
- immunocompromised adults at increased risk of pneumococcal disease (eg, those with nephrotic syndrome, multiple myeloma, lymphoma and Hodgkin's disease)
- individuals of any age who have had one episode of IPD
- smokers.

PCV13 is funded but 23PPV is also recommended and not funded for individuals with:

- intracranial shunts
- cerebrospinal fluid leakage.

For those individuals who choose to purchase PCV13 and 23PPV vaccines, providers may follow the age-appropriate schedules in Table 17.4 and Table 17.5.

### Adults aged 65 years and older with no other risk factors

Give one dose of PCV13 followed at least eight weeks later with 23PPV (not funded).

## 17.5.5 Pregnancy and breastfeeding

Pneumococcal vaccines are not routinely recommended for pregnant women.

Women of childbearing age who are eligible for funded PCV13 and 23PPV should be vaccinated before a planned pregnancy or as soon as possible after delivery (see Table 17.5). Administration of these vaccines in pregnancy is unlikely to result in serious adverse effects and may be considered in individuals at the very high risk of IPD who were not vaccinated prior to pregnancy.<sup>71</sup>

PCV13 and 23PPV may be given to breastfeeding women.<sup>71</sup>

## 17.6 Contraindications and precautions

See section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

## 17.6.1 Contraindications

There are no specific contraindications to pneumococcal polysaccharide or conjugate vaccines apart from a severe reaction to a previous dose or known hypersensitivity to any components of either vaccine.

## 17.6.2 Precautions

Systemic reactions (chills, rash and myalgia) may occur when PCV13 and influenza vaccine are administered at the same time. PCV13 has been associated with a slightly higher risk of fever over 39°C and febrile convulsions when co-administered with inactivated influenza vaccine in infants and young children, compared to when administered separately.<sup>72</sup> Febrile convulsion history is not a contraindication to PCV13 immunisation. If indicated, PCV13 and influenza vaccines may be given to a child aged under 5 years at the same visit.<sup>71</sup> Parents/guardians should be informed of the small risk of febrile convulsions, and separation of vaccines by two days can be offered. If the child has a history of febrile convulsions, separation of the vaccines is recommended.

23PPV should not be given to children aged under 2 years due to the reduced immune response associated with polysaccharide vaccines (see section 1.4.3).

# 17.7 Potential responses and AEFIs

## 17.7.1 Pneumococcal conjugate vaccines

Pneumococcal conjugate vaccines have excellent safety profiles. A 2016 systematic review found that pneumococcal conjugate vaccines are considered safe for use in children, and serious adverse events are detected very rarely by post-marketing surveillance.<sup>73</sup>

The most commonly reported adverse reactions after PCV13 are injection-site reactions, fever, irritability, decreased appetite and increased or decreased sleep.<sup>74</sup> An increase in injection-site reactions was reported in children older than 12 months compared to rates observed in infants during the primary series with PCV13.

No serious adverse events have been identified in adults or children, associated with underlying disease or immunocompromise.<sup>75-77</sup>

## 17.7.2 Pneumococcal polysaccharide vaccine

Local discomfort, erythema and induration lasting a couple of days are potential responses.<sup>78</sup> Local and systemic reactions, such as self-limiting mild fever, myalgia and



decreased arm movement in injected limb, may occur after revaccination of adults, particularly when the second dose is given within five years of the first dose.<sup>71</sup>

## 17.8 Public health measures

IPD is a notifiable condition, and if confirmed, the laboratory undertaking the testing must notify the local medical officer of health.

Local public health action is not expected in response to individual notifications of this disease. Passive surveillance for IPD and pneumococcal serotypes help to inform the immunisation schedule.

Antimicrobial prophylaxis is not indicated for close contacts of cases of IPD. For those at high risk of pneumococcal disease where response to vaccination may be poor, antimicrobial prophylaxis may be indicated. Discuss with an appropriate specialist.

For more details on control measures, refer to the '*Invasive pneumococcal disease*' chapter of the *Communicable Disease Control Manual* (available at [www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual](http://www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual) ).

## 17.9 Variations from the vaccine data sheet

The PCV13 (Prevenar 13) data sheet states that there is no data on the interchangeability of PCV13 with other pneumococcal conjugate vaccines containing a protein carrier different from CRM197. Health New Zealand | Te Whatu Ora recommends that those who started with PCV10 may complete with PCV13 (see section 17.5).

Children aged 24–59 months who have not received any PCV, or only one dose of PCV10 before the age of 12 months, are recommended to receive two doses of PCV13 given 8 weeks apart rather than one dose as given on the PCV13 (Prevenar 13) datasheet (see Appendix 2, Table A2.6).

## References

1. American Academy of Pediatrics. 2021. Pneumococcal infections. in *Red Book: 2021 Report of the Committee on Infectious Diseases*, Kimberlin D, Brady M, Jackson M, and Long S (eds). Elk Grove Village, IL. p. 639-650. URL: <https://redbook.solutions.aap.org/redbook.aspx>. (accessed 3 Nov 2022)
2. World Health Organization. Pneumococcal vaccines – WHO position paper, 2012. *Weekly Epidemiological Record*, 2012. 87(14): p. 129–44.
3. Shea KM, Edelsberg J, Weycker D, et al. Rates of pneumococcal disease in adults with chronic medical conditions. *Open Forum Infect Dis*, 2014. 1(1): p. ofu024.
4. Morton JB, Morrill HJ, LaPlante KL, Caffrey AR. Risk stacking of pneumococcal vaccination indications increases mortality in unvaccinated adults with *Streptococcus pneumoniae* infections. *Vaccine*, 2017. 35(13): p. 1692-1697.
5. Dirmesropian S, Liu B, Wood JG, et al. Pneumonia hospitalisation and case-fatality rates in older Australians with and without risk factors for pneumococcal disease: implications for vaccine policy. *Epidemiology and Infection*, 2019. 147: p. e118.
6. Seminog OO, Goldacre MJ. Risk of pneumonia and pneumococcal disease in people with severe mental illness: English record linkage studies. *Thorax*, 2013. 68(2): p. 171-176.
7. Chapman KE, Wilson D, Gorton R. Invasive pneumococcal disease and socioeconomic deprivation: A population study from the North East of England. *Journal of Public Health (United Kingdom)*, 2013. 35(4): p. 558-569.
8. World Health Organization. Pneumococcal conjugate vaccines in infants and children under 5 years of age: WHO position paper – February 2019. *Weekly Epidemiological Record*, 2019. 94(8): p. 85-104.
9. De Wals P, Lefebvre B, Deceuninck G, Longtin J. Incidence of invasive pneumococcal disease before and during an era of use of three different pneumococcal conjugate vaccines in Quebec. *Vaccine*, 2018. 36(3): p. 421-426.
10. Rinta-Kokko H, Palmu AA, Auranen K, et al. Long-term impact of 10-valent pneumococcal conjugate vaccination on invasive pneumococcal disease among children in Finland. *Vaccine*, 2018. 36(15): p. 1934-1940.
11. Shiri T, McCarthy ND, Petrou S. The impact of childhood pneumococcal vaccination on hospital admissions in England: a whole population observational study. *BMC Infectious Diseases*, 2019. 19(1): p. 510.
12. Lucero MG, Dulalia VE, Nillos LT, et al. Pneumococcal conjugate vaccines for preventing vaccine-type invasive pneumococcal disease and X-ray defined pneumonia in children less than two years of age. *Cochrane Database Syst Rev*, 2009(4): p. CD004977.
13. Fitzwater SP, Chandran A, Santosham M, Johnson HL. The worldwide impact of the seven-valent pneumococcal conjugate vaccine. *Pediatric Infectious Disease Journal*, 2012. 31(5): p. 501-8.
14. Taylor S, Marchisio P, Vergison A, et al. Impact of pneumococcal conjugate vaccination on otitis media: a systematic review. *Clinical Infectious Diseases*, 2012. 54(12): p. 1765-73.
15. Fortanier AC, Venekamp RP, Boonacker CW, et al. Pneumococcal conjugate vaccines for preventing acute otitis media in children. *Cochrane Database Syst Rev*, 2019. 5: p. CD001480.
16. Simonsen L, Taylor RJ, Young-Xu Y, et al. Impact of pneumococcal conjugate vaccination of infants on pneumonia and influenza hospitalization and mortality in all age groups in the United States. *MBio*, 2011. 2(1): p. e00309-10.
17. Ahmed SS, Pondo T, Xing W, et al. Early impact of 13-valent pneumococcal conjugate vaccine use on invasive pneumococcal disease among adults with and

- without underlying medical conditions – United States. *Clinical Infectious Diseases*, 2019.
18. Centers for Disease Control and Prevention. Direct and indirect effects of routine vaccination of children with 7-valent pneumococcal conjugate vaccine on incidence of invasive pneumococcal disease – United States, 1998–2003. *Morbidity and Mortality Weekly Report*, 2005. 54(36): p. 893–7.
  19. Demczuk WH, Martin I, Griffith A, et al. Serotype distribution of invasive *Streptococcus pneumoniae* in Canada after the introduction of the 13-valent pneumococcal conjugate vaccine, 2010–2012. *Canadian Journal of Microbiology*, 2013. 59(12): p. 778–88.
  20. Elberse KE, van der Heide HG, Witteveen S, et al. Changes in the composition of the pneumococcal population and in IPD incidence in The Netherlands after the implementation of the 7-valent pneumococcal conjugate vaccine. *Vaccine*, 2012. 30(52): p. 7644–51.
  21. Griffin MR, Zhu Y, Moore MR, et al. U.S. hospitalizations for pneumonia after a decade of pneumococcal vaccination. *New England Journal of Medicine*, 2013. 369(2): p. 155–63.
  22. Ingels H, Rasmussen J, Andersen PH, et al. Impact of pneumococcal vaccination in Denmark during the first 3 years after PCV introduction in the childhood immunization programme. *Vaccine*, 2012. 30(26): p. 3944–50.
  23. Miller E, Andrews NJ, Waight PA, et al. Herd immunity and serotype replacement 4 years after seven-valent pneumococcal conjugate vaccination in England and Wales: an observational cohort study. *Lancet Infectious Diseases*, 2011. 11(10): p. 760–8.
  24. Pilishvili T, Lexau C, Farley MM, et al. Sustained reductions in invasive pneumococcal disease in the era of conjugate vaccine. *Journal of Infectious Diseases*, 2010. 201(1): p. 32–41.
  25. Steens A, Bergsaker MA, Aaberge IS, et al. Prompt effect of replacing the 7-valent pneumococcal conjugate vaccine with the 13-valent vaccine on the epidemiology of invasive pneumococcal disease in Norway. *Vaccine*, 2013. 31(52): p. 6232–8.
  26. Vestheim DF, Hoiby EA, Bergsaker MR, et al. Indirect effect of conjugate pneumococcal vaccination in a 2+1 dose schedule. *Vaccine*, 2010. 28(10): p. 2214–2221.
  27. Bigogo GM, Audi A, Auko J, et al. Indirect effects of 10-valent pneumococcal conjugate vaccine against adult pneumococcal pneumonia in rural Western Kenya. *Clinical Infectious Diseases*, 2019.
  28. Sando E, Suzuki M, Furumoto A, et al. Impact of the pediatric 13-valent pneumococcal conjugate vaccine on serotype distribution and clinical characteristics of pneumococcal pneumonia in adults: The Japan Pneumococcal Vaccine Effectiveness Study (J-PAVE). *Vaccine*, 2019. 37(20): p. 2687–2693.
  29. Naucler P, Galanis I, Morfeldt E, et al. Comparison of the Impact of Pneumococcal Conjugate Vaccine 10 or Pneumococcal Conjugate Vaccine 13 on Invasive Pneumococcal Disease in Equivalent Populations. *Clinical Infectious Diseases*, 2017. 65(11): p. 1780–1789.
  30. Levy C, Varon E, Ouldali N, et al. Changes in invasive pneumococcal disease spectrum after 13 valent pneumococcal conjugate vaccine implementation. *Clinical Infectious Diseases*, 2019.
  31. Singh KP, Voolmann T, Lang SD. Pneumococcal bacteraemia in south Auckland: a five year review with emphasis on prescribing practices. *New Zealand Medical Journal*, 1992. 105(943): p. 394–5.
  32. Murdoch DR, Jennings LC. Association of respiratory virus activity and environmental factors with the incidence of invasive pneumococcal disease. *Journal of Infection*, 2009. 58(1): p. 37–46.

33. Voss L, Lennon D, Okesene-Gafa K, et al. Invasive pneumococcal disease in a pediatric population, Auckland, New Zealand. *Pediatric Infectious Disease Journal*, 1994. 13(10): p. 873-8.
34. Chambers S, Laing R, Murdoch D, et al. Maori have a much higher incidence of community-acquired pneumonia and pneumococcal pneumonia than non-Maori: findings from two New Zealand hospitals. *New Zealand Medical Journal*, 2006. 119(1234): p. U1978.
35. Heffernan HM, Martin DR, Woodhouse RE, et al. Invasive pneumococcal disease in New Zealand 1998-2005: capsular serotypes and antimicrobial resistance. *Epidemiology and Infection*, 2008. 136(3): p. 352-9.
36. Anglemeyer A, McNeill A, DuBray K, et al. Invasive Pneumococcal Disease: Concerning Trends in Serotype 19A Notifications in New Zealand. *Clinical Infectious Diseases*, 2022. 74(10): p. 1859-1861.
37. Institute of Environmental Science and Research. 2022 *Invasive pneumococcal disease quarterly report, July-September 2022*. Porirua. URL: [https://surv.esr.cri.nz/surveillance/IPD.php?we\\_objectID=5257](https://surv.esr.cri.nz/surveillance/IPD.php?we_objectID=5257). (accessed 13 December 2022)
38. Petousis-Harris H, Howe AS, Paynter J, et al. Pneumococcal conjugate vaccines turning the tide on inequity: a retrospective cohort study of New Zealand children born 2006–2015. *Clinical Infectious Diseases*, 2019. 68(5): p. 818-826.
39. Kyaw MH, Lynfield R, Schaffner W, et al. Effect of introduction of the pneumococcal conjugate vaccine on drug-resistant *Streptococcus pneumoniae*. *New England Journal of Medicine*, 2006. 354(14): p. 1455-63.
40. Institute of Environmental Science and Research Ltd (ESR). 2019. *Invasive pneumococcal disease in New Zealand, 2016* (ed.), Porirua: ESR. URL: [https://surv.esr.cri.nz/PDF\\_surveillance/IPD/2016/2016IPDAnnualReport.pdf](https://surv.esr.cri.nz/PDF_surveillance/IPD/2016/2016IPDAnnualReport.pdf) (accessed 25 November 2019)
41. Tin Tin Htar M, van Den Biggelaar AHJ, Sings H, et al. The impact of routine childhood immunization with higher-valent pneumococcal conjugate vaccines on antimicrobial-resistant pneumococcal diseases and carriage: a systematic literature review. *Expert Rev Vaccines*, 2019. 18(10): p. 1069-1089.
42. Hume-Nixon M, Lim R, Russell F, et al. Systematic review of the clinical outcomes of pneumonia with a penicillin-group resistant pneumococcus in respiratory and blood culture specimens in children in low- and middle-income countries. *J Glob Health*, 2022. 12: p. 10004.
43. Temple B, Toan NT, Dai VTT, et al. Immunogenicity and reactogenicity of ten-valent versus 13-valent pneumococcal conjugate vaccines among infants in Ho Chi Minh City, Vietnam: a randomised controlled trial. *The Lancet Infectious Diseases*, 2019. 19(5): p. 497-509.
44. Centers for Disease Control and Prevention. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine among children aged 6–18 years with immunocompromising conditions: recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morbidity and Mortality Weekly Report*, 2013. 62(25): p. 521–4.
45. Plosker GL. 13-valent pneumococcal conjugate vaccine: a review of its use in infants, children, and adolescents. *Paediatric Drugs*, 2013. 15(5): p. 403-23.
46. Bhorat AE, Madhi SA, Laudat F, et al. Immunogenicity and safety of the 13-valent pneumococcal conjugate vaccine in HIV-infected individuals naive to pneumococcal vaccination. *AIDS*, 2015. 29(11): p. 1345-54.
47. Pittet LF, Posfay-Barbe KM, Chehade H, et al. Optimizing seroprotection against pneumococcus in children with nephrotic syndrome using the 13-valent pneumococcal conjugate vaccine. *Vaccine*, 2016. 34(41): p. 4948-4954.

48. Esposito S, Terranova L, Patria MF, et al. *Streptococcus pneumoniae* colonisation in children and adolescents with asthma: impact of the heptavalent pneumococcal conjugate vaccine and evaluation of potential effect of thirteen-valent pneumococcal conjugate vaccine. *BMC Infectious Diseases*, 2016. 16(1): p. 12.
49. Esposito S, Colombo C, Tosco A, et al. *Streptococcus pneumoniae* oropharyngeal colonization in children and adolescents with cystic fibrosis. *J Cyst Fibros*, 2016. 15(3): p. 366-71.
50. Principi N, Iughetti L, Cappa M, et al. *Streptococcus pneumoniae* oropharyngeal colonization in school-age children and adolescents with type 1 diabetes mellitus: Impact of the heptavalent pneumococcal conjugate vaccine. *Human Vaccines & Immunotherapeutics*, 2016. 12(2): p. 293-300.
51. Principi N, Preti V, Gaspari S, et al. *Streptococcus pneumoniae* pharyngeal colonization in school-age children and adolescents with cancer. *Human Vaccines & Immunotherapeutics*, 2016. 12(2): p. 301-7.
52. Jackson LA, Gurtman A, van Cleeff M, et al. Immunogenicity and safety of a 13-valent pneumococcal conjugate vaccine compared to a 23-valent pneumococcal polysaccharide vaccine in pneumococcal vaccine-naïve adults. *Vaccine*, 2013. 31(35): p. 3577-84.
53. Shiramoto M, Irie S, Juergens C, et al. Immunogenicity and safety of 13-valent pneumococcal conjugate vaccine when administered to healthy Japanese adults aged  $\geq 50$  years. An open-label trial. *Human Vaccines & Immunotherapeutics*, 2014. 10(7): p. 1850-8.
54. Bryant KA, Frenck R, Gurtman A, et al. Immunogenicity and safety of a 13-valent pneumococcal conjugate vaccine in adults 18-49 years of age, naïve to 23-valent pneumococcal polysaccharide vaccine. *Vaccine*, 2015. 33(43): p. 5854-5860.
55. Tinoco JC, Juergens C, Ruiz Palacios GM, et al. Open-label trial of immunogenicity and safety of a 13-valent pneumococcal conjugate vaccine in adults  $\geq 50$  years of age in Mexico. *Clinical and Vaccine Immunology*, 2015. 22(2): p. 185-92.
56. Jackson LA, Gurtman A, Rice K, et al. Immunogenicity and safety of a 13-valent pneumococcal conjugate vaccine in adults 70 years of age and older previously vaccinated with 23-valent pneumococcal polysaccharide vaccine. *Vaccine*, 2013. 31(35): p. 3585-93.
57. Jackson LA, Gurtman A, van Cleeff M, et al. Influence of initial vaccination with 13-valent pneumococcal conjugate vaccine or 23-valent pneumococcal polysaccharide vaccine on anti-pneumococcal responses following subsequent pneumococcal vaccination in adults 50 years and older. *Vaccine*, 2013. 31(35): p. 3594-602.
58. Plosker GL. 13-Valent Pneumococcal Conjugate Vaccine: A Review of Its Use in Adults. *Drugs*, 2015. 75(13): p. 1535-46.
59. Bonten MJ, Huijts SM, Bolkenbaas M, et al. Polysaccharide conjugate vaccine against pneumococcal pneumonia in adults. *New England Journal of Medicine*, 2015. 372(12): p. 1114-25.
60. Leesa F, Spiller MT, Effectiveness of PCV13 in Adults Hospitalized with Pneumonia Using Centers for Medicare & Medicaid Services Data, 2014–2017 in *ACIP meeting February 2019*. 2019, National Center for Immunization & Respiratory Diseases,.
61. Hanquet G, Krizova P, Valentiner-Branth P, et al. Effect of childhood pneumococcal conjugate vaccination on invasive disease in older adults of 10 European countries: implications for adult vaccination. *Thorax*, 2019. 74(5): p. 473-482.
62. Falkenhorst G, Remschmidt C, Harder T, et al. Effectiveness of the 23-valent pneumococcal polysaccharide vaccine (PPV23) against pneumococcal disease in the elderly: systematic review and meta-analysis. *PLoS One*, 2017. 12(1): p. e0169368.
63. Huss A, Scott P, Stuck AE, et al. Efficacy of pneumococcal vaccination in adults: a meta-analysis. *CMAJ: Canadian Medical Association Journal*, 2009. 180(1): p. 48-58.



64. Vila-Corcoles A, Ochoa-Gondar O, Guzman JA, et al. Effectiveness of the 23-valent polysaccharide pneumococcal vaccine against invasive pneumococcal disease in people 60 years or older. *BMC Infectious Diseases*, 2010. 10(73): p. 73.
65. Cadeddu C, De Waure C, Gualano MR. 23-valent pneumococcal polysaccharide vaccine (PPV23) for the prevention of invasive pneumococcal diseases (IPDs) in the elderly: is it really effective? *Journal of Preventive Medicine and Hygiene*, 2012. 53(2): p. 101–103.
66. Suzuki M, Dhoubhadel BG, Ishifuji T, et al. Serotype-specific effectiveness of 23-valent pneumococcal polysaccharide vaccine against pneumococcal pneumonia in adults aged 65 years or older: a multicentre, prospective, test-negative design study. *Lancet Infectious Diseases*, 2017. 17(3): p. 313–321.
67. Cook IF, Pond D, Hartel G. Comparative reactogenicity and immunogenicity of 23 valent pneumococcal vaccine administered by intramuscular or subcutaneous injection in elderly adults. *Vaccine*, 2007. 25(25): p. 4767–74.
68. Curcio D, Cané A, Isturiz R. Redefining risk categories for pneumococcal disease in adults: critical analysis of the evidence. *International Journal of Infectious Diseases*, 2015. 37: p. 30–5.
69. Pelton SI, Shea KM, Weycker D, et al. Rethinking risk for pneumococcal disease in adults: the role of risk stacking. *Open Forum Infect Dis*, 2015. 2(1): p. ofv020.
70. Baxter R, Yee A, Aukes L, et al. Risk of underlying chronic medical conditions for invasive pneumococcal disease in adults. *Vaccine*, 2016. 34(36): p. 4293–7.
71. Australian Technical Advisory Group on Immunisation (ATAGI). 2018. Pneumococcal disease. in *Australian Immunisation Handbook*. Canberra. URL: <https://immunisationhandbook.health.gov.au/vaccine-preventable-diseases/pneumococcal-disease>. (accessed 25 April 2020)
72. Tse A, Tseng HF, Greene SK, et al. Signal identification and evaluation for risk of febrile seizures in children following trivalent inactivated influenza vaccine in the Vaccine Safety Datalink Project, 2010–2011. *Vaccine*, 2012. 30(11): p. 2024–31.
73. Esposito S, Principi N. Safety and tolerability of pneumococcal vaccines in children. *Expert Opin Drug Saf*, 2016. 15(6): p. 777–85.
74. Thompson A, Gurtman A, Patterson S, et al. Safety of 13-valent pneumococcal conjugate vaccine in infants and children: meta-analysis of 13 clinical trials in 9 countries. *Vaccine*, 2013. 31(45): p. 5289–95.
75. Ho YL, Brandao AP, de Cunto Brandileone MC, Lopes MH. Immunogenicity and safety of pneumococcal conjugate polysaccharide and free polysaccharide vaccines alone or combined in HIV-infected adults in Brazil. *Vaccine*, 2013. 31(37): p. 4047–53.
76. Cordonnier C, Ljungman P, Juergens C, et al. Immunogenicity, safety, and tolerability of 13-valent pneumococcal conjugate vaccine followed by 23-valent pneumococcal polysaccharide vaccine in recipients of allogeneic hematopoietic stem cell transplant aged  $\geq 2$  years: an open-label study. *Clinical Infectious Diseases*, 2015. 61(3): p. 313–23.
77. Glesby MJ, Watson W, Brinson C, et al. Immunogenicity and safety of 13-valent pneumococcal conjugate vaccine in HIV-infected adults previously vaccinated with pneumococcal polysaccharide vaccine. *Journal of Infectious Diseases*, 2015. 212(1): p. 18–27.
78. Bentley D, Ita K, Moon D. Pneumococcal vaccine in the institutional elderly: design of a non-randomized trial and preliminary results. *Reviews of Infectious Diseases*, 1981. 3(Suppl): p. 571.

# 18 Poliomyelitis

## Key information

Mode of transmission	Faecal–oral route or by ingestion of pharyngeal secretions.
Incubation period	Paralytic disease usually 7–14 days, with a reported range of 3–35 days.
Period of communicability	Most infectious in the days immediately before and after the onset of any symptoms. Transmission is possible for as long as the virus is shed (can be years in immunocompromised individuals).
Incidence and burden of disease	Globally, endemic wild-type poliovirus 1 in Afghanistan and Pakistan. Circulating vaccine-derived poliovirus outbreaks continue. Wild-types 2 and 3 have been eradicated.
Funded vaccines	As inactivated polio vaccine (IPV), in combination with other antigens, or on its own: <ul style="list-style-type: none"><li>• DTaP-IPV-HepB/Hib (Infanrix-hexa)</li><li>• DTaP-IPV (Infanrix-IPV)</li><li>• IPV (IPOL).</li></ul>
Dose, presentation, route	All 0.5 mL per dose. DTaP-IPV-HepB/Hib: pre-filled syringe and glass vial, the vaccine must be reconstituted prior to intramuscular injection. DTaP-IPV: pre-filled syringe, intramuscular injection. IPV: pre-filled syringe, subcutaneous injection.
Funded vaccine indications and schedule	Usual childhood schedule: <ul style="list-style-type: none"><li>• at age 6 weeks, 3 months and 5 months: DTaP-IPV-HepB/Hib (primary series)</li><li>• at age 4 years: DTaP-IPV (booster).</li></ul> For non-immune adults, 3 doses of IPV 8 weeks apart (may be shortened to 4-week intervals). For (re)vaccination of eligible patients: DTaP-IPV-HepB/Hib, DTaP-IPV or IPV.
Vaccine efficacy	Greater than 90 percent.
Precautions and special considerations	Non-immune pregnant women may be immunised if they are travelling to a region where polio is endemic.
Public health measures	All suspected cases of poliomyelitis be notified immediately on suspicion. (see section 18.8)



## 18.1 Virology

Poliomyelitis (polio) is a highly transmissible infectious disease caused by poliovirus, a small, non-enveloped enterovirus of the family Picornaviridae. There are three serotypes of poliovirus (types 1, 2 and 3). Wild types 2 and 3 have now been eradicated, but vaccine-derived poliovirus continue to circulate in some countries.

## 18.2 Clinical features

Poliovirus is transmitted by the faecal–oral route or by ingestion of pharyngeal secretions. The incubation period for poliomyelitis is commonly 7–14 days for paralytic disease, with a reported range of 3–35 days. The risk of transmission of infection is greatest shortly before to shortly after the onset of symptoms. The virus persists in the pharynx for approximately one week, and in the faeces for three to six weeks or longer, particularly in immunocompromised individuals, where cases have been reported shedding for many years.

The virus is highly neurotropic and its primary effect occurs in the neurones of the spinal anterior horn or the motor ganglia of the brain stem. In up to 95 percent of infections are clinically inapparent; clinical cases range in severity from a non-paralytic fever to viral meningitis and acute flaccid paralysis.

Symptoms include fever; headache; gastrointestinal disturbances; malaise; stiffness of the neck and back; and pain in the limbs, back and neck, with or without paralysis. In children who develop paralysis, the illness may be biphasic with the initial phase of one to three days' duration being indistinguishable from that of other viral infections. The patient appears to recover, only to be struck down abruptly two to five days later with meningism, followed by paralysis. In adults and adolescents, the illness usually presents with a gradual onset of paralysis and pain without the early symptoms.

Infected asymptomatic people will shed the virus in their stool and may spread the infection to others. Infection rates may be as high as 100 percent in households where there are non-immune young children.

Paralysis may occur in 0.1–2 percent of infected individuals. It is more common in adults, occurring in up to 1 in 75 cases of infection. Case fatalities from paralytic polio vary from 2–5 percent among children and up to 15–30 percent for adults, increasing to 25–75 percent with bulbar involvement.

Post-polio syndrome may occur some 30–40 years after poliomyelitis. The cause is unknown but is probably related to the ageing or death of nerves and muscles that were compensating for the original damage. Patients experience muscle pain and exacerbation of existing muscle weakness. The risk of developing post-polio syndrome is greater in women than in men, and the risk increases with time from the episode of acute polio.

## 18.3 Epidemiology

### 18.3.1 Global burden of disease

In the pre-vaccination era, cases of poliomyelitis occurred sporadically with epidemics in high-income countries in temperate zones. In tropical countries, where the virus still circulates, there is no seasonal pattern.

Classically, poliomyelitis is a disease of young children and adolescents. In countries where polio was endemic, most children acquired antibodies to all three subtypes by age 5 years and most paralytic disease occurred in children aged under 3 years. However, with improvements in living standards a greater number of cases have occurred at an older age, particularly in early adult life, with an associated higher frequency of paralytic disease.

In the 30 years since the Global Polio Eradication Initiative began, an estimated 18 million cases of paralytic poliomyelitis have been prevented, and out of 125 countries, two have ongoing transmission of wild-type 1 disease (Afghanistan and Pakistan).<sup>1</sup> No wild-type disease has been detected in Nigeria since 2016, and the WHO hopes to declare Africa wild poliovirus free in 2020.<sup>2</sup> Although wild-type 2 and 3 polio have been eradicated, there was a dramatic increase in polio cases during 2019, primarily due to outbreaks in Pakistan which spread across its borders to Afghanistan and Iran.<sup>1</sup> Disruption of immunisation programmes and poor sanitary conditions has enabled polio to spread, and in some countries, there are pockets of children unable to be accessed for vaccination due to conflict.

The risk of international spread of poliovirus was declared as a Public Health Emergency of International Concern in May 2014. Further to wild-type 1 disease, the incidence of circulating vaccine-derived poliovirus types (cVDPV) within under-vaccinated populations is of significant international concern, particularly in Africa and South-East Asia (China, Malaysia, Philippines and Indonesia).<sup>3</sup> For up-to-date surveillance information and countries at risk of potential international spread of polioviruses, see the 'Polio Now' section of the Global Polio Eradication Initiative website ([polioeradication.org/polio-today/polio-now](http://polioeradication.org/polio-today/polio-now)).

There was a synchronised global switch to bivalent oral polio vaccine (bOPV) in 2016 in countries with circulating polio once the wild-type 2 disease was declared eradicated. In these countries, OPV is used together with inactivated poliovirus vaccine (IPV). Many countries without circulating virus have discontinued OPV and provide only IPV to eliminate the risk vaccine-associated paralytic poliomyelitis (VAPP). However, shortages of IPV supply led to delays in this switch and mixed schedules have continued. A revised Polio Eradication & Endgame Strategic Plan 2019–2023 has been developed by the Global Polio Eradication Initiative.<sup>4</sup> Its goal is 'the complete eradication and containment of all polioviruses'. Vaccination will continue worldwide until all polio has been eradicated.<sup>1</sup>

## 18.3.2 New Zealand epidemiology

Since 1962 only six polio cases have been reported. Four of these cases were laboratory confirmed as VAPP and two were classified as probable VAPP.<sup>5</sup> The last case of VAPP was reported in 1999.<sup>6</sup> No cases have been reported since IPV replaced OPV in 2002.

The New Zealand Paediatric Surveillance Unit carries out active surveillance of acute flaccid paralysis (AFP). In 2019 there were nine notifications: all were reviewed by the New Zealand National Certification Committee for the Eradication of Polio and all were classified as non-polio (ESR, 8 June 2020).

The risk of importing wild-type or neurovirulent oral vaccine-derived (cVDPV) strains means that maintaining high IPV coverage in New Zealand is essential.

For further details, refer to the ESR annual notifiable disease reports (available at [www.esr.cri.nz/digital-library/notifiable-disease-dashboard/](http://www.esr.cri.nz/digital-library/notifiable-disease-dashboard/)).

## 18.4 Vaccines

New Zealand switched from OPV to IPV in 2002 (see Appendix 1).

### 18.4.1 Available vaccines

#### Funded polio vaccines

The polio-containing vaccines funded as part of the Schedule are:

- DTaP-IPV-HepB/Hib (Infanrix-hexa, GSK): diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and *Haemophilus influenzae* type b vaccine (see section 6.4.1 for more information)
- DTaP-IPV (Infanrix-IPV, GSK): diphtheria, tetanus, acellular pertussis and inactivated polio vaccine (see section 6.4.1 for more information)
- IPV (IPOL, Sanofi): contains three strains of poliovirus (40D antigen units of the Mahoney, 8D antigen units of the MEF-1 and 32D antigen units of the Saukett strains), inactivated by formaldehyde and containing phenoxyethanol as a preservative; trace amounts of neomycin, streptomycin, polymyxin B, polysorbate 80 and bovine serum albumin may be present.

## Other vaccine

Adacel Polio (Sanofi) is a Tdap-IPV vaccines registered (approved for use) and available (marketed) in New Zealand.

### 18.4.2 Efficacy and effectiveness

See also section 16.4.2 for information about DTaP-IPV-HepB/Hib vaccine.

#### Immunogenicity and efficacy

IPV induces good systemic immune responses to protect against paralytic polio, but does not induce adequate intestinal neutralising antibody to interrupt faecal-oral transmission in regions with circulating polioviruses and with poor sanitation.<sup>7</sup>

Virtually all infants (99–100 percent) will seroconvert against all three strains after three doses of IPV vaccine, and more than 95 percent will seroconvert after two doses.<sup>8</sup> The efficacy of IPV is greater than 90 percent and immunity is expected to be long lasting.<sup>9</sup> Although antibody may decline over time in some individuals, there is no evidence that this leads to increased susceptibility to poliomyelitis.<sup>10</sup>

The combined IPV-containing vaccines induce immune responses against polioviruses superior to IPV stand-alone vaccines. This is due to the effect of the aluminium adjuvant present in these combination vaccines.<sup>9</sup>

Although immunocompetent adults previously immunised with OPV are expected to have lifelong protection against paralytic disease,<sup>10</sup> a study in Australia found that adolescents and young adults who were primed only with OPV had lower levels of serum neutralising antibody than the younger cohorts who had received OPV and at least one dose of IPV.<sup>11</sup> This data suggests that immunity provided by OPV primary schedule can be boosted by IPV to maintain individual immunity.

### 18.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at [www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

Store at +2°C to +8°C. Do not freeze. DTaP-IPV-HepB/Hib vaccine should be stored in the dark.

DTaP-IPV-HepB/Hib (Infanrix-hexa) must be reconstituted by adding the entire contents of the supplied container of the DTap-IPV-HepB vaccine to the vial containing the Hib pellet. After adding the vaccine to the pellet, the mixture should be shaken until the pellet is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.

## 18.4.4 Dosage and administration

The dose of DTap-IPV-HepB/Hib (Infanrix-hexa) and DTap-IPV (Infanrix-IPV) is 0.5 mL, administered by intramuscular injection (see section 2.2.3).

The dose of IPV (IPOL) is 0.5 mL, administered by subcutaneous injection.

### Co-administration with other vaccines

DTaP-IPV-HepB/Hib, DTap-IPV and IPV may be given at the same time as inactivated or live attenuated vaccines, at separate sites and in separate syringes.

## 18.5 Recommended immunisation schedule

**Table 18.1: Immunisation schedule for IPV-containing vaccines (excluding catch-up)**

Age	Vaccine	Comment
6 weeks	DTaP-IPV-HepB/Hib	Primary series
3 months	DTaP-IPV-HepB/Hib	Primary series
5 months	DTaP-IPV-HepB/Hib	Primary series
4 years	DTaP-IPV	Booster

### 18.5.1 Usual childhood schedule

A primary course of poliomyelitis vaccine is given as DTap-IPV-HepB/Hib at ages 6 weeks, 3 months and 5 months, followed by a booster dose given as DTap-IPV at age 4 years (see Table 18.1).

## 18.5.2 Unimmunised adults and children

For partially immunised or previously unimmunised individuals, a primary immunisation course consists of three doses of IPV-containing vaccine (funded). The recommended interval is eight weeks between doses, but the minimum interval can be as short as four weeks for catch-up of children or adults (see Appendix 2).<sup>12</sup>

If a course of vaccine is interrupted, it may be resumed without repeating prior doses. A booster may be given if 10 years have elapsed since the last dose and exposure is possible (eg, in the case of a traveller to an area where the virus circulates; this is not funded).

If a child who began a course of OPV in another country moves to New Zealand, they can switch to IPV to complete the final doses. A further dose of IPV should be administered even if they have completed a full OPV (OPV or bOPV) course.

Note: All immunocompromised individuals and their household members may receive IPV. OPV was contraindicated in the immunocompromised because of the risk of VAPP. There is no risk of VAPP with IPV.

## 18.5.3 Pregnancy and breastfeeding

No adverse effects on the fetus have been reported following administration of IPV during pregnancy, but immunisation should not be carried out during the first or second trimester unless there are compelling reasons to do so, such as planned travel to an endemic area. However, bear in mind that pregnant women are particularly susceptible to paralytic polio.

If a previously unvaccinated pregnant woman is travelling to a country where polio is occurring, two doses should be administered four weeks apart prior to departure. If departure cannot be delayed allowing a four-week gap, give two doses at the maximum possible interval, though protection cannot be guaranteed. If the available interval is less than two weeks, a single dose is recommended, with further doses given on arrival where possible.

IPV may be given to breastfeeding women.

## 18.5.4 (Re)vaccination

Polio-containing vaccines are funded for (re)vaccination of eligible patients, as follows. See also sections 4.2 and 4.3.

## DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV)

An additional four doses (as appropriate) of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for (re)vaccination of patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- prior to planned or following other severely immunosuppressive regimens.

Up to an additional four doses (as appropriate) of DTaP-IPV-HepB/Hib are funded for children aged 10 years to under 18 years for (re)vaccination of patients post HSCT. This is an off-label use of this vaccine which requires a prescription from an authorised prescriber or the patient's specialist. In this group, all prior immunity will have been lost and revaccination is equivalent to a primary immunisation schedule. DTaP-IPV-HepB/Hib not recommended for other severely immunocompromised individuals aged 10-18 years that require revaccination as they may have residual immune memory.

## IPV (IPOL)

IPV is funded for patients following immunosuppression.

## 18.5.5 Recommendations for other groups

Booster doses of IPV are recommended (but not funded) for:

- all travellers to areas or countries where poliomyelitis remains endemic or with cVDPV (see section 18.3.1), who should receive a pre-travel polio booster
  - Under the Public Health Emergency of International Concern (PHEIC) regarding polio, proof of polio vaccination is required on **departure** from certain countries. See Global Polio Eradication Initiative website for the current country list: [polioeradication.org/polio-today/polio-now/public-health-emergency-status](http://polioeradication.org/polio-today/polio-now/public-health-emergency-status)
  - Evidence of polio vaccination (a booster dose of IPV given 4 weeks to 12 months prior to exit from these countries) must be recorded on an International Certificate of Vaccination and Prophylaxis (ICVP).
  - An adult polio booster is recommended also for those travelling to countries that have cVDPV-2 only.<sup>1</sup>
- health care workers in direct contact with a case of poliomyelitis
- individuals at particular risk of exposure (eg, laboratory workers routinely handling faecal specimens from persons recently arriving from high-risk countries, which may contain wild or vaccine-derived polioviruses); a booster dose of IPV is recommended every 10 years.

All the above should have completed a primary course of polio vaccines. See Table 4.9 for those for whom IPV is particularly recommended. Where there is uncertainty about



previous immunisation, a full course of IPV is recommended (see Appendix 2). There is no evidence for the need for routine boosters, but they are recommended to reduce any possible risk from waning immunity in situations of increased risk of exposure.

## 18.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

### 18.6.1 Contraindications

IPV-containing vaccines are contraindicated if there is a history of an anaphylactic reaction to a previous dose or to any of the vaccine components.

See also section 16.6 for information about DTaP-IPV-HepB/Hib vaccine.

### 18.6.2 Precautions

Pregnancy is a precaution for IPV-containing vaccination, but may be given to women who clearly need it. See section 18.5.3.

## 18.7 Potential responses and AEFIs

See also section 16.7 for information about DTaP-IPV-HepB/Hib and DTaP-IPV vaccines.

### 18.7.1 Potential responses

A small proportion of individuals experience mild local symptoms following IPV. Injection-site erythema is seen in 1–2 percent of infants, induration in 3–11 percent and pain in 14–29 percent. Similar local reactions are seen with combination vaccines.<sup>9</sup> There is no poliovirus excretion following IPV.

## 18.7.2 AEFIs

Serious adverse events are very rare following administration of the IPV currently manufactured.<sup>8</sup> See section 16.6 for information about DTaP-IPV-HepB/Hib vaccine.

## 18.8 Public health measures

It is a legal requirement that all suspected cases of poliomyelitis be notified immediately on suspicion to the local medical officer of health.

For more details on control measures, refer to the 'Poliomyelitis' chapter of the *Communicable Disease Control Manual* at [www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual](http://www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual)

## 18.9 Variations from the vaccine data sheets

See section 16.9 for variations from the DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV) data sheets.

The IPV (IPOL) data sheet recommends three doses of vaccine administered at eight-week intervals.<sup>13</sup> Health New Zealand | Te Whatu Ora recommends that this schedule may be shortened to four-week intervals for catch-up (see Appendix 2).

## References

1. World Health Organization. Progress towards poliovirus containment worldwide, 2018–2019. *Weekly Epidemiological Record*, 2019. 94(39): p. 441–448.
2. World Health Organization. 2019 *Polio: Statement of the Twenty-Third IHR Emergency Committee Regarding the International Spread of Poliovirus (Press release)*. World Health Organization: Geneva. 7 January 2020 URL: <https://www.who.int/news-room/detail/20-12-2019-statement-o-the-twenty-third-ih-emergency-committee-regarding-the-international-spread-of-poliovirus>. (accessed 3 July 2020)
3. Global Polio Eradication Initiative. 2020 *Public Health Emergency Status*. World Health Organization; 2020; URL: <https://polioeradication.org/polio-today/polio-now/public-health-emergency-status/>. (accessed 10 May 2022)
4. Global Polio Eradication Initiative. 2019 *Polio Endgame Strategy 2019–2023*. World Health Organization; 2019; URL: <https://polioeradication.org/who-we-are/polio-endgame-strategy-2019-2023/>. (accessed 10 May 2022)

5. Institute of Environmental Science and Research Ltd. 2019 *Notifiable Diseases in New Zealand: Annual Report 2017*. Porirua, New Zealand. URL: [https://surv.esr.cri.nz/PDF\\_surveillance/AnnualRpt/AnnualSurv/2017/2017AnnualNDReport\\_FINAL.pdf](https://surv.esr.cri.nz/PDF_surveillance/AnnualRpt/AnnualSurv/2017/2017AnnualNDReport_FINAL.pdf). (accessed 3 July 2020)
6. Edwards EA, Grant CC, Huang QS, et al. A case of vaccine-associated paralytic poliomyelitis. *Journal of Paediatrics and Child Health*, 2000. 36(4): p. 408-11.
7. Macklin GR, Grassly NC, Sutter RW, et al. Vaccine schedules and the effect on humoral and intestinal immunity against poliovirus: a systematic review and network meta-analysis. *Lancet Infectious Diseases*, 2019. 19(10): p. 1121-1128.
8. American Academy of Pediatrics. 2018. Poliovirus Infections. in *Red Book: 2018 Report of the Committee on Infectious Diseases*, Kimberlin D, Brady M, Jackson M, and Long S (eds). URL: <https://redbook.solutions.aap.org/redbook.aspx>. (accessed 3 July 2020)
9. Vidor E. 2018. Poliovirus Vaccine - Inactivated, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
10. World Health Organization. 2016. Polio vaccines: WHO position paper – March 2016. *Weekly Epidemiological Record*. 91(12): p. 145–68. URL: <http://www.who.int/wer/2016/wer9112.pdf?ua=1> (accessed 29 March 2020)
11. Hendry AJ, Beard FH, Dey A, et al. Lower immunity to poliomyelitis viruses in Australian young adults not eligible for inactivated polio vaccine. *Vaccine*, 2020. 38(11): p. 2572-2577.
12. Australian Technical Advisory Group on Immunisation. 2018. *Australian Immunisation Handbook* (ed.), Canberra: Australian Government Department of Health. URL: <https://immunisationhandbook.health.gov.au/> (accessed October 2019)
13. Sanofi-aventis New Zealand, NZ Datasheet: IPOL. 2019, Medsafe.

# 19 Respiratory syncytial virus

## Key information

Mode of transmission	Transmitted from respiratory secretions to nasopharyngeal or conjunctival mucosa, through close or direct contact with large droplets or fomites.
Incubation period	Ranges from two to eight days
Period of communicability	Average eight days, up to three weeks
Available vaccines	Unfunded – RSVpreF vaccine (Arexvy) – for active immunisation Unfunded – palivizumab – for passive immunoprophylaxis
Dose, presentation, route	<b>RSV vaccine (Arexvy)</b> <ul style="list-style-type: none"><li>- 0.5 mL per dose</li><li>- Two glass vials – antigen powder must be reconstituted with adjuvant suspension.</li><li>- Intramuscular injection</li></ul> <b>Palivizumab</b> <ul style="list-style-type: none"><li>- Single-use vials containing 50 mg / 0.5 mL or 100 mg / 1.0 mL palivizumab</li><li>- Recommended dose 15 mg/Kg, monthly during RSV season</li><li>- Intramuscular injection</li></ul>
Vaccine indications and schedule	<b>RSV vaccine (Arexvy)</b> Unfunded One dose, for use in adults aged 60 years and over For use prior to or during RSV season (autumn/winter months) <b>Palivizumab</b> Unfunded For use in infants aged under 24 months at high risk of severe RSV-LRTI, particularly recommended for: <ul style="list-style-type: none"><li>- born preterm <math>\leq</math>28 weeks gestation</li><li>- born preterm <math>\leq</math>32 weeks gestation with chronic lung disease of prematurity</li><li>- with haemodynamically significant congenital heart disease</li><li>- severely immunocompromised infants.</li></ul>

*Continued overleaf*

Vaccine effectiveness	<p><b>RSV vaccine (Arexvy):</b></p> <p>Clinical trial data: efficacy of 83 percent against RSV-LRTI and 94 percent against severe RSV disease in adults aged over 60 and over 70 years.</p> <p>Protection is maintained for at least two RSV seasons.</p>
Precautions and special considerations	<p>Allow spacing of at least a week between rZV (zoster vaccine) and RSVPreF as a precaution against potentially increased reactivity.</p>

## 19.1 Virology

Respiratory syncytial virus (RSV) is an Orthopneumovirus of the *Pneumoviridae* family. There are two main antigenic subtypes in humans, subtype A and B. Virus-induced fusion of infected cells forms multinucleated cells known as syncytia.

## 19.2 Clinical features

Respiratory syncytial virus is a highly contagious and common virus that can cause lower respiratory tract infections (LRTIs), particularly in the late autumn and winter months. Most children will have been exposed to RSV by the age of 2 years but reinfection is common.<sup>1</sup>

It is transmitted in large droplets or on fomites from respiratory secretions, infecting the nasopharyngeal or conjunctiva mucosa.<sup>2</sup> Incubation period ranges from two to eight days and viral shedding can last for an average of eight days to up to three weeks from immunocompetent individuals.<sup>2</sup>

Infection starts in the upper respiratory tract and then spreads rapidly by intercellular transmission to the lower airways to the terminal bronchioles.<sup>2</sup> RSV infection disrupts ciliated epithelial cells in the airways, stimulating mononuclear cell infiltration, mucosal oedema and syncytia formation. It disrupts the cell-cycle regulatory proteins to boost viral replication. Severity and infectivity is directly related to viral load.<sup>3</sup>

With subsequent infections, acquired humoral and cell-mediated immunity attenuate the severity of each infection assisted by increasing age, size and maturity of the airways during childhood. Conversely, in older adults, declines in cell-mediated immunity and lung function increase the severity of RSV infection.

### 19.2.1 Adults

RSV is a major cause of upper respiratory tract infection (URTI) in adults. By adulthood, individuals are unlikely to be immunologically naïve to RSV, with repeat exposures occurring throughout our lifetimes.<sup>3</sup> Most infected adults experience mild to moderate clinical disease. RSV-associated hospitalisation rates increase exponentially from the

age of 60 years. For those with immunocompromise and older age, RSV infection can result in hospitalisation for severe lower respiratory tract disease (LRTD), viral pneumonia and exacerbation of underlying comorbidities.<sup>4</sup>

RSV is a highly prevalent disease and the virus has been identified as the causative agent in up to 12 percent of medically-attended acute respiratory illnesses.<sup>4</sup> It is associated with exacerbation of pre-existing illness in adults and with excess deaths predominantly in elderly adults. Hospital admission is on average three to six days and overall mortality is 6–8 percent in adults. Among hospitalised adults with a positive-RSV test, 10–31 percent require intensive care admission and 3–17 percent need mechanical ventilation.<sup>4</sup>

Risk factors for progression of RSV infection to viral pneumonia include Down syndrome, immunocompromise, underlying lung or heart disease, increasing age from 65 years, frailty, living in long-term care facilities and living at high altitudes.<sup>4</sup> Further factors associated with more severe RSV-LRTD include vitamin D deficiency, colder weather, air pollution and exposure to tobacco smoke.<sup>4</sup> The burden of RSV in adults is likely to be higher when consideration is given to the exacerbation of underlying disease, such as heart and lung disease, beyond those recorded as having RSV-LRTI.<sup>5</sup> In New Zealand, being of Māori or Pacific ethnicity, and/or living in areas of high deprivation independently increases the risk of RSV-associated hospitalisation.<sup>6</sup>

## 19.2.2 Infants

Compared with less than one percent of all adults, a higher proportion (around 12 percent) of young children with RSV require hospital care. Risk factors for poor outcomes in infants are: age under 3 months and gradually decreasing with increasing age, congenital heart disease, chronic conditions diagnosed before age 6 months, including congenital heart, congenital lung and chronic lung disease or neurological disease; prematurity (born before 37 weeks gestation) and extreme prematurity (born before 32 weeks gestation).<sup>7-9</sup> Another risk factor for hospitalisation with RSV-LRTI in infants are young maternal age (under 20 years). Preschool and primary school children in the household are significant sources of infection to infants.<sup>10</sup> In New Zealand, being of Māori or Pacific ethnicity, and/or living in areas of high deprivation is also independently associated with an increased risk for RSV-associated hospitalisation of infants.<sup>11</sup>

# 19.3 Epidemiology

## 19.3.1 Global burden of disease

More than 80 percent of children are infected with RSV at least once by the age of 2 years, and half of these have been infected twice.<sup>12</sup> Globally, RSV is associated with a substantial burden in young infants and is the most common cause of hospitalisation

of infants under 2 years for acute LRTI. The virus is also linked to an increased risk of childhood asthma.<sup>9, 13</sup>

In adults, the available epidemiology of RSV is less robust than for children. The frequency of clinical testing is lower, and in ambulatory settings, adults often present later to clinical care. Despite this, RSV is a highly prevalent disease associated with excess deaths predominantly in the older adults. The incidence of medically-attended RSV infection in adults generally increases with age, and RSV-associated pneumonia in adults age 65 years and over has the highest annual mortality rate (7.2 per 100,000 persons per year).<sup>4</sup> The odds of an adult with comorbidity being hospitalised with RSV acute respiratory illness is approximately four times that of individuals without comorbidity.<sup>5</sup> The burden is likely to be underestimated, and would be greater if exacerbation of underlying diseases, such as heart and lung disease, due to RSV infection was considered.

### 19.3.2 New Zealand epidemiology

RSV is not a notifiable disease in Aotearoa New Zealand, but the Institute of Environmental Surveillance and Research (ESR) maintains several surveillance systems to monitor respiratory virus activity and severity for the Public Health Agency. Virus detection forms part of the surveillance for community respiratory infections and severe acute respiratory infection (SARI) hospitalisation, including RSV testing. In 2023, like other seasonal respiratory viruses, RSV was predominantly detected in the community during the winter months but RSV-SARI occurred throughout the year.<sup>14</sup>

One study examining the RSV-associated hospitalisation rates in adults in Auckland during 2012–2015 found that approximately 8 percent of SARI hospitalisations were associated with RSV infection and 90 percent of these cases occurred during winter.<sup>6</sup> Adults aged over 80 years had the highest incidence of RSV-SARI, at 190.8 (95% CI 137.6–244.0) per 100,000 compared with 23.6 (21.0–26.1) per 100,000 for all adults. The incidence rate ratio was over 30 times higher for oldest adults than those aged under 50 years.<sup>6</sup>

## 19.4 Vaccines

An early respiratory syncytial virus vaccine candidate in the 1960s, containing formalin-inactivated whole virus, was discontinued due to the occurrence of vaccine-associated enhanced disease. During a clinical trial some participants experienced more severe RSV after exposure to RSV infection following vaccination. Advances in virology have since identified two forms of the F protein, the protein used by the virus to attach to epithelial cells of the airways: namely, a prefusion form and a post fusion form. DNA technology to produce recombinant proteins has enabled the production of the F protein in its prefusion conformation only. The risk of vaccine-associated enhanced disease, which is driven by T cell and antibody responses against the post-fusion F protein, has been overcome in the current vaccines by targeting specific antigenic sites expressed on the prefusion F protein only.



## 19.4.1 Available vaccines

### New Zealand approved vaccine (unfunded)

#### **Adjuvanted RSVpreF vaccine (Arexvy, GSK)**

Each 0.5 ml dose of RSVpreF contains:

- 120 µg RSV glycoprotein F stabilized in the prefusion conformation (RSVPreF3) produced by recombinant DNA technology in Chinese hamster ovary (CHO) cells
- AS01E adjuvant, containing 25 µg *Quillaja saponaria* Molin fraction 21 (QS-21) and 25 µg 3-O-desacyl-4'-monophosphoryl lipid A (MPL) from *Salmonella minnesota*
- it also contains trehalose dihydrate, polysorbate 80, monobasic potassium phosphate, dibasic potassium phosphate, dioleoyl phosphatidylcholine, cholesterol, sodium chloride and water.

#### **Palivizumab (Synagis, AstraZeneca)**

Palivizumab is a humanised IgG1κ monoclonal antibody targeting antigen site A (II) of the RSV fusion protein F to provide monthly passive immunity (immunoprophylaxis) against RSV in infants and young children at very high risk of RSV disease.

Each 0.5 mL dose contains 50mg or 1 mL dose contains 100 mg of palivizumab.

- Palivizumab is produced by DNA technology in recombinant mouse myeloma cells. It also contains histidine, glycine and water.

Other RSV vaccines, for use in older adults or during pregnancy to provide passive protection for infants, and immunoprophylactic candidates for young children, are approved for use or under regulatory review elsewhere, including in Australia, Europe and North America.<sup>15</sup> Some of which are also undergoing regulatory review in New Zealand.

## 19.4.2 Efficacy and effectiveness

### Immunogenicity of adjuvanted RSVpreF vaccine, Arexvy

One dose of adjuvanted RSVpreF vaccine (Arexvy) induces robust RSV-A and RSV-B neutralising antibodies that are likely to be seroprotective for at least one year after vaccination in older adults (aged ≥60 years).<sup>16</sup> The T cell profile is strongly CD4+ Th1-driven, and there is no evidence of induction of CD8+ T cells associated with risk for vaccine-associated enhanced respiratory disease.<sup>17</sup> An anamnestic response is seen after a booster dose given 20 months after the first dose.<sup>18</sup> Although clinical trials evaluated a two-dose primary course, it appears that one dose induces an adequate immune response to provide protection for longer than one year.<sup>16, 17</sup>

RSVpreF vaccine has similar immunogenicity in adults aged 18–50 years to that seen in older adults. Similar efficacy is also seen in those aged 50–59 years with comorbidities that increase the risk of severe RSV (study to date included chronic heart failure, disease, chronic respiratory disease, advanced renal or liver disease, diabetes mellitus type 1 or 2, but exclude those with immunocompromise).<sup>19, 20</sup> Further data is anticipated over more than two RSV seasons, in special high-risk groups and immunocompromised groups.

No clinically relevant interference of antibody responses were shown following coadministration of RSVPreF3 with aQIV (FluAd Quad), or for RSVPreF3 with rZV (Shingrix) when compared with sequential administration.<sup>21, 22</sup> Further coadministration data is anticipated for other vaccines given to older adults.

### Efficacy of adjuvanted RSVpreF vaccine, Arexvy

Vaccine efficacy of adjuvanted RSVpreF was consistently high among adults aged from 60 years against RSV-LRTI, severe RSV-LRTD and RSV-ARI during a first RSV season in a phase 3 RCT (NCT0488659).<sup>23</sup> Over one RSV season, vaccine efficacy was around 83 percent (96.95% CI: 58 – 94 percent) against RSV-LRTI; 94 percent (97.5% CI: 62 – 99.9 percent) against severe RSV-LRTD; and 72 percent (56 – 82 percent) against RSV-ARI in adults aged from 60 years,<sup>23</sup> and was similar in adults over 70 years. Similarly, efficacy of 95 percent (66–99.9 percent) was also shown against RSV-LRTD in those with at least one comorbidity that increases the risk of severe RSV.<sup>19</sup> A second dose, given a year after the first, provided little additional benefit than that provided by one dose over two seasons.<sup>24</sup> The efficacy of one dose over two seasons (adjusted for seasonality) was maintained around 80 percent (53–92 percent) against severe RSV-LRTD and 67 percent (48–80) against all RSV-LRTI.<sup>24</sup> Further data is required to assess the optimal timing of revaccination.

### Efficacy of palivizumab

Licensure was based on the IMpact-RSV randomised control trial, conducted during the 1996–1997 RSV season, which included 1502 infants and young children born at or before 35 weeks gestation (some with chronic lung disease (CLD) associated with prematurity).<sup>25</sup> Compared with the placebo cohort (RSV hospitalisation rate of 10.6 percent), an absolute reduction of 5.8% ( $p < 0.001$ ) was seen in hospitalisation of those who received palivizumab (4.8 percent); equivalent to a relative risk reduction of 54.7 percent.<sup>25</sup> A second clinical trial in 1287 children with haemodynamically significant congenital heart disease reported an absolute reduction in hospitalisation of 4.4 percent ( $p < 0.003$ ; 9.7 percent in placebo group and 5.3 percent in palivizumab group); with relative risk reduction of 45.3 percent.<sup>25</sup>

There is limited and conflicting data on effectiveness of palivizumab. Whilst retrospective studies have not shown consistent increases nor decrease in RSV-related hospitalisation for those born 29–35 weeks receiving palivizumab, many did not examine cohorts separately based on comorbidities, such as chronic lung disease of prematurity, and acknowledge that adherence with injections is challenging.<sup>25–27</sup> A systematic review reported that palivizumab reduces hospitalisation due to RSV

infection by 56 percent (relative risk 0.44; 95% CI 0.30-0.64), but evidence is uncertain around mortality (relative risk 0.69; 0.42-1.15).<sup>28</sup>

### 19.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at [www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

Store at +2°C to +8°C. Do not freeze. Protect from light.

### 19.4.4 Dosage and administration

#### Adjuvanted RSVpreF vaccine, Arexvy

A single 0.5 mL dose of Arexvy is administered by intramuscular injection (see section 2.2.3).

This vaccine requires reconstitution prior to administration. It consists of two components, a vial containing powder of recombinant prefusion F protein and a vial containing a suspension of adjuvant, AS01<sub>E</sub>. Draw up the adjuvant suspension into a syringe and add the entire contents into the powder. Gently swirl until the powder is dissolved. Use within 4 hours of reconstitution.

Both vials have a non-latex, butyl rubber stopper.

#### Palivizumab

Palivizumab is administered by intramuscular injection, monthly according to infant weight at 15 mg/Kg. Injection volumes of over 1mL should be given as a divided dose. Single-use vials contain 50 mg / 0.5 mL or 100 mg / 1.0 mL of palivizumab.

#### Co-administration with other vaccines

RSVpreF vaccine can be given concomitantly with standard and adjuvanted seasonal quadrivalent influenza vaccines. RSVpreF can also be given concomitantly with rZV, preferably in separate limbs. Note that mild to moderate reactions, such as injection-site pain and fatigue, can occur more frequently with coadministration than when these are given separately due to receiving additional AS01 adjuvant.

Palivizumab can be administered with any routine childhood immunisations. Since the monoclonal antibody in palivizumab is specific for RSV, it is not expected to interfere with the immune response to vaccines, including live viral vaccines.

## 19.5 Recommended immunisation schedule

### 19.5.1 Recommended groups (unfunded) for RSVpreF vaccine

RSVpreF (Arexvy) is indicated for active immunisation for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus RSV-A and RSV-B subtypes in adults 60 years of age and older.

It is currently unfunded. It can be considered for individuals who are aged over 60, especially the very elderly and those with multiple comorbidities that increase the risk of severe RSV-ARI. Offered as one dose of RSVpreF vaccine given prior to the start of the RSV season in late autumn or as soon as possible during the RSV season in the winter.

### 19.5.2 Recommended groups (unfunded) for palivizumab

For use in infants at high risk of severe RSV-LRTI, particularly recommended for those aged under 1 year prior to or during the RSV season :

- born preterm up to 28 weeks gestation
- born preterm up to 32 weeks gestation with chronic lung disease of prematurity
- with haemodynamically significant congenital heart disease
- severely immunocompromised infants.

### 19.5.3 Pregnancy and breastfeeding

RSVpreF (Arexvy) is indicated from the age of 60 years and is not recommended for use in pregnancy or while lactating/breast-feeding.

Palivizumab is not indicated for adolescent or adult use.

### 19.5.4 Immunocompromised individuals

Although safety and immunogenicity data are not yet available in immunocompromised adults, as a non-live vaccine, there are no safety concerns around giving RSVpreF to individuals who are immunocompromised and who are at increased risk of being hospitalised with severe RSV infection. Individuals receiving immunosuppressive therapy or who have immunodeficiency could have a reduced immune response to RSV vaccine.

Palivizumab is available for use in infants with immunocompromise, particularly those with severe immunodeficiencies, that increases their risk of severe RSV-LRTD up to age 24 months.

## 19.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

### 19.6.1 Contraindications

There are no specific contraindications to RSVpreF (Arexvy) or palivizumab, except for anaphylaxis to a previous dose or any component of the vaccine.

### 19.6.2 Precautions

The RSVpreF, Arexvy, is not recommended for use during pregnancy. During a single clinical trial, a 1.5-times increase in preterm births was observed in the vaccinated cohort compared to placebo following administration of an investigational unadjuvanted formulation of RSVpreF3 to 3,557 pregnant women; the clinical trial was discontinued. Stratification by economic region showed that the increase in preterm births was seen in low-income and not in high-income countries.<sup>29</sup> The mechanism for this is unknown.

## 19.7 Potential responses and AEFIs

### 19.7.1 Potential responses

During clinical trials, RSVpreF was well-tolerated in adults aged from 18 years and aged from 50 years. The most frequently reported responses were injection-site pain, headache, fatigue, myalgia and arthralgia.<sup>23</sup> Co-administration with seasonal influenza vaccine increased the incidence of pain at the RSV vaccine injection site but there are no concerns about safety.<sup>30</sup>

The reported responses to palivizumab were not significantly different from placebo and the adverse event profiles were similar during clinical studies.

## 19.7.2 AEFI

No serious adverse events or potential immune-mediated disease were attributed to RSVPreF3 OA in diverse older populations (aged over 60 years)<sup>23</sup> or in adults aged 50-59 years with comorbidities that increase the risk for severe RSV.<sup>31</sup> Clinical trial safety follow-up has been reported for at least 18 months, to date.<sup>24</sup> One case of Guillain-Barré syndrome (GBS) was temporally associated with vaccination but diagnosis of this was inconclusive as it did not meet the Brighton Collaboration Working Group case definition.<sup>16</sup>

Consistent with clinical trial data, early findings reported by the CDC identified a potential safety concern for GBS in adults aged 60 years and over who received RSVpreF vaccines. Reports of GBS were more common than expected background rates in those who received Abrysvo (5.0 excess cases per million doses, based on 11 reports that met the case definition) and Arexvy (1.5 excess cases per million doses, based on 17 reports that met the case definition).<sup>32</sup> It was noted that VAERS data cannot determine a causal association between the adverse event and the vaccination.

When RSVPreF was coadministered with adjuvanted influenza vaccine (FluAd Quad) to clinical trial participants aged 65 years and over, most solicited responses were mild or moderate and transient. Serious adverse events were balanced between the coadministration and control groups, and none were considered due to coadministration of these vaccines.<sup>21</sup> Another clinical trial demonstrated no safety concerns around giving RSVPreF and rZV (both contain AS01 adjuvant). Mild to moderate solicited local AE at either injection site and systemic AE were reported by 74 percent of coadministered participants, 60 percent of controls post-RSVPreF only and 49 percent of controls post-rZV only. For both groups the duration of AE were short and most frequently reported were pain, fatigue and myalgia.<sup>22</sup>

## 19.8 Public health measures

Respiratory syncytial virus is not a notifiable infection in Aotearoa New Zealand. The methods of preventing and controlling RSV are the same as those for other seasonal respiratory viruses.

- breastfeeding
- hand hygiene (ie, regularly washing hands for at least 20 seconds and drying them for 20 seconds, or regularly using an alcohol-based hand rub)
- respiratory hygiene (ie, cough and sneeze etiquette, and wearing of face masks in some settings for example poorly ventilated or overcrowded)
- social distancing (ie, persuading those with symptoms to avoid others in the community by staying away from school and work when sick; in particular, infected individuals should avoid contact with the elderly, the chronically ill, and infants and babies)
- regularly cleaning flat surfaces such as bathroom sinks, bedside cabinets, desks and tabletops

- immunisation (as available).
- Consider healthy homes initiatives (see [www.tewhatauora.govt.nz/health-services-and-programmes/healthy-homes/](http://www.tewhatauora.govt.nz/health-services-and-programmes/healthy-homes/))

## 19.9 Variations from the vaccine data sheet

None

### References

1. Andeweg SP, Schepp RM, van de Kasstele J, et al. Population-based serology reveals risk factors for RSV infection in children younger than 5 years. *Scientific Reports*, 2021. 11(1): p. 8953.
2. Piedimonte G ,Perez MK. Respiratory syncytial virus infection and bronchiolitis. *Pediatrics in Review*, 2014. 35(12): p. 519-30.
3. Taleb SA, Al Thani AA, Al Ansari K,Yassine HM. Human respiratory syncytial virus: pathogenesis, immune responses, and current vaccine approaches. *European Journal of Clinical Microbiology and Infectious Diseases*, 2018. 37(10): p. 1817-1827.
4. Nam HH ,Ison MG. Respiratory syncytial virus infection in adults. *BMJ*, 2019. 366: p. I5021.
5. Shi T, Vennard S, Jasiewicz F, et al. Disease burden estimates of respiratory syncytial virus related acute respiratory infections in adults with comorbidity: A systematic review and meta-analysis. *Journal of Infectious Diseases*, 2022. 226(Suppl 1): p. S17-S21.
6. Prasad N, Newbern EC, Trenholme AA, et al. The health and economic burden of respiratory syncytial virus associated hospitalizations in adults. *PloS One*, 2020. 15(6): p. e0234235.
7. Hardelid P, Verfuerden M, McMenamin J, et al. The contribution of child, family and health service factors to respiratory syncytial virus (RSV) hospital admissions in the first 3 years of life: birth cohort study in Scotland, 2009 to 2015. *Euro Surveillance*, 2019. 24(1).
8. Munro APS, Martinon-Torres F, Drysdale SB,Faust SN. The disease burden of respiratory syncytial virus in infants. *Current Opinion in Infectious Diseases*, 2023. 36(5): p. 379-384.
9. Shi T, Vennard S, Mahdy S,Nair H. Risk factors for poor outcome or death in young children with respiratory syncytial virus-associated acute lower respiratory tract infection: A systematic review and meta-analysis. *Journal of Infectious Diseases*, 2022. 226(Suppl 1): p. S10-S16.
10. Agoti CN, Phan MVT, Munywoki PK, et al. Genomic analysis of respiratory syncytial virus infections in households and utility in inferring who infects the infant. *Scientific Reports*, 2019. 9(1): p. 10076.
11. Prasad N, Newbern EC, Trenholme AA, et al. Respiratory syncytial virus hospitalisations among young children: a data linkage study. *Epidemiology and Infection*, 2019. 147.



12. Eiland LS. Respiratory syncytial virus: diagnosis, treatment and prevention. *J Pediatr Pharmacol Ther*, 2009. 14(2): p. 75-85.
13. Brenes-Chacon H, Garcia-Maurino C, Moore-Clingenpeel M, et al. Age-dependent interactions among clinical characteristics, viral loads and disease severity in young children with respiratory syncytial virus infection. *Pediatric Infectious Disease Journal*, 2021. 40(2): p. 116-122.
14. Institute of Environmental Surveillance and Research (ESR). 2024 *Influenza and other viral respiratory surveillance*. ESR; 2024 [updated 26 May 2024]; URL: <https://www.esr.cri.nz/our-research/nga-kete/infectious-disease-intelligence/influenza-and-respiratory-surveillance/>. (accessed 31 May 2024)
15. Ruckwardt TJ. The road to approved vaccines for respiratory syncytial virus. *npj Vaccines*, 2023. 8(1).
16. Schwarz TF, Hwang SJ, Ylisastigui P, et al. Immunogenicity and safety following one dose of AS01E-adjuvanted respiratory syncytial virus prefusion F protein vaccine in older adults: a phase 3 trial. *Journal of Infectious Diseases*, 2023.
17. Leroux-Roels I, Davis MG, Steenackers K, et al. Safety and immunogenicity of a respiratory syncytial virus prefusion F (RSVPreF3) candidate vaccine in older adults: Phase 1/2 randomized clinical trial. *Journal of Infectious Diseases*, 2023. 227(6): p. 761-772.
18. Leroux-Roels I, Van Ranst M, Vandermeulen C, et al. Safety and immunogenicity of a revaccination with a respiratory syncytial virus prefusion F vaccine in older adults: A Phase 2b study. *Journal of Infectious Diseases*, 2023.
19. Feldman RG, Antonelli-Incalzi R, Steenackers K, et al. Respiratory syncytial virus prefusion F protein vaccine is efficacious in older adults with underlying medical conditions. *Clinical Infectious Diseases*, 2023.
20. Gerber S. 2023 *GSK's RSVPreF3 + AS01E vaccine (Arexvy)*. ACIP meeting 25 October 2023. URL: <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-10-25-26/02-gerber-adult-RSV-508.pdf>. (accessed 31 May 2024)
21. Clark R, Davies S, Labrador J, et al. Safety and immunogenicity of respiratory syncytial virus prefusion F protein vaccine when co-administered with adjuvanted seasonal quadrivalent influenza vaccine in older adults: A phase 3 randomized trial. *Clinical Infectious Diseases*, 2024.
22. Dennis P, Roussy J-F, Gupta A, et al., Co-administration of the adjuvanted respiratory syncytial virus (RSV) prefusion F protein vaccine (RSVPreF3 OA) with the adjuvanted recombinant zoster vaccine (RZV) in adults  $\geq 50$  years of age, in *European Geriatric Medicine Society Congress*. 2024 (unpublished): Valencia, Spain.
23. Papi A, Ison MG, Langley JM, et al. Respiratory syncytial virus Prefusion F protein vaccine in older adults. *New England Journal of Medicine*, 2023. 388(7): p. 595-608.
24. Ison MG, Papi A, Athan E, et al. Efficacy and safety of respiratory syncytial virus prefusion F protein vaccine (RSVPreF3 OA) in older adults over 2 RSV seasons. *Clinical Infectious Diseases*, 2024.
25. Caserta MT, O'Leary ST, Munoz FM, Ralston SL. Palivizumab Prophylaxis in Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection. *Pediatrics*, 2023. 152(1).
26. Link-Gelles R, Ciesla AA, Mak J, et al. Early estimates of updated 2023-2024 (monovalent XBB.1.5) COVID-19 vaccine effectiveness against symptomatic SARS-CoV-2 infection attributable to co-circulating omicron variants among immunocompetent adults - Increasing Community Access to Testing Program, United States, September 2023-January 2024. *MMWR: Morbidity and Mortality Weekly Report*, 2024. 73(4): p. 77-83.
27. Wu P, Escobar GJ, Gebretsadik T, et al. Effectiveness of respiratory syncytial virus immunoprophylaxis in reducing bronchiolitis hospitalizations among high-risk infants. *American Journal of Epidemiology*, 2018. 187(7): p. 1490-1500.

28. Garegnani L, Styrnisdóttir L, Roson Rodriguez P, et al. Palivizumab for preventing severe respiratory syncytial virus (RSV) infection in children. *Cochrane Database Syst Rev*, 2021. 11(11): p. CD013757.
29. Department of Health and Social Care. 2023 *Respiratory syncytial virus (RSV) immunisation programme for infants and older adults: JCVI full statement, 11 September 2023*. Crown. URL: <https://www.gov.uk/government/publications/rsv-immunisation-programme-jcvi-advice-7-june-2023/respiratory-syncytial-virus-rsv-immunisation-programme-for-infants-and-older-adults-jcvi-full-statement-11-september-2023>. (accessed 2023 February 7)
30. Chandler R, Montenegro N, Llorach C, et al. Immunogenicity, reactogenicity, and safety of AS01E-adjuvanted RSV prefusion F protein-based candidate vaccine (RSVPreF3 OA) when co-administered with a seasonal quadrivalent influenza vaccine in older adults: results of a phase 3, open-label, randomized controlled trial. *Clinical Infectious Diseases*, 2024.
31. Ferguson M, Schwarz TF, Núñez SA, et al., Respiratory syncytial virus prefusion F protein vaccine (RSVPreF3 OA) is immunogenic and well-tolerated in adults 50–59 years, including adults at increased risk for RSV disease, in *8th ReSViNET Conference*. 2024: Mumbai, India.
32. Hause AM, Moro PL, Baggs J, et al. Early Safety Findings Among Persons Aged  $\geq 60$  Years Who Received a Respiratory Syncytial Virus Vaccine - United States, May 3, 2023-April 14, 2024. *MMWR: Morbidity and Mortality Weekly Report*, 2024. 73(21): p. 489-494.

# 20 Rotavirus

## Key information

Mode of transmission	Faecal–oral route through close personal contact and fomites.
Incubation period	1–3 days.
Period of communicability	During symptoms and until approximately 8 days after onset of symptoms. Up to 30 days after onset of symptoms in immunocompromised patients.
Burden of disease	All children during infancy or early childhood. Severe disease occurs most often in children aged 3 months to 2 years.
Funded vaccine	Oral live attenuated monovalent rotavirus: RV1 (Rotarix).
Dose, presentation, route	1.5 mL per dose. Oral suspension in an oral applicator, Administered orally.
Funded vaccine indications and schedule	2 doses for infants, at ages 6 weeks and 3 months. For catch-up schedules, the first dose should be given before age 15 weeks (latest is 14 weeks and 6 days), and the 2nd dose should be given before age 25 weeks (latest is 24 weeks and 6 days).
Vaccine effectiveness	Highly effective against severe rotavirus diarrhoea; some evidence for efficacy against all-cause diarrhoea and herd protection.
Contraindications	Previous intussusception and with conditions that predispose the infant to intussusception. Severe combined immune deficiency.
Precautions and special considerations	Infants living in households with immunocompromised persons or pregnant women should still be vaccinated. Hand washing and the careful disposal of soiled nappies are likely to minimise any risk of vaccine transmission to household members. Immunosuppressed infants including those on immunosuppressive therapy (other than SCID, where it is contraindicated). Infants born to mothers on immunosuppressive biologic agents (see section 20.6.2).
Potential responses to vaccine	A possible, very small risk for intussusception; the benefits of immunisation considerably outweigh this potential risk.

## 20.1 Virology

The rotaviruses are segmented, double-stranded RNA viruses of the family Reoviridae.<sup>1</sup> They are classified according to two surface proteins on the outer capsid: VP4 protease cleaved 'P' protein and VP7, the 'G' glycoprotein, which allows a binary classification system. The G and P proteins are immunological targets for neutralising antibodies protecting against disease and re-infection.<sup>2</sup> While more than 60 G and P combinations have been found in humans, there are only five strains (P[8]G1, P[4]G2, P[8]G3, P[8]G4, and P[8]G9) that are associated with 80–90 percent of the global burden of disease in children.<sup>3</sup> For simplicity, these strains are commonly referred to by their G serotype as G1, G2, G3, G4 and G9.

## 20.2 Clinical features

Rotavirus infects almost all children during infancy or early childhood. Transmission occurs through the faecal–oral route through close personal contact and through fomites. Aerosol transmission has been hypothesised but remains unproven.<sup>1</sup>

The incubation period is one to three days, after which illness can begin abruptly, with fever and vomiting often preceding the onset of diarrhoea.<sup>1,4</sup> Up to one-third of children will develop a fever of greater than 39°C.<sup>5,6</sup> The illness lasts from three to eight days.

Children with rotavirus are infectious while they have symptoms and until approximately eight days after the onset of symptoms. Immunocompromised patients may be infectious for up to 30 days after the onset of symptoms.<sup>7</sup> Large quantities of rotavirus are shed in the stool, and only a few virions are required to cause infection in a susceptible host.<sup>8</sup>

Rotavirus infection in the first three months of life is frequently mild or asymptomatic. This is possibly due to passive protection from maternally acquired antibodies, being breastfed and the intestinal cell structure of newborn infants.<sup>1,9</sup>

The burden of severe dehydrating gastroenteritis caused by rotavirus occurs predominantly in infants and children aged 3 months to 2 years.<sup>3</sup>

The clinical spectrum ranges from asymptomatic infection to an acute severe illness with frequent and large-volume diarrhoea and vomiting, leading to dehydration, electrolyte disturbance and their sequelae. The illness spectrum from rotavirus is more severe than from other common causes of diarrhoea in children.<sup>1</sup>

## 20.3 Epidemiology

### 20.3.1 Global burden of disease

Rotavirus gastroenteritis is a significant cause of infant diarrhoea worldwide, both in high- and low-income countries. Virtually all children are infected by age 5 years.<sup>1</sup> Each year rotavirus causes the death of approximately 200,000 to 450,000 children aged under 5 years worldwide<sup>10, 11</sup> and results in 2.4 million paediatric hospital admissions.<sup>12</sup> Virtually all of the deaths occur in low-income countries. Prior to the introduction of licensed rotavirus vaccines in high-income countries, more than 220,000 children were hospitalised with rotavirus gastroenteritis every year.<sup>13, 14</sup>

Rates of rotavirus illness in children before the introduction of vaccine were similar in high- and low-income countries, indicating that good hygiene and clean water supplies are unlikely to have a significant impact on disease prevention. As a result, immunisation is the primary public health measure for the reduction of rotavirus disease burden.<sup>1</sup>

In countries with a temperate climate, rotavirus epidemics occur every winter and spring. Factors associated with an increased risk of severe rotavirus gastroenteritis include age under 2 years, low birthweight, premature gestation, lack of breastfeeding, socioeconomic disadvantage, malnutrition and impaired immunity.<sup>1, 15-18</sup> Rotavirus gastroenteritis is not, however, more severe in HIV-infected children, although viral shedding may be longer.<sup>3</sup>

Rotavirus is an important cause of hospital-acquired infection<sup>19</sup> and can also cause disease in adults, especially those caring for children<sup>20</sup> and those living in aged-care facilities. During outbreaks in early childhood settings, rotavirus has been isolated from telephone receivers, drinking fountains, water-play tables and toilet handles.<sup>21</sup> Outbreaks in elderly populations may be linked to waning immunity, institutional crowding or both.

Children and adults can be infected with rotavirus several times in their lives. After a single natural infection during infancy, approximately one-third are protected against subsequent rotavirus infection, more than three-quarters are protected against subsequent rotavirus gastroenteritis and 85–90 percent are protected against severe rotavirus gastroenteritis.<sup>22</sup> The proportion with protection against both infection and symptomatic rotavirus gastroenteritis increases with successive episodes.<sup>22</sup>

These observations serve as the biological basis for rotavirus vaccines, whereby live attenuated strains can induce cumulative protective immunity similar to that following natural infection by wild-type rotaviruses. Although the immune mechanism and correlates of protection against rotavirus infection are incompletely understood, it is likely that both mucosal and serum antibodies are associated with protection against rotavirus infection and disease.<sup>23</sup>

Since the introduction of the vaccine in other high-income countries, there have been reductions in all-cause and rotavirus gastroenteritis in age groups not eligible for the vaccine, suggesting herd immunity effects as a result of rotavirus vaccines<sup>3, 24, 25</sup> (see 'Herd immunity in the post-licensure period' in section 20.4.2).

## 20.3.2 New Zealand epidemiology

Rotavirus vaccine was introduced in July 2014, as a three-dose schedule to infants at ages 6 weeks, 3 months and 5 months, using the RV5 vaccine (RotaTeq) (see Appendix 1).

At present rotavirus is not a notifiable disease, so there is no national surveillance data available. National hospital discharge rates, community and hospital laboratory data plus a sentinel hospital-based surveillance system have been used to monitor rotavirus disease since vaccine introduction. The sentinel hospital-based rotavirus surveillance was introduced in December 2014 at Kidz First Children's Hospital in Counties Manukau district and extended to Wellington, Hutt and Christchurch Hospitals in April 2016.

For detailed information about rotavirus surveillance and rotavirus infections in New Zealand, see the ESR website ([www.esr.cri.nz/expertise/public-health/](http://www.esr.cri.nz/expertise/public-health/)).

### Pre-vaccine epidemiology

Prior to the introduction of vaccine, by the age of 5 years, it is estimated 1 in 5 children had sought medical advice for rotavirus gastroenteritis and 1 in 43 children had been hospitalised.<sup>13</sup>

From 2010 to 2014, the average annual national hospitalisation rate for rotavirus in children aged under 5 years was 215.4 per 100,000.<sup>26</sup> The highest hospitalisation rates for children aged under 5 years were in those from the Middle Eastern/Latin American/African ethnic group, followed by Pacific and Māori ethnic groups. Hospitalisation rates in children aged under 5 years who reside in the most deprived NZDep2013 quintiles (quintiles 4 and 5) were significantly higher than those who reside in the least deprived quintile. There is a seasonal peak for rotavirus hospitalisations, usually occurring around September each year.

### Post-vaccine epidemiology

The introduction of rotavirus vaccination in Australia resulted in a 70 percent decrease in rotavirus hospitalisations in the two and a half years post-vaccine introduction.<sup>27</sup>

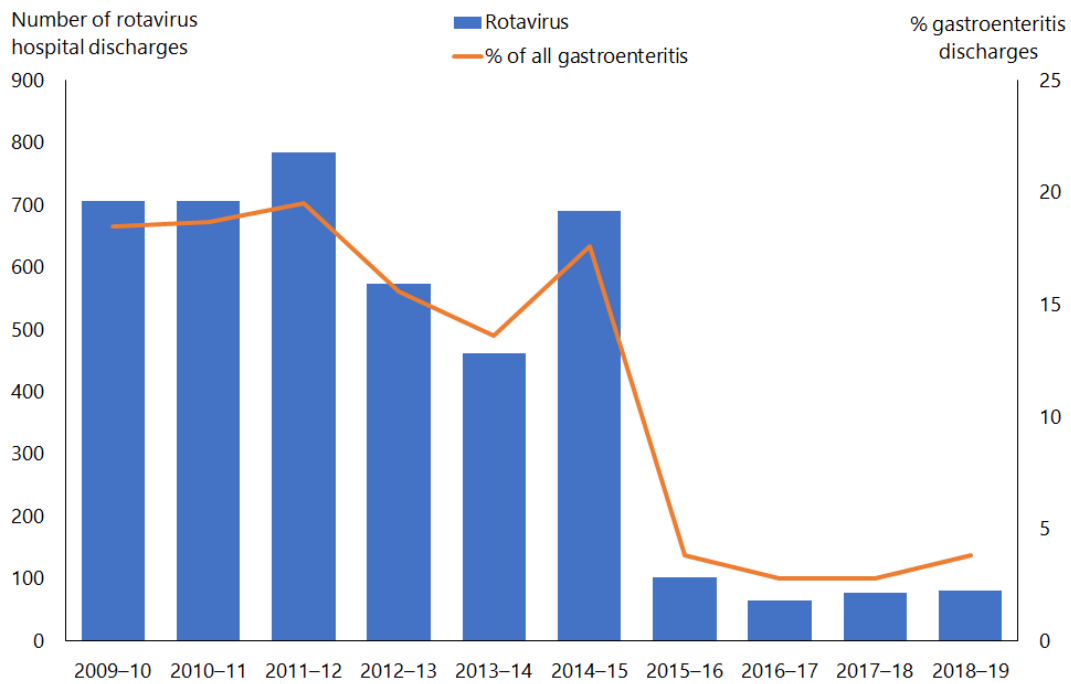
A similar decline has been noted in New Zealand in the first year post-vaccine introduction, where rotavirus hospitalisation rates for children aged under 5 years declined by 85 percent in 2015 compared with the previous five-year average (2010–2014)<sup>26</sup> (Figure 20.1). The vaccine has been effective in decreasing the most severe rotavirus disease. Hospitalisation rates decreased for all ethnic groups and levels of socioeconomic deprivation. Community laboratory data also supports the large decrease in rotavirus infections in the community.

Although only children aged under 1 year were eligible for rotavirus vaccination, hospital discharge rates decreased in all children aged under 5 years in 2015<sup>26</sup> (Figure 20.2). Older children are more likely to have been exposed to rotavirus already, and are less likely to benefit from vaccination.

Hospital discharges for rotavirus ranged from 510 to 822 cases per year in the four years prior to vaccine introduction (2010–2013).<sup>26</sup> There were 99 hospital discharges for rotavirus in children aged under 5 years in New Zealand in 2015, compared with 770 in 2014. This reduction in rotavirus hospitalisations of children aged under 5 years was maintained to 2019, with 80 cases hospitalised in the year to June 2019.

There was a 93.6 percent decrease in rotavirus outbreaks (three outbreaks reported in 2015 compared with 47 in 2014) after the introduction of vaccine in New Zealand.<sup>26</sup> This demonstrates that universal rotavirus vaccination is an effective public health intervention.

**Figure 20.1: Rotavirus hospital discharges and as a percentage of all gastroenteritis discharges for children aged under 5 years, all New Zealand, June 2009–June 2019**

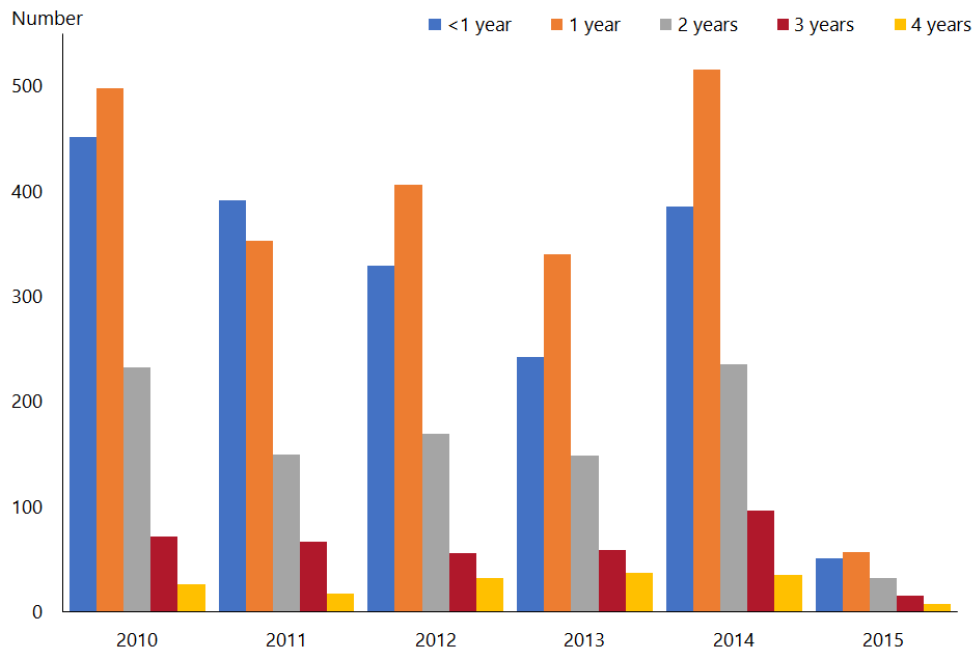


Note: Rotavirus vaccine introduced in July 2014.

Source: Ministry of Health.



**Figure 20.2: Rotavirus hospital discharge rates for children aged under 5 years by age and year, all New Zealand, 2010–2015**



Source: ESR

## 20.4 Vaccines

### 20.4.1 Available vaccines

The types of virus assessed for use as rotavirus vaccines have included live attenuated virus, both human and animal strains of the virus, and human–animal reassortant viruses. Two rotavirus vaccines have been used in New Zealand. Both are orally administered live attenuated vaccines and have been extensively evaluated.<sup>28, 29</sup> The live attenuated vaccine viruses replicate in the intestinal mucosa and are shed in the stools of vaccine recipients.<sup>28, 30, 31</sup>

#### Funded vaccine

RV1 (Rotarix, GSK) is a live attenuated monovalent human G1P1A[8] strain rotavirus vaccine. It protects against non-G1 serotypes (these include G2P[4], G3P[8], G8P[4], G9P[8] and G12P[6]) on the basis of other shared epitopes. Each 1.5 mL dose contains:

- at least 106 CCID50 (cell culture infective dose 50 percent) of the RIX 4414 strain of human rotavirus
- other components and residuals, including sucrose, disodium adipate and culture medium.

## 20.4.2 Efficacy and effectiveness

### Prevention of disease

A 2012 Cochrane review<sup>32</sup> of the efficacy of rotavirus vaccines for the prevention of rotavirus diarrhoea assessed 41 trials which met the inclusion criteria, involving 186,263 enrolled participants. Of these, 29 trials assessed the monovalent vaccine (RV1; Rotarix) and 12 trials assessed the pentavalent vaccine (RV5; RotaTeq).

For the first two years of life in countries with low mortality rates, both vaccines prevented over 80 percent of cases of severe rotavirus diarrhoea (Table 20.1). Both vaccines impact severe all-cause diarrhoea (moderate to low quality of evidence). See also Figure 20.1 and Figure 20.2 above, which show a reduction in rotavirus hospitalisations in New Zealand children aged under 5 years after rotavirus vaccine was introduced in 2014.

**Table 20.1: Cochrane review: percentage of severe rotavirus and all-cause diarrhoea cases prevented in children by RV1 and RV5, compared to placebo (low mortality rate countries)**

Vaccine	Percentage of cases prevented	Risk ratio (95% confidence interval)	Number of participants (number of trials)	Quality of evidence
<b>Severe rotavirus diarrhoea: infants aged under 1 year</b>				
RV1	86	0.14 (0.07–0.26)	40,631 (6)	High
RV5	87	0.13 (0.04–0.45)	2,344 (3)	Moderate
<b>Severe rotavirus diarrhoea: children aged under 2 years</b>				
RV1	85	0.15 (0.12–0.2)	32,854 (8)	High
RV5	82	0.18 (0.07–0.5)	3,190 (3)	Moderate
<b>Severe all-cause diarrhoea: infants aged under 1 year</b>				
RV1	40	0.60 (0.5–0.72)	17,867 (1)	Moderate
RV5	72	0.28 (0.16–0.48)	1,029 (1)	Low
<b>Severe all-cause diarrhoea: children aged under 2 years</b>				
RV1	37	0.63 (0.56–0.71)	39,091 (2)	Moderate
RV5	96	0.04 (0.00–0.70)	5,916 (1)	Low

Adapted from: Soares-Weiser K, MacLehose H, Bergman H, et al. 2012. Vaccines for preventing rotavirus diarrhoea: vaccines in use. *Cochrane Database of Systematic Reviews* Issue 11, Art. No. CD008521. DOI: 10.1002/14651858.CD008521.pub3 (accessed 24 June 2020).

## Effectiveness

In pre-marketing clinical trials, rotavirus vaccination prevented 42–58 percent of all-cause hospital admissions for acute gastroenteritis, suggesting it is responsible for more gastroenteritis than is detected by routine testing.<sup>28, 33, 34</sup>

Post-licensure surveillance studies have demonstrated large reductions in rotavirus-positive stool isolates from children with gastroenteritis (US)<sup>35</sup> and in diarrhoea-related deaths (Mexico).<sup>36, 37</sup> Summarised, post-licensure vaccine effectiveness studies in high-income countries have shown an 89–100 percent reduction in emergency department visits or hospitalisation; a 74–90 percent decline in hospitalisations for rotavirus gastroenteritis in children aged under 2 years; and a 29–50 percent decline in 'all-cause' acute gastroenteritis hospitalisations for children aged under 5 years.<sup>38</sup>

A protective association between rotavirus vaccine and childhood seizures has been reported in the US<sup>39</sup> and Australia.<sup>40</sup> In US children, a full course of rotavirus vaccination was associated with an 18–21 percent reduction in the risk of seizure requiring hospitalisation or emergency department care in the year following vaccination, compared with unvaccinated children.<sup>39</sup> In the Australian state of Queensland, rotavirus vaccine was 35.8 percent effective at preventing emergency department presentation for febrile seizures and 38.0 percent effective at preventing subsequent hospitalisation in children up to two years following vaccination.<sup>40</sup>

## Herd immunity in the post-licensure period

Since the beginning of the post-licensure period, over 80 countries have introduced the rotavirus vaccine into their national immunisation programmes.<sup>41</sup> There has been substantial though somewhat variable efficacy data to show a decline in rotavirus infections in the different country environments. In the US, there was a 73 percent reduction in rotavirus infections among infants from 2003 to 2014.<sup>42</sup> The effectiveness tends to wane with age, and rotavirus 'seasons' appear to be longer in the post-licensure period.<sup>42</sup>

While a decline has occurred in rotavirus infection alone, there has also been a reduction in all-cause diarrhoeal illnesses.<sup>41</sup> Furthermore, the protective effect of the vaccine has surpassed the expected level of vaccine efficacy and coverage, resulting in a herd protection. Therefore, the immunised proportion of the population is causing a reduction of infection in the unimmunised portion of the community.<sup>43</sup>

## Duration of protection

Prior to the introduction of rotavirus vaccines in Europe, extension studies of the pivotal phase III RV5 trial showed protection lasting up to three years from the last vaccine dose.<sup>44</sup> The duration of protection provided by rotavirus vaccines is difficult to measure because of the herd immunity effect that occurs after the vaccine is implemented. Some studies indicate waning immunity after the first year of life, particularly in low-income countries.<sup>45, 46</sup> In a large multicentre study in the US, both RV1 and RV5 vaccines were found to provide lasting and broadly heterologous protection against infection. Vaccine effectiveness persisted to the seventh year of life for RV5 and through the third year of life for RV1.<sup>47</sup> Note that the differences in duration are because RV1 was licensed in the US approximately two years later than RV5, affecting vaccination coverage and corresponding study power for older age groups for RV1 analyses.<sup>47</sup>

## Partial vaccination

Studies in partially vaccinated infants (ie, those who had not completed the three-dose course of RV5 or the two-dose course of RV1) found that protection against rotavirus gastroenteritis ranged from 51–55 percent in low- and middle-income countries, and from 69–93 percent in high-income countries.<sup>48</sup>

## Cross-protection

Rotavirus vaccine strains vary considerably, and multiple wild-type strains can occur at the same time. In high-income countries, both vaccines appear to provide some cross-protection against non-vaccine serotypes.<sup>49, 50</sup> Vaccine protection against newly emerging genotypes is not well known, and national surveillance of circulating rotavirus types post-vaccination is necessary.<sup>51</sup>

## 20.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at [www.tewhaturora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhaturora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

Store in the dark at +2°C to +8°C. Do not freeze.

## 20.4.4 Dosage and administration

The dose of RV1 (Rotarix) is 1.5 mL, administered orally (for administration instructions see section A7.2.4 of this *Handbook* or the vaccine data sheet, available at [medsafe.govt.nz](https://www.medsafe.govt.nz)). Do not inject RV1.

Two doses are given, at ages 6 weeks and 3 months. See section 20.5 below for more information.

### Co-administration with other vaccines

Rotavirus vaccines can be administered at the same time as other scheduled vaccines. Note that no time interval is required between administration of rotavirus and BCG vaccines; the two live vaccines likely to be administered to infants aged under 6 months.

### If the dose is regurgitated or vomited

If an infant spits out or vomits most of a vaccine dose within minutes of receiving it, give one repeat dose during the same visit. If an infant spits out or vomits only a small part of a vaccine dose, the dose is still considered valid and does not need to be repeated.<sup>52</sup> It is safe for the infant to have the entire volume of a repeat dose even if some of the first dose had been swallowed.

## 20.5 Recommended immunisation schedule

RV1 is recommended and funded for all infants. See section 20.5.2 for RV1 age limit information.

Immunisation is especially encouraged for those who will be attending early childhood education services or where there is an immunocompromised individual living in the household.

Infants who have already had rotavirus gastroenteritis should still receive the full course of immunisation. Initial rotavirus infection only provides partial protection against subsequent infection.<sup>1, 22</sup>

## 20.5.1 Routine schedule

Two RV1 doses are given orally, at ages 6 weeks and 3 months.

**Table 20.2: The infant RV1 (Rotarix) schedule**

Dose	Usual scheduled age	Recommended age limits for dosing
Dose 1	6 weeks	6–14 weeks <sup>a</sup>
Dose 2 <sup>b</sup>	3 months	10–24 weeks <sup>c</sup>

- The upper age limit for receipt of the first dose of RV1 is immediately prior to turning 15 weeks old (14 weeks and 6 days).
- The minimum interval between doses 1 and 2 is 4 weeks.
- The upper age limit for receipt of the second dose of RV1 is immediately prior to turning 25 weeks old (24 weeks and 6 days).

## 20.5.2 Catch-up schedules

The first dose of RV1 should be given before age 15 weeks (ie, 14 weeks and 6 days), and the second dose administered at least four weeks later (see Table 20.2). An infant who has not had the first dose before age 15 weeks will not be able to commence the rotavirus course. Where the first dose is inadvertently given at age 15 weeks or older, the second dose should be given, but both doses should be given before age 25 weeks (ie, the latest is 24 weeks and 6 days).<sup>1</sup> Rotavirus vaccine is not intended for use in older children, adolescents or adults.

The age limits for initiating and completing the vaccine series are recommended because there is insufficient safety data on the use of these vaccines outside this age range. If a partially vaccinated infant reaches age 25 weeks before the second dose is given, the first dose already given will offer them partial protection against disease.

The severity of rotavirus infection decreases with age, so a cost–benefit analysis for vaccinating older children is a low priority and has not been done.

## 20.5.3 Preterm infants

Vaccination as per the Schedule (ie, at the usual chronological age, with the usual vaccine dosage and interval) is recommended for preterm infants and infants with low birthweight, including those still in hospital (see below). Rotavirus vaccine can be given to preterm infants born who are receiving corticosteroids. (See also 4.2.1 for more immunisation recommendations for preterm infants.)

## 20.5.4 Hospitalised infants

Rotavirus vaccine should be given on time to any infant admitted to a general hospital ward (where other patients are not high risk). If standard infection control precautions are maintained, there is no risk of transmission of vaccine strain rotavirus when rotavirus vaccine is administered to hospitalised infants, including hospitalised preterm infants and those in neonatal units.<sup>53, 54</sup> (See also section 4.2 for more information about infants with special immunisation recommendations.)

## 20.5.5 Pregnancy and breastfeeding

There is no concern caused by vaccine exposure during pregnancy. There is no restriction for breastfeeding before or after vaccination of the infant (see 'Shedding' in section 20.6.2).

# 20.6 Contraindications and precautions

See section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

## 20.6.1 Contraindications

Rotavirus vaccine should not be given to infants with:

- a history of a severe (anaphylactic) allergic reaction after a previous dose or to a vaccine component
- a history of intussusception or an uncorrected congenital malformation of the gastrointestinal tract that would predispose the infant to intussusceptions (see section 20.7.1).
- severe combined immunodeficiency (SCID).<sup>55</sup>

## 20.6.2 Precautions

Rotavirus vaccine can be administered to infants with a mild illness, including gastroenteritis and upper respiratory tract infections. Infants with moderate to severe gastroenteritis should not be vaccinated until symptoms resolve.



There is very little safety data on infants with predisposing conditions such as metabolic disorders and chronic gastrointestinal diseases (Hirschsprung's, malabsorption syndromes or short gut syndromes). Since there is a greater risk of serious wild-type rotavirus disease, the benefits outweigh the risk, and vaccination is encouraged.<sup>52</sup>

Infants who have received antibody-containing blood products and are the appropriate age should be vaccinated. Rotavirus vaccine and antibody-containing blood products can be administered simultaneously.<sup>52</sup> There is a theoretical risk of interference in the immune response to the vaccine; therefore the interval between vaccination and receipt of blood products should ideally be as long as possible within the age limits of the vaccine schedule.

Administration of RV1 in immunosuppressed infants, including infants on immunosuppressive therapy, should be based on careful consideration of potential benefits and risks.

### Infants born to mothers on immunosuppressive therapies

There is limited data on rotavirus vaccination safety when given to infants born to mothers receiving immunosuppressive therapy during pregnancy.<sup>19, 36, 56</sup> Although in most cases it is likely to be safe, caution is required. The level of circulating wild-type rotavirus is currently very low in New Zealand; therefore, the risk of gastroenteritis following rotavirus vaccination in this cohort of infants may be greater than the risk of acquiring the disease. The decision to administer rotavirus vaccine to infants born to mothers who received immunosuppressive agents (biologic agents) during pregnancy should be determined case by case.

If an infant turns 15 weeks of age before the first rotavirus vaccine dose can be administered, they will not be able to receive any rotavirus vaccine doses.

See section 4.2.5 / Infants of mothers who received immunomodulatory biologic agents during pregnancy and Table 4.2 for a list of the highly immunomodulatory biologic agents with long half-lives that require a prolonged delay before vaccination (for up to one year in those being treated). These include monoclonal antibody (mab) agents that readily cross the placenta.

Each case should be assessed on a risk–benefit basis and with specialist advice.

### Shedding

Since rotavirus vaccine virus replicates in the gastrointestinal tract, it can be shed in stools – especially after the first dose.<sup>57</sup> Shedding is also more likely in immunocompromised patients (eg, children with HIV). The vaccine virus could then be transmitted to unvaccinated populations; a feature that is generally beneficial as it promotes herd immunity.

Infants living in households with immunocompromised individuals should be vaccinated. So far there are no safety concerns, but there is also no data to confirm the

safety of these vaccines for immunocompromised patients. Infants living in households with pregnant women should also be vaccinated. Hand washing and the careful disposal of soiled nappies are likely to minimise any risk of vaccine transmission to household members.<sup>52, 53</sup>

## 20.7 Potential responses and AEFIs

The 2012 Cochrane review<sup>32</sup> described in section 20.4.2 also reviewed the safety of RV1 and RV5 vaccines. No significant difference was found between children receiving RV1 or RV5 and placebo in the number of serious adverse events, particularly intussusception (see below). No statistical differences were observed for fever, diarrhoea and vomiting between cases and placebo groups. There was no significant difference between cases and placebos in the number of adverse events leading to discontinuation of the schedule.

In 2010 porcine circovirus or porcine circovirus DNA was detected in both rotavirus vaccines. However, there is no evidence that this virus is a safety risk or causes illness in humans.<sup>52</sup>

### 20.7.1 Intussusception

Intussusception is a cause of an acute abdomen when one part of the intestine telescopes into another part of the intestine; the mechanism by which these events occur remains uncertain. In 1999 an oral human–rhesus rotavirus quadrivalent vaccine (RotaShield) was licensed in the US and on the infant schedule but was withdrawn later that year after reports of an association with intussusception (a risk of approximately one case in 5,000–10,000 vaccine recipients).

No increased risk of intussusception was detected in the large phase III pre-licensure clinical trials of RV1 (Rotarix) and RV5 (RotaTeq), despite this being a specifically monitored adverse event. However, post-marketing surveillance of both rotavirus vaccines indicates the possibility of an increased risk of intussusception shortly after the first dose of rotavirus vaccination. Evidence from Australia<sup>58</sup> indicates that after the first dose, RV1 had a relative incidence (relative risk) of 6.8 (95% CI: 2.4–19.0,  $p < 0.001$ ) and 3.5 (95% CI: 1.3–8.9,  $p = 0.01$ ) for the periods of 1–7 days and 8–21 days after vaccination, respectively. For RV5, the relative incidence was 9.9 (95% CI: 3.7–26.4,  $p < 0.001$ ) and 6.3 (95% CI: 2.8–14.4,  $p < 0.001$ ) for the same time periods.

There was also some elevated risk of intussusception 1 to 7 days after the second dose of both vaccines. The relative incidence for RV1 was 2.8 (95% CI: 1.1–7.3,  $p = 0.03$ ) and for RV5 was 2.8 (95% CI: 1.2–6.8,  $p = 0.02$ ). There was no evidence of increased risk of intussusception following a third dose of RV5.<sup>58</sup> The increased risk of intussusception following rotavirus vaccination is estimated at approximately 6 additional cases of intussusception among every 100,000 infants vaccinated (approximately 1 in 15,500 vaccine recipients), or 14 additional cases per year in Australia.<sup>58</sup>

Studies in the post-licensure period continue to show small increases in risk for both RV1 and RV5 and primarily within seven days of the first dose of vaccine.<sup>59, 60</sup> Recent safety data has continued to emphasise the clear and dramatic benefit of vaccination over the very low risk of vaccine-associated intussusception.<sup>41</sup> For example, a self-controlled case-series study estimated that the RV1 programme in England caused 21 intussusception admissions annually and prevented 25,000 gastrointestinal infection admissions with a clear risk–benefit ratio.<sup>61</sup>

While there appears to be an increased relative risk of intussusception, the condition remains rare, and this risk is outweighed by the benefits of rotavirus vaccination in preventing rotavirus infections; there was an estimated 70 percent reduction in hospitalisations in young children after the vaccine’s introduction to the Australian schedule.<sup>62</sup> It is uncertain whether rotavirus vaccine administration affects the overall incidence of intussusception: US data suggests no increased overall rate in infants despite a small cluster effect.<sup>63</sup> Both the WHO<sup>64</sup> and the Australian Technical Advisory Group on Immunisation<sup>62</sup> continue to recommend the use of rotavirus vaccine for infants.

Although the risk of intussusception after rotavirus immunisation is very small, it is recommended that parents seek medical advice and health care professionals are attentive if the baby develops intermittent crying or screaming episodes, pulling their knees towards their chest and vomiting, or pink- or red-coloured jelly-like stools.

A recent study has described the epidemiology of intussusception in New Zealand children aged 0–36 months (794 cases) for a 16-year period before the introduction of routine rotavirus vaccination.<sup>65</sup> This study will provide a valuable baseline to determine if the introduction of the vaccine has significant effects on intussusception rates in the New Zealand population.

## 20.8 Public health measures

Prevention of spread is by contact precautions, including careful handwashing. In an early childhood service setting where there has been a child known to have had a rotavirus infection, the surfaces should be washed with sodium hypochlorite (bleach) and water. Disinfectants inactivate rotavirus and may help to prevent disease transmission resulting from contact with environmental surfaces.<sup>52</sup>

For more details on control measures, refer to the ‘Acute gastroenteritis’ chapter of the *Communicable Disease Control Manual* [www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual](http://www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual)

## 20.9 Variations from the vaccine data sheet

The RV1 data sheet recommends postponing the administration of the vaccine in infants suffering from diarrhoea or vomiting. Health New Zealand recommends vaccinating infants with mild gastroenteritis, and to wait until symptoms have resolved for infants with moderate to severe gastroenteritis (see section 20.6.2).

The RV1 data sheet states that the vaccine should not be administered to subjects with any chronic gastrointestinal disease. Health New Zealand recommends instead that pre-existing chronic gastrointestinal disease is not a contraindication to rotavirus vaccination, with the exception of those conditions that may predispose the infant to intussusceptions (see sections 20.6.1 and 20.7.1).<sup>53</sup>

## References

1. Cortese MM, Parashar UD, Centers for Disease C, Prevention. Prevention of rotavirus gastroenteritis among infants and children: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR: Recommendations and Reports*, 2009. 58(RR-2): p. 1-25.
2. Cunliffe NA, Nakagomi O. A critical time for rotavirus vaccines: a review. *Expert Rev Vaccines*, 2005. 4(4): p. 521-32.
3. Parashar U, Cortese MM, Offit P. 2018. Rotavirus vaccines, in *Plotkin's Vaccines, 7th edition*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
4. Parashar UD, Nelson EA, Kang G. Diagnosis, management, and prevention of rotavirus gastroenteritis in children. *BMJ*, 2013. 347(30 December): p. f7204.
5. Rodriguez WJ, Kim HW, Arrobio JO, et al. Clinical features of acute gastroenteritis associated with human reovirus-like agent in infants and young children. *Journal of Pediatrics*, 1977. 91(2): p. 188-93.
6. Ruuska T, Vesikari T. Rotavirus disease in Finnish children: use of numerical scores for clinical severity of diarrhoeal episodes. *Scandinavian Journal of Infectious Diseases*, 1990. 22(3): p. 259-67.
7. Ministry of Health. 2012. *Communicable Disease Control Manual* (ed.), Wellington: Ministry of Health. URL: <https://www.health.govt.nz/publication/communicable-disease-control-manual> (accessed 10 May 2022)
8. Bishop RF. Natural history of human rotavirus infection. *Archives of Virology. Supplementum*, 1996. 12: p. 119-28.
9. Bishop RF, Barnes GL, Cipriani E, Lund JS. Clinical immunity after neonatal rotavirus infection. A prospective longitudinal study in young children. *New England Journal of Medicine*, 1983. 309(2): p. 72-6.
10. Tate JE, Burton AH, Boschi-Pinto C, et al. 2008 estimate of worldwide rotavirus-associated mortality in children younger than 5 years before the introduction of universal rotavirus vaccination programmes: a systematic review and meta-analysis. *Lancet Infectious Diseases*, 2012. 12(2): p. 136-41.

11. Fischer Walker CL, Rudan I, Liu L, et al. Global burden of childhood pneumonia and diarrhoea. *The Lancet*, 2013. 381(9875): p. 1405-1416.
12. Grimwood K, Lambert SB. Rotavirus vaccines: opportunities and challenges. *Hum Vaccin*, 2009. 5(2): p. 57-69.
13. Milne RJ, Grimwood K. Budget impact and cost-effectiveness of including a pentavalent rotavirus vaccine in the New Zealand childhood immunization schedule. *Value in Health*, 2009. 12(6): p. 888-98.
14. Parashar UD, Hummelman EG, Bresee JS, et al. Global illness and deaths caused by rotavirus disease in children. *Emerging Infectious Diseases*, 2003. 9(5): p. 565-72.
15. Dennehy PH, Cortese MM, Begue RE, et al. A case-control study to determine risk factors for hospitalization for rotavirus gastroenteritis in U.S. children. *Pediatric Infectious Disease Journal*, 2006. 25(12): p. 1123-31.
16. Huppertz H-I, Salman N, Giaquinto C. Risk factors for severe rotavirus gastroenteritis. *Pediatric Infectious Disease Journal*, 2008. 27(1): p. S11-19.
17. Newman RD, Grupp-Phelan J, Shay DK, Davis RL. Perinatal risk factors for infant hospitalization with viral gastroenteritis. *Pediatrics*, 1999. 103(1): p. E3.
18. Sethi D, Cumberland P, Hudson MJ, et al. A study of infectious intestinal disease in England: risk factors associated with group A rotavirus in children. *Epidemiology and Infection*, 2001. 126(1): p. 63-70.
19. Chandran A, Heinzen RR, Santosham M, Siberry GK. Nosocomial rotavirus infections: a systematic review. *Journal of Pediatrics*, 2006. 149(4): p. 441-7.
20. Grimwood K, Abbott GD, Fergusson DM, et al. Spread of rotavirus within families: a community based study. *British Medical Journal (Clinical Research Ed.)*, 1983. 287(6392): p. 575-7.
21. Butz AM, Fosarelli P, Dick J, et al. Prevalence of rotavirus on high-risk fomites in day-care facilities. *Pediatrics*, 1993. 92(2): p. 202-5.
22. Velázquez FR, Matson DO, Calva JJ, et al. Rotavirus infection in infants as protection against subsequent infections. *New England Journal of Medicine*, 1996. 335(14): p. 1022-8.
23. Angel J, Franco MA, Greenberg HB. Rotavirus immune responses and correlates of protection. *Current Opinion in Virology*, 2012. 2(4): p. 419-25.
24. Buttery JP, Lambert SB, Grimwood K, et al. Reduction in rotavirus-associated acute gastroenteritis following introduction of rotavirus vaccine into Australia's National Childhood vaccine schedule. *Pediatric Infectious Disease Journal*, 2011. 30(1 Suppl): p. S25-9.
25. Parashar UD, Johnson H, Steele AD, Tate JE. Health impact of rotavirus vaccination in developing countries: progress and way forward. *Clinical Infectious Diseases*, 2016. 62 Suppl 2(Supplement 2): p. S91-5.
26. Institute of Environmental Science and Research Ltd. 2016. *Rotavirus in New Zealand, 2015* (ed.), Porirua: Institute of Environmental Science and Research Ltd. URL: [https://surv.esr.cri.nz/PDF\\_surveillance/Rotavirus/2015Rotavirus.pdf](https://surv.esr.cri.nz/PDF_surveillance/Rotavirus/2015Rotavirus.pdf) (accessed 19 January 2017)
27. Macartney KK, Porwal M, Dalton D, et al. Decline in rotavirus hospitalisations following introduction of Australia's national rotavirus immunisation programme. *Journal of Paediatrics and Child Health*, 2011. 47(5): p. 266-70.
28. Vesikari T, Matson DO, Dennehy P, et al. Safety and efficacy of a pentavalent human-bovine (WC3) reassortant rotavirus vaccine. *New England Journal of Medicine*, 2006. 354(1): p. 23-33.
29. Vesikari T, Karvonen A, Prymula R, et al. Efficacy of human rotavirus vaccine against rotavirus gastroenteritis during the first 2 years of life in European infants: randomised, double-blind controlled study. *Lancet*, 2007. 370(9601): p. 1757-63.
30. Phua KB, Quak SH, Lee BW, et al. Evaluation of RIX4414, a live, attenuated rotavirus vaccine, in a randomized, double-blind, placebo-controlled phase 2 trial involving



- 2464 Singaporean infants. *Journal of Infectious Diseases*, 2005. 192 Suppl 1(Suppl 1): p. S6-S16.
31. Salinas B, Perez Schael I, Linhares AC, et al. Evaluation of safety, immunogenicity and efficacy of an attenuated rotavirus vaccine, RIX4414: A randomized, placebo-controlled trial in Latin American infants. *Pediatric Infectious Disease Journal*, 2005. 24(9): p. 807-16.
  32. Soares-Weiser K, Macle hose H, Bergman H, et al. Vaccines for preventing rotavirus diarrhoea: vaccines in use. *Cochrane Database Syst Rev*, 2012. 11(Art. No. CD008521): p. CD008521.
  33. Ruiz-Palacios GM, Perez-Schael I, Velazquez FR, et al. Safety and efficacy of an attenuated vaccine against severe rotavirus gastroenteritis. *New England Journal of Medicine*, 2006. 354(1): p. 11-22.
  34. Vesikari T, Giaquinto C, Huppertz HI. Clinical trials of rotavirus vaccines in Europe. *Pediatric Infectious Disease Journal*, 2006. 25(1 Suppl): p. S42-7.
  35. Clark HF, Offit PA, Parashar UD. 2013. Rotavirus vaccines, in *Vaccines*, Plotkin SA, Orenstein WA, Offit PA (eds) (eds). Elsevier Saunders: Philadelphia, PA.
  36. Richardson V, Hernandez-Pichardo J, Quintanar-Solares M, et al. Effect of rotavirus vaccination on death from childhood diarrhea in Mexico. *New England Journal of Medicine*, 2010. 362(4): p. 299-305.
  37. Gastañaduy PA, Sánchez-Urbe E, Esparza-Aguilar M, et al. Effect of rotavirus vaccine on diarrhea mortality in different socioeconomic regions of Mexico. *Pediatrics*, 2013. 131(4): p. e1115-20.
  38. Sheridan S, Lambert S, Grimwood K. Impact of rotavirus vaccination on childhood gastroenteritis. *Microbiology Australia*, 2012. 33(May): p. 56-60.
  39. Payne DC, Baggs J, Zerr DM, et al. Protective association between rotavirus vaccination and childhood seizures in the year following vaccination in US children. *Clinical Infectious Diseases*, 2014. 58(2): p. 173-7.
  40. Sheridan SL, Ware RS, Grimwood K, Lambert SB. Febrile seizures in the era of rotavirus vaccine. *J Pediatric Infect Dis Soc*, 2016. 5(2): p. 206-9.
  41. Yen C, Healy K, Tate JE, et al. Rotavirus vaccination and intussusception - Science, surveillance, and safety: A review of evidence and recommendations for future research priorities in low and middle income countries. *Human Vaccines & Immunotherapeutics*, 2016. 12(10): p. 2580-2589.
  42. Kaufman HW, Chen Z. Trends in Laboratory Rotavirus Detection: 2003 to 2014. *Pediatrics*, 2016. 138(4): p. 1-6.
  43. Pollard SL, Malpica-Llanos T, Friberg IK, et al. Estimating the herd immunity effect of rotavirus vaccine. *Vaccine*, 2015. 33(32): p. 3795-800.
  44. Vesikari T, Karvonen A, Ferrante SA, et al. Sustained efficacy of the pentavalent rotavirus vaccine, RV5, up to 3.1 years following the last dose of vaccine. *Pediatric Infectious Disease Journal*, 2010. 29(10): p. 957-63.
  45. Correia JB, Patel MM, Nakagomi O, et al. Effectiveness of monovalent rotavirus vaccine (Rotarix) against severe diarrhea caused by serotypically unrelated G2P[4] strains in Brazil. *Journal of Infectious Diseases*, 2010. 201(3): p. 363-9.
  46. Yen C, Figueroa JR, Uribe ES, et al. Monovalent rotavirus vaccine provides protection against an emerging fully heterotypic G9P[4] rotavirus strain in Mexico. *Journal of Infectious Diseases*, 2011. 204(5): p. 783-6.
  47. Payne DC, Selvarangan R, Azimi PH, et al. Long-term consistency in rotavirus vaccine protection: RV5 and RV1 vaccine effectiveness in US children, 2012-2013. *Clinical Infectious Diseases*, 2015. 61(12): p. 1792-9.
  48. Patel MM, Glass R, Desai R, et al. Fulfilling the promise of rotavirus vaccines: how far have we come since licensure? *Lancet Infectious Diseases*, 2012. 12(7): p. 561-70.

49. Steele AD, Neuzil KM, Cunliffe NA, et al. Human rotavirus vaccine Rotarix provides protection against diverse circulating rotavirus strains in African infants: a randomized controlled trial. *BMC Infectious Diseases*, 2012. 12(213): p. 213.
50. Armah GE, Sow SO, Breiman RF, et al. Efficacy of pentavalent rotavirus vaccine against severe rotavirus gastroenteritis in infants in developing countries in sub-Saharan Africa: a randomised, double-blind, placebo-controlled trial. *Lancet*, 2010. 376(9741): p. 606-14.
51. Kirkwood CD. Genetic and antigenic diversity of human rotaviruses: potential impact on vaccination programs. *Journal of Infectious Diseases*, 2010. 202 Suppl(S1): p. S43-8.
52. American Academy of Pediatrics. 2018. Rotavirus infections. in *Red Book: 2018 Report of the Committee on Infectious Diseases*, Kimberlin D, Brady M, Jackson M, and Long S (eds). Elk Grove Village, IL. p. 700-705. URL: <https://redbook.solutions.aap.org/redbook.aspx>. (accessed 3 July 2020)
53. Australian Technical Advisory Group on Immunisation (ATAGI). 2018. Rotavirus. in *Australian Immunisation Handbook*. Canberra. URL: <https://immunisationhandbook.health.gov.au/vaccine-preventable-diseases/rotavirus>. (accessed 25 April 2020)
54. Sicard M, Bryant K, Muller ML, Quach C. Rotavirus vaccination in the neonatal intensive care units: where are we? A rapid review of recent evidence. *Current Opinion in Pediatrics*, 2020. 32(1): p. 167-191.
55. Centers for Disease Control and Prevention. 2010. Addition of severe combined immunodeficiency as a contraindication for administration of rotavirus vaccine. *Morbidity and Mortality Weekly Report*. 59(22): p. 687-8. <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5922a3.htm> (accessed 30 May 2020)
56. Østensen M. Safety issues of biologics in pregnant patients with rheumatic diseases. *Annals of the New York Academy of Sciences*, 2014. 1317(1): p. 32-8.
57. Boom JA, Sahni LC, Payne DC, et al. Symptomatic infection and detection of vaccine and vaccine-reassortant rotavirus strains in 5 children: a case series. *Journal of Infectious Diseases*, 2012. 206(8): p. 1275-9.
58. Carlin JB, Macartney KK, Lee KJ, et al. Intussusception risk and disease prevention associated with rotavirus vaccines in Australia's National Immunization Program. *Clinical Infectious Diseases*, 2013. 57(10): p. 1427-34.
59. Tate JE, Yen C, Steiner CA, et al. Intussusception rates before and after the introduction of rotavirus vaccine. *Pediatrics*, 2016. 138(3): p. e20161082.
60. Walter EB, Staat MA. Rotavirus vaccine and intussusception hospitalizations. *Pediatrics*, 2016. 138(3): p. e20161952.
61. Stowe J, Andrews N, Ladhani S, Miller E. The risk of intussusception following monovalent rotavirus vaccination in England: A self-controlled case-series evaluation. *Vaccine*, 2016. 34(32): p. 3684-9.
62. Therapeutic Goods Administration. 2013 *Rotavirus vaccination and the risk of intussusception*. Australian Government, Department of Health; 2013 [updated 28 August 2013]; URL: <https://www.tga.gov.au/safety/alerts-medicine-rotavirus-130828.htm>. (accessed 3 July 2020)
63. Yen C, Tate JE, Steiner CA, et al. Trends in intussusception hospitalizations among US infants before and after implementation of the rotavirus vaccination program, 2000-2009. *Journal of Infectious Diseases*, 2012. 206(1): p. 41-8.
64. World Health Organization. Position paper on rotavirus vaccines. *Weekly Epidemiological Record*, 2013. 88(5): p. 49-64.
65. Rosie B, Dalziel S, Wilson E, Best EJ. Epidemiology of intussusception in New Zealand pre-rotavirus vaccination. *New Zealand Medical Journal*, 2016. 129(1442): p. 36-45.





# 21 Rubella

## Key information

Mode of transmission	By contact with infected nasopharyngeal secretions. Infants with congenital rubella syndrome (CRS) shed rubella virus in their pharyngeal secretions and urine.
Incubation period	14–23 days, usually 16–18 days. Up to 50 percent of rubella infections are subclinical.
Period of communicability	7 days before until 7 days after the onset of the rash. Infants with CRS may be infectious for months.
Incidence and burden of disease	Endemic rubella was verified as eliminated in 2017. One imported case of rubella was notified in 2018. Cases continue in other regions, including China.
Funded vaccine	MMR is a live attenuated vaccine.
Dose, presentation, route	0.5 mL per dose after reconstitution. Pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. Intramuscular or subcutaneous injection.
Funded vaccine indications and schedule	Children at ages 12 months and 15 months. Adults who are susceptible to one or more of measles, mumps and rubella. For (re)vaccination following immunosuppression, if the individual is immunocompetent enough to safely receive the vaccine.
Recommended	All adults born since January 1969 should be up to date with two doses of MMR or have evidence of immunity to all three vaccine components. It is particularly important for health care workers, individuals who work with children, armed forces personnel, staff of correctional facilities, long-term care facilities and immigration/refugee centres and laboratory staff. All vaccine-eligible travellers, particularly to high-risk countries.
Vaccine efficacy/effectiveness	Highly effective, 2 doses are anticipated to provide lifelong protection. Protection is best achieved through herd immunity from high immunisation coverage.
Contraindication	MMR is contraindicated for those with anaphylaxis to neomycin, immunocompromise and in pregnancy. See section 12.6 for cautions around receipt of blood products and other live vaccines, and other precautions.

*Continued overleaf*

Precautions and special considerations	<p>All pregnant women and women planning pregnancy should have their immunisation history checked.</p> <p>A woman is immune to rubella if she has had two documented doses of a rubella-containing vaccine given at least 4 weeks apart and given after age 12 months, regardless of serology.</p> <p>Pregnant non-immune women should avoid contact with known cases of rubella and should receive MMR after delivery.</p>
Potential response to vaccine	<p>MMR is generally well tolerated. Temporary joint pain 2–4 weeks after vaccination due to rubella component of the vaccine is more common in adults than children. See section 12.7.</p> <p>Alert parents of possible febrile seizure risk, particularly for those with a history of seizure.</p>
Public health measures	All suspected cases must be notified immediately on suspicion. (see section 21.8)
Post-exposure prophylaxis	For management and vaccination of contacts, see section 21.8

## 21.1 Virology

Rubella is an enveloped RNA virus from the family *Togaviridae* and the genus *Rubivirus*. It is less stable than measles virus and can be inactivated by solvents, trypsin, formalin, extremes of heat and pH, and light.<sup>1</sup>

## 21.2 Clinical features

The purpose of the rubella immunisation programme is to prevent congenital rubella syndrome (CRS).

Rubella infection during pregnancy can result in fetal infection, causing CRS in a high proportion of cases. Rubella infection in the first 12 weeks of pregnancy results in fetal damage in up to 85 percent of infants, and multiple defects are common. The risk of damage declines to 50 percent by about 16 weeks' gestation and 25 percent by the end of the second trimester.<sup>2</sup> Fetal abnormalities are rare from infection in the third trimester of pregnancy.

Infants born with CRS may have cataracts, nerve deafness, cardiac malformations, microcephaly, mental retardation and behavioural problems. Inflammatory changes may also be found in the liver, lungs and bone marrow. Some infected infants may appear normal at birth, but have nerve deafness, oesophageal and eye defects, and diabetes detected later.<sup>3</sup> CRS is one of the few known causes of autism.<sup>2</sup>

Clinical features of rubella in children and adults include a transient erythematous rash and lymphadenopathy without respiratory symptoms. Arthritis or arthralgia is relatively common and a classic feature of infection in adults. While usually a mild childhood

illness, rubella may also present as a more severe illness, clinically indistinguishable from measles. Encephalitis occurs with a prevalence of approximately 1 in 6,000 cases and may result in residual neurological damage or, occasionally, death. Thrombocytopenia rarely occurs.

Clinical diagnosis is unreliable because the symptoms are often fleeting and can be mimicked by other viruses. In particular, the rash is not diagnostic of rubella. Up to 50 percent of rubella infections are subclinical or asymptomatic. Asymptomatic cases are also able to transmit the virus. A history of rubella should therefore never be accepted as proof of immunity without laboratory confirmation.<sup>3</sup>

Transmission of rubella is through direct or indirect contact with infected nasopharyngeal secretions and droplets. The incubation period is usually 16–18 days (range 14–23 days) and infectivity is between seven days before and seven days after the onset of the rash. Infants with congenital rubella syndrome (CRS) shed rubella virus in their pharyngeal secretions and urine for months after birth and should be considered infectious until they are aged 12 months.

Although the vaccine virus is excreted after vaccination, mostly from the pharynx, transmission to susceptible contacts has not been demonstrated (see section 12.7.2). Therefore, a recently immunised contact is not a risk to a pregnant woman.

The frequency of complications and consequences of rubella infection are best described from the 1963/1964 US outbreak, involving 12.5 million cases of rubella and 30,000 infants damaged by intrauterine rubella, an incidence rate of 1 per 100 pregnancies (see Table 21.1).

**Table 21.1: Estimated morbidity and mortality associated with the 1963/64 US rubella epidemic**

<b>Total number of cases of rubella:</b>	<b>12,500,000</b>
<b>Complications of rubella</b>	<b>Risk per case</b>
Arthritis or arthralgia	13 per 1,000
Encephalitis	17 per 100,000
Neonatal deaths	17 per 100,000
<b>Complications caused by congenital rubella syndrome (CRS)</b>	<b>Numbers of cases (% of CRS cases)</b>
Total number with CRS	20,000
Deaf children	8,055 (40%)
Deaf-blind children	3,580 (18%)
Mentally disabled children	1,790 (9%)

Adapted from: Reef SE, Plotkin S. 2018. Rubella vaccines. In: Plotkin S, Orenstein W, Offit P, et al (eds) *Plotkin's Vaccines (7th Edition)*. Philadelphia, US: Elsevier. Table 53.7.

Rubella infection can occur (very rarely) in individuals with either naturally acquired or vaccine-induced antibody.<sup>3</sup> Rare cases of CRS have been reported after reinfection during pregnancy.<sup>3</sup>

As with measles, public health measures of accurately diagnosing potential cases of rubella with notification and contact tracing are critical (see section 21.8).

## 21.3 Epidemiology

### 21.3.1 Global burden of disease

Humans are the only source of rubella infection. Infection is often asymptomatic. In the pre-vaccine era the highest incidence of clinical cases occurred in the spring among 5–9-year-old children, and 80–90 percent of adults were immune to rubella. Extensive outbreaks of rubella occurred every six to nine years, in which many children were affected by CRS. Immunisation against rubella, introduced to prevent the occurrence of CRS, has resulted in a very significant reduction in infection, especially once vaccination was introduced to boys and girls.

The Global Vaccine Action Plan set a specific target to eliminate measles and rubella by 2020 and to reduce the incidence of CRS from 100,000 cases per year. The number of notified rubella cases fell from over 670,000 in 2000 to just over 22,000 in 2016. However, from January to September 2019, nearly 40,000 cases were reported: 92 percent of those cases were in China and 7 percent in Japan.<sup>4</sup>

Although rubella elimination has been verified in 81 countries, less than 70 percent of infants across 168 countries worldwide were immunised against rubella by the end of 2018.<sup>5</sup>

### 21.3.2 New Zealand epidemiology

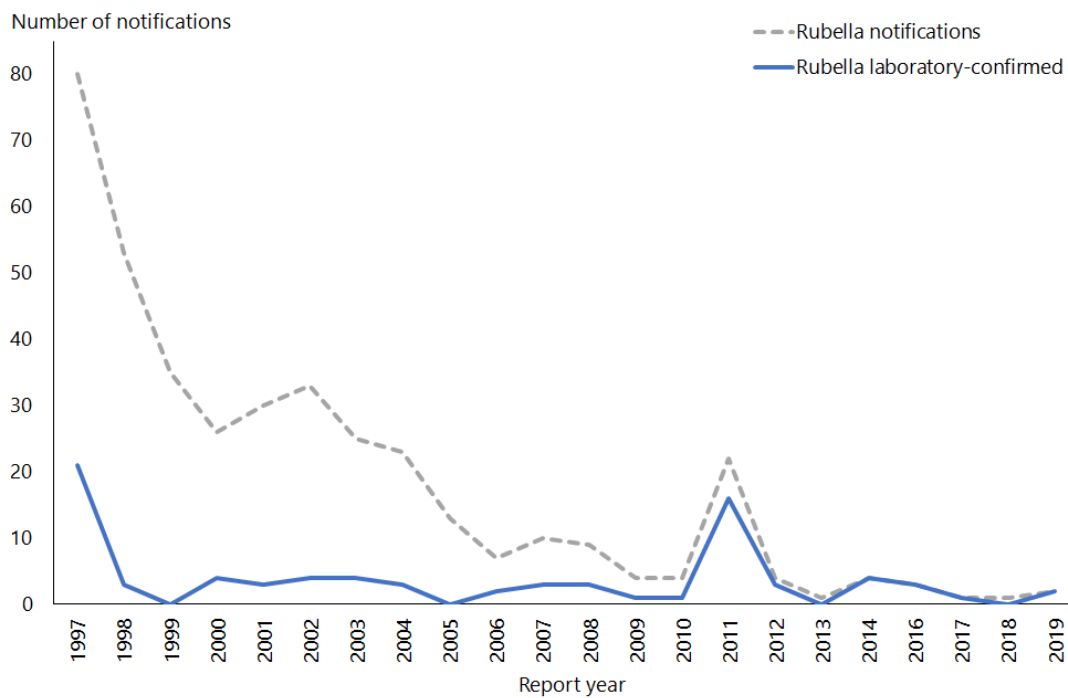
Rubella immunisation was introduced in 1970 (see Appendix 1), and rubella has been a notifiable disease since 1996. The last large rubella outbreak in 1995–1996 mostly involved young adult males, who would not have been offered immunisation. This emphasises the need to immunise both boys and girls to reduce the risk of exposure in pregnant women, as well as to reduce illness in men.

Two cases of rubella were notified in 2019, in a male and a female both aged 30–39 years.

Rubella was verified as eliminated from New Zealand in October 2017. There have been no reported cases of CRS in New Zealand since 1998.

For further information, see the ESR's notifiable disease reports (available at [www.esr.cri.nz/digital-library/notifiable-disease-dashboard/](http://www.esr.cri.nz/digital-library/notifiable-disease-dashboard/)).

**Figure 21.1: Rubella notifications and laboratory-confirmed cases by year, 1997–2019**



Source: ESR

## 21.4 Vaccines

### 21.4.1 Available vaccines

Rubella vaccine is one of the components of the live attenuated MMR vaccine (see section 12.4.1) (and also MMRV vaccine mentioned in section 24.4.1).

#### Funded vaccine

MMR funded as part of the Schedule is Priorix (GSK), which contains attenuated Schwarz strain measles, RA 27/3 rubella and Jeryl Lynn mumps. (See section 12.4.1 for more information.)

#### Other vaccines

MMR II (MSD) was the funded vaccine prior to the 1 July 2017 Schedule change (see section 12.4.1).

## 21.4.2 Efficacy and effectiveness

The rubella vaccine has been shown to be 90–97 percent effective in an outbreak after a single dose, and this is likely to be higher with a two-dose schedule. One dose of rubella vaccine at 12 months or older induces an antibody response in at least 95 percent of recipients. Studies have found no evidence of waning of protection over decades of follow-up.<sup>3</sup> In more than 90 percent of recipients, antibodies persisted for at least 16 years; other studies have reported persistence up to 21 years.<sup>3</sup> A few recipients fail to produce antibodies following immunisation, and a small number of individuals lose antibodies, whether they are derived from natural infection or the vaccine. As part of a follow-up of those who received MMR in Finland, it was shown that while antibodies wane over time, immunity to rubella remained secure 20 years after the second dose of MMR.<sup>6</sup>

## 21.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at [www.tewhātuora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhātuora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

Store at +2°C to +8°C. Do not freeze.

MMR must be reconstituted only with the diluents supplied by the manufacturer. Use MMR as soon as possible after reconstitution. If storage is necessary, reconstituted vaccine can be stored at +2°C to +8°C for up to eight hours.

## 21.4.4 Dosage and administration

The dose of MMR is all of the reconstituted vaccine (approximately 0.5 mL) administered by intramuscular injection, or subcutaneous injection if indicated (see section 2.2.3).

### Co-administration with other vaccines

MMR can be given concurrently with other vaccines, as long as separate syringes are used and the injections are given at different sites. If not given concurrently, live vaccines should be given at least four weeks apart. (See also section 2.2.7 for information about multiple injections at the same visit.)

### Interchangeability

The two brands of MMR (Priorix and MMR II) may be used interchangeably for completion of a course.<sup>1</sup>



## 21.5 Recommended immunisation schedule

To prevent all cases of CRS, rubella must not circulate in the community. Achieving at least 95 percent coverage of two doses of MMR prevents the circulation of rubella (which is much less infectious than measles). As in other high-income countries, New Zealand's primary strategy for preventing and maintaining elimination of rubella is to vaccinate both boys and girls (Table 21.2).

Historically, a targeted individual protection approach was used in which only 11-year-old girls were immunised with one dose of rubella vaccine. Even with high coverage, there remained women of childbearing age who were susceptible to rubella due to failure to be vaccinated or vaccine failure and cases of CRS continued to occur albeit at a reduced rate. Rubella remained in circulation in New Zealand because children aged under 11 years and males were not vaccinated.

**Table 21.2: Recommended MMR vaccination schedule**

	Schedule
Usual childhood schedule <sup>a</sup>	2 doses: at ages 12 months and 15 months
Catch-up <sup>b</sup> for children adolescents and adults	2 doses: at least 4 weeks apart

- If MMR is given to children aged 6–12 months for outbreak control, 2 further MMR doses are still required at ages 12 months (at least 4 weeks after previous dose) and 15 months.
- MMR is funded for those who are susceptible to 1 or more of the 3 diseases. See sections 21.5.2 and 21.5.3.

### 21.5.1 Usual childhood schedule

Two doses of rubella vaccine as MMR are recommended at age 12 months and 15 months. Over 95 percent of individuals will become immune to rubella after one dose.<sup>2</sup> The second dose is not a booster. Two doses are recommended because nearly all the 2–5 percent not protected by the first dose will be protected by the second. The second dose of vaccine can be given as soon as four weeks after the first dose. (See below for the recommendations for other groups.)

Children who receive MMR vaccination during an outbreak (of measles, mumps or rubella) when aged under 11 months (MMR0) require two further doses administered at age 12 months and 15 months. No opportunity should be missed to achieve immunity, if not contraindicated.

## 21.5.2 Catch-up

Any individual born on or after 1 January 1969 (see section 12.5.2) who does not have two documented doses of MMR, given at least four weeks apart with the first dose given any time after age 12 months, should be offered either one or two doses (four weeks apart) to bring them up to two doses (funded).

Even if the individual has previously received single-antigen measles vaccine, up to two doses of MMR (ie, additional doses of measles vaccine) may be given to these individuals to ensure rubella and mumps protection. There are no significant adverse effects from further vaccinating individuals who are already immune to measles, mumps and/or rubella, and no reliance can be placed on a prior clinical history of rubella infection.

### Immigrants to New Zealand

The vaccination status of immigrants should be checked as a priority group: particularly, those born overseas (especially in Asia, the Pacific Islands, sub-Saharan Africa and South America) who entered New Zealand after the age of routine vaccination.

Anyone who does not have two documented doses of MMR, given any time after age 12 months, should be offered either one or two doses (four weeks apart) to bring them up to two doses (funded if eligible). Some countries provide a rubella-containing vaccine before the age of 12 months; these children may require extra MMR doses to be fully immunised.

### Occupational risk

Visitors to countries with circulating rubella virus, including those travelling for work or humanitarian purposes, are at highest risk of importing disease. It is recommended to be fully immunised prior to departure from New Zealand. During an outbreak, health care workers and those working with infants in day care facilities are at high risk of transmitting disease to pregnant women and their infants. MMR is funded for all New Zealand residents born since 1 January 1969 if they have not previously had two documented doses of MMR.

## 21.5.3 Pregnancy and breastfeeding

### Women planning pregnancy

It is particularly important to ensure that women of child-bearing age are immune to rubella.<sup>1</sup> Women who are planning pregnancy should have their immunisation history checked for having received two documented doses of a rubella-containing vaccine given at least four weeks apart and given after age 12 months. Non-immune women may receive MMR before pregnancy, but pregnancy should be avoided for four weeks after the last MMR vaccination.<sup>7, 8</sup>

As seen with recent measles and mumps outbreaks, community immunity in the 15–29 years age group is low due to historically poor MMR vaccination coverage during the 1990s and early 2000s; there is a cohort of women of child-bearing age potentially susceptible to rubella.

## Pregnant women

MMR is contraindicated during pregnancy.

All pregnant women should have their immunisation history checked. A pregnant woman is considered immune to rubella if she has had two documented doses of a rubella-containing vaccine given at least four weeks apart and given after age 12 months, *regardless of serology*. As soon as possible following delivery, as appropriate, give one or two doses of MMR four weeks apart to women who are not immune (funded).

Serological testing for immunity to rubella is not usually performed in New Zealand except as part of routine antenatal care. Improved documentation and effective surveillance showing the rarity of CRS when there is high immunisation coverage has led to some countries, such as England, discontinuing routine antenatal rubella screening.<sup>9</sup> Also, the screening tests used for rubella serology can potentially give inaccurate results and may cause unnecessary stress for women.<sup>9</sup>

In general, it should be remembered that the great majority of New Zealand-born individuals who received all scheduled childhood vaccines will be immune to rubella. Although the chance of being exposed in New Zealand to an infectious case is becoming increasingly rare, rubella remains endemic in some countries, and the risk remains to those who are unimmunised when travelling overseas or through an imported case. (If exposure during pregnancy does occur, see the guidelines in section 21.8.2.)

## After delivery

If MMR and Rhesus anti-D IG are required after delivery, both the vaccine and anti-D IG may be given at the same time, in separate sites with separate syringes. The vaccine may be given at any time after the delivery. Anti-D IG does not interfere with the antibody response to the vaccine, but whole blood transfusion does inhibit the response in up to 50 percent of vaccine recipients (see section A6.4.1).

## Breastfeeding

There is no risk to the mother or child in giving MMR to breastfeeding women.<sup>3</sup>

## 21.5.4 Immunocompromise

MMR is contraindicated in immunocompromised children (see section 4.3). They can be partially protected from exposure to infection by ensuring that all contacts are fully immunised, including hospital staff and family members. There is no risk of transmission of MMR vaccine viruses from a vaccine recipient to the immunocompromised individual. See section 12.7.2.

MMR is funded for (re)vaccination following immunosuppression. However, it is important to be sure that the individual is immunocompetent enough to safely receive the vaccine.

### HIV infection

Discuss vaccination of individuals with HIV infection with their specialists (see 'HIV infection' in section 4.3.12).

MMR is recommended for all HIV-positive children, whether symptomatic or asymptomatic, if their CD4+ lymphocyte percentage is 15 percent or greater. It is recommended that asymptomatic children who are not severely immunocompromised receive MMR from age 12 months to provide early protection against the three diseases. Susceptible HIV-positive children and adults aged 14 years and older may receive MMR if the CD4+ lymphocyte count is 200 cells/mm<sup>3</sup> or greater. Administration of MMR with CD4+ counts below these recommended levels has been associated with vaccine-related pneumonitis (from the measles component).<sup>7</sup>

## 21.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general vaccine contraindications.

### 21.6.1 Contraindications

See section 12.6.1 for specific MMR contraindications.

The general contraindications that apply to all immunisations are relevant to MMR.

Anaphylaxis to a previous dose of MMR or any of the vaccine components (including neomycin) is a contraindication to a further dose of MMR.

MMR should not be given to women who are pregnant, and pregnancy should be avoided for four weeks after immunisation.<sup>2, 3</sup> However, inadvertent immunisation with a rubella-containing vaccine in early pregnancy is no longer considered an indication for termination of pregnancy. There have been no cases of teratogenic damage from vaccine virus despite intensive surveillance in the US, the UK and Germany.<sup>3</sup>

## 21.6.2 Precautions

Egg allergy, including anaphylaxis, is **not** a contraindication for MMR. See section 12.6.3 for more information, and section 12.6.2 for further precautions.

For infants aged under 12 months, please discuss immunomodulatory therapies taken during pregnancy with infant's mother or specialist, or contact IMAC before administration of MMR0 in an outbreak situation. See section 4.2.5.

# 21.7 Potential responses and AEFIs

See also section 12.7.

## 21.7.1 Potential responses

A fever of 39.4°C or more occurs in 5–15 percent of children 6 to 12 days after immunisation and generally lasts 1 to 2 days.<sup>7</sup> A rash may also occur in approximately 5 percent of children at the same interval post-vaccination: these children are not infectious to others, unless the rash is caused by a different concurrent illness.<sup>7</sup> The majority of these events are coincidental and not caused by the vaccine.<sup>10</sup> Serological tests or PCR can be expected to be positive if performed during this time, so testing should not be routinely performed.

Joint symptoms may be reported in 0.5 percent of young children and 10–25 percent of post-pubertal women.<sup>2</sup> Symptoms begin one to three weeks after immunisation and are usually transient. The prevalence of joint symptoms following rubella immunisation is lower than occurs with natural infection at a corresponding age.<sup>2</sup>

It was previously thought that the rubella vaccine might lead to long-term arthritis. A 2012 Institute of Medicine review concluded that the evidence was inadequate to accept or reject a causal relationship between MMR and chronic arthritis in women.<sup>11</sup>

## 21.7.2 AEFIs

ITP and, rarely, neurological disturbances have been reported (see section 12.7.2).

## 21.8 Public health measures

Rubella (including congenital rubella syndrome) is a notifiable disease, and suspected cases should be notified by the clinician on suspicion to the local medical officer of health. Accurate diagnosis requires laboratory confirmation.

For detailed information about disease control measures see the 'Rubella' chapter of the *Communicable Disease Control Manual* at [www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/rubella/](http://www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/rubella/)

### 21.8.1 Management of non-pregnant contacts

The local medical officer of health will advise on contact management. Check the immunisation status of all close contacts.

Rubella-containing vaccine does not provide protection if given after exposure to rubella. However, if the exposure did not result in infection, the vaccine would induce protection against subsequent infection. Human normal immunoglobulin does not prevent rubella infection after exposure and should not be used for that purpose.<sup>12</sup>

### 21.8.2 Management of pregnant contacts

It is critical to accurately document the rubella status of all people who may have rubella and potentially exposed a pregnant woman to the virus. Such people will have travelled overseas or had contact with an infected returned traveller. As described in section 21.3.2, rubella virus does not circulate in New Zealand. Rubella infection in the first half of pregnancy is potentially devastating, and every possible exposure of a pregnant woman should be discussed with the local medical officer of health, obstetrician and microbiologist or infectious diseases physician.

Pregnant contacts with confirmed immunity can be reassured that the likelihood of rubella infection is remote. This applies if:

- she has received at least two documented doses of rubella-containing vaccine, or
- a previous antibody screening test has detected a protective level of antibodies, and this has been documented, or
- one dose of vaccine followed by a rubella antibody screening test showing a protective level of antibodies has been documented.

### Coordinated care and management

Coordinated care and management are essential (Table 21.3). An obstetrician (or a maternal fetal medicine specialist) and an infectious diseases specialist/microbiologist

should be consulted when the diagnosis of possible rubella infection in a pregnant woman is first considered. The clinical picture and all test results should be discussed by all involved in the care of the woman, to enable an accurate interpretation of the serological results before advising the woman about the risk to her fetus and options regarding the continuation of pregnancy.

Pregnant women whose immunity to rubella has not been confirmed for the current pregnancy, **and who have been exposed to rubella in the first half of pregnancy**, must be investigated serologically irrespective of immunisation history or history of previous clinical rubella. Serum should be obtained as soon as possible, with the clinical details included on the request form. The laboratory should be asked to store an aliquot of serum for later testing in tandem with a follow-up sample. These results must be interpreted in conjunction with the time since exposure, to determine whether acute infection has occurred.

It is essential to discuss testing with the local clinical microbiologist before taking samples, to ensure that the right samples are obtained, and the best tests performed expeditiously. All requests to laboratories must state the:

- duration of pregnancy and last menstrual period
- date of exposure to possible rubella
- date of blood specimen
- name of the index case who is thought to have rubella.

The use of IG is not recommended for post-exposure prophylaxis of rubella in early pregnancy or any other circumstance. However, IG may be considered if termination of the pregnancy is not an option, but termination must be discussed when maternal infection is confirmed. Although IG has been shown to reduce clinically apparent infection in the mother, there is no guarantee that fetal infection will be prevented.

**Table 21.3: Suggested roles of health professionals**

	Lead maternity carer	Medical officer of health	GP	Obstetrician/ infectious diseases specialist/ maternal fetal medicine specialist
Check rubella status in every pregnancy (2 documented doses of rubella-containing vaccine)	✓			
Investigate initial suspected rubella case and trace contacts		✓		
Coordinate care of exposed non-immune pregnant woman		✓	✓	
Review clinical and laboratory results, and discuss options with the pregnant woman if rubella is confirmed				✓
AFTER delivery – vaccinate any woman who is not immune	✓		✓	



## 21.9 Variations from the vaccine data sheet

See section 12.9 for variations from the MMR (Priorix) data sheet.

### References

1. Australian Technical Advisory Group on Immunisation. 2018. *Australian Immunisation Handbook* (ed.), Canberra: Australian Government Department of Health. URL: <https://immunisationhandbook.health.gov.au/> (accessed October 2019)
2. American Academy of Pediatrics. 2018. Rubella. in *Red Book: 2018 Report of the Committee on Infectious Diseases*, Kimberlin D, Brady M, Jackson M, and Long S (eds). Elk Grove Village, IL. URL: <https://redbook.solutions.aap.org/redbook.aspx>. (accessed 3 July 2020)
3. Reef SE, Plotkin S. 2018. Rubella Vaccines, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
4. World Health Organization. *Measles and Rubella Surveillance Data*.: WHO; [updated 13 March 2020]; URL: [https://www.who.int/immunization/monitoring\\_surveillance/burden/vpd/surveillance\\_type/active/measles\\_monthlydata/en/](https://www.who.int/immunization/monitoring_surveillance/burden/vpd/surveillance_type/active/measles_monthlydata/en/) (accessed 25 April 2020)
5. Grant GB, Desai S, Dumolard L, et al. Progress toward rubella and congenital rubella syndrome control and elimination – worldwide, 2000–2018. *MMWR: Morbidity and Mortality Weekly Report*, 2019. 68(39): p. 855-859.
6. Davidkin I, Jokinen S, Broman M, et al. Persistence of measles, mumps, and rubella antibodies in an MMR-vaccinated cohort: a 20-year follow-up. *Journal of Infectious Diseases*, 2008. 197(7): p. 950-6.
7. American Academy of Pediatrics. 2018. Measles. in *Red Book: 2018 Report of the Committee on Infectious Diseases*, Kimberlin D, Brady M, Jackson M, and Long S (eds). Elk Grove Village, IL. p. 537-550. URL: <https://redbook.solutions.aap.org/redbook.aspx>. (accessed 3 July 2020)
8. Strebel P, Papania M, Gastañaduy P, Goodson J. 2018. Measles Vaccine, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
9. Public Health England. 2016 *Rubella susceptibility screening in pregnancy to end in England (Press release)*. Public Health England. 27 January 2016 URL: <https://www.gov.uk/government/news/rubella-susceptibility-screening-in-pregnancy-to-end-in-england>. (accessed 10 May 2022)
10. Peltola H, Heinonen OP. Frequency of true adverse reactions to measles-mumps-rubella vaccine. A double-blind placebo-controlled trial in twins. *Lancet*, 1986. 1(8487): p. 939-42.
11. Institute of Medicine: Committee to Review Adverse Effects of Vaccines. 2012. *Adverse effects of vaccines: Evidence and causality* (ed.), Washington, DC: The National Academies Press. URL: <https://www.nap.edu/catalog/13164/adverse-effects-of-vaccines-evidence-and-causality> (accessed January 2020)
12. McLean HQ, Fiebelkorn AP, Temte JL, Wallace GS. Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013: summary recommendations of the

Advisory Committee on Immunization Practices (ACIP). *MMWR: Recommendations and Reports*, 2013. 62(RR-04): p. 1-34.

# 22 Tetanus

## Key information

Mode of transmission	Environmental exposure to the bacillus, usually through contaminated wounds. The disease is not directly transmitted from person to person.	
Incubation period	Between 3 and 21 days, commonly about 10 days; may vary from 1 day to several months.	
Period of communicability	A person with tetanus is not infectious to others.	
Incidence and burden of disease	Older individuals, usually women, who are less likely to have received a primary series of tetanus vaccine; and in unvaccinated children.	
Funded vaccines	DTaP-IPV-HepB/Hib (Infanrix-hexa). DTaP-IPV (Infanrix-IPV). Tdap (Boostrix).	
Dose, presentation, route	Intramuscular injection. 0.5 mL per dose. DTaP-IPV-HepB/Hib: pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. DTaP-IPV, Tdap: pre-filled syringe.	
Funded vaccine indications and schedule	During each pregnancy (recommended from 16 weeks' gestation) for pertussis protection	Tdap
	6 weeks, 3 months and 5 months	DTaP-IPV-HepB/Hib
	4 years	DTaP-IPV
	11 years	Tdap
	45 years (catch-up, if individual has not received 4 previous tetanus doses)	Tdap
	65 years	Tdap
	Parents or primary caregivers of infants admitted to neonatal intensive or specialist baby care units for more than 3 days and whose mothers had not received Tdap at least 14 days prior to birth for pertussis protection	Tdap
	For vaccination of previously unimmunised or partially immunised patients	DTaP-IPV-HepB/Hib, DTaP-IPV or Tdap
	For (re)vaccination of eligible patients	
	For boosting of patients with tetanus-prone wounds	Tdap
Public health measures	All cases of tetanus must be notified immediately on suspicion to the local medical officer of health (see section 22.8)	
Post-exposure prophylaxis	If an injury is tetanus prone <i>and</i> there is any doubt about previous tetanus immunisation, the individual must be given tetanus immunoglobulin (TIG) and a 3-dose primary immunisation course (see section 22.5.6).	

## 22.1 Bacteriology

Tetanus is caused by the action of tetanus toxin released by *Clostridium tetani*, a spore-forming gram-positive, motile, anaerobic bacillus. The most common source of environmental exposure to *C. tetani* spores and bacilli is soil. However, soil is not the only reservoir of the organism. Animals, both herbivores and omnivores, can carry *C. tetani* bacilli and spores in their intestines, and the organism is readily disseminated in their faeces. Once introduced into the relatively anaerobic conditions found in wound tissue, they germinate and produce toxin.

Tetanus spores or bacilli can easily be introduced into a wound at the time of injury, even when the injury is quite trivial. Contaminated wounds, especially wounds with devitalised tissue and deep-puncture trauma, are at greatest risk.

## 22.2 Clinical features

The clinical diagnosis of tetanus is characterised by muscular rigidity and very painful contraction spasms. When severe, it is associated with a characteristic facial grimace (risus sardonicus) and arching of the back (opisthotonus). The patient suffering from tetanus remains alert unless they become severely hypoxic.

The *C. tetani* toxin reaches the central nervous system via the axons and irreversibly binds to nerve terminals at the neuromuscular junction, blocking the release of inhibitory neurotransmitters and leading to the tetanic muscle spasms.

The incubation period is between 3 and 21 days, commonly about 10 days, but it has been reported to vary from one day to several months. The bacteria need an anaerobic environment in which to grow, and this is often found in damaged and necrotic tissue, although the inoculation site may appear insignificant. Initial symptoms include weakness, stiffness or cramps, and difficulty chewing or swallowing food. Reflex muscle spasms usually occur within one to four days of the initial symptoms, the interval being called the onset period. The shorter the incubation and onset periods, the more severe the disease. Even with modern intensive care, tetanus mortality is about 10 percent overall, and much higher in older people.

Neonatal tetanus, from infection of the umbilical stump, is the commonest form of the disease in some low-income countries, particularly where births take place at home without adequate sterile procedures and antenatal screening and immunisation programmes are disrupted.<sup>1</sup>

A person with tetanus is not infectious to others, and vaccination provides individual protection only, with no herd immunity. Protective immunity can only be conferred by vaccination with tetanus toxoid and not through exposure to the natural pathogen or suffering tetanus. See section 22.5.2.

## 22.3 Epidemiology

### 22.3.1 Global burden of disease

Tetanus infection continues to occur globally but is rare in high income countries. The estimated total number of tetanus cases (including neonatal cases) globally fell from more than 110,000 in 1980 to 15,000 in 2018.<sup>2</sup> The highest numbers of cases were in India, Uganda and other sub-Saharan African countries.<sup>2</sup> Tetanus in males in some sub-Saharan countries has been associated with voluntary circumcision aimed at reducing the risk of HIV infection.<sup>3</sup>

There were 1,803 neonatal tetanus cases reported worldwide in 2018, two-thirds of which were in Africa, and all the cases of tetanus reported in Afghanistan, Chad and Yemen were neonatal.<sup>4</sup> Maternal and neonatal tetanus is described as a silent killer, since many cases are unreported.<sup>5</sup> Worldwide, all countries are committed to 'elimination' of maternal and neonatal tetanus; that is, a reduction of neonatal tetanus incidence to below one case per 1,000 live births per year in every district.<sup>1</sup> However, this goal has not yet been reached in 14 countries.

The incidence of tetanus reflects the effectiveness of the local immunisation programme, with low incidence in regions with high immunisation coverage. Global immunisation coverage for DTP is around 86 percent and 129 countries have reached at least 90 percent coverage for three doses of the DTP vaccine. In 2018, an estimated 19.4 million children aged under 1 year did not receive DTP. Of these, 13.5 million lack access to vaccination service and live in the poorest most fragile or conflicted states, and 60 percent live in 10 countries: Nigeria, India, Pakistan, Indonesia, Ethiopia, Philippines, Brazil, Angola and Vietnam.<sup>6</sup>

### 22.3.2 New Zealand epidemiology

No cases of tetanus were notified during 2017-2019. There were 33 tetanus cases notified between 1997 and 2017.<sup>7</sup> There were four cases in unvaccinated children (aged under 10 years), 14 cases in unvaccinated adults and three cases in vaccinated adults (the time since vaccination is not known). Two females aged 70 years or older died (one was not vaccinated and the vaccination status of the other was unknown).<sup>8</sup>

For further information, see to the ESR's notifiable disease reports (available at [www.esr.cri.nz/digital-library/notifiable-disease-dashboard/](http://www.esr.cri.nz/digital-library/notifiable-disease-dashboard/)).

## 22.4 Vaccines

Tetanus immunisation protects by stimulating the production of antitoxin, providing immunity against the effects of the toxin. It does not prevent *C. tetani* growing in a contaminated wound. The tetanus vaccine is prepared from cell-free toxin treated with formaldehyde to produce a toxoid. The toxoid is adsorbed onto an aluminium salt adjuvant to improve immunogenicity.

### 22.4.1 Available vaccines

#### Funded vaccines

Tetanus vaccine as a single antigen is no longer available in New Zealand. It is only available in combination with other vaccines.

The tetanus toxoid-containing vaccines funded as part of the Schedule are:

- DTaP-IPV-HepB/Hib (Infanrix-hexa, GSK): diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and Haemophilus influenzae type b vaccine
- DTaP-IPV (Infanrix-IPV, GSK): diphtheria, tetanus, acellular pertussis and inactivated polio vaccine
- Tdap (Boostrix, GSK): a lower adult dose of diphtheria and pertussis vaccine, together with tetanus vaccine.

See section 6.4.1 for more detailed vaccine information.

#### Other vaccines

Other tetanus toxoid-containing vaccines registered (approved for use) and available (marketed) in New Zealand are:

- Tdap: Adacel (Sanofi)
- Tdap-IPV: Adacel Polio (Sanofi).

### 22.4.2 Efficacy and effectiveness

#### Efficacy and effectiveness

Tetanus toxoid vaccine administered to pregnant women can prevent tetanus in their newborns (neonatal tetanus). Subsequent field assessments of the efficacy of two or more tetanus toxoid doses using data collected during neonatal tetanus mortality surveys demonstrated effectiveness of 70–100 percent.

A systematic review and meta-analysis concluded that immunisation of pregnant or childbearing-age women with two or more doses of tetanus toxoid reduces neonatal tetanus mortality by 94 percent (95% CI: 80–98).<sup>9</sup>

Tetanus in adults is too rare for vaccine efficacy to be tested in a clinical trial. However, the effectiveness of tetanus vaccine was clearly demonstrated in World War II, when only 12 cases of tetanus occurred among the 2.7 million wounded US army personnel (0.44 per 100,000), compared to 70 cases out of 520,000 wounded in World War I (13.4 per 100,000).<sup>9</sup> Of the 12 cases, only four had completed primary immunisation. Immunised cases have less severe disease and a lower case-fatality.

### Duration of protection

Serological studies show that the three-dose primary series of a tetanus vaccine given in infancy plus a booster during the second year of life, provide 3–5 years of protection against tetanus. WHO recommends six doses of tetanus-containing vaccine before age 18 years to induce immunity that lasts for much of adulthood.<sup>1</sup> It is recommended that adults receive at least one booster dose, particularly where fewer than six doses have been given in childhood.

Over the last two decades, there has been a significant increase in the proportion of the adult population with protective antitoxin levels by mid-life.<sup>10</sup> One mathematical model estimated protection to last for at least 30 years in most adults after vaccination.<sup>11</sup> But as age increases, by every 10 years there is an associated 50 percent reduction in antitoxin levels.<sup>12, 13</sup> Even if documented as fully immunised, older adults are likely to have had fewer tetanus doses in their lifetime than adults younger than 30 years.<sup>14</sup> Protection against the effects of tetanus toxin may be insufficient in adults who have not been adequately primed, and those aged over 65 years are at particularly increased risk of tetanus.<sup>10</sup>

A single dose of tetanus toxoid produces a rapid anamnestic response.<sup>15-18</sup> To ensure that there is adequate antitoxin to neutralise tetanus toxin in the case of a tetanus-prone injury, a booster dose is advised if it has been longer than 10 years since the last tetanus vaccine dose. The extent of wound contamination and delays in seeking medical assistance can result in high levels of tetanus toxin being released. (See also sections 6.4.2 and 16.4.2.)

## 22.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at [www.tewhātuora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhātuora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

Store at +2°C to +8°C. Do not freeze. DTaP-IPV-HepB/Hib and Tdap should be stored in the dark.



DTaP-IPV-HepB/Hib (Infanrix-hexa) must be reconstituted by adding the entire contents of the supplied container of the DTap-IPV-HepB vaccine to the vial containing the Hib pellet. After adding the vaccine to the pellet, the mixture should be shaken until the pellet is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.

## 22.4.4 Dosage and administration

The dose of DTap-IPV-HepB/Hib, DTap-IPV or Tdap is 0.5 mL administered by intramuscular injection (see section 2.2.3).

### Co-administration with other vaccines

DTaP-IPV-HepB/Hib, DTap-IPV and Tdap can be administered simultaneously (at separate sites) with other vaccines or IGs.

## 22.5 Recommended immunisation schedule

**Table 22.1: Immunisation schedule for tetanus-containing vaccines (excluding catch-up)**

Age	Vaccine	Comment
Pregnant women: recommended from 16 weeks' gestation of every pregnancy, preferably in the second trimester (funded when given any time in second or third trimester)	Tdap	Booster for mother Passive immunity for infant
6 weeks	DTaP-IPV-HepB/Hib	Primary series
3 months	DTaP-IPV-HepB/Hib	Primary series
5 months	DTaP-IPV-HepB/Hib	Primary series
4 years	DTaP-IPV	Booster
11 years	Tdap	Booster
45 years (individuals who have not received 4 tetanus vaccinations in their lifetime)	Tdap	Booster
65 years	Tdap	Booster

## 22.5.1 Usual childhood schedule

A primary course of tetanus vaccine is given as DTaP-IPV-HepB/Hib (Infanrix-hexa) at ages 6 weeks, 3 months and 5 months, followed by a dose of DTaP-IPV (Infanrix-IPV) at age 4 years (Table 22.1). A further booster is given at age 11 years (school year 7) as Tdap (Boostrix).

If a course of immunisation is late or interrupted for any reason, it may be resumed without repeating prior doses (see Appendix 2).

## 22.5.2 Catch-up immunisation for individuals aged 10 years and older

For adults and children who present with a tetanus-prone wound, boosters are recommended in accordance with the guidelines in the following sections and Table 22.2.

See Appendix 2 for detailed catch-up immunisation information.

Tdap may be used for primary immunisation of children aged 7 to under 18 years. Tdap can be given for vaccination of previously unimmunised or partially immunised adult patients.

Prior clinical tetanus does not usually confer immunity, and immunisation is required. In 1995, a 40-year-old man developed tetanus for a second time because he failed to complete the recommended course of immunisation after the first episode of tetanus.<sup>19</sup>

### Dose intervals between Td and Tdap

When Tdap is to be given to adolescents or adults, no minimum interval between Td and Tdap is required,<sup>20-22</sup> unless Tdap is being given as part of a primary immunisation course.

## 22.5.3 Booster doses for adolescents and adults

Adults are recommended to have their tetanus immunisation status assessed at ages 45 and 65 years, and given either a booster dose of tetanus toxoid-containing vaccine if more than 10 years has elapsed since the previous dose, or a primary course, if there is any doubt about the adequacy of previous tetanus immunisation (uncertain or no history of a prior primary course). Protection against tetanus is expected to last at least 20 years following a booster dose after the primary series.

Tdap is recommended and funded:

- as a booster dose to all adolescents at school year 7 or age 11 years
- as a single dose for vaccination of individuals from aged 65 years old
- as a single dose for catch-up vaccination of individuals aged from 45 years old who have not had four previous tetanus doses.

These age-specific recommendations may facilitate the linkage of adult immunisation to the delivery of other preventive health measures. Offer a booster dose of Tdap for someone travelling overseas if it has been more than 10 years since the last dose (unfunded) (see section 6.5.3).

The administration of tetanus and diphtheria (Tdap) boosters given at ages 45 and 65 years, is also funded.

See Table 4.9 for occupational groups specifically recommended Tdap (not funded) vaccination due to risk of tetanus or pertussis.

## 22.5.4 Pregnancy and breastfeeding

Pregnant women should receive a dose of Tdap in every pregnancy so that antibodies can pass to the fetus to provide pertussis protection from birth (funded when given any time in second or third trimester). It is recommended to be given from 16 weeks' gestation of every pregnancy, preferably in the second trimester to protect both the mother and her infant from pertussis (see section 16.5.2).<sup>23</sup>

Tdap vaccine may also be given to pregnant women when catch-up is needed for an under-immunised woman, or for management of a tetanus-prone wound (see section 22.5.5).<sup>23, 24</sup>

Tdap can be given to breastfeeding women.<sup>24</sup>

## 22.5.5 (Re)vaccination

Tetanus toxoid-containing vaccines are funded for (re)vaccination of eligible patients as follows, including prior to planned immunosuppression regimes or following immunosuppression. See also sections 4.2 and 4.3.

### DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV)

An additional four doses (as appropriate) of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for (re)vaccination of patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis

- prior to planned or following other severely immunosuppressive regimens.

Up to an additional four doses (as appropriate) of DTaP-IPV-HepB/Hib are funded for children aged 10 years to under 18 years for (re)vaccination of patients post HSCT. This is an off-label use of this vaccine which requires a prescription from an authorised prescriber or the patient's specialist. In this group, all prior immunity will have been lost and revaccination is equivalent to a primary immunisation schedule. DTaP-IPV-HepB/Hib not recommended for other severely immunocompromised individuals aged 10-18 years that require revaccination as they may have residual immune memory.

### Tdap (Boostrix)

An additional four doses (as appropriate) of Tdap (Boostrix) are funded for patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- prior to planned or following other severely immunosuppressive regimens.

A single dose of Tdap is funded for parents or primary caregivers of infants admitted to a neonatal intensive care unit or special care baby unit for more than three days and whose mothers had not received Tdap at least 14 days prior to baby's birth.

## 22.5.6 Prevention of tetanus following injury

Following injury, it is essential that all wounds be adequately cleaned and devitalised tissue removed to reduce the level of contamination and tetanus toxin release. Further treatment depends on the circumstances of each case.

If the injury is considered to be tetanus-prone and there is any doubt about the adequacy of previous tetanus immunisation, the individual must have tetanus immunoglobulin (TIG) and commence or complete the recommended primary course of three doses of a tetanus toxoid-containing vaccine (depending on age and other antigens required: DTaP-containing vaccine or Tdap).

The definition of a tetanus-prone injury is not straightforward, because tetanus can occur after apparently trivial injury, such as from a rose thorn, or with no history of injury. However, there are certain types of wounds likely to favour the growth of tetanus organisms. These include:

- compound fractures
- bite wounds
- deep, penetrating wounds
- wounds containing foreign bodies (especially wood splinters)
- wounds complicated by pyogenic (pus-forming) infections
- wounds with extensive tissue damage (eg, crush injuries, avulsions, contusions or burns)

- wounds associated with vascular insufficiency (eg, leg or foot ulcers in the elderly)
- any superficial wound obviously contaminated with soil, dust or horse manure (especially if topical disinfection is delayed more than four hours)
- re-implantation of an avulsed tooth – in this case, minimal washing and cleaning of the tooth is conducted to increase the likelihood of successful reimplantation.

## General measures for the treatment of tetanus-prone wounds

Wounds or injuries should be classified as tetanus-prone or non-tetanus-prone as follows (see Table 22.2):

- non-tetanus-prone wounds – clean, minor wounds that are less than six hours old, non-penetrating and with negligible tissue damage
- tetanus-prone wounds – all wounds that may be contaminated or infected, and are penetrating, more than six hours old and with tissue damage.

Immunised individuals respond rapidly to a booster injection of tetanus toxoid-containing vaccine, even after a prolonged interval. Tetanus toxoid-containing vaccine and TIG should be given at the same time, but into different limbs and using separate syringes.

See also the IMAC factsheet *Guidelines for the management of tetanus-prone wounds* (available at [immune.org.nz/resources/factsheets](http://immune.org.nz/resources/factsheets)).

**Table 22.2: Guide to tetanus prophylaxis in wound management**

History of tetanus vaccination <sup>a</sup>	Time since last dose	Type of wound	Tdap <sup>b</sup>	TIG <sup>c</sup>
≥3 doses	<5 years	Tetanus-prone wounds	No	No
≥3 doses	>5 years	Clean minor wounds	No	No
≥3 doses	>5 years	Tetanus-prone wounds	Booster dose <sup>d</sup>	No
≥3 doses	>10 years	Clean minor wounds	Booster dose <sup>d</sup>	No
<3 doses or uncertain		Clean minor wounds	Complete the course <sup>e</sup>	No
<3 doses or uncertain		Tetanus-prone wounds	Complete the course <sup>e</sup>	Yes

- People who have experienced Arthus-type hypersensitivity reactions (see 22.7.2) after a previous dose of a tetanus toxoid-containing preparation should not receive tetanus toxoid-containing preparation more frequently than every 10 years, even if they have a wound that is neither clean nor minor.
- See Appendix 2 for catch-up schedules for previously unimmunised children. DTaP-containing vaccine may be used in children aged under 10 years.
- TIG = tetanus immunoglobulin. The recommended dose is 250 IU given by IM injection as soon as practicable after injury. If more than 24 hours has elapsed, 500 IU is recommended. A dose of TIG can be given for up to 3 weeks after injury.
- If appropriate, this may count as the booster dose at age 45 or 65 years.
- To complete the 3-dose primary immunisation course, give 1–3 doses at not less than 4-weekly intervals.

## Tetanus immunoglobulin availability and storage

Tetanus immunoglobulin (TIG) is issued in ampoules, each containing 250 IU of human tetanus antitoxin. (Ampoules of 2,000 IU are used for treatment and not for prophylaxis.) These should be protected from light and stored in a refrigerator at +2°C to +8°C. They must never be frozen. TIG is given intramuscularly.

### TIG dose

The recommended dose to prevent tetanus is 250 IU of TIG for recent injuries, but this should be increased to 500 IU if more than 24 hours has elapsed since injury, or if there is a risk of heavy contamination or following burns. A dose of TIG can be given for up to 3 weeks after injury.

There is no need to test the patient's sensitivity before administering TIG, but caution is necessary if the patient is known to suffer complete immunoglobulin A (IgA) deficiency. In this situation, specialist help should be sought (see section 4.3).

Patients with impaired immunity who suffer a tetanus-prone wound may have failed to respond to prior vaccination and may therefore require TIG.

TIG can be given in pregnancy if clinically indicated. Whilst the safety of TIG for use in pregnancy has not been established in controlled clinical trials, no known risk to the fetus has been associated with use in pregnancy.

## 22.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

### 22.6.1 Contraindications

Immunisation with Tdap or another tetanus toxoid-containing vaccine should not be repeated in individuals who have had previous severe hypersensitivity reactions to the vaccine or a vaccine component. Most cases of hypersensitivity have been reported in individuals who have had an excessive number of booster injections outside the guidelines noted above.

### 22.6.2 Precautions

Protection against the risk of tetanus is paramount if the wound is thought to be tetanus-prone. Immunisation should not be postponed because the patient has a minor infection.

People who have experienced Arthus-type hypersensitivity reactions (see section 22.7.2) after a previous dose of a tetanus toxoid-containing preparation should not receive tetanus toxoid-containing preparation more frequently than every 10 years, even if they have a wound that is neither clean nor minor. Arthus-type reactions are rare in children and did not occur during the clinical trial of Tdap vaccines.<sup>25</sup>

Guillain–Barré Syndrome within six weeks of a tetanus toxoid-containing vaccine weeks is a precaution to receiving a further dose (see section 22.7.2).<sup>22</sup>

See section 16.6.2 for precautions to pertussis-containing vaccines, including DTaP-IPV-HepB/Hib.

## 22.7 Potential responses and AEFIs

See also sections 6.7 and 16.7 for potential responses and AEFIs to DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap vaccines.

### 22.7.1 Potential responses

Tetanus toxoid combination vaccines have not been associated with any safety concerns. Sterile abscesses and persistent nodules at the injection site may develop if the injection is not given deeply enough into the muscle.<sup>26</sup> Mild discomfort or pain at the injection site persisting for up to a few days is common.<sup>24</sup>

Tdap has a safety profile similar to Td and is generally well tolerated.<sup>27, 28</sup>

### 22.7.2 AEFIs

The 1994 US Institute of Medicine review of adverse events from tetanus vaccine concluded that the evidence supported a link with brachial plexus neuropathy (brachial neuritis) at a rate of 0.5–1 per 100,000 doses within four weeks of immunisation.<sup>29</sup> Occurrence of brachial neuritis following vaccination does not preclude the future use of a tetanus-toxoid containing vaccine in the same person.<sup>22</sup>

Severe local reactions (including large injection-site swelling) called Arthus reactions, immune-complex mediated hypersensitivity reactions that were associated with older tetanus and diphtheria toxoid-containing vaccines. Historical data on multiple doses of Td and tetanus toxoid vaccines indicate that hypersensitivity was associated with very high levels of pre-existing antibody.<sup>9, 30</sup>

No increased risk of GBS has been observed with use of tetanus toxoid-containing vaccines, and therefore a history of GBS is not a contraindication to receiving a tetanus toxoid-containing vaccine. However, out of prudence, it is recommended that having GBS within six weeks of a tetanus toxoid-containing vaccine is a precaution to receiving a further dose.<sup>9, 30</sup>



## 22.8 Public health measures

All cases of tetanus must be notified immediately on suspicion to the local medical officer of health, who should be provided with as accurate an immunisation history as possible.

See section 22.5.6 'Prevention of tetanus following injury'. See also the 'Tetanus' chapter of the *Communicable Disease Control Manual* available online at [www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/tetanus/](http://www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/tetanus/)

## 22.9 Variations from the vaccine data sheets

Tdap vaccine is not approved for use (registered) for primary immunisation. However, adults aged over 18 years may receive Tdap (funded) for catch-up of the primary schedule (see Appendix 2).

See section 16.9 for variations from the DTaP-IPV-HepB/Hib (Infanrix-hexa), DTaP-IPV (Infanrix-IPV) and Tdap (Boostrix) data sheets.

## References

1. World Health Organization. Tetanus vaccines: WHO position paper - February 2017. *Weekly Epidemiological Record*, 2017. 92(6): p. 53-76.
2. World Health Organization. 2021 *Tetanus (total) reported cases*. 2021 [updated 10 December ]; URL: <https://immunizationdata.who.int/pages/incidence/ttetanus.html>. (accessed 10 May 2022)
3. Dalal S, Samuelson J, Reed J, et al. Tetanus disease and deaths in men reveal need for vaccination. *Bulletin of the World Health Organization*, 2016. 94(8): p. 613-21.
4. World Health Organization. 2021 *Tetanus (neonatal) reported cases*. WHO; 2021 [updated 10 December]; URL: <https://immunizationdata.who.int/pages/incidence/ttetanus.html>. (accessed 10 May 2022)
5. World Health Organization. 2019. *Protecting All Against Tetanus: Guide to sustaining maternal and neonatal tetanus elimination (MNTE) and broadening tetanus protection for all populations*. . Licence: CC BY-NC-SA 3.0 IGO ed (ed.), Geneva: World Health Organization. URL:

- <https://apps.who.int/iris/bitstream/handle/10665/329882/9789241515610-eng.pdf?ua=1> (accessed 20 May 2020)
6. World Health Organization ,UNICEF. 2019 *Progress and challenges with achieving universal immunisation coverage: 2018 WHO/UNICEF estimates of National Immunization Coverage*. Monitoring and Surveillance Monitoring and Surveillance; 2019 [updated July 2019]; URL: [https://www.who.int/immunization/monitoring\\_surveillance/who-immuniz.pdf?ua=1](https://www.who.int/immunization/monitoring_surveillance/who-immuniz.pdf?ua=1). (accessed 3 July 2020)
  7. Institute of Environmental Science and Research Ltd. 2019 *Notifiable Diseases in New Zealand: Annual Report 2017*. Porirua, New Zealand. URL: [https://surv.esr.cri.nz/PDF\\_surveillance/AnnualRpt/AnnualSurv/2017/2017AnnualNDReport\\_FINAL.pdf](https://surv.esr.cri.nz/PDF_surveillance/AnnualRpt/AnnualSurv/2017/2017AnnualNDReport_FINAL.pdf). (accessed 3 July 2020)
  8. Institute of Environmental Science and Research Ltd. 2016. *Notifiable Diseases in New Zealand: Annual Report 2015* (ed.), Porirua, New Zealand: The Institute of Science and Environmental Research Ltd. URL: [https://surv.esr.cri.nz/PDF\\_surveillance/AnnualRpt/AnnualSurv/2015/2015AnnualReportFinal.pdf](https://surv.esr.cri.nz/PDF_surveillance/AnnualRpt/AnnualSurv/2015/2015AnnualReportFinal.pdf) (accessed 3 July 2020)
  9. Roper MH, Wassilak SGF, Scobie HM, et al. 2018. Tetanus Toxoid, in *Plotkin's Vaccines (7th edition)*, Plotkin SA, Orenstein WA, Offit PA, and Edwards KM (eds). Elsevier: Philadelphia, PA.
  10. Lu X, Quinn HE, Menzies RI, et al. Tetanus immunity and epidemiology in Australia, 1993-2010. *Infect Disord Drug Targets*, 2018.
  11. Hammarlund E, Thomas A, Poore EA, et al. Durability of vaccine-induced immunity against tetanus and diphtheria toxins: a cross-sectional analysis. *Clinical Infectious Diseases*, 2016. 62(9): p. 1111-1118.
  12. Maple PA, Jones CS, Wall EC, et al. Immunity to diphtheria and tetanus in England and Wales. *Vaccine*, 2000. 19(2-3): p. 167-73.
  13. Moughty A, Donnell JO ,Nugent M. Who needs a shot ... a review of tetanus immunity in the West of Ireland. *Emergency Medicine Journal*, 2013. 30(12): p. 1009-11.
  14. Weinberger B, Schirmer M, Matteucci Gothe R, et al. Recall responses to tetanus and diphtheria vaccination are frequently insufficient in elderly persons. *PLoS One*, 2013. 8(12): p. e82967.
  15. Alagappan K, Rennie W, Lin D,Auerbach C. Immunologic response to tetanus toxoid in the elderly: one-year follow-up. *Annals of Emergency Medicine*, 1998. 32(2): p. 155-60.
  16. Björkholm B, Hagberg L, Sundbeck G,Granstrom M. Booster effect of low doses of tetanus toxoid in elderly vaccinees. *European Journal of Clinical Microbiology and Infectious Diseases*, 2000. 19(3): p. 195-9.
  17. Shohat T, Marva E, Sivan Y, et al. Immunologic response to a single dose of tetanus toxoid in older people. *Journal of the American Geriatrics Society*, 2000. 48(8): p. 949-51.
  18. Van Damme P, McIntyre P, Grimprel E, et al. Immunogenicity of the reduced-antigen-content dTpa vaccine (Boostrix®) in adults 55 years of age and over: a sub-analysis of four trials. *Vaccine*, 2011. 29(35): p. 5932-9.
  19. Smith J. Tetanus infection may not confer immunity. *New Zealand Public Health Report*, 1995. 6: p. 53.
  20. Beytout J, Launay O, Guiso N, et al. Safety of Tdap-IPV given one month after Td-IPV booster in healthy young adults: a placebo-controlled trial. *Hum Vaccin*, 2009. 5(5): p. 315-21.
  21. Talbot EA, Brown KH, Kirkland KB, et al. The safety of immunizing with tetanus-diphtheria-acellular pertussis vaccine (Tdap) less than 2 years following previous

- tetanus vaccination: Experience during a mass vaccination campaign of healthcare personnel during a respiratory illness outbreak. *Vaccine*, 2010. 28(50): p. 8001-7.
22. Liang JL, Tiwari T, Moro P, et al. Prevention of pertussis, tetanus, and diphtheria with vaccines in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR: Recommendations and Reports*, 2018. 67(2): p. 1-44.
  23. Havers FP, Moro PL, Hunter P, et al. Use of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccines: updated recommendations of the Advisory Committee on Immunization Practices – United States, 2019. *MMWR: Morbidity and Mortality Weekly Report*, 2020. 69(3): p. 77-83.
  24. Australian Technical Advisory Group on Immunisation. 2018. *Australian Immunisation Handbook* (ed.), Canberra: Australian Government Department of Health. URL: <https://immunisationhandbook.health.gov.au/> (accessed October 2019)
  25. American Academy of Pediatrics. 2018. Tetanus. in *Red Book: 2018 Report of the Committee on Infectious Diseases*, Kimberlin D, Brady M, Jackson M, and Long S (eds). Elk Grove Village, IL. URL: <https://redbook.solutions.aap.org/redbook.aspx>. (accessed 3 July 2020)
  26. Mark A, Carlsson RM, Granstrom M. Subcutaneous versus intramuscular injection for booster DT vaccination of adolescents. *Vaccine*, 1999. 17(15-16): p. 2067-72.
  27. Klein NP, Hansen J, Lewis E, et al. Post-marketing safety evaluation of a tetanus toxoid, reduced diphtheria toxoid and 3-component acellular pertussis vaccine administered to a cohort of adolescents in a United States health maintenance organization. *Pediatric Infectious Disease Journal*, 2010. 29(7): p. 613-7.
  28. Yih WK, Nordin JD, Kulldorff M, et al. An assessment of the safety of adolescent and adult tetanus-diphtheria-acellular pertussis (Tdap) vaccine, using active surveillance for adverse events in the Vaccine Safety Datalink. *Vaccine*, 2009. 27(32): p. 4257-62.
  29. Vaccine Safety Committee: Institute of Medicine. 1994. Diphtheria and tetanus toxoids, in *Adverse Events Associated with Childhood Vaccines: Evidence bearing on causality*, Stratton KR, Howe CJ, Johnston RB (eds) (eds). National Academies Press: Washington, DC.
  30. Edsall G, Elliott MW, Peebles TC, Eldred MC. Excessive use of tetanus toxoid boosters. *JAMA*, 1967. 202(1): p. 111-3.

# 23 Tuberculosis

## Key information

Mode of transmission	<p>Inhalation of airborne droplets produced by people with pulmonary or laryngeal tuberculosis (TB).</p> <p>People with latent TB infection and non-pulmonary TB disease are not infectious.</p>
Incubation period	<p>Between 2 and 10 weeks from infection to primary lesion or significant tuberculin skin test (Mantoux) reaction.</p>
Period of communicability	<p>May be years with untreated pulmonary TB.</p> <p>See the <i>Guidelines for Tuberculosis Control in New Zealand 2019</i> (or current edition) – see section 23.5.3.</p>
Burden of disease	<p>Disseminated and meningeal TB are more common in very young children.</p> <p>The immunocompromised individuals, particularly HIV-infected, are more at risk of disease and complications.</p> <p>In New Zealand, TB incidence is highest in those born in high prevalence countries.</p>
Funded vaccine	<p>Bacillus Calmette-Guérin (BCG) Vaccine SSI.</p>
Dose, presentation and route	<p>Vaccine can only be administered intradermally by an authorised vaccinator with BCG endorsement.</p> <p>Live attenuated vaccine, which must be reconstituted.</p>
Funded vaccine indications and recommended schedule	<p>Neonatal BCG vaccine should be offered to infants at increased risk of TB, as defined in section 23.5.2.</p> <p>(See section 23.5.2 for countries with a TB rate <math>\geq 40</math> per 100,000.)</p>
Contraindications	<p>Individuals with primary or secondary immunocompromise, including:</p> <ul style="list-style-type: none"><li>• receiving immunosuppressive treatment</li><li>• malignant conditions of the reticulo-endothelial system (eg, lymphoma, leukaemia)</li><li>• HIV-positive or potentially HIV-positive individuals</li><li>• infants of mothers who received biologic immunosuppressive agents during pregnancy</li><li>• other individuals in whom immunocompromise is known or suspected (see section 23.6.1).</li></ul> <p>Individuals with generalised infected skin conditions.</p>
Potential responses	<p>A local reaction develops in 90–95% of those vaccinated with BCG, which may scar within 3 months.</p> <p>A minor degree of adenitis is normal, not a complication.</p> <p>Suppurative adenitis may take months to resolve; usually no treatment is required.</p>

*Continued overleaf*

Public health measures	All cases of active TB must be notified to the local medical officer of health. (see section 23.8)
Post-exposure prophylaxis	Vaccine prophylaxis is only applicable for young children

## 23.1 Bacteriology

Human tuberculosis (TB) is caused by infection with *Mycobacterium tuberculosis* or *Mycobacterium bovis*.

## 23.2 Clinical features

*M. tuberculosis* or *M. bovis* infection most commonly causes disease in the lungs, but any part of the body can be affected.

The initial infection with *M. tuberculosis* usually goes unnoticed. Early infections can be cleared, progress rapidly to primary TB, or be contained in a latent phase (LTBI): see Figure 23.1.

Primary TB occurs most commonly in young children aged under 5 years, individuals with immunocompromise and those infected by particularly transmissible isolates of TB.

Latent TB infection has no symptoms and is diagnosed by a positive tuberculin skin test or interferon gamma release assay after the exclusion of active TB. Latent infection progressing to active TB is also called reactivation TB.

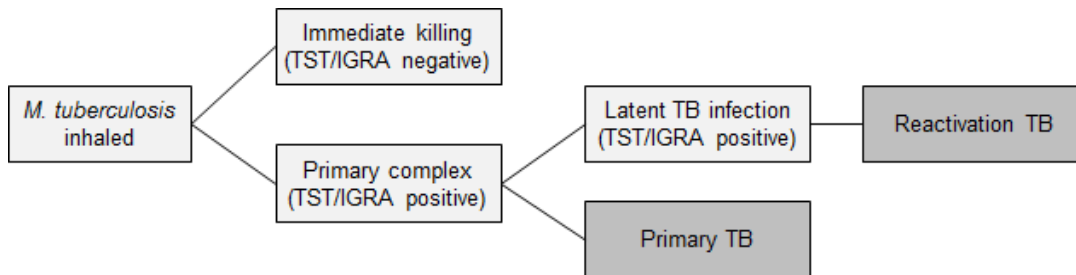
The lifetime risk for infected people progressing from this latent phase to active TB disease is on average 5-10 percent, usually within the first five years of initial infection. This risk is strongly affected by infecting dose, the age of the person, the presence of healed lesions on chest X-ray, and particularly, immunocompromise.<sup>1-4</sup>

The time from infection to clinical manifestations of primary TB varies, from one to six months after infection. Reactivation TB can occur at any time thereafter, even decades after infection. The most common site of infection is the lung (pulmonary TB), where TB infection classically causes an asymmetrical pulmonary infiltrate. The 'classic' TB pathology of caseation, cavity formation and fibrosis occurs late and in a minority of cases. Young children with active TB disease may be asymptomatic or present with symptoms of fever, lassitude and failure to thrive. Older children and adults with active TB disease may present with symptoms of anorexia, fatigue, weight loss, chills, night sweats, cough, haemoptysis and chest pain.

Any organ can be affected by extrapulmonary TB, causing meningitis, pleurisy, pericarditis, bone or joint infection, renal infection, gastrointestinal tract infection, peritonitis or lymphadenitis, or disseminating via the bloodstream and affecting multiple organs (disseminated TB). Disseminated and meningeal TB are more common

in very young children. Immunocompromise, like HIV, is associated with higher rates of disseminated TB and less specific clinical features.<sup>5</sup>

**Figure 23.1: Stages in the natural history of tuberculosis**



Key: TST = tuberculin skin test; IGRA = interferon gamma release assay; TB = tuberculosis.

## 23.3 Epidemiology

### 23.3.1 Global epidemiology

Around a quarter of the global population is estimated to have been infected with TB bacteria. Worldwide, the incidence of TB has increased, reversing the downward trend observed prior to 2020.<sup>6</sup> Of those infected, about 5–10 percent will develop symptoms and progress to TB disease. The estimated TB incidence rate (new cases per 100,000 population per year) increased by 1.9 percent from 2020 to 2021, and a further 1.9 percent from 2021 to 2022. Disruptions in TB diagnosis and treatment at the start of the COVID-19 pandemic during 2020 led to increases in new cases reporting and TB incidence during the subsequent years. TB remained the world's second leading cause of death from a single infectious agent in 2022, after COVID-19, with estimated 1.3 million deaths. An estimated 10.6 million people worldwide were diagnosed with TB in 2022, which translates to 133 new cases per 100,000 population. Of these cases, 6.3 percent were among individuals living with HIV.<sup>6</sup>

Most TB cases were reported in the WHO regions of South-East Asia (46 percent), Africa (23 percent), and the Western Pacific (18 percent), with smaller proportions in the Eastern Mediterranean (8.1 percent), the Americas (3.1 percent), and Europe (2.2 percent). There has been an increasing burden of multidrug-resistant TB (defined as resistance to at least isoniazid and rifampicin) with an estimated 410,000 new cases of multidrug-resistant TB in 2022.<sup>6, 7</sup>

In low-burden countries, such as New Zealand, the peak age for TB is in older adults, reflecting their exposure to TB in the past when incidence was higher. In high-burden countries TB is most common in children and young adults. The risk of TB in people who emigrate from high-burden countries is proportionate to the incidence in their country of origin.<sup>8</sup>



## 23.3.2 New Zealand epidemiology

For detailed TB information, see the notifiable disease dashboard at ESR: [www.esr.cri.nz/digital-library/notifiable-disease-dashboard/](http://www.esr.cri.nz/digital-library/notifiable-disease-dashboard/)

### Notification rates and risk factors

TB remains one of the most common notifiable infectious diseases in New Zealand. Cases of TB declined substantially between 1980 and 2007, but they have remained relatively stable since then.<sup>9</sup>

In 2023, there were 317 notifications for TB (notification rate of 6.1 per 100,000), which was higher than 2022 (5.2 per 100,000) (ESR, 24 September 2024). Notification rates were highest in those aged 20–29 years (8.5 per 100,000), 40–49 years (8.4 per 100,000) and 30–39 years (8.0 per 100,000), with similar rates in males and females (6.1 and 6.0 per 100,000, respectively).

Asian ethnic groups had the highest notification rate in 2023 (28.2 per 100,000, 224 cases), followed by Middle Eastern/Latin American/African (15.8 per 100,000, 12 cases) and Pacific peoples (13.1 per 100,000, 46 cases). Of the 304 new cases recorded in 2023 with TB risk factors, 267 (87.8 percent) were born overseas (ESR, 24 September 2024). The highest disease rate was among those born in Southern and Central Asia (68.2 per 100,000), followed by those born in South-East Asia (63.4 per 100,000), and the Pacific Islands (20.4 per 100,000). The most reported countries of birth were India (92.2 percent) and the Philippines (77.4 percent). Of the 82 percent of new TB cases in 2023 with date of arrival recorded, the median interval between arrival and the TB notification ranged from 0 to 62 years (mean 9 years and median 6 years) (ESR, 24 September 2024).

The notification rate was considerably lower for Māori (2.0 per 100,000, 17 cases) and European/ Other (0.5 per 100,000, 15 cases) groups (ESR, 24 September 2024). There was substantial regional variation in TB notification rates: the highest rates were in Auckland (11.2 per 100,000), Counties Manukau (10.7 per 100,000), Whanganui (7.1 per 100,000) and Capital and Coast (6.4 per 100,000).

Three children aged under 5 years were notified with TB in 2023 (ESR, 24 September 2024). The children were born in New Zealand and not vaccinated with BCG.

### Multidrug-resistant TB

Multidrug-resistant TB is rare but does occur in New Zealand. Over 10 years (2012–2021), a total of 39 cases were multidrug resistant (annual average rate of 1.6 percent). (ESR, 24 September 2024) All these cases were born and assumed to have acquired the infection overseas: 87.2 percent were born in an Asian country.<sup>10</sup>



## 23.4 Vaccine

Note: Depending on world supply, BCG vaccine may not be available in New Zealand.

BCG vaccine types vary widely, with different strains. The incidence of side-effects with BCG vaccination differs between strains that are considered more reactogenic (ie, those that elicit stronger immune responses in animal models) and strains that are considered less reactogenic.<sup>11</sup> The more reactogenic strains have also been associated with a higher rate of lymphadenitis and osteitis, especially among neonates. Reducing the vaccination dosage for the more reactogenic strains also reduces the incidence of lymphadenitis.

### 23.4.1 Licensed vaccine

BCG Vaccine SSI (Seqirus (NZ) Ltd) is a live attenuated vaccine, containing the less reactogenic Danish 1331 strain of *M. bovis*. The 0.1 mL dose for children aged 12 months and older contains  $2-8 \times 10^5$  colony-forming units of *M. bovis*, and the 0.05 mL dose for infants contains  $1-4 \times 10^5$  colony-forming units. Other components and residuals include sodium glutamate, magnesium sulphate heptahydrate, dipotassium phosphate, citric acid, L-asparagine monohydrate, ferric ammonium citrate and glycerol.

### 23.4.2 Efficacy and effectiveness

The exact immune response elicited by BCG vaccination and the mechanism of action in the host are still not well understood. There is no reliable established laboratory correlate for immunity to *M. tuberculosis*,<sup>12</sup> though this remains an active area of study.<sup>13</sup>

BCG protection is partial and varies according to the age at which vaccination is administered and the disease phenotype in question. A meta-analysis of randomised controlled trials showed neonatal BCG had 59 percent efficacy against pulmonary TB (95% CI: 0.42–0.71) and 90 percent efficacy against meningeal TB (95% CI: 0.23–0.99).<sup>14</sup> Studies conducted since the advent of interferon gamma release assays suggest BCG may also be effective against *M. tuberculosis* infection. A meta-analysis of 26 cohort studies has estimated the overall effectiveness of BCG against all tuberculosis at 18 percent (aOR 0.82, 95% CI 0.74–0.91).<sup>15</sup> When stratified by age, BCG vaccination at birth only significantly protected children under 5 years (aOR 0.63, 0.49–0.81). The study concluded that BCG vaccination at birth is effective at preventing TB in young children but is ineffective in adolescents and adults.<sup>15</sup> Thus, the principal role of BCG in New Zealand is to protect young children who are at greatest risk of disease, particularly miliary and meningeal disease.<sup>11</sup> BCG is less effective in adults and older children, particularly if they already have latent infection.

As BCG has been propagated *in vitro* for over 40 years, there are now several strains being manufactured.<sup>16</sup> Immunological responses vary considerably across vaccine strains, but the data to date cannot differentiate which strains, if any, are overall more effective.<sup>17, 18</sup>

In low-income countries, a birth dose of BCG significantly reduces overall infant mortality.<sup>19, 20</sup>

BCG has had little effect in reducing the population rate and transmission of TB,<sup>21</sup> so there are no herd immunity effects. Duration of protection is unknown, possibly 10 to 15 years, but it may be much longer in some populations.<sup>11</sup>

There have been a number of different approaches to using BCG in the control of TB in middle- and high-income countries.<sup>22</sup> For example, the US has not had a BCG programme, whereas New Zealand (see Appendix 1) and the UK had programmes until 1990 and 2005, respectively. The WHO recommends that countries with low rates of active TB, such as New Zealand, target BCG vaccination at children who are at significantly increased risk of TB exposure through household contact.<sup>7</sup> New Zealand (see section 23.5) and the UK now only offer BCG vaccine to high-risk individuals. A study from the Netherlands suggests that around 9,000 children from countries with rates greater than 50 per 100,000 population would have to be given BCG to prevent a severe case.<sup>23</sup>

The current recommendation to use neonatal BCG vaccination in populations with high rates of active TB is part of a control and treatment programme for TB in New Zealand, which includes active contact tracing and treatment of latent TB infection.

There are large international efforts working to improve BCG vaccines and develop new, more effective vaccines.<sup>24</sup>

### 23.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at [www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

Store in the dark at +2°C to +8°C. Do not freeze.

There are variances in strain potency between brands of BCG vaccine so vaccinators should always follow the instructions in the vaccine data sheet (available on [www.medsafe.govt.nz](http://www.medsafe.govt.nz)).

BCG vaccine requires reconstitution before administration. It is presented as freeze-dried vaccine in a multi-dose vial with diluent in a separate vial. The diluent must be added to the freeze-dried vaccine vial and mixed gently (do not shake vigorously). Protect the vial from light. Leave the reconstituted vaccine to stand for one minute until it forms an opalescent liquid. Reconstituted vaccine should be stored at 4°C, protected from sunlight and used within four hours.

## 23.4.4 Dosage and administration

Only authorised vaccinators with BCG endorsement can administer BCG vaccine (see A3.6).

Administer a dose of:

- 0.05 mL to infants aged under 12 months
- 0.1 mL to children aged 12 months or older.

The vaccine is administered by intradermal injection over the point of insertion of the left deltoid muscle (see sections 2.2.3 and 2.2.4).

No follow-up tuberculin skin testing is required.

Repeat BCG vaccination is not recommended.

### BCG immunisation given in other countries

BCG is one of the vaccines that are part of the WHO Expanded Programme on Immunization. It is given at birth in most low-income countries.

The following Pacific Island countries<sup>25</sup> recommend BCG vaccination at birth: Cook Islands, Fiji, Kiribati, Nauru, Niue, Papua New Guinea, Samoa, Solomon Islands, Tonga, Tuvalu and Vanuatu.

Usually BCG vaccine is administered in the left deltoid area, but other sites of administration have also (although uncommonly) been used, such as the right deltoid. Revaccination with BCG is not recommended by the WHO.<sup>7</sup>

### Co-administration with other vaccines

BCG can be given simultaneously with any other vaccine. However, it must be administered into a separate site in a separate syringe. Because of the risk of local

lymphadenitis, no further vaccinations should be given into the arm used for BCG for at least three months. If not given concurrently, BCG should be given at least four weeks after MMR or VV. Note that no time interval is required between administration of BCG and rotavirus vaccines.

HBIG (given at birth to babies of mothers with chronic HBV infection) or human normal immunoglobulin is thought not to reduce the effectiveness of BCG immunisation, which principally acts through cell-mediated immunity.

## 23.5 Recommended immunisation schedule

### 23.5.1 Tuberculin skin testing (Mantoux) or interferon-gamma release assay before BCG vaccination

Tuberculin skin testing is not needed if BCG is given before age 6 months unless a history of contact with a known or possible case of TB is obtained. Although the tuberculin skin test is usually positive in the year following BCG vaccination, at least 50 percent of children will be negative beyond that time, so tuberculin skin testing still has utility for diagnosing TB infection.

Children eligible for BCG vaccine who have missed vaccination at birth may be vaccinated at any time up to age 5 years (see section 23.5.3). If the child is aged 6 months to <2 years, they should have a pre-vaccination tuberculin skin test or an interferon-gamma release assay (IGRA; Quantiferon) if aged 2 to <5 years to detect whether they have already been infected: BCG vaccination only to be given if the child is uninfected.

### 23.5.2 BCG eligibility criteria

TB is more common in migrants or families of migrants from high-incidence countries. However, anyone who is pregnant should have a discussion with their lead maternity carer about the risk of TB for their baby.

Neonatal BCG is recommended and funded for infants at increased risk of TB, as defined in Table 23.1.

**Table 23.1: Neonatal BCG eligibility criteria**

Neonatal BCG is recommended and funded for infants at increased risk of TB, defined as those who:

- will be living in a house or family/whānau with a person with either current TB or a history of TB
- have one or both parents or household members or carers who within the last five years lived for a period of six months or longer in countries with a TB rate  $\geq 40$  per 100,000\*
- during their first five years will be living for three months or longer in a country with a TB rate  $\geq 40$  per 100,000.\*

\* For TB incidence rates in specific countries see [https://worldhealthorg.shinyapps.io/tb\\_profiles/](https://worldhealthorg.shinyapps.io/tb_profiles/).

The WHO Global Tuberculosis 2021 report showed that the highest burden for TB was seen in 30 countries. For more detail see [www.who.int/publications/digital/global-tuberculosis-report-2021](http://www.who.int/publications/digital/global-tuberculosis-report-2021)

As a general indication, the following global areas have TB rates  $\geq 40$  per 100,000:

- most of Africa
- much of South America
- Russia and the former Soviet states
- the Indian subcontinent
- Eastern Mediterranean
- China (including Hong Kong) and Taiwan
- South-East Asia
- some parts of the Pacific (Kiribati and Papua New Guinea have consistently high rates).

For TB incidence rates in specific countries see [https://worldhealthorg.shinyapps.io/tb\\_profiles/](https://worldhealthorg.shinyapps.io/tb_profiles/)

Neonates at risk should be identified antenatally by lead maternity care providers and antenatal referral made to the neonatal BCG service. Health care providers can also identify and refer neonates at risk. Immunisation is desirable before infants leave hospital. If this does not happen, immunisation should be arranged through the local medical officer of health.

Infants born before 34 weeks' gestation should have their BCG vaccination delayed until 34 weeks' post-conceptual age.<sup>26</sup> Babies born after this or with low birthweight appear to produce an adequate response, based on tuberculin skin test responses.<sup>27, 28</sup>

If the baby has not been vaccinated before leaving hospital, and if there is a history of *current* TB in a relative who has had contact with the baby, *do not vaccinate immediately*. Withhold vaccination, conduct tuberculin skin testing, seek paediatric advice and vaccinate only after the possibility of infection in the baby has been excluded. Vaccination may not protect the baby who is incubating disease and may prevent the tuberculin test from assisting with the diagnosis of disease.

A parent's/guardian's request should not be accepted as an indication for immunisation. Parents/guardians seeking vaccination of children who do not meet the

above criteria should be referred to the local medical officer of health to discuss the risks and benefits of immunisation before a final decision is made.

## BCG vaccine information for parents

Information about the BCG vaccine is available in English and other languages from the HealthEd website ([healthed.govt.nz](https://healthed.govt.nz)). This includes information for parents on why the vaccine is recommended, what to expect and how to care for the vaccination site.

### 23.5.3 Children aged under 5 years at high TB risk

Repeat BCG vaccination is not recommended. Vaccination for overseas travel is not available in New Zealand.

Funded BCG may be offered to children aged under 5 years if they are tuberculin skin test- or interferon gamma-release assay negative and are at increased risk of TB because they:

- will be living in a house or family/whānau with a person with either current TB or a history of TB or
- have one or both parents, household members or carers who within the last five years lived for a period of six months or longer in countries with a TB rate  $\geq 40$  per 100,000\* or
- during their first five years will be living for three months or longer in a country with a TB rate  $\geq 40$  per 100,000\*.

\* For TB incidence rates in specific countries see [https://worldhealthorg.shinyapps.io/tb\\_profiles/](https://worldhealthorg.shinyapps.io/tb_profiles/)

Refer to the *Guidelines for Tuberculosis Control in New Zealand 2019* (available at <https://www.tewhatauora.govt.nz/publications/guidelines-for-tuberculosis-control-in-new-zealand-2019>).

### 23.5.4 Pregnancy and breastfeeding

BCG vaccine is not recommended for when someone is pregnant or breastfeeding.

## 23.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

### 23.6.1 Contraindications

BCG vaccine should not be given to individuals:

- known to be hypersensitive to any component of the vaccine
- receiving corticosteroids or other immunosuppressive treatment, including radiotherapy (see section 4.3)
- suffering from malignant conditions such as lymphoma, leukaemia, Hodgkin's disease or other tumours of the reticulo-endothelial system
- in whom immunocompromise is known or suspected, such as individuals with hypogammaglobulinaemia – primary immune deficiencies in children are often not detected until after the first few weeks of life (ie, after BCG vaccine is given), so a family history of immune deficiency should be sought and, if present, discussed with a paediatrician before vaccination
- known to be infected with HIV, including neonates where the mother's HIV status is unknown – maternal HIV infection should be excluded prior to neonatal vaccination; testing should have been offered as part of the National Antenatal HIV Screening Programme, and infants born to HIV-infected mothers should be under the care of a paediatrician
- with generalised infected skin conditions.

Infants born to those who received immunomodulatory biologic agents during pregnancy must not be vaccinated with a BCG vaccine until they are identified as being immunocompetent. See section 4.2.5 and Table 4.2 for a list of the highly immunosuppressive medications with long half-lives that require a prolonged delay before vaccination (for up to one year in those being treated). These include monoclonal antibody (mab) agents that readily cross the placenta. Each case should be assessed with specialist advice.

### 23.6.2 Precautions

- BCG vaccine should be avoided in those who are pregnant (this is a counsel of caution, as no harmful effects to the fetus have been observed following accidental immunisation of the mother during pregnancy).
- In the case of eczema, an immunisation site should be chosen that is free of skin lesions.
- Infants born before 34 weeks' gestation should have their BCG vaccination delayed until 34 weeks' post-conceptual age.<sup>26</sup>



- Avoid or defer immunisation in a child born with a condition that may require immunosuppressive therapy in future.
- Before BCG vaccination is scheduled for neonates (up to 4 weeks of age), a normal metabolic/immune deficiency (Guthrie test) result needs to have been confirmed, specifically for severe combined immunodeficiency (SCID).

## 23.7 Potential responses and AEFIs

### 23.7.1 Potential responses

Following the BCG injection, a white weal should appear. This should subside in approximately 30 minutes. The site requires no swabbing or dressing.

A local reaction develops in 90–95 percent of people vaccinated with BCG, which may include shallow ulceration, followed by healing and scar formation within three months. To ensure appropriate healing, encourage parents/caregivers to keep the injection site clean and dry, to allow sore to scab and to avoid ointments and scratching. A minor degree of adenitis developing in the weeks following immunisation should be regarded as normal, not a complication. It may take months to resolve. Suppurative adenitis may also take months to resolve; usually no treatment is required.

### 23.7.2 AEFIs

AEFIs with BCG vary with age and vaccine strain and are summarised in Table 23.2.

**Table 23.2: Age-specific estimated risks for complications after administration of BCG vaccine**

Complication	Incidence per 1 million vaccinations	
	Age <1 year	Age 1–20 years
Local subcutaneous abscess; regional lymphadenopathy	387	25
Musculoskeletal lesions	0.39–0.89	0.06
Multiple lymphadenitis; non-fatal disseminated lesions	0.31–0.39	0.36
Fatal disseminated lesions	0.19–1.56	0.06–0.72

Reprinted with permission of the International Union Against Tuberculosis and Lung Disease. Copyright © The Union. Lotte A, Wasz-Hockert O, Poisson N, et al. 1988. Second IUATLD study on complications induced by intradermal BCG-vaccination. *Bulletin of the International Union against Tuberculosis and Lung Disease* 63: 47–59.

The risk of BCG adverse reactions depends on many factors, including strain type, route of administration and the underlying immune state of the patient. Severe injection-site reactions, large ulcers and abscesses can occur in individuals who are tuberculin positive. Special care is needed both in interpreting initial tuberculin skin results and in delivering the BCG vaccine.

Rarely, osteitis and osteomyelitis, lupoid and other types of skin disorders, and neurological disorders have been reported following BCG vaccination. Although rare, disseminated BCG disease is the most severe BCG vaccine complication occurring in immunocompromised people, such as children with primary immune deficiency. This needs rapid and aggressive treatment and has a high mortality.

Keloid scars at the injection-site, although not uncommon, are largely avoidable. Some sites are more prone to keloid formation than others and vaccinators should adhere to the site recommended (mid-upper arm). Most experience has been with the upper arm site, and it is known that the risk of keloid formation increases greatly if the injection is given higher than the insertion of the deltoid muscle into the humerus.

Every effort should be made to recover and identify the causative organism from any lesions that constitute a serious complication.

Most local and regional adenopathy resulting from BCG vaccination will resolve spontaneously, and there is rarely a need for medical or surgical intervention. Treatment recommendations for local abscess formation and suppurative lymphadenitis remain controversial.<sup>29</sup> If suppurative adenitis reactions persist for longer than three months, seek specialist opinion. However, anyone presenting with more widespread or distant disease needs referral to a specialist.

Abscesses and more serious complications should be reported to CARM (see 'AEFI reporting process – notifying CARM' in section 1.6.3), and also reported to the local medical officer of health in the interests of quality control of the BCG vaccination technique.

## 23.8 Public health measures

It is a legal requirement that all cases of active TB be notified to the local medical officer of health. While there is no legal requirement to notify cases of latent TB infection that are being treated, for surveillance purposes and with the patient's consent they should be reported to the local medical officer of health.

For more information refer to the 'Tuberculosis' chapter of the Communicable Disease Control Manual at [www.tewhaturora.govt.nz/for-health-professionals/clinical-guidance/communicable-disease-control-manual/tuberculosis/](http://www.tewhaturora.govt.nz/for-health-professionals/clinical-guidance/communicable-disease-control-manual/tuberculosis/) and see the 'Tuberculosis' page for the health sector guidance available at [www.tewhaturora.govt.nz/for-the-health-sector/health-sector-guidance/diseases-and-conditions/tuberculosis](http://www.tewhaturora.govt.nz/for-the-health-sector/health-sector-guidance/diseases-and-conditions/tuberculosis).

Under the Health (Protection) Amendment Act 2016, the medical officer of health is given wide powers to investigate and control all TB cases and their contacts, while

districts are required to make provision for the treatment and supervision of patients and their contacts.

The primary purpose of neonatal BCG vaccination is to protect child case contacts from TB disease and its most devastating consequences. Screening of certain risk groups and case contact management are other elements of TB control in New Zealand. These programmes do not obviate the need for BCG vaccination, as screening coverage is partial and contact tracing may not occur in time to prevent illness in child contacts. The local medical officer of health can advise on local TB control policies, including issues in BCG immunisation.

Both TB infection and BCG immunisation lead to the development of a cellular immune response, which can be detected by measuring dermal induration after the injection of tuberculin-purified protein derivative (eg, via the tuberculin skin test). A positive response to a tuberculin skin test may be an indication of current infection, previous natural infection or prior BCG immunisation. However, the false positive effect after vaccination will wane, rapidly in all individuals who receive the vaccine in the neonatal period and more slowly in those who are vaccinated at an older age such as during the primary-school years.<sup>30</sup>

*In vitro* tests have been developed to measure the release of interferon-gamma from host lymphocytes in response to well-defined antigens. The antigens used are not present in BCG strains of *M. bovis* or most non-tuberculous mycobacteria. Interferon gamma release assay has the advantage of greater specificity and convenience, but it is more expensive.<sup>31</sup>

## 23.9 Variations from the vaccine data sheet

The data sheet states that BCG vaccine should not be given to infants born to HIV-positive mothers. Health New Zealand | Te Whatu Ora recommends that BCG may be given to HIV-negative infants born to HIV-positive mothers – providing that the infant is confirmed to be HIV negative by appropriately-timed PCR tests before the vaccine is given.<sup>32, 33</sup> Seek specialist advice.

## References

1. Getahun H, Matteelli A, Chaisson R. Latent *Mycobacterium tuberculosis* infection. *New England Journal of Medicine*, 2015. 372(22): p. 2127–35.
2. Marais BJ, Gie RP, Schaaf HS, et al. The natural history of childhood intra-thoracic tuberculosis: a critical review of literature from the pre-chemotherapy era. *International Journal of Tuberculosis and Lung Disease*, 2004. 8(4): p. 392-402.

3. World Health Organization. 2018 *Latent tuberculosis infection: updated and consolidated guidelines for programmatic management.*: Geneva. URL: <https://www.who.int/publications/i/item/9789241550239>. (accessed 20 August 2024)
4. World Health Organization. 2018 *Latent tuberculosis infection: updated and consolidated guidelines for programmatic management.* World Health Organization,| CC BY-NC-SA 3.0 IGO. URL: <https://www.who.int/publications/i/item/9789241550239>. (accessed 24 September 2024)
5. Schaaf H ,Zumla Ae, *Tuberculosis: A Comprehensive Clinical Reference.* 2009, London, UK: WB Saunders Elsevier.
6. Global Tuberculosis Programme (GTB). 2023 *Global tuberculosis report 2023.* World Health Organization. URL: <https://www.who.int/publications/i/item/9789240083851>. (accessed 24 September 2024)
7. World Health Organization. BCG vaccines: WHO position paper – February 2018. *Weekly Epidemiological Record*, 2018. 93(8): p. 73-96.
8. Pareek M, Watson JP, Ormerod LP, et al. Screening of immigrants in the UK for imported latent tuberculosis: a multicentre cohort study and cost-effectiveness analysis. *Lancet Infectious Diseases*, 2011. 11(6): p. 435-44.
9. Institute of Environmental Science and Research Ltd. 2016. *Notifiable Diseases in New Zealand: Annual Report 2015* (ed.), Porirua, New Zealand: The Institute of Science and Environmental Research Ltd. URL: [https://surv.esr.cri.nz/PDF\\_surveillance/AnnualRpt/AnnualSurv/2015/2015AnnualReportFinal.pdf](https://surv.esr.cri.nz/PDF_surveillance/AnnualRpt/AnnualSurv/2015/2015AnnualReportFinal.pdf) (accessed 3 July 2020)
10. Institute of Environmental Science and Research. 2023 *Tuberculosis in New Zealand: Annual Report 2020.*: Porirua, New Zealand. (accessed
11. Hanekom W, Hawn T ,Ginsberg A. 2018. Tuberculosis Vaccines, in *Plotkin's Vaccines (7th Edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
12. Nunes-Alves C, Booty MG, Carpenter SM, et al. In search of a new paradigm for protective immunity to TB. *Nature Reviews: Microbiology*, 2014. 12(4): p. 289-99.
13. Tanner R, O'Shea MK, Fletcher HA,McShane H. *In vitro* mycobacterial growth inhibition assays: A tool for the assessment of protective immunity and evaluation of tuberculosis vaccine efficacy. *Vaccine*, 2016. 34(39): p. 4656-4665.
14. Mangtani P, Abubakar I, Ariti C, et al. Protection by BCG vaccine against tuberculosis: a systematic review of randomized controlled trials. *Clinical Infectious Diseases*, 2014. 58(4): p. 470-80.
15. Martinez L, Cords O, Liu Q, et al. Infant BCG vaccination and risk of pulmonary and extrapulmonary tuberculosis throughout the life course: a systematic review and individual participant data meta-analysis. *Lancet Glob Health*, 2022. 10(9): p. e1307-e1316.
16. Copin R, Coscolla M, Efstathiadis E, et al. Impact of in vitro evolution on antigenic diversity of *Mycobacterium bovis* bacillus Calmette-Guerin (BCG). *Vaccine*, 2014. 32(45): p. 5998-6004.
17. Anderson EJ, Webb EL, Mawa PA, et al. The influence of BCG vaccine strain on mycobacteria-specific and non-specific immune responses in a prospective cohort of infants in Uganda. *Vaccine*, 2012. 30(12): p. 2083-9.
18. Ritz N, Hanekom WA, Robins-Browne R, et al. Influence of BCG vaccine strain on the immune response and protection against tuberculosis. *FEMS Microbiology Reviews*, 2008. 32(5): p. 821-41.

19. Thyssen SM, Benn CS, Gomes VF, et al. Neonatal BCG vaccination and child survival in TB-exposed and TB-unexposed children: a prospective cohort study. *BMJ Open*, 2020. 10(2): p. e035595.
20. Biering-Sørensen S, Jensen KJ, Monterio I, et al. Rapid protective effects of early BCG on neonatal mortality among low birth weight boys: observations from randomized trials. *Journal of Infectious Diseases*, 2018. 217(5): p. 759-766.
21. World Health Organization. *BCG Vaccine*. URL: <https://www.who.int/teams/health-product-policy-and-standards/standards-and-specifications/norms-and-standards/vaccines-quality/bcg>. (accessed 24 September 2024)
22. Zwerling A, Behr MA, Verma A, et al. The BCG World Atlas: a database of global BCG vaccination policies and practices. *PLoS Medicine*, 2011. 8(3): p. e1001012.
23. Altes HK, Dijkstra F, Lugner A, et al. Targeted BCG vaccination against severe tuberculosis in low-prevalence settings: epidemiologic and economic assessment. *Epidemiology*, 2009. 20(4): p. 562-8.
24. Ottenhoff TH, Kaufmann SH. Vaccines against tuberculosis: where are we and where do we need to go? *PLoS Pathogens*, 2012. 8(5): p. e1002607.
25. World Health Organization, WHO Vaccine-preventable Diseases: Monitoring system: 2016 global summary. 2016: Online.
26. Sedaghatian MR, Hashem F, Moshaddeque Hossain M. Bacille Calmette-Guérin vaccination in pre-term infants. *International Journal of Tuberculosis and Lung Disease*, 1998. 2(8): p. 679-82.
27. Badurdeen S, Marshall A, Daish H, et al. Safety and Immunogenicity of Early Bacillus Calmette-Guérin Vaccination in Infants Who Are Preterm and/or Have Low Birth Weights: A Systematic Review and Meta-analysis. *JAMA Pediatr*, 2019. 173(1): p. 75-85.
28. Saroha M, Faridi MM, Batra P, et al. Immunogenicity and safety of early vs delayed BCG vaccination in moderately preterm (31-33 weeks) infants. *Human Vaccines & Immunotherapeutics*, 2015. 11(12): p. 2864-71.
29. Caglayan S, Yegin O, Kayran K, et al. Is medical therapy effective for regional lymphadenitis following BCG vaccination? *American Journal of Diseases of Children*, 1987. 141(11): p. 1213-4.
30. Farhat M, Greenaway C, Pai M, Menzies D. False-positive tuberculin skin tests: what is the absolute effect of BCG and non-tuberculous mycobacteria? *International Journal of Tuberculosis and Lung Disease*, 2006. 10(11): p. 1192-204.
31. Centers for Disease Control and Prevention. Updated guidelines for using interferon gamma release assays to detect mycobacterium tuberculosis infection – United States, 2010. *Morbidity and Mortality Weekly Report: Recommendations and Reports*, 2010. 59(RR05): p. 1–25.
32. UK Health Security Agency. 2018. Tuberculosis. in *The Green Book*. URL: <https://www.gov.uk/government/publications/tuberculosis-the-green-book-chapter-32>. (accessed 24 September 2024)
33. Australian Technical Advisory Group on Immunisation. 2018. *Australian Immunisation Handbook* (ed.), Canberra: Australian Government Department of Health. URL: <https://immunisationhandbook.health.gov.au/> (accessed October 2019)

# 24 Varicella (chickenpox)

## Key information

Mode of transmission	Airborne droplets from, or contact with, vesicular lesions or possibly respiratory secretions.
Incubation period	Usually 14–16 days (range 10–21 days).
Period of communicability	From 2 days before onset of the rash until all lesions have crusted.
Incidence and burden of disease	Without immunisation, most people have infection during childhood. Groups at risk of severe complications include pregnant women and their unborn babies, and immunocompromised individuals.
Funded vaccine	VV (Varilrix) is a live attenuated vaccine.
Dose, presentation, route	0.5 mL per dose after reconstitution. Pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. Intramuscular or subcutaneous injection.
Funded vaccine indications and schedule	1 dose is funded for: <ul style="list-style-type: none"><li>• children at age 15 months; or</li><li>• previously unvaccinated children turning 11 years old on or after 1 July 2017 who have not previously had a varicella infection (as determined by clinical history).</li></ul> Up to 2 doses are funded for certain special groups and their household members if non-immune to varicella.
Recommended	Susceptible children and adults who are not eligible by age for funded vaccine.
Vaccine effectiveness	One dose confers approximately 99% protection against severe disease and 80% protection against varicella disease of any severity. Breakthrough disease is usually mild. Herd immunity has been documented.
Contraindications	Pregnancy Certain immune deficiency and immunocompromised states Known anaphylaxis to neomycin, gelatin or other vaccine components Active untreated TB (see section 24.6)
Potential responses to vaccine	Generally mild and self-limiting, and include local reactions, fever and mild papulo-vesicular rash in normal healthy individuals.

*Continued overleaf*



Post-exposure prophylaxis VV may be used for post-exposure prophylaxis for immune-competent people if given within 5 days of exposure. Zoster immunoglobulin (ZIG) is most effective if given as soon as possible after exposure but may be given up to 10 days post-exposure (see section 24.8.2).

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## 24.1 Virology

Varicella (chickenpox) is a highly infectious disease caused by human herpes virus type 3 (varicella zoster virus or VZV). Reactivation of latent VZV results in herpes zoster (zoster; shingles), a disease with considerable morbidity (see chapter 25).

## 24.2 Clinical features

Varicella is one of the most infectious diseases known (along with pertussis and measles). Transmission occurs via airborne droplets from, or contact with, vesicular lesions and possibly respiratory tract secretions. The incubation period is usually 14–16 days (range 10–21 days but can be longer in immunocompromised individuals and those who have received ZIG), and cases are infectious from two days before the onset of the rash until all the lesions have crusted. A maculopapular rash, which becomes vesicular, appears in crops over several days, first on the face and scalp, later spreading to the trunk and then the limbs. Vesicles, ranging in number from few to many hundred, dry and crust after three to four days. A hallmark of the rash is lesions in varying stages of development. Lesions on mucosal surfaces (mouth, vagina) can cause considerable distress. The rash is pruritic and is usually associated with mild fever, malaise, anorexia and listlessness.

In most children, varicella is a mild disease but complications requiring hospitalisation and fatalities do occur. Secondary bacterial skin infections are common. Serious complications include central nervous system involvement (encephalitis, cerebellar ataxia, stroke), pneumonia, secondary invasive bacterial infections, and even death. Adults are 25 times more likely to develop severe disease than children, with pneumonia being the most common complication, often requiring mechanical ventilation. VZV pneumonia carries an overall mortality rate of 10–30 percent.

Maternal varicella occurring in the first half of pregnancy can cause the rare but devastating congenital varicella syndrome (see Table 24.4), whereas disease very late in pregnancy (from five days before to two days after delivery) may cause severe neonatal varicella infection. Pregnant women who contract varicella have an estimated 10–20 percent risk of developing VZV pneumonia.

Others vulnerable to both VZV and zoster are those who are immunocompromised, such as people taking immunosuppressive medications (eg, cancer treatment or organ transplant patients) and those with HIV infection. Varicella can be a fatal disease in immunocompromised individuals.



VZV infection is followed by the production of VZV-specific T-cell mediated immunity, necessary to maintain the latency of VZV in the ganglia and prevent reactivation as zoster. The immune response is boosted by subclinical reactivation of latent virus. The incidence of zoster increases with age as VZV-specific T cell-mediated immunity declines (see chapter 25).

## 24.3 Epidemiology

### 24.3.1 Global burden of disease

In temperate climates, winter-spring epidemics occur with peak incidence in preschool and early primary school ages (1–9 years). Around 90 percent of individuals have been infected by adolescence and fewer than 5 percent of adults are susceptible. The annual number of infections therefore approximates the birth cohort.<sup>1, 2</sup>

Transmission of the virus is less efficient in tropical climates. Adolescent and adult immigrants to New Zealand from such countries are more likely to be susceptible, placing them at risk of contracting chickenpox in their new environment. Being older, they are more likely to suffer severe disease.

The long incubation and high transmissibility of VZV conspire to maximise disruption to families: by the time the rash occurs a child will have been infectious for two days; any susceptible household members will then become unwell just as the first child recovers. This results not only in morbidity but also in financial consequences for parents missing work.

Crude hospitalisation admission rates in high-income countries range from around 2–6 per 100,000 population-year. Most of these admissions are children, consistent with the high incidence of varicella in children. Crude mortality rates ranged from 0.3–0.5 per million population-year with overall case fatality ratios of around 2–4 per 100,000 cases. Almost 90 percent of varicella hospital admissions occur in otherwise healthy and immunocompetent individuals.<sup>1, 2</sup>

VV has been introduced into childhood immunisation programmes overseas, including the US from 1995 and Australia from 2005, resulting in dramatic reductions in varicella morbidity, hospitalisations and mortality.<sup>3–5</sup> By 2005 in the US, vaccine coverage was approximately 90 percent and varicella incidence had declined by more than 90 percent. Herd immunity was observed outside of age groups targeted for vaccination.<sup>1</sup>

Following the introduction of VV onto the childhood schedule, exposure to wild-type virus decreases. It has been theorised that a lack of boosting may lead to an increase in zoster in older adults. However, studies that have investigated this issue have been unable to attribute any increase in incidence of zoster to the childhood VZV vaccine programme.<sup>6, 7</sup> Studies from the UK and Canada reported increases in zoster not associated with a vaccination programme, and some US data showed zoster rates were increasing prior to the initiation of their varicella vaccination programme.<sup>8, 9</sup>

## 24.3.2 New Zealand epidemiology

Varicella is not a notifiable disease, so data is limited for uncomplicated varicella, but the epidemiology is likely to be as described above for temperate climates. With increasing participation in early childhood services, a greater proportion of infections may now be occurring in preschool-aged children. It is expected that zoster numbers will rise in New Zealand as the population ages.

Prospective nationwide surveillance of varicella in New Zealand children, conducted from November 2011 to October 2013, found that the incidence of varicella-related hospitalisation was 8.3 per 100,000 children per year – although this is likely to be a significant underestimate.<sup>10</sup> Māori and Pacific children were disproportionately affected, with an almost three- and four-fold increase in the relative risk of hospitalisation for varicella or its complications, respectively. Of the hospitalised children, 9 percent required ICU admission and most of them were previously healthy. Almost one-third of hospitalised children had multiple complications from varicella, and those with neurological complications were more likely to have ongoing problems at discharge.

A retrospective survey of admissions to the paediatric intensive care unit at Auckland's Starship Children's Hospital during 2001–2011 found 26 children admitted for varicella or its secondary complications.<sup>11</sup> The main admission reasons were neurological (38.5 percent) and secondary bacterial sepsis or shock (26.9 percent). Four children died (15 percent), three of whom were immunocompromised. A further eight children (31 percent) had ongoing disability at discharge, most having had no prior medical condition.

Based on overseas rates, it is estimated that up to one case of congenital varicella syndrome may be expected in New Zealand each year, although few have been reported.

In 2017, adults (aged 20 years and older) accounted for 25 percent of varicella related hospital admissions;<sup>12</sup> approximately one person per year dies from VZV infection, and most VZV-related deaths occur in adults.<sup>13</sup>

## 24.4 Vaccines

### 24.4.1 Available vaccines

There are two live attenuated monovalent VVs registered (approved for use) and available (marketed) in New Zealand. Two quadrivalent live attenuated MMRV vaccines are registered but not currently available in New Zealand.

## Funded vaccine

### Monovalent VV

Varilrix, (GSK): each 0.5 mL dose contains no less than  $10^{3.3}$  PFU (plaque-forming units) of the varicella virus (VZV Oka strain). Other components include amino acids, lactose monohydrate and polyalcohols (mannitol and sorbitol) and residual neomycin sulphate.

### Other vaccines

Monovalent VV (Varivax, MSD) contains not less than 1,350 PFU of the varicella-zoster virus (Oka/Merck strain). Other components and residuals include sucrose, gelatin, urea, sodium chloride, monosodium L-glutamate, potassium chloride, MRC-5 cells, neomycin and bovine calf serum. This vaccine is not currently available in New Zealand.

Quadrivalent MMRV is not available in New Zealand

- Priorix-Tetra (GSK) contains the Schwarz measles, RIT 4385 mumps, Wistar RA 27/3 rubella and varicella (Oka/Merck VZV) virus strains.
- ProQuad (MSD) contains Enders' attenuated Edmonston (Moraten) measles virus strain, Wistar RA 27/3 rubella virus, Jeryl Lynn mumps virus and live varicella virus vaccines (Oka/Merck VZV)

See also section 12.4.1 for more information about MMR vaccines.

## 24.4.2 Efficacy and effectiveness

Single-dose varicella vaccination programmes have had a dramatic impact on the incidence of VZV infections,<sup>14-16</sup> hospitalisations<sup>3, 4, 17</sup> and serious outcomes,<sup>5</sup> particularly when high coverage rates are achieved. Indirect effects are also apparent. A 2014 systematic review of varicella vaccines found that a single dose of VV is moderately effective for preventing any severity of varicella (approximately 80 percent) in immune-competent individuals, highly effective for preventing moderate-severe disease (approximately 95 percent) and highly effective in preventing severe disease only (approximately 99 percent).<sup>18</sup> However, single-dose programmes are associated with outbreaks even among highly vaccinated groups.<sup>19, 20</sup>

The use of a second dose during outbreaks has been an effective strategy to prevent further cases. Catch-ups for non-immunised groups without a previous history of varicella are also important. There is a significant reduction in breakthrough disease when two doses are given. After a second dose in children the immune response is markedly enhanced, with over 99 percent of children attaining an immune response thought to provide protection, and the geometric mean antibody titre is also significantly increased.

Over a 10-year period the estimated vaccine efficacy of two doses for prevention of any varicella disease is 98 percent (compared to 94 percent for a single dose), with 100 percent efficacy for the prevention of severe varicella. The likelihood of breakthrough varicella is reduced by a factor of 3.3.<sup>21, 22</sup> Because of this data, in 2006 the US authorities recommended a two-dose strategy for varicella prevention, with the first dose at age 12–15 months and the second at age 4–6 years, as for MMR.<sup>19, 21</sup> A Hong Kong study recommended reducing the time between doses, to age 12 months and 18 months, to reduce breakthrough cases and outbreaks in preschools.<sup>23</sup>

The antigenic components of MMRV vaccines are non-inferior compared with simultaneous administration of MMR and VV,<sup>24, 25</sup> for both the first and second doses.

## Herd immunity

In regions where universal varicella vaccination programmes have been implemented, significant declines in varicella cases and hospitalisation have been observed. These programmes also reduce circulating VZV and provide protection through herd immunity for those who are unable to be immunised, such as infants and immunocompromised individuals.

In the US, the annual average age-adjusted mortality rate for varicella was 0.05 per million population during 2008–2011, an 87 percent reduction from the pre-vaccine years.<sup>26</sup> In Canada between 2000 and 2007, a single dose of VV was introduced to the immunisation schedules of different provinces at 12 months of age; most provinces also included catch-ups for susceptible children at preschool or school. An ecological study of varicella-related hospitalisations in Canada between 1990 and 2010 found that hospitalisation rates decreased in all age groups, including infants and those aged 20–39 years.<sup>27</sup> Similar herd effects were seen in Germany, with declines in varicella cases and hospitalisations in infants and adolescents who were not eligible for VV.<sup>28</sup>

## Duration of immunity

Varicella vaccination provides long-term but probably not lifelong immunity against VZV, in contrast to VZV natural infection. The duration of protection after a single dose of vaccine is difficult to study – especially if wild-type varicella continues to circulate liberally in the community, providing natural boosting and prolonging the duration of protection.<sup>18</sup> Many countries that initially introduced a single-dose vaccination programme have subsequently changed to a two-dose programme as the epidemiology of the disease has changed over time.

## 24.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at [www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

VV requires reconstitution with the supplied diluent before administration.

Varilrix is presented as a lyophilised powder for reconstitution with the supplied diluent. The vaccine should be stored in the refrigerator at +2°C to +8°C, although the diluent may be stored at room temperature (to a maximum of 25°C). Reconstituted vaccine should be used immediately, if possible, and discarded if reconstituted vaccine is not used within 90 minutes (1½ hours) at room temperature. Do not freeze reconstituted vaccine.<sup>29</sup>

## 24.4.4 Dosage and administration

The dose of monovalent VV is 0.5 mL, administered by intramuscular or subcutaneous injection in the deltoid area (see section 2.2.3).

### Co-administration with other vaccines

Monovalent VV can be administered concurrently with other vaccines, but in a separate syringe and at a different site. If not administered concurrently, the vaccine must be separated from other live vaccines (eg, MMR, BCG) by at least four weeks.

## 24.5 Recommended immunisation schedule

Recommendations for VV are summarised in Table 24.1 and discussed below.

VV is recommended to be administered with the second MMR dose and Hib-PRP at age 15 months. VV can be used for a second (unfunded) dose or first dose after age 4 years, as appropriate for those not in eligible special groups.

**Table 24.1: Varicella vaccine recommendations and schedule**

**Funded individuals are shown in shaded boxes.** See the Pharmaceutical Schedule ([pharmac.govt.nz](http://pharmac.govt.nz)) for any changes to funding decisions.

<b>Recommended and funded</b>
1 dose of VV for: <ul style="list-style-type: none"><li>• children at age 15 months; or</li><li>• previously unvaccinated children turning 11 years old on or after 1 July 2017 who have not previously had a varicella infection.</li></ul>
2 doses of VV, at least 6 weeks apart, for the following special groups <sup>a</sup> <ul style="list-style-type: none"><li>• non-immune patients:<ul style="list-style-type: none"><li>– with chronic liver disease who may in future be candidates for transplantation<sup>b</sup></li><li>– with deteriorating renal function before transplantation<sup>b,c</sup></li><li>– prior to solid organ transplant</li><li>– prior to any planned immunosuppression<sup>d</sup></li><li>– for post-exposure prophylaxis of immune-competent in-patients</li></ul></li><li>• patients at least 2 years after bone marrow transplantation, on the advice of their specialist</li><li>• patients at least 6 months after completion of chemotherapy, on the advice of their specialist</li><li>• HIV-positive patients who are non-immune to varicella, with mild or moderate immunosuppression, on the advice of an HIV specialist</li><li>• patients with inborn errors of metabolism at risk of major metabolic decompensation, with no clinical history of varicella</li><li>• household contacts of paediatric patients who are immunocompromised or undergoing a procedure leading to immunocompromise, where the household member has no clinical history of varicella</li><li>• household contacts of adult patients who have no clinical history of varicella and who are severely immunocompromised or undergoing a procedure leading to immunocompromise, where the household member has no clinical history of varicella.</li></ul>
<b>Recommended, not funded</b>
1 dose for all susceptible healthy children aged under 13 years who do not meet the eligibility criteria for the funded dose.
2 doses, at least 6 weeks apart, for all susceptible adolescents and adults.
a. See chapter 4 'Immunisation of special groups' for more information.
b. See Table 4.4 for an accelerated immunisation schedule for infants in whom liver or kidney transplant is likely.
c. Check Starship Children's Hospital guidelines for children with chronic kidney disease, dialysis and renal transplant, (available at <a href="http://www.starship.org.nz/guidelines/renal-vaccination-record-for-starship-paediatric-ckd">www.starship.org.nz/guidelines/renal-vaccination-record-for-starship-paediatric-ckd</a> ).
d. Note that immunosuppression due to steroid or other immunosuppressive therapy must be for a treatment period of greater than 28 days.

### 24.5.1 Usual childhood schedule

From 1 July 2020, one dose of VV is funded for children at age 15 months. A second VV dose is not currently funded but may be purchased for those who wish to reduce the risk of breakthrough disease.

A catch-up dose of VV is funded for previously unvaccinated children turning 11 years old on or after 1 July 2017, who have not previously had a varicella infection (as determined by clinical history). This dose aims to protect those who have not become

immune to varicella before adolescence, as disease in adolescents and adults can be more severe.

Regardless of clinical history of varicella, children are recommended to receive one dose of VV at age 15 months (or as part of a catch-up immunisation) due to a risk of misdiagnosis of varicella, particularly in young children with a mild infection. There is no harm to vaccinate if they have previously had varicella. Serology is not routinely suggested.

## 24.5.2 Special groups

Two doses of VV at least six weeks apart, are recommended and funded for the special groups listed in Table 24.1 above from age 9 months.

### Immunocompromised (including immunosuppressed) individuals

The vaccine should not be given to immunocompromised individuals except under the direction and care of a specialist, following a suitable protocol<sup>19</sup> (see section 4.3).

Some clinical trials of the original vaccine formulations were conducted in immunocompromised children (with leukaemia in remission or with HIV infection on antiretroviral treatment). One study found that half the vaccinated children receiving maintenance chemotherapy developed a rash up to one month after vaccination (40 percent of these required acyclovir treatment), compared with 5 percent of those no longer on chemotherapy.<sup>30</sup> Despite this, the study concluded that the vaccine, Varivax, was safe, immunogenic and effective in these children.<sup>30, 31</sup>

Varicella immunisation of children with congenital T-cell immune deficiency syndromes is generally contraindicated, but those with impaired humoral immunity may be immunised (see section 24.6.1 for further contraindications). Seek specialist advice.

### Household contacts of immunocompromised individuals

Immunocompromised individuals are at highest risk of severe varicella and zoster infections.

Where such individuals cannot be vaccinated, it is important to vaccinate the non-immune household members and other close contacts (funded for household contacts) to provide 'ring-fence' protection (see sections 4.2, 4.3 and 24.7.1).

## 24.5.3 Recommended but not funded

A single dose of VV is recommended for susceptible children who do not meet the eligibility criteria for funded vaccine (Table 24.1). A second dose may also be purchased for those who wish to reduce the risk of breakthrough disease.



VV in a two-dose schedule is recommended but not funded for the following groups:<sup>19</sup>

- adults and adolescents who were born and resided in tropical countries, if they have no history of varicella infection
- susceptible adults and adolescents (ie, those who have no prior history of chickenpox)
- susceptible individuals who live or work in environments where transmission of VZV is likely (see Table 4.9 for occupational groups)
- susceptible non-pregnant women of childbearing age
- susceptible international travellers<sup>19</sup>
- health care workers (see below)
- susceptible individuals who have been exposed to varicella (see section 24.8.3).

See section 24.8.1 for information about assessing susceptibility.

### Health care workers

All health care workers should be immunised with VV if they are susceptible to varicella (not funded), particularly those within obstetric, paediatric and neonatal units, and those caring for immunocompromised children and adults. When a health care worker has a good history of prior varicella infection, no blood test is required.<sup>32</sup> If there is not a good history of varicella infection, a blood test to assess susceptibility will be necessary, as many individuals with no clinical history of varicella are immune (see section 24.8).

If a health care worker who has clinical contact with patients develops a rash as a result of the vaccine (around 5 percent), they must be excluded from contact with immunocompromised or other at-risk patients and allocated other duties, or excluded from their place of work, for the duration of the rash.

## 24.5.4 Pregnancy and breastfeeding

Varicella vaccines are contraindicated in pregnant women. Pregnancy should be avoided for at least four weeks after vaccination.<sup>33</sup> The vaccine's safety for the fetus has not yet been demonstrated, although no congenital defects have been described following inadvertent administration to pregnant women.

A pregnant woman in the household is not a contraindication for immunisation of a child, and the vaccine can be administered to non-immune mothers who are breastfeeding.

## 24.6 Contraindications and precautions

See section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

### 24.6.1 Contraindications

Varicella vaccines are contraindicated for the following people:

- individuals with primary or acquired T-cell immune deficiency states – consult the child’s paediatrician for advice<sup>33</sup>
- individuals with blood dyscrasias, leukaemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic systems.
- individuals on high-dose steroids for more than two weeks (ie, children on 2 mg/kg per day or more of prednisone or its equivalent, or 20mg per day if their weight is over 10 kg)
- individuals are receiving or who have recently received chemotherapy (consult with specialist)
- individuals with a family history of congenital or hereditary immunodeficiency, unless the immune competence of the potential vaccine recipient is demonstrated.
- individuals with a history of an anaphylactic reaction to a prior dose of VV or any component of the vaccine, including neomycin and gelatin.
- individuals with active untreated TB
- pregnant women – women should avoid pregnancy for at least four weeks after vaccination<sup>33</sup> (see section 24.5.4).

### 24.6.2 Precautions

There is no need to avoid salicylates before or after receiving VV. People taking long-term salicylate therapy (aspirin) can receive varicella-containing vaccine, if needed. No association has been shown between the vaccine and Reye syndrome. Children on low-dose aspirin following cardiac surgery would be more at risk of thrombosis from stopping their aspirin<sup>34</sup> than from any theoretical risk of Reye syndrome with VV.

If tuberculin testing has to be done, it should be carried out before or simultaneously with vaccination because it has been reported that live viral vaccines may cause a temporary depression (anergy) of tuberculin skin sensitivity.<sup>35</sup> As this anergy may last up to a maximum of six weeks, tuberculin testing should not be performed within that period after vaccination to avoid false negative results.

On the advice of their specialist, VV may be administered to:

- patients at least two years after bone marrow transplantation

- patients at least six months after completion of chemotherapy
- HIV-positive patients who are non-immune to varicella, with mild or moderate immunosuppression.

For suggested intervals between receipt of human normal immunoglobulin or other blood products and VV, see Table A6.1 in Appendix 6.

Antiviral medications with anti-VZV activity, such as acyclovir, valaciclovir and famciclovir, can interfere with the replication of the VZV strain in VV. It is recommended that antiviral medication be stopped at least 24 hours before vaccination and recommenced at least 14 days after vaccination.

## 24.7 Potential responses and AEFIs

### 24.7.1 Potential responses

A 2013 systematic review of varicella vaccines found that mild adverse events were the most frequently reported AEFIs.<sup>36</sup> This includes injection-site reactions such as pain, swelling and redness, which occurred in up to 28 percent of recipients. There was no increased risk of cerebellar ataxia, encephalitis or ischaemic stroke following vaccination. Post-marketing surveillance in the US found the rate of AEFIs to be 30 per 100,000 doses of VV, and the rate of serious AEFIs was less than 4 per 100,000 doses. Fever has been reported in 15 percent of healthy children following VV and 10 percent of adults.<sup>33, 37</sup>

#### Post-VV rash

In approximately 1–3 percent of immunised children, a localised rash develops, and in an additional 3–5 percent a generalised varicella-like rash develops.<sup>33</sup> These rashes typically consist of two to five lesions and may be maculopapular rather than vesicular; lesions usually appear 5–26 days after immunisation. Not all rashes can be attributable to the vaccine;<sup>33</sup> some may be due to exposure to wild-type virus, prior to vaccination.

#### Transmission of vaccine virus to contacts of vaccinated individuals

In healthy vaccine recipients, transmission of vaccine virus to contacts is exceedingly rare, documented in nine immunised people and resulting in 11 secondary cases. The documented risk exists only if the immunised person develops a rash.<sup>33</sup> Err on the side of caution and isolate the vaccine recipient if they are a household contact of an immunocompromised individual and a post-immunisation rash occurs. If an immunocompromised individual inadvertently comes in contact with a vaccine recipient who has a varicella-like rash, the administration of zoster immunoglobulin (ZIG) and/or acyclovir should be considered (see below).<sup>33</sup> Intravenous acyclovir may be required if symptoms develop.

## 24.7.2 AEFIs

### Vaccine virus shingles

The Oka strain of VZV used in the available vaccines can establish latent ganglionic infection in vaccine recipients and later reactivate to produce clinical zoster (shingles). The risk of zoster is lower, and the clinical severity milder, in immunocompetent vaccine recipients than in naturally infected children. A cohort study in children with acute lymphoblastic leukaemia (who have a high rate of zoster in childhood) showed that vaccine recipients had less than one-fifth the zoster rate of their naturally infected counterparts.<sup>30, 38</sup> Some zoster lesions in vaccine recipients have been shown to contain wild-type virus, likely acquired prior to vaccination.<sup>33</sup>

### Febrile seizures with MMRV vaccine

MMRV vaccines are not currently available in New Zealand. Compared with the use of MMR and VV at the same visit, use of MMRV vaccine requires one fewer injection but is associated with a higher risk of fever and febrile seizures 5 to 12 days after the first dose among children aged 12–23 months (approximately one extra febrile seizure for every 2,300–2,600 MMRV vaccine doses).<sup>39</sup>

After the second dose, there are no differences in incidence of fever, rash or febrile seizures among recipients of MMRV vaccine compared with recipients of MMR and VV.<sup>39</sup> There is no evidence of an association with increased febrile seizures when MMRV is given to toddlers as a second dose of MMR.<sup>40</sup> For example, in Australia, the first dose of MMR is given at 12 months and the second dose is given as MMRV at 18 months.

## 24.8 Control measures

At present, VZV is not a notifiable disease in New Zealand.

### 24.8.1 Susceptibility

In general, a positive history of chickenpox can be taken as indicating immunity, provided there has not been an intervening bone marrow transplant or other immunosuppressive therapy. Recall of varicella or characteristic rash is reliable evidence of immunity. In people with no history or recall of the rash, 70–90 percent are found to be immune.<sup>33</sup> Consult with the local laboratory about the availability and interpretation of varicella serology.

## 24.8.2 Post-exposure prophylaxis with zoster immunoglobulin

Zoster immunoglobulin (ZIG) is a high-titre immunoglobulin available from the New Zealand Blood Service for passive immunisation of varicella in high-risk individuals. It is most effective if given within 96 hours after exposure, but may have some efficacy if given up to 10 days post-exposure.<sup>39, 41-43</sup> ZIG should be given intramuscularly.<sup>43</sup> Intravenous immunoglobulin (IVIG) can be given when ZIG is unavailable. For further information, see Starship Child Health guidelines (available at [starship.org.nz/guidelines/zoster-immunoglobulin](http://starship.org.nz/guidelines/zoster-immunoglobulin)).

The decision whether to offer ZIG depends on:<sup>43</sup>

- the likelihood that the exposed person is susceptible to varicella
- the probability that a given exposure to varicella will result in infection
- the likelihood that complications would develop if the person exposed is infected.

**Contact** (exposure) can be classified as follows:<sup>43</sup>

- household contact – infection is very likely to occur in a susceptible individual living with an infected contact
- playmate contact – more than one hour of play indoors with infected individual
- newborn infant contact – when the mother of a newborn infant develops chickenpox (but not shingles) from seven days before to seven days after delivery
- hospital contact – individuals in the same two-bed room or have face-to-face contact for longer than five minutes.

Provided exposure has occurred and susceptibility is likely, **ZIG is recommended for:**

- pregnant non-immune women (see section 24.8.6 below and discuss with an infectious diseases physician)
- newborn infants whose mother had onset of chickenpox (but not shingles) within seven days before or after delivery (see section 24.8.6)
- hospitalised premature infants whose mothers have no history of chickenpox, or who were born at less than 28 weeks' gestation, or with birthweight less than 1,000 g, irrespective of maternal history
- immunocompromised individuals – discuss the use of ZIG with their specialists, as appropriate.

### Dosage of ZIG

ZIG prepared by CSL Behring in Melbourne, derived from human plasma donated in New Zealand, is available in single vials containing 200 IU varicella-zoster antibody. The actual volume in the vial is stated on the label. The recommended dose is based on body weight and is shown in Table 24.2 below. ZIG should be given intramuscularly, not intravenously.<sup>43</sup>

**Table 24.2: Dose of ZIG based on body weight**

Weight of patient (kg)	Dose (IU)	Number of vials
0–10	125	1
10.1–20	250	2
20.1–30	375	2
30.1–40	500	3
over 40	600	3

Source: CSL Behring, 2022. *Zoster Immunoglobulin-VF New Zealand Data Sheet*. URL: [www.nzblood.co.nz/Clinical-information/Transfusion-medicine/Health-professionals-medicine-datasheets/Immunoglobulins](http://www.nzblood.co.nz/Clinical-information/Transfusion-medicine/Health-professionals-medicine-datasheets/Immunoglobulins) (accessed 17 September 2024).

If ZIG is not available, IVIG can be used. The titre of anti-varicella antibody will vary between lots, and the blood transfusion centre haematologist needs to be contacted to confirm the appropriate dose when IVIG is used. Refer to the immunoglobulin preparations section in the **Transfusion Medicine Handbook**.

## 24.8.3 Post-exposure vaccination and outbreak control

VV may be used for post-exposure prophylaxis of susceptible individuals aged 9 months or older, if there are no contraindications to vaccine use<sup>33</sup> – see Table 24.3. Data from the US and Japan from household, hospital and community settings indicates that VV is effective in preventing illness or modifying varicella severity if used within three days, and possibly up to five days, of exposure.

**Table 24.3: Post-exposure varicella vaccination recommendations**

Note: **Funded individuals are shown in the shaded rows below.** See the Pharmaceutical Schedule ([pharmac.govt.nz](http://pharmac.govt.nz)) for any changes to the funding decisions.

	Schedule
Immune-competent hospital in-patients who are susceptible to varicella, from age 9 months <sup>a</sup>	First dose within 3 days of exposure (up to a maximum of 5 days) Second dose at least 6 weeks later
Susceptible individuals aged from 9 months – who are not eligible for age-appropriate funded vaccine <sup>a,b,c</sup>	Give 1 dose within 3 days of exposure (up to a maximum of 5 days) A second dose can be given at least 6 weeks later

- The funded 15-month VV dose can be given from 12 months of age for post-exposure prophylaxis
- VV can be purchased for individuals who are not eligible to receive funded VV, including infants aged 9 months to under 12 months who do not have an eligible condition listed in Table 24.1.
- Children who were under age 12 months when they received VV for post-exposure prophylaxis will still be eligible for the age 15-month dose. Ensure there are at least 6 weeks between doses.

VV may not prevent disease in all cases because some individuals may have been exposed to the same source as the index case.<sup>33</sup> If exposure to varicella does not result in infection, post-exposure vaccination should induce protection against subsequent exposure. If the exposure results in infection, no evidence indicates that administration of VV during the pre-symptomatic or prodromal stage of illness increases the risk for AEFIs. Note that although this method of immunisation may be successful, it is not necessarily reliable. Immunisation before exposure is therefore recommended as the preferred method of preventing outbreaks.

## 24.8.4 In-hospital exposure

In the event of an exposure:

- susceptible staff should be excluded from contact with high-risk patients from day 8 to day 21 after exposure to varicella (or shingles in an immunocompromised patient)
- hospital staff who have no history of chickenpox and who will be in contact with pregnant women or high-risk patients should be tested for varicella zoster antibodies; vaccination is recommended for those who are not immune or whose serostatus cannot be promptly determined.

Two doses of VV are funded for post-exposure prophylaxis of immune-competent in-patients who are susceptible to varicella (see section 24.8.3).

## 24.8.5 Exclusion from school or early childhood education services

Parents/guardians should be advised that:

- infected children should be excluded from early childhood education services or school until fully recovered, or all lesions have crusted. Lesions from mild breakthrough disease in immunised children may not crust but these children should be excluded until no new lesions appear for 24 hours<sup>33</sup>
- immune-deficient children should be excluded from early childhood education services or school until three weeks after the last documented case.

## 24.8.6 Care of pregnant women after exposure

Pregnant women are at higher risk of severe complications from varicella. If an immune-competent pregnant woman with no history of varicella or vaccination is exposed to varicella, it is recommended, where possible, that her varicella antibodies be assessed (Figure 24.1). If there is no evidence of immunity, two possible courses of action are available: either administer ZIG, or await the onset of symptoms and as soon as possible commence the administration of acyclovir, which is effective in this

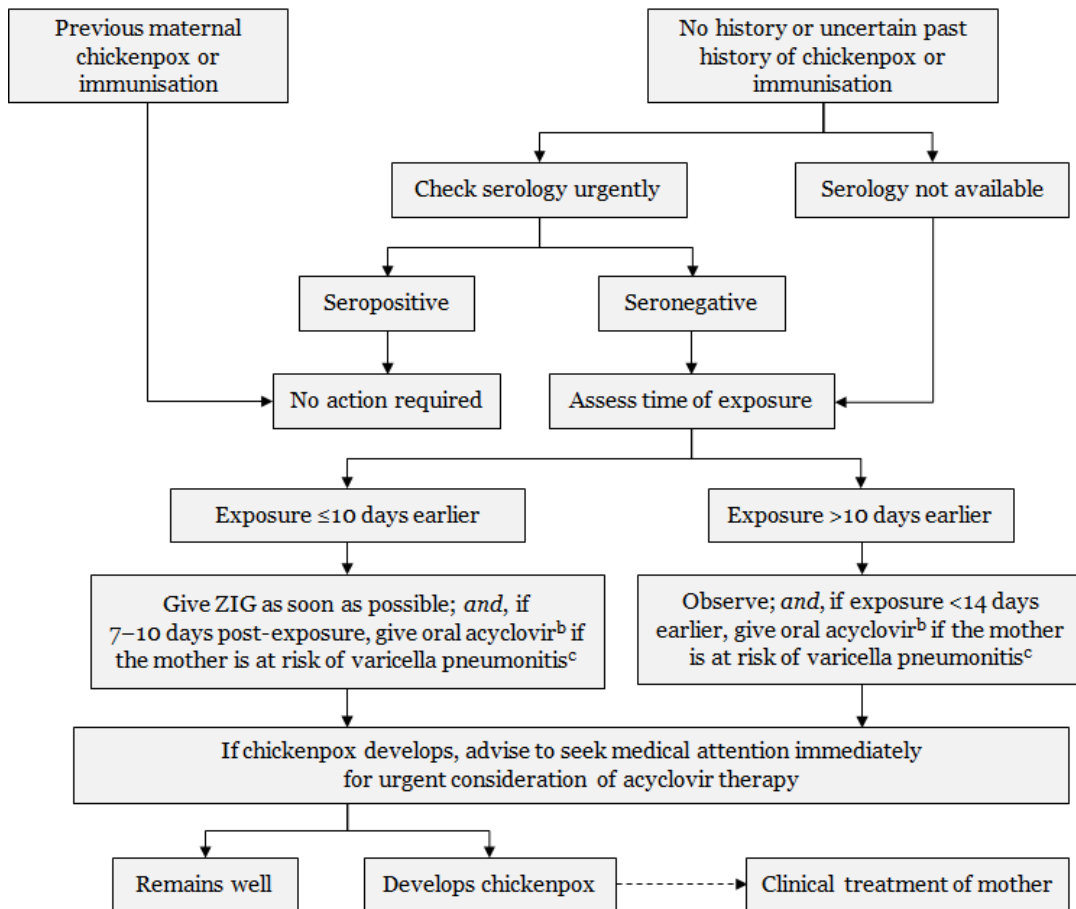


situation and now regarded as safe in pregnancy. Discuss the clinical circumstances with an infectious diseases physician before deciding on which course of action is best.

Intravenous acyclovir is recommended for the pregnant woman with severe complications of varicella. ZIG given to a pregnant woman within five days of delivery may not protect the fetus/neonate: the neonate should receive ZIG on delivery and may need treatment with acyclovir (Figure 24.2).

**Figure 24.1: Management of pregnant women exposed to varicella or zoster**

Every effort should be made to confirm the diagnosis in the suspected positive contact and assess significance of exposure.<sup>a</sup> Exposure or symptoms in the final two weeks of pregnancy should always be discussed with a specialist.



- a. Exposure to varicella or zoster for which ZIG is indicated for susceptible persons includes: living in the same household as a person with active chickenpox or herpes zoster; face-to-face contact with a case of chickenpox for at least 5 minutes; close contact (eg, touching, hugging) with a person with active zoster.
- b. Efficacy of acyclovir for post-exposure prophylaxis has not been tested in controlled trials. Dose is 800 mg orally, 5 times per day for 7 days.
- c. The mother is at risk of pneumonitis if she is in the second half of pregnancy; has underlying lung disease; is immunocompromised; or is a smoker.

Adapted from: Australasian Society for Infectious Diseases. 2014. Varicella zoster virus. In: Palasanthiran P, Starr M, Jones C, et al (eds) *Management of Perinatal Infections*. Sydney: Australasian Society for Infectious Diseases.

Pregnant women exposed to VZV should be counselled about the risks of congenital varicella syndrome (CVS), a rare but devastating disorder that can occur following varicella zoster infection during pregnancy (see Table 24.4). The risk of CVS is greatest in the first 20 weeks of pregnancy. Large case studies suggest that the rate of CVS is 0.4 percent when maternal infection occurs up to week 12 of pregnancy, and 2 percent from weeks 13 to 20.

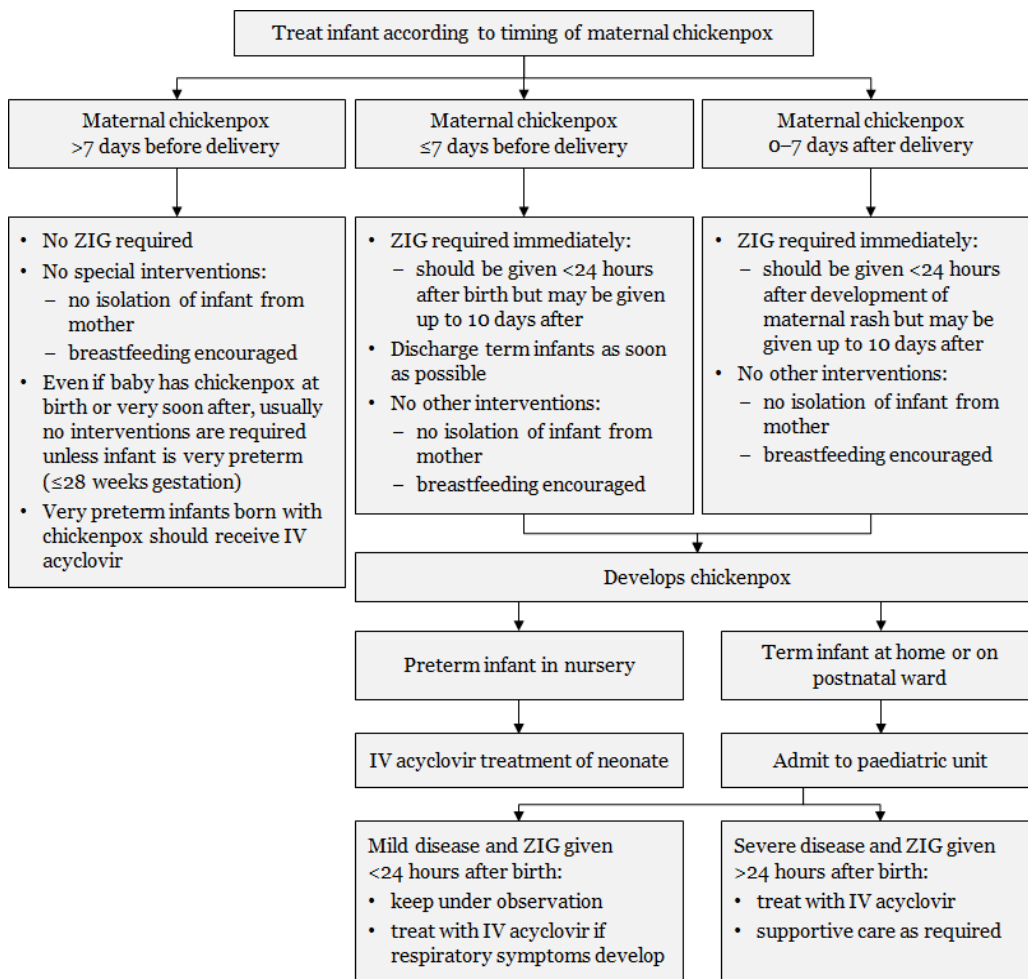
There is no single diagnostic test available for CVS. Regular fetal ultrasound for developmental anomalies is recommended. VZV fetal serology is unhelpful but amniocentesis may be considered; negative VZV PCR may be reassuring.

**Table 24.4: Sequelae of congenital varicella**

Sequelae	Frequency
Skin scars	78%
Eye abnormalities	60%
Limb abnormalities	68%
Prematurity, low birthweight	50%
Cortical atrophy, severe developmental delay	46%
Poor sphincter control	32%
Early death	29%

Adapted from: Australasian Society for Infectious Diseases. 2014. Varicella zoster virus. In: Palasanthiran P, Starr M, Jones C, et al (eds) *Management of Perinatal Infections*. Sydney: Australasian Society for Infectious Diseases.

**Figure 24.2: Management of infants from mothers with perinatal varicella or zoster**



Notes:

- Transplacentally acquired VZV is high risk and severity is reduced by ZIG.
- ZIG is not always effective in preventing severe disease.

Adapted from: Australasian Society for Infectious Diseases. 2014. Varicella zoster virus. In: Palasanthiran P, Starr M, Jones C, et al (eds) *Management of Perinatal Infections*. Sydney: Australasian Society for Infectious Diseases.

## 24.9 Variations from the vaccine data sheet

The VV (Varilrix) data sheet recommends that children aged 9 months to 12 years receive a second dose administered at least six weeks after the first to ensure optimal protection against varicella.<sup>29</sup> Health New Zealand | Te Whatu Ora instead recommends a single dose of VV for healthy children at 15 months or for catch-up at 11 years of age (see section 24.5.1) and two doses for individuals with a special groups condition given 6 weeks apart (see section 24.5.2).

The datasheet that Varilrix is to be administered subcutaneously. Health New Zealand | Te Whatu Ora recommends that parenteral live vaccines on the Schedule (MMR and varicella) be administered via intramuscular (IM) route, unless the patient is on an

anticoagulant or has a bleeding disorder, in which case the preferred route is subcutaneous (SC). There are no immunogenicity concerns when varicella vaccine is given either SC or IM (see section 2.2.3).

Due to an association with Reye syndrome, salicylates and varicella infection, the vaccine manufacturers advised against the use of salicylates for six weeks after VV is given. No association has been seen with Reye syndrome, salicylates and the use of varicella vaccine. Health New Zealand recommends that non-immune individuals receiving long term salicylate therapy can receive VV, if not otherwise contraindicated, as the benefit of the vaccine likely outweighs any theoretical risk.

## References

1. World Health Organization. 2014 *Background paper on varicella vaccine*. SAGE Working Group on Varicella and Herpes Zoster Vaccines. WHO: Geneva. URL: [https://terrance.who.int/mediacentre/data/sage/SAGE\\_Docs\\_Ppt\\_Apr2014/6\\_session\\_varicella\\_herpes\\_zoster/Apr2014\\_session6\\_varicella.pdf](https://terrance.who.int/mediacentre/data/sage/SAGE_Docs_Ppt_Apr2014/6_session_varicella_herpes_zoster/Apr2014_session6_varicella.pdf). (accessed 16 May 2022)
2. Sengupta N, Breuer J. A global perspective of the epidemiology and burden of varicella-zoster virus. *Current Pediatric Reviews*, 2009. 5(4): p. 207-228.
3. Lopez AS, Zhang J, Brown C, Bialek S. Varicella-related hospitalizations in the United States, 2000–2006: the 1-dose varicella vaccination era. *Pediatrics*, 2011. 127(2): p. 238-45.
4. Shah SS, Wood SM, Luan X, Ratner AJ. Decline in varicella-related ambulatory visits and hospitalizations in the United States since routine immunization against varicella. *Pediatric Infectious Disease Journal*, 2010. 29(3): p. 199-204.
5. Khandaker G, Marshall H, Peadar E, et al. Congenital and neonatal varicella: impact of the national varicella vaccination programme in Australia. *Archives of Disease in Childhood*, 2011. 96(5): p. 453-6.
6. Carville KS, Riddell MA, Kelly HA. A decline in varicella but an uncertain impact on zoster following varicella vaccination in Victoria, Australia. *Vaccine*, 2010. 28(13): p. 2532-8.
7. Leung J, Harpaz R, Molinari NA, et al. Herpes zoster incidence among insured persons in the United States, 1993–2006: evaluation of impact of varicella vaccination. *Clinical Infectious Diseases*, 2011. 52(3): p. 332-40.
8. Reynolds MA, Chaves SS, Harpaz R, et al. The impact of the varicella vaccination program on herpes zoster epidemiology in the United States: a review. *Journal of Infectious Diseases*, 2008. 197 Suppl 2(Suppl 2): p. S224-7.
9. Hales CM, Harpaz R, Joesoef MR, Bialek SR. Examination of links between herpes zoster incidence and childhood varicella vaccination. *Annals of Internal Medicine*, 2013. 159(11): p. 739-45.
10. Wen SC, Best E, Walls T, et al. Prospective surveillance of hospitalisations associated with varicella in New Zealand children. *Journal of Paediatrics and Child Health*, 2015. 51(11): p. 1078-83.
11. Wen SC, Miles F, McSharry B, Wilson E. Varicella in a paediatric intensive care unit: 10-year review from Starship Children's Hospital, New Zealand. *Journal of Paediatrics and Child Health*, 2014. 50(4): p. 280-5.
12. Ministry of Health. *Hospital event data and stats*. [updated 28 October 2021]; URL: <https://www.health.govt.nz/nz-health-statistics/health-statistics-and-data-sets/hospital-event-data-and-stats>. (accessed 10 May 2022)

13. Ministry of Health. *Mortality data and stats*. [updated 16 December 2021]; URL: <https://www.health.govt.nz/nz-health-statistics/health-statistics-and-data-sets/mortality-data-and-stats>. (accessed 10 May 2021)
14. Chang LY, Huang LM, Chang IS, Tsai FY. Epidemiological characteristics of varicella from 2000 to 2008 and the impact of nationwide immunization in Taiwan. *BMC Infectious Diseases*, 2011. 11(16 Dec): p. 352.
15. Pozza F, Piovesan C, Russo F, et al. Impact of universal vaccination on the epidemiology of varicella in Veneto, Italy. *Vaccine*, 2011. 29(51): p. 9480-7.
16. Siedler A, Arndt U. Impact of the routine varicella vaccination programme on varicella epidemiology in Germany. *Euro Surveillance*, 2010. 15(13): p. pii=19530.
17. Tan B, Bettinger J, McConnell A, et al. The effect of funded varicella immunization programs on varicella-related hospitalizations in IMPACT centers, Canada, 2000-2008. *Pediatric Infectious Disease Journal*, 2012. 31(9): p. 956-63.
18. World Health Organization. 2014 *Systematic review of available evidence on effectiveness and duration of protection of varicella vaccines*. SAGE Working Group on Varicella and Herpes Zoster Vaccines. Geneva. URL: [http://www.who.int/immunization/sage/meetings/2014/april/presentations\\_background\\_docs/en/](http://www.who.int/immunization/sage/meetings/2014/april/presentations_background_docs/en/). (accessed 3 July 2020)
19. Marin M, Guris D, Chaves SS, et al. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR: Recommendations and Reports*, 2007. 56(RR-4): p. 1-40.
20. Quinn HE, Gidding HF, Marshall HS, et al. Varicella vaccine effectiveness over 10 years in Australia; moderate protection from 1-dose program. *Journal of Infection*, 2019. 78(3): p. 220-225.
21. American Academy of Pediatrics Committee on Infectious Diseases. Prevention of varicella: recommendations for use of varicella vaccines in children, including a recommendation for a routine 2-dose varicella immunization schedule. *Pediatrics*, 2007. 120(1): p. 221-31.
22. Marin M, Meissner HC, Seward JF. Varicella prevention in the United States: a review of successes and challenges. *Pediatrics*, 2008. 122(3): p. e744-51.
23. Chan YD, Edmunds WJ, Chan HL, et al. Varicella vaccine dose depended effectiveness and waning among preschool children in Hong Kong. *Human Vaccines & Immunotherapeutics*, 2019: p. 1-7.
24. Gershon A, Marin M, Seward JF. 2018. Varicella vaccines, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
25. Halperin SA, Ferrera G, Scheifele D, et al. Safety and immunogenicity of a measles-mumps-rubella-varicella vaccine given as a second dose in children up to six years of age. *Vaccine*, 2009. 27(20): p. 2701-6.
26. Leung J, Bialek SR, Marin M. Trends in varicella mortality in the United States: Data from vital statistics and the national surveillance system. *Human Vaccines & Immunotherapeutics*, 2015. 11(3): p. 662-8.
27. Waye A, Jacobs P, Tan B. The impact of the universal infant varicella immunization strategy on Canadian varicella-related hospitalization rates. *Vaccine*, 2013. 31(42): p. 4744-8.
28. Streng A, Grote V, Carr D, et al. Varicella routine vaccination and the effects on varicella epidemiology - results from the Bavarian Varicella Surveillance Project (BaVariPro), 2006-2011. *BMC Infectious Diseases*, 2013. 13: p. 303.
29. GSK, Varilrix New Zealand Data Sheet. 2019.
30. LaRussa P, Steinberg S, Gershon AA. Varicella vaccine for immunocompromised children: results of collaborative studies in the United States and Canada. *Journal of Infectious Diseases*, 1996. 174 Suppl 3(Suppl 3): p. S320-3.

31. Son M, Shapiro ED, LaRussa P, et al. Effectiveness of varicella vaccine in children infected with HIV. *Journal of Infectious Diseases*, 2010. 201(12): p. 1806-10.
32. Holmes CN, Iglar KT, McDowell BJ, Glazier RH. Predictive value of a self-reported history of varicella infection in determining immunity in adults. *CMAJ: Canadian Medical Association Journal*, 2004. 171(10): p. 1195-6.
33. American Academy of Pediatrics. 2018. Varicella-zoster infections. in *Red Book: 2018 Report of the Committee on Infectious Diseases*, Committee on Infectious Diseases, Kimberlin D, Brady M, et al. (eds). URL: <https://redbook.solutions.aap.org/redbook.aspx>. (accessed 3 July 2020)
34. Li JS, Yow E, Berezny KY, et al. Clinical outcomes of palliative surgery including a systemic-to-pulmonary artery shunt in infants with cyanotic congenital heart disease: does aspirin make a difference? *Circulation*, 2007. 116(3): p. 293-7.
35. Brickman HF, Beaudry PH, Marks MI. The timing of tuberculin tests in relation to immunization with live viral vaccines. *Pediatrics*, 1975. 55(3): p. 392-6.
36. World Health Organization. 2013 *Safety of varicella and MMRV vaccines: a systematic review*. SAGE Working Group on Varicella and Herpes Zoster Vaccines. WHO: Geneva. URL: [https://terrace.who.int/mediacentre/data/sage/SAGE\\_Docs\\_Ppt\\_Apr2014/6\\_session\\_varicella\\_herpes\\_zoster/Apr2014\\_session6\\_varicella\\_MMRV\\_safety.pdf](https://terrace.who.int/mediacentre/data/sage/SAGE_Docs_Ppt_Apr2014/6_session_varicella_herpes_zoster/Apr2014_session6_varicella_MMRV_safety.pdf). (accessed 16 May 2022)
37. Australian Technical Advisory Group on Immunisation. 2018. *Australian Immunisation Handbook* (ed.), Canberra: Australian Government Department of Health. URL: <https://immunisationhandbook.health.gov.au/> (accessed October 2019)
38. Weinmann S, Chun C, Schmid DS, et al. Incidence and clinical characteristics of herpes zoster among children in the varicella vaccine era, 2005-2009. *Journal of Infectious Diseases*, 2013. 208(11): p. 1859-68.
39. Marin M, Broder KR, Temte JL, et al. Use of combination measles, mumps, rubella, and varicella vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR: Recommendations and Reports*, 2010. 59(RR-3): p. 1-12.
40. Macartney K, Gidding HF, Trinh L, et al. Evaluation of combination measles-mumps-rubella-varicella vaccine introduction in Australia. *JAMA Pediatr*, 2017. 171(10): p. 992-998.
41. Centers for Disease Control and Prevention. FDA approval of an extended period for administering VariZIG for postexposure prophylaxis of varicella. *Morbidity and Mortality Weekly Report*, 2012. 61(12): p. 212.
42. Centers for Disease Control and Prevention. Updated recommendations for use of VariZIG--United States, 2013. *MMWR: Morbidity and Mortality Weekly Report*, 2013. 62(28): p. 574-6.
43. Starship Child Health. *Zoster Immunoglobulin – Starship Clinical Guidelines*. [updated 22 February 2017 ]; URL: <https://www.starship.org.nz/guidelines/zoster-immunoglobulin/>. (accessed 17 February 2020)



# 25 Zoster (herpes zoster/shingles)

## Key information

Mode of transmission	<p>Zoster is a reactivation of the varicella-zoster virus in someone who has previously had varicella disease (most often as chickenpox).</p> <p>Direct contact with zoster vesicles has a low risk of causing varicella in non-immune individuals – can be prevented by covering the rash.</p> <p>There is potential for aerosol transmission from some immunocompromised cases with viraemia.</p>
Period of communicability	Until lesions have crusted.
Incidence and burden of disease	Increasing incidence with age; lifetime risk about 1 in 3. For those aged over 85 years, the risk is 1 in 2. Complications include post-herpetic neuralgia and herpes zoster ophthalmicus.
Funded vaccine	Recombinant zoster vaccine – rZV; Shingrix
Dose, presentation, route	<ul style="list-style-type: none"> <li>• 0.5 ml per reconstituted dose</li> <li>• vial of vaccine powder and vial of suspension for one dose. The vaccine must be reconstituted prior to injection.</li> <li>• Intramuscular injection only</li> </ul>
Funded vaccine indications and recommended schedule	<p>Two doses of rZV given 2 to 6 months apart.</p> <ul style="list-style-type: none"> <li>• Funded for individuals <b>at</b> age 65 years.</li> <li>• Funded for certain groups at increased risk of zoster due to immunocompromise, from age 18 years and over, including individuals aged 66 years and over.</li> </ul>
Recommended, not funded	<ul style="list-style-type: none"> <li>• for use from age 50 years, including those aged 66 years and older, due to older age and comorbidity</li> <li>• for other individuals aged 18 years or older with increased risk of zoster due to immunocompromise not eligible for funded vaccine.</li> </ul>
Vaccine efficacy/ effectiveness	rZV showed efficacy against both zoster and post herpetic neuralgia of over 90 percent in participants aged over 50 years and over 70 years, including those with comorbidities, maintained at 84 percent for at least 7 years and at 70 percent for up to 10 years.
Contraindications and precautions	For contraindications and precautions see section 25.6.1. Use in pregnancy is limited and not routinely recommended.
Potential responses to vaccine	Injection-site pain, myalgia, headache and fatigue are the most common responses.



## 25.1 Virology

Varicella-zoster virus (VZV) is a DNA virus from the herpesvirus family. The virus is usually acquired in childhood and primary infection with VZV causes varicella disease (chickenpox). Herpes zoster (zoster), or 'shingles', is a clinical syndrome caused reactivation of latent VZV, which resides in the dorsal root or trigeminal nerve ganglia after primary infection. VZV is usually acquired in childhood, but it is often many decades before the virus reactivates, at times when cellular immunity is compromised and is unable to maintain suppression of the virus.

## 25.2 Clinical features

Herpes zoster (shingles) occurs when the cell-mediated immune response is impaired and unable to maintain suppression of latent varicella-zoster virus reactivation (see chapter 24). Zoster occurs only by loss of suppression and reactivation of the patient's own virus – which is often acquired in childhood; it is not acquired from other patients with zoster or varicella.<sup>1</sup>

VZV, present at low levels in lesions of zoster rash, is transmissible via direct contact with fluid in the rash vesicles to VZV-naïve or other susceptible individuals (causing chickenpox). Episodes of zoster in older individuals provide a constant mechanism for reintroducing the virus, causing varicella in non-immune individuals who are in close contact, who then spread the virus to other susceptible individuals. Covering the rash can reduce this risk of transmission.

Zoster presents clinically as a unilateral vesicular rash, which in most cases is in a dermatomal distribution. The dermatomal distribution of the rash is the key diagnostic feature. In 70–80 percent of zoster cases in older adults, prodromal pain and/or itching occurs three to four days before the appearance of the rash.<sup>2</sup> In the majority of patients, zoster is an acute and self-limiting disease, with the rash lasting 10–15 days. However, complications can occur, especially with increasing age.

Although most zoster cases occur in adults aged 40 years or older, it may be seen less commonly in infants and children. In those aged under 2 years may reflect *in utero* chickenpox, with the greatest risk arising following exposure between 25 and 36 weeks' gestation, and reactivation in early life. Infants who get varicella at a young age have a higher chance of having zoster before the age 20 years.

A common complication of zoster is post-herpetic neuralgia (PHN), a chronic, often debilitating pain condition that can last several months or even years. A systematic review of the incidence and complications of zoster found that the risk of developing post-herpetic neuralgia ranges between 5 percent and about 30 percent (depending on the type of study design, age distribution of the study populations and definition).<sup>3</sup> The risk rises with age, and it is uncommon in healthy children and young people.

Herpes zoster ophthalmicus (HZO) is another complication of zoster, which occurs when VZV reactivation affects the ophthalmic branch of the trigeminal nerve. HZO can

occur with or without eye involvement, and can result in prolonged or permanent pain, facial scarring and loss of vision. About 10 percent of zoster patients develop HZO, if that dermatome is affected, and the risk is similar across all age groups.<sup>3</sup>

The incidence of zoster is highest in immunocompromised individuals,<sup>4,5</sup> including:

- following HSCT
- solid organ transplants<sup>6</sup>
- haematological malignancy<sup>7</sup>
- immunomodulatory treatments and immune-mediated inflammatory diseases including treatments for
  - rheumatoid arthritis<sup>8</sup>
  - systemic lupus erythematosus
  - inflammatory bowel disease
  - cancer
- those living with HIV infection.

Up to 10 percent of children treated for a malignant neoplasm may develop zoster. In immunocompromised patients, extensive viraemia in the absence of a vigorous immune response can result in a disseminated form of zoster that includes severe multi-organ disease.<sup>2,9</sup> There is an increased risk of airborne transmission of VZV for immunocompromised individuals with viraemia.

Other factors associated with an increased risk of developing zoster include splenectomy, chronic pancreatitis, chronic kidney disease, chronic inflammatory skin disease,<sup>10</sup> anxiety and depression,<sup>11,12</sup> sleep disorders<sup>13</sup> and type 1 and type 2 diabetes,<sup>14-16</sup> chronic obstructive pulmonary disease and adult asthma.<sup>17</sup> Environmental factors such as exposure to high ambient temperature, UV radiation<sup>18,19</sup> and high altitudes<sup>20</sup> have also been proposed as potential triggers. There is some evidence that a family (sibling or parent) history of zoster is also a potential risk factor in elderly individuals.<sup>21</sup> Incidence of zoster is higher in women than men.<sup>4</sup>

## 25.3 Epidemiology

### 25.3.1 Global burden of disease

Zoster is a sporadic disease occurring as a reactivation of the VZV in individuals who have previously had chickenpox. Approximately one in three people will develop zoster during their lifetime with the incidence rising as cell-mediated immunity to VZV declines with age;<sup>22</sup> 50 percent of those aged 85 years or over will suffer zoster.<sup>23,24</sup> A systematic review documented an incidence rate between 3 and 5 per 1,000 person-years in North America, Europe and Asia-Pacific.<sup>3</sup> The incidence rate was about 6–8 per 1,000 person-years at age 60 years and 8–12 per 1,000 person-years at age 80 years.

Recurrence is greater in females than males (about 7 percent after eight years compared with 4 percent for males), and in those who are immunocompromised. Third

episodes are rare. In those who have zoster at a younger age (45–54 years) the time from the first episode to recurrence is shorter than for those who are aged over 55 years (mean time 2 years [IQR 1.0–2.3] vs 3 years [1.4–4.2], respectively).<sup>25</sup>

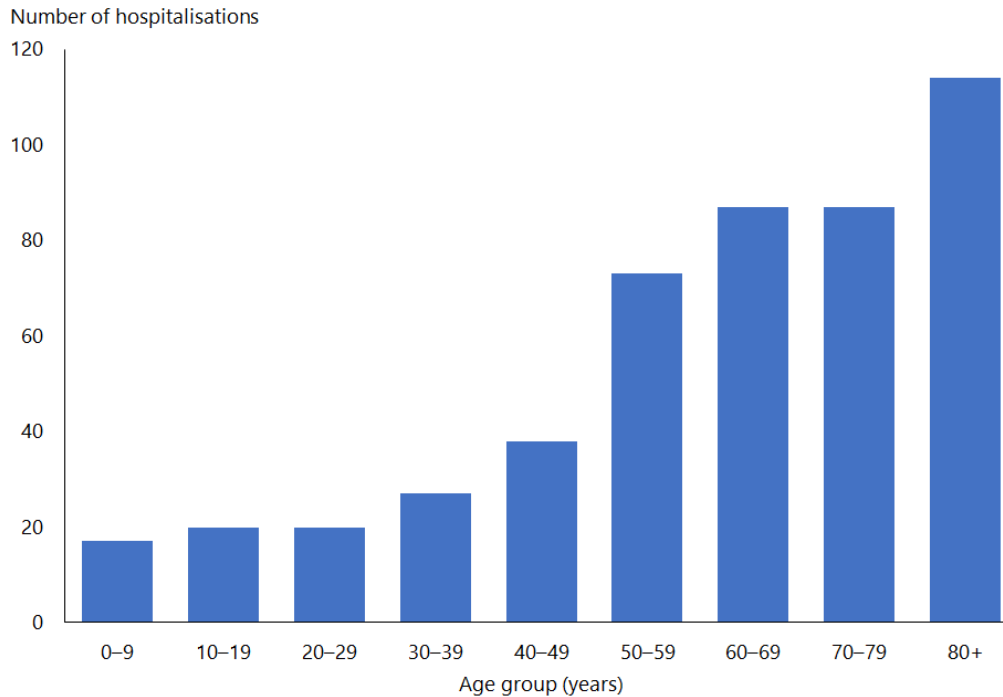
VZV is present in lesions of zoster and is transmissible via direct contact with the vesicles to other susceptible individuals (causing chickenpox). Airborne transmission can occur from immunocompromised individuals with disseminated zoster. Episodes of zoster in older individuals provide a constant mechanism for reintroducing the virus, causing varicella in non-immune individuals who are in close contact, who then spread the virus to other susceptible individuals.

Following the introduction of VV onto the childhood schedule, exposure to wild-type virus decreases. It has been theorised that a lack of boosting may lead to an increase in zoster in older adults. However, several studies that have investigated this issue, observed an increase in zoster prior to VV programme introductions and have been unable to attribute any increase in incidence of zoster to childhood VV programmes.<sup>11, 12, 13, 14</sup> Such increases have been observed in countries both with and without childhood varicella immunisation.

### 25.3.2 New Zealand epidemiology

Zoster hospitalisations by age group during 2018/2019 are shown in Figure 25.1, with around 60 percent occurring in adults aged 60 years and older. Hospitalisations are predicted to account for only a very small proportion of the overall zoster cases as most are managed in primary care. Interrogation of general practice electronic records found the incidence of zoster in New Zealand to be similar (approximately 5 per 100,000 patient-years rising to 12.8 per 100,000 in those aged 80–90 years) to the global incidence estimates described in section 25.3.1.<sup>26</sup> In 2018/2019, there were 483 hospitalisations associated with herpes zoster.

**Figure 25.1: Hospitalisations with herpes zoster as primary diagnosis by age group, 2018/2019**



Source: Ministry of Health.

## 25.4 Vaccine

### 25.4.1 Available vaccines

#### Funded vaccine

The funded vaccine is an adjuvanted recombinant subunit zoster vaccine (Shingrix, GSK) containing recombinant VZV glycoprotein E and a proprietary AS01<sub>B</sub> adjuvant system that is designed to specifically boost T-cell immunity against VZV.<sup>27</sup>

Each 0.5 ml dose contains:

- 50 µg of recombinant VZV glycoprotein E
- AS01<sub>B</sub> liposome-based adjuvant containing two immunostimulants: 50 µg of *Quillaja saponaria* (soapbark tree) saponin fraction 21 (QS-21) with 50 µg detoxified lipopolysaccharide fraction, 3-O-desacyl-4'-monophosphoryl lipid A (MPL), from *Salmonella minnesota*.
- It also contains dioleoylphosphatidylcholine, cholesterol, sodium chloride, dibasic sodium phosphate, monobasic potassium phosphate and water.

#### Historical vaccines

A live attenuated varicella-zoster virus vaccine (Zostavax, MSD) is approved for use from the age of 50 years and used as part of the Schedule at age 65 years from 2018 to August 2022. It is no longer available in New Zealand.

## 25.4.2 Efficacy and effectiveness

### Efficacy in adults aged 50 years and over

Two phase III clinical trials (ZOE-50 and ZOE-70) demonstrated vaccine efficacy of over 90 percent in adults aged from 50 years and aged over 70 years, and those with medical conditions that increase their risk of zoster.<sup>28-32</sup> Pooled data gave vaccine efficacy of 91 percent (95% CI 87–95 percent) against the incidence of zoster overall, and 91 percent (86–98 percent) against post-herpetic neuralgia across all age groups. No decline in efficacy was observed with increasing age; in those aged over 80 years efficacy was 91 percent (80–97 percent) against zoster.<sup>33</sup>

Immunogenicity of rZV was shown to be similar in adults aged 65 or over who have previously received live zoster vaccine compared with those who were live ZV naive. A strong humoral and polyfunctional cell-mediated immune response was shown to persist for at least 1 year after dose 2 of rZV.<sup>34</sup>

Post-hoc analysis, long term follow-up of trial participants found rZV efficacy against zoster plateaued after four to six years and was sustained overall at 84 percent for at least seven years and 70 percent at up to ten years post-vaccination, including in individuals aged 70 years and over and people with pre-existing medical conditions.<sup>29, 33, 35</sup>

### Effectiveness in adults aged 50 years and over

Many of the effectiveness studies of recombinant ZV have been conducted in the US.. A systematic review reported that observational studies have confirmed the high effectiveness of two doses of rZV against zoster (ranging from 70 to 85 percent).<sup>36</sup>

One observational study involving 1.74 million people found the vaccine effectiveness of two doses of rZV against zoster overall was 85.5 percent (95% CI 83.5–87.3 percent), 86.8 percent (84.6–88.7 percent) in those aged 50 to 79 years and 80.3% (75.4–84.3 percent) for those aged 80 years and over. In those who had received live ZV within the previous 5 years, vaccine effectiveness of recombinant ZV was 84.8 percent (75.3–90.7 percent) compared with unvaccinated people. Adjusted effectiveness of two doses rZV against herpes zoster ophthalmicus was 89.1 percent (82.9–93.0 percent).<sup>37</sup>

Another real-world study of Medicare beneficiaries in the US found that administering the second dose beyond six months after the first dose did not impair effectiveness in community-dwelling adults aged over 65 years (approximately 1.5 million participants received one dose and 1.0 million received two doses, compared with 15.6 million unvaccinated controls).<sup>38</sup> One dose was 59.5 percent (57.4–61.4 percent) effective for up to six months and 43.5 percent (37.9–48.7 percent) after six months; whereas, two doses were 70.0 percent (68.4–71.5 percent) effective for up to six months after the second dose, and effectiveness was maintained beyond six months.<sup>38</sup> This study

showed that vaccine effectiveness of two doses was lower for those with immunosuppressive conditions (64.1 percent; 95% CI 57.2-69.8) and those with autoimmune disease (68.0 percent; 95% CI 62.3-72.8) than immunocompetent individuals (70.5 percent; 95% CI 69.0-72.0).<sup>38</sup>

### Severely immunocompromised adults

Good immunogenicity was also shown in younger immunocompromised participants, including those aged from 18 years with solid organ transplants, solid organ tumours, haematopoietic stem cell transplants or living with HIV infection.<sup>39-43</sup> In HSCT recipients, efficacy of 72 percent (39-88%) was shown in those aged 18-49 years and 67 percent (53-78 percent) in those aged 50 or older with 21 months follow-up; in those aged from 18 years with haematological malignancies, efficacy was estimated at 87.2 percent (44.3-98.6 percent) for up to 13 months post vaccination.<sup>40</sup> To date, there is limited data in real-world settings or long term follow-up for those aged 18-49 years with severe immunocompromise.

## 25.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at [www.tewhaturora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhaturora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

The recombinant rZV (Shingrix) must be reconstituted before use with supplied diluent. Once reconstituted, if not used promptly, can be store in a refrigerator (+2°C to +8°C) for up to 6 hours. Do not freeze. Protect from light.

## 25.4.4 Dosage and administration

Two doses of 0.5 ml are administered intramuscularly from two to six months apart.

If a shortened schedule is required, the second dose can be given optimally at two months after the first dose.

Serological testing for previous VZV infection is not necessary prior to administration of this rZV to individuals with immunocompromise.

Individuals who are receiving antiviral medications, such as acyclovir, can be given rZV at any time without discontinuing their treatment. This vaccine does not contain live varicella-zoster virus.

### Co-administration with other vaccines

Recombinant ZV can be co-administered with all the vaccines available on the Schedule, including seasonal influenza vaccine, mRNA-CV, 23PPV and Tdap. It can also be given at any time with the adjuvanted influenza vaccine aQIV (FluAd Quad) or

RSVPreF, preferably in a different limb. When RSVPreF and rZV are given together, mild to moderate reactions, such as injection-site pain and fatigue, can occur more frequently than when given separately due to receiving additional AS01 adjuvant.

## 25.5 Recommended immunisation schedule

**Table 25.1: Herpes zoster vaccine (rZV) recommendations**

Note: Neither history of previous varicella infection nor evidence of prior immunity to VZV is required prior to the routine administration of rZV. **Funded individuals are shown in the shaded row.** See the Pharmaceutical Schedule ([pharmac.govt.nz](http://pharmac.govt.nz)) for any changes to funding decisions.

<b>Recommended and funded</b>
<p>Two doses of recombinant rZV are funded:</p> <ul style="list-style-type: none"> <li>• at age 65 years <sup>a</sup></li> <li>• for those aged 18 years and over, including those aged 66 years and over, with the following immunocompromising conditions: <ul style="list-style-type: none"> <li>– pre- and post-haematopoietic stem cell transplant or cellular therapy</li> <li>– pre- or post-solid organ transplant</li> <li>– haematological malignancies <sup>b</sup></li> <li>– people living with poorly controlled <sup>c</sup> HIV infection</li> <li>– planned or receiving <sup>d</sup> disease-modifying anti-rheumatic drugs (DMARDs – targeted synthetic, biologic, or conventional synthetic) for polymyalgia rheumatica, systemic lupus erythematosus or rheumatoid arthritis</li> <li>– end stage kidney disease (CKD 4 or 5)</li> <li>– primary immunodeficiency.</li> </ul> </li> </ul>
<p><b>For consideration, but not funded</b></p> <p>Two doses of recombinant rZV are recommended but not funded for all individuals aged from 50 years, including those aged over 66 years; and for individuals aged from 18 years who are at increased risk of zoster<sup>5, 6, 44-46</sup> including:</p> <ul style="list-style-type: none"> <li>• prior to planned, receiving <sup>d</sup> or post immunosuppressive therapy <ul style="list-style-type: none"> <li>– including receiving immunomodulatory agents for the treatment of other immune-mediated inflammatory (autoimmune) diseases, such as inflammatory bowel disease, Crohn’s disease, ulcerative colitis and psoriasis</li> <li>– chemotherapy or radiotherapy</li> </ul> </li> <li>• those potentially immunocompromised following cancer treatment</li> <li>• With well-controlled HIV infection.</li> </ul> <p>Other conditions that can increase risk of zoster in older adults include: <sup>10, 12, 14</sup></p> <ul style="list-style-type: none"> <li>• diabetes</li> <li>• chronic obstructive pulmonary disease</li> <li>• chronic inflammatory skin diseases</li> <li>• splenectomy</li> <li>• chronic pancreatitis</li> <li>• psychiatric disorders, including depression and anxiety</li> <li>• sleep disorders.</li> </ul>

a. The second dose is funded at age 66 years if the first dose was given at age 65 years.

b. Including those with a past-history of haematological malignancy who remain immunocompromised



- c. People living with advanced or untreated HIV infection with CD4 counts <350/μL or those with a higher CD4 count not established on effective anti-retroviral therapy (i.e. with a viral load of >500 copies / mL or 2.7 Log<sub>10</sub>)
- d. Ideally, vaccinate prior to planned immunosuppression. If rZV is given during treatment regimen, take timing of treatment and level of immunosuppression into consideration when timing vaccinations. If a shortened schedule is required, the second doses can be given optimally at two months after the first dose.

## 25.5.1 Recommended and funded

Two doses of adjuvanted recombinant zoster vaccine (rZV; Shingrix) are recommended and funded for all adults at the age of 65 years. The second dose continues to be funded for those who turn age 66 years between doses, but not beyond the age of 66 (ie age 67 years and over), unless eligible as below.

RZV is also available for individuals aged 18 years and older at increased risk of zoster, particularly those who are at increased risk of zoster due to comorbidities.<sup>4, 7, 44</sup> Two doses of rZV are funded for individuals aged 18 years and over, including those aged 66 years and over, who are pre and post haematopoietic stem cell transplantation or cellular therapy; due to receive or following solid organ transplant; with haematological malignancies; living with poorly controlled HIV infection; with certain immune-mediated inflammatory disease (autoimmune diseases) receiving disease-modifying immunomodulatory agents (formerly known as DMARDS, biologic, synthetic or conventional); with end-stage chronic kidney disease (CKD-4 or -5); or primary immunodeficiencies (see Table 24.1 for funded groups).

It is recommended to discuss the optimal timing for vaccination with a specialist before the vaccine appointments for those who are severely immunocompromised. Ideally, vaccination should be conducted prior to any planned immunosuppression (see section 4.3.6). If a shortened schedule is required, the second doses can be given optimally at two months after the first dose.

## 25.5.2 Recommended not funded

rZV is approved for use in New Zealand for all individuals aged 50 years or older, including those aged 66 years and over, not eligible to funded vaccine.

It is also available (unfunded) for individuals aged 18 years and older at increased risk of zoster. This particularly includes those with comorbidities,<sup>4, 7, 44</sup> and includes individuals aged 66 years and over who did not receive rZV at age 65 years. These groups include individuals who are immunocompromised due to an existing illness and/or its treatment or prior to planned immunosuppression; those receiving immunomodulatory therapy; or chemotherapy or systemic radiotherapy; or living with well-controlled HIV infection (see Table 24.1 for recommended but not funded groups).

It is recommended to discuss the optimal timing for vaccination with a specialist before the vaccine appointments for those who are severely immunocompromised. Ideally,

vaccination should be conducted prior to any planned immunosuppression (see section 4.3.6). If a shortened schedule is required, the second doses can be given optimally at two months after the first dose.

### 25.5.3 Individuals with a history of zoster (shingles)

Individuals with a history of zoster episodes can be given rZV. It is possible that a history of previous zoster may be inaccurate or a mistaken diagnosis.<sup>44</sup> In addition, the risk of a repeat episode of zoster has been estimated at approximately 5 percent in immunocompetent individuals.<sup>25, 44</sup> The incidence of recurrence is higher in women than men, in people who are immunosuppressed, and in those aged 45–64 years compared with those aged over 65 years at the time of the first episode.<sup>25</sup>

There are no recognised safety concerns in giving zoster vaccines to people with a history of zoster episodes.<sup>47, 48</sup> The length of time following an episode of zoster after which it may be beneficial to vaccinate has not been established.<sup>49</sup> Recombinant ZV is recommended to be given from 12 months after zoster has resolved from which time the rate of recurrence is increased.<sup>25, 49</sup> Caution is required for individuals who have previously experienced ocular complications of zoster, such as herpes zoster ophthalmicus and uveitis, in this case vaccination is not recommended until at least 12 months after the inflammation has completely resolved.

### 25.5.4 Individuals with a history of zoster vaccination

The optimal time for administration of recombinant zoster vaccine following live zoster vaccination (Zostavax) is not yet established.<sup>49</sup> Effectiveness of live zoster vaccine wanes significantly within three to five years of vaccination in adults aged 60 or older.<sup>34</sup> Individuals who previously received live zoster vaccine can receive two doses of recombinant ZV (see Table 24.1 for funded and recommended groups). Spacing of at least 12 months after live zoster vaccine is recommended but timing may be shortened to three months for the use of rZV in individuals who are immunocompromised with an increased risk of zoster recurrence or prior to planned immunosuppression.

## 25.6 Contraindications and precautions

See section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

## 25.6.1 Contraindications

Recombinant rZV (Shingrix) is contraindicated to individuals with a history of hypersensitivity to a previous dose or to any component of the vaccine.

## 25.6.2 Precautions

There is limited data on the use of rZV in human pregnancy however, since it is a non-live vaccine, there are no theoretical safety concerns should it be inadvertently administered during pregnancy.

# 25.7 Potential responses and AEFIs

## 25.7.1 Potential responses

During clinical trials, rZV was generally well tolerated. The most commonly reported responses were injection-site pain, myalgia and fatigue; other responses included headache, shivering, fever and gastrointestinal symptoms. These were mild to moderate and lasting for one to three days post vaccination, with higher incidence in those aged under 70 years than in the older age groups.<sup>31</sup> Adverse events were also more frequently reported in younger age groups (ages 18 to 49 years compared with those aged over 50 years). In clinical studies in those aged 50 years and over, a higher incidence of fever and shivering was reported when rZV was co-administered with 23PPV.<sup>50</sup>

Fever and shivering are reported more frequently when rZV is coadministered with 23PPV than when rZV is given alone.

## 25.7.2 AEFIs

Injection-site reactions (eg redness or swelling) were more common after vaccination with rZV than live ZV according to a meta-analysis of clinical trial data (risk difference of 30 percent; 95% CI 2 to 51 percent). There was no statistical difference between serious adverse events or study withdrawal due to adverse events.<sup>51</sup> No safety concerns in immunocompromised populations were associated with rZV across six clinical trials; most adverse events reported were consistent with the underlying diseases or treatments and similar between vaccinated and placebo controls.<sup>52</sup> A post-market surveillance study in adults aged 65 years or over observed a slightly increased risk of Guillain-Barré syndrome (estimated three excess cases per million doses) during 42 days following vaccination with rZV.<sup>50</sup>

There have been rare reports of flares of pre-existing inflammatory eye disease including uveitis and herpes zoster ophthalmicus following rZV administration.<sup>53, 54</sup> It is recommended to allow at least 12 months after ocular zoster episode had resolved prior to administering rZV.

In a small clinical trial (865 adults aged 50 years and over), fever and shivering were reported more frequently when PPV23 was co-administered with rZV than when rZV was given alone (16 percent and 21 percent versus 7 percent each).<sup>50</sup>

## 25.8 Variations from the vaccine data sheet

None.

### References

1. Gilden D. Efficacy of live zoster vaccine in preventing zoster and postherpetic neuralgia. *Journal of Internal Medicine*, 2011. 269(5): p. 496-506.
2. Gershon A, Marin M, Seward JF. 2018. Varicella vaccines, in *Plotkin's Vaccines (7th edition)*, Plotkin S, Orenstein W, Offit P, and Edwards K (eds). Elsevier: Philadelphia, US.
3. Kawai K, Gebremeskel BG, Acosta CJ. Systematic review of incidence and complications of herpes zoster: towards a global perspective. *BMJ Open*, 2014. 4(6): p. e004833.
4. Kawai K, Yawn BP. Risk factors for herpes zoster: a systematic review and meta-analysis. *Mayo Clinic Proceedings*, 2017. 92(12): p. 1806-1821.
5. Muñoz-Quiles C, López-Lacort M, Díez-Domingo J, Orrico-Sánchez A. Herpes zoster risk and burden of disease in immunocompromised populations: a population-based study using health system integrated databases, 2009-2014. *BMC Infectious Diseases*, 2020. 20(1): p. 905.
6. Kho MML, Roest S, Bovée DM, et al. Herpes zoster in solid organ transplantation: incidence and risk factors. *Frontiers in Immunology*, 2021. 12: p. 645718.
7. Yenikomshian MA, Guignard AP, Haguinet F, et al. The epidemiology of herpes zoster and its complications in Medicare cancer patients. *BMC Infectious Diseases*, 2015. 15: p. 106.
8. Che H, Lukas C, Morel J, Combe B. Risk of herpes/herpes zoster during anti-tumor necrosis factor therapy in patients with rheumatoid arthritis. Systematic review and meta-analysis. *Joint, Bone, Spine: Revue du Rhumatisme*, 2014. 81(3): p. 215-21.
9. Gnann JW, Jr., Whitley RJ. Clinical practice. Herpes zoster. *New England Journal of Medicine*, 2002. 347(5): p. 340-6.
10. Chovatiya R, Silverberg JI. Association of herpes zoster and chronic inflammatory skin disease in US inpatients. *Journal of the American Academy of Dermatology*, 2021. 85(6): p. 1437-1445.
11. Liao CH, Chang CS, Muo CH, Kao CH. High prevalence of herpes zoster in patients with depression. *Journal of Clinical Psychiatry*, 2015. 76(9): p. e1099-104.
12. Choi HG, Kim EJ, Lee YK, Kim M. The risk of herpes zoster virus infection in patients with depression: A longitudinal follow-up study using a national sample cohort. *Medicine (Baltimore)*, 2019. 98(40): p. e17430.

13. Chung WS, Lin HH ,Cheng NC. The incidence and risk of herpes zoster in patients with sleep disorders: a population-based cohort study. *Medicine (Baltimore)*, 2016. 95(11): p. e2195.
14. Huang CT, Lee CY, Sung HY, et al. Association between diabetes mellitus and the risk of herpes zoster: A systematic review and meta-analysis. *Journal of Clinical Endocrinology and Metabolism*, 2022. 107(2): p. 586-597.
15. Lai SW, Liu CS, Kuo YH, et al. The incidence of herpes zoster in patients with diabetes mellitus: A meta-analysis of cohort studies. *Medicine (Baltimore)*, 2021. 100(16): p. e25292.
16. Guignard AP, Greenberg M, Lu C, et al. Risk of herpes zoster among diabetics: a matched cohort study in a US insurance claim database before introduction of vaccination, 1997-2006. *Infection*, 2014. 42(4): p. 729-35.
17. Peng YH, Fang HY, Wu BR, et al. Adult asthma is associated with an increased risk of herpes zoster: A population-based cohort study. *Journal of Asthma*, 2017. 54(3): p. 250-257.
18. Kawai K, VoPham T, Drucker A, et al. Ultraviolet radiation exposure and the risk of herpes zoster in three prospective cohort studies. *Mayo Clinic Proceedings*, 2020. 95(2): p. 283-292.
19. Lai SW, Liao KF, Kuo YH, et al. The impacts of ambient temperature and ultraviolet radiation on the incidence of herpes zoster: An ecological study in Taiwan. *International Journal of Clinical Practice*, 2021. 75(4): p. e13854.
20. Singh GK, Deora MS, Grewal R, et al. Is high altitude a risk factor in development of herpes zoster? *High Altitude Medicine & Biology*, 2018. 19(3): p. 244-248.
21. Tseng HF, Chi M, Hung P, et al. Family history of zoster and risk of developing herpes zoster. *International Journal of Infectious Diseases*, 2018. 66: p. 99-106.
22. Wehrhahn M ,Dwyer D. Herpes zoster: epidemiology, clinical features, treatment and prevention. *Australian Prescriber*, 2012. 35(5): p. 143-7.
23. Brisson M, Edmunds WJ, Law B, et al. Epidemiology of varicella zoster virus infection in Canada and the United Kingdom. *Epidemiology and Infection*, 2001. 127(2): p. 305-14.
24. Schmader K. Herpes zoster in older adults. *Clinical Infectious Diseases*, 2001. 32(10): p. 1481-6.
25. Qian J, Macartney K, Heywood AE, et al. Risk of recurrent herpes zoster in a population-based cohort study of older adults. *Journal of the American Academy of Dermatology*, 2021. 85(3): p. 611-618.
26. Turner NM, MacRae J, Nowlan ML, et al. Quantifying the incidence and burden of herpes zoster in New Zealand general practice: a retrospective cohort study using a natural language processing software inference algorithm. *BMJ Open*, 2018. 8(5): p. e021241.
27. Heineman TC, Cunningham A ,Levin M. Understanding the immunology of Shingrix, a recombinant glycoprotein E adjuvanted herpes zoster vaccine. *Current Opinion in Immunology*, 2019. 59: p. 42-48.
28. Cunningham AL, Lal H, Kovac M, et al. Efficacy of the herpes zoster subunit vaccine in adults 70 years of age or older. *New England Journal of Medicine*, 2016. 375(11): p. 1019-32.
29. Dagnew AF, Rausch D, Hervé C, et al. Efficacy and serious adverse events profile of the adjuvanted recombinant zoster vaccine in adults with pre-existing potential immune-mediated diseases: a pooled post hoc analysis on two parallel randomized trials. *Rheumatology (Oxford, England)*, 2021. 60(3): p. 1226-1233.
30. Oostvogels L, Heineman TC, Johnson RW, et al. Medical conditions at enrollment do not impact efficacy and safety of the adjuvanted recombinant zoster vaccine: a pooled post-hoc analysis of two parallel randomized trials. *Human Vaccines & Immunotherapeutics*, 2019. 15(12): p. 2865-2872.

31. Syed YY. Recombinant zoster vaccine (Shingrix®): a review in herpes zoster. *Drugs and Aging*, 2018. 35(12): p. 1031-1040.
32. Lal H, Cunningham AL, Godeaux O, et al. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. *New England Journal of Medicine*, 2015. 372(22): p. 2087-96.
33. Boutry C, Hastie A, Diez-Domingo J, et al. The adjuvanted recombinant zoster vaccine confers long-term protection against herpes zoster: Interim results of an extension study of the pivotal phase III clinical trials (ZOE-50 and ZOE-70). *Clinical Infectious Diseases*, 2022. 74(8): p. 1459-1467.
34. Dagneu AF, Klein NP, Hervé C, et al. The Adjuvanted Recombinant Zoster Vaccine in Adults Aged ≥65 Years Previously Vaccinated With a Live-Attenuated Herpes Zoster Vaccine. *Journal of Infectious Diseases*, 2021. 224(7): p. 1139-1146.
35. Strezova A, Diez-Domingo J, Al Shawafi K, et al. Long-term Protection Against Herpes Zoster by the Adjuvanted Recombinant Zoster Vaccine: Interim Efficacy, Immunogenicity, and Safety Results up to 10 Years After Initial Vaccination. *Open Forum Infect Dis*, 2022. 9(10): p. ofac485.
36. Zeevaert R, Thiry N, Maertens de Noordhout C, Roberfroid D. Efficacy and safety of the recombinant zoster vaccine: A systematic review and meta-analysis. *Vaccine X*, 2023. 15: p. 100397.
37. Lu A, Sun Y, Porco TC, et al. Effectiveness of the recombinant zoster vaccine for herpes zoster ophthalmicus in the United States. *Ophthalmology*, 2021. 128(12): p. 1699-1707.
38. Izurieta HS, Wu X, Forshee R, et al. Recombinant zoster vaccine (Shingrix): Real-world effectiveness in the first 2 years post-licensure. *Clinical Infectious Diseases*, 2021. 73(6): p. 941-948.
39. Anderson TC, Masters NB, Guo A, et al. Use of recombinant zoster vaccine in immunocompromised adults aged ≥19 years: Recommendations of the Advisory Committee on Immunization Practices - United States, 2022. *MMWR: Morbidity and Mortality Weekly Report*, 2022. 71(3): p. 80-84.
40. Racine E, Gilca V, Amini R, et al. A systematic literature review of the recombinant subunit herpes zoster vaccine use in immunocompromised 18-49 year old patients. *Vaccine*, 2020. 38(40): p. 6205-6214.
41. Berkowitz EM, Moyle G, Stellbrink HJ, et al. Safety and immunogenicity of an adjuvanted herpes zoster subunit candidate vaccine in HIV-infected adults: a phase 1/2a randomized, placebo-controlled study. *Journal of Infectious Diseases*, 2015. 211(8): p. 1279-87.
42. Vink P, Delgado Mingorance I, Maximiano Alonso C, et al. Immunogenicity and safety of the adjuvanted recombinant zoster vaccine in patients with solid tumors, vaccinated before or during chemotherapy: A randomized trial. *Cancer*, 2019. 125(8): p. 1301-1312.
43. Vink P, Ramon Torrell JM, Sanchez Fructuoso A, et al. Immunogenicity and safety of the adjuvanted recombinant zoster vaccine in chronically immunosuppressed adults following renal transplant: A phase 3, randomized clinical trial. *Clinical Infectious Diseases*, 2020. 70(2): p. 181-190.
44. Australian Technical Advisory Group on Immunisation (ATAGI). 2022. Zoster (herpes zoster). in *Australian Immunisation Handbook*. Canberra. URL: <https://immunisationhandbook.health.gov.au/vaccine-preventable-diseases/zoster-herpes-zoster>. (accessed 2 August 2022)
45. Gilbert L, Wang X, Deiss R, et al. Herpes zoster rates continue to decline in people living with human immunodeficiency virus but remain higher than rates reported in the general US population. *Clinical Infectious Diseases*, 2019. 69(1): p. 155-158.



46. Lai SW, Kuo YH, Lin CL, Liao KF. Risk of herpes zoster among patients with predialysis chronic kidney disease in a cohort study in Taiwan. *International Journal of Clinical Practice*, 2020. 74(10): p. e13566.
47. Centers for Disease Control and Prevention. 2018 *Zostavax recommendations*. 2018; URL: <https://www.cdc.gov/vaccines/vpd/shingles/hcp/zostavax/recommendations.html>. (accessed 20 May 2020)
48. Godeaux O, Kovac M, Shu D, et al. Immunogenicity and safety of an adjuvanted herpes zoster subunit candidate vaccine in adults  $\geq 50$  years of age with a prior history of herpes zoster: A phase III, non-randomized, open-label clinical trial. *Human Vaccines & Immunotherapeutics*, 2017. 13(5): p. 1051-1058.
49. ATAGI. 2022 *Statement on the clinical use of zoster vaccines in adults in Australia*. Australian Government Department of Health. URL: <https://www.health.gov.au/resources/publications/statement-on-the-clinical-use-of-zoster-vaccine-in-older-adults-in-australia>. (accessed 2 August 2022)
50. GlaxoSmithKline NZ Ltd. 2022 *New Zealand datasheet: Shingrix*. URL: <https://www.medsafe.govt.nz/profs/datasheet/s/shingrixinj.pdf>. (accessed 3 August 2022)
51. Tricco AC, Zarin W, Cardoso R, et al. Efficacy, effectiveness, and safety of herpes zoster vaccines in adults aged 50 and older: systematic review and network meta-analysis. *BMJ*, 2018. 363: p. k4029.
52. López-Fauqued M, Co-van der Mee M, Bastidas A, et al. Safety profile of the adjuvanted recombinant zoster vaccine in immunocompromised populations: An overview of six trials. *Drug Safety*, 2021. 44(7): p. 811-823.
53. Tavares-Da-Silva F, Co MM, Dessart C, et al. Review of the initial post-marketing safety surveillance for the recombinant zoster vaccine. *Vaccine*, 2020. 38(18): p. 3489-3500.
54. Walia A, Sun Y, Acharya NR. Risk of Herpes Zoster Ophthalmicus Recurrence After Recombinant Zoster Vaccination. *JAMA Ophthalmol*, 2024. 142(3): p. 249-256.



# Appendix 1: The history of immunisation in New Zealand

This appendix details the history of immunisation in New Zealand. Section A1.1 is a summary of when each vaccine was introduced to the National Immunisation Schedule (the Schedule). This summary includes vaccines which were initially introduced as targeted programmes for a defined population and were then added to the Schedule, and those vaccines which were introduced to the Schedule and then changed to targeted programmes. Section A1.2 shows the historical immunisation schedules for New Zealand. Section A1.3 provides detailed information about the history of the Schedule<sup>1-3</sup> – this information was previously contained within the disease chapters of earlier editions of the *Handbook*.

## A1.1 History of the Schedule – summary tables

**Table A1.1: Summary of when each vaccine was introduced to New Zealand**

Vaccine	Year the vaccine was introduced, plus comments
Diphtheria	1926 Became available in New Zealand for selected schools and orphanages.
	1941 Offered routinely to children aged under 7 years. See DTWP for more information.
Tetanus	1940–1955 Tetanus toxoid became available as a voluntary vaccination. See DTWP for more information.
Pertussis	1945 Introduced by the Department of Health – given on request.
	1953 Combined pertussis-diphtheria vaccine became available, although usage was restricted. See DTWP for more information.
BCG	1948 Initially introduced for nurses, then later extended to all adolescents.
	1963 Adolescent BCG programme was discontinued in the South Island. Phased out in the North Island by 1990.
	1976 Neonatal BCG was introduced initially in high-risk districts, and then variably implemented throughout New Zealand.
	1990 Neonatal BCG was given for high-risk groups only. This continues in 2020.
Salk poliomyelitis (IPV)	1956 Became available; initially 8–9-year-olds were targeted, then 5–10-year-olds, then 11–15-year-olds.
	1960 Offered to all those aged 6 months to 21 years.
	2002 IPV replaced OPV on the Schedule, either as IPV or combined with the DTaP vaccine. See Hib for more information.
	2014 IPV became available for (re)vaccination following immunosuppression (see also DTaP).

*Continued overleaf*

Vaccine	Year the vaccine was introduced, plus comments	
DTwP (diphtheria, tetanus, whole-cell pertussis)	1958	DTwP became available and the first Schedule commences.
	1960	DTwP was supplied to medical practitioners free of charge. See Hib for more information.
Sabin poliomyelitis (OPV)	1961	Initially introduced for children aged under 12 months, administered by the Department of Health.
	1962	In April 95% of all school children received 2 doses; in September it was offered to all adults and adolescents (administered by the Department of Health).
	1967	From April GPs were able to administer OPV along with DTwP at ages 3, 4, 5 and 18 months.
	2002	Sabin OPV was replaced by Salk-derived IPV on the Schedule, as DTaP-IPV at ages 6 weeks, 3 and 5 months, and at 4 years, and as IPV at age 11 years. See Hib for more information.
Measles	1969	Introduced for children aged 10 months to 5 years and those aged under 10 years at special risk. Due to adverse reactions, the measles programme was suspended in late 1969 until the Edmonston B strain vaccine became available in February 1970.
	1974	The recommended age changed to age 12 months.
	1981	The recommended age changed to age 12–15 months.
	1990	Measles, mumps and rubella (MMR) vaccine was introduced to the Schedule for all infants at age 12–15 months, replacing monovalent measles vaccine. See MMR for more information.
Rubella	1970	Introduced to the Schedule for all children at age 4 years.
	1979	Low uptake at age 4 years, especially by boys, spurred a change to a vaccination for girls at age 11 years (year 7/form 1).
	1990	MMR was introduced to the Schedule for all infants at age 12–15 months. See MMR for more information.
Hepatitis B	1985	Plasma-derived vaccine was introduced for newborn babies born to HBeAg-positive mothers.
	1987	Extended to newborns of HBsAg-positive mothers and newborns in high-risk districts (eg, Northland, South Auckland, Rotorua, Napier, Gisborne).
	1988	In February 1988 it was introduced to the Schedule for all infants (catch-up programmes for preschoolers are implemented during 1988).
	1989	In December 1989 recombinant HepB replaced the plasma-derived vaccine.
	1990	Funded hepatitis B immunisation was extended to all children aged under 16 years (catch-up school programmes were also implemented).
	1996	The third HepB dose was brought forward from 12–15 months to age 5 months. See Hib for more information.
	2014	HepB vaccine became available to individuals at high risk of hepatitis B or its complications (see also DTaP).
	2015	Funding extended to include other high-risk conditions.

*Continued overleaf*

Vaccine	Year the vaccine was introduced, plus comments	
Measles, mumps and rubella (MMR)	1990	Introduced to the Schedule for all infants at age 12–15 months.
	1992	A second dose was introduced for 11-year-old (school year 7/form 1) boys and girls.
	2001	The second dose of MMR was changed from age 11 years to age 4 years. A school-based catch-up programme was offered for all 5–10-year-olds.
	2014	The 2-dose schedule at ages 15 months and 4 years continues. MMR became available for (re)vaccination following immunosuppression.
	2020	In October 2020, the recommended age for MMR dose one changed to 12 months with dose 2 recommended at 15 months.
<i>Haemophilus influenzae</i> type b (Hib-PRP)	1994	Hib-PRP vaccine was introduced to the Schedule as DTwPH (replacing DTwP) at ages 6 weeks, 3 months and 5 months, and as monovalent Hib at age 18 months. All children aged under 5 years were offered vaccination against Hib.
	1996	Given as DTwPH at ages 6 weeks, 3 months and 5 months, with a booster at age 15 months.
	2000	Given as Hib-HepB at ages 6 weeks and 3 months, and as DTaP/Hib at age 15 months.
	2006	Given as Hib-HepB at ages 6 weeks and 3 months, and as monovalent Hib at age 15 months. Monovalent Hib-PRP became available to older children and adults pre- or post-splenectomy.
	2008	Given as DTaP-IPV-HepB/Hib at ages 6 weeks, 3 months and 5 months, and as monovalent Hib-PRP at age 15 months. This schedule continues in 2020.
	2014	Monovalent Hib-PRP became available for additional high-risk conditions (see also DTaP).
Td (Tetanus-diphtheria)	1994	Introduced to the Schedule, replacing tetanus toxoid. See Tdap for more information.
	2002	Adult Td boosters are introduced at ages 45 and 65 years.
	2014	Td became available for (re)vaccination following immunosuppression.
	2020	Adult Td replaced with Tdap at ages 45 years (if not had previously had 4 doses of Td) and 65 years.
Influenza	1997	Introduced to the Schedule for adults aged 65 years and older.
	1999	Introduced to the Schedule for those aged under 65 years with certain medical conditions.
	2010	Pregnant women became eligible to receive the funded vaccine.
	2013	Children aged under 5 years who have been hospitalised for respiratory illness or have a history of significant respiratory illness became eligible to receive the funded vaccine.
	2015	Funding extended to include other high-risk conditions.
	2023	For 2023 only, influenza vaccine was funded for all children age 6 months to 12 years and for adults aged 55 years and over with Māori and Pacific ethnicity.
Acellular pertussis (DTaP)	1999	Introduced for infants/children aged under 7 years who have a previous reaction to the whole-cell pertussis in DTwPH.
	2000	In August, DTaP was introduced for all infants to replace whole cell pertussis vaccine at ages 6 weeks, 3 months and 5 months (see also Hib).
	2014	DTaP-IPV-HepB/Hib and DTaP-IPV became available for (re)vaccination of children with certain high-risk conditions.

*Continued overleaf*

Vaccine	Year the vaccine was introduced, plus comments	
Meningococcal B (MeNZB)	2004–2008	MeNZB was used as an epidemic control vaccine between 2004 and 2008. It was offered in a three-dose schedule to all aged under 20 years. The vaccination programme ceased in 2008 following a decline in the incidence of group B disease and because the immune response to the vaccine was short-lived. The vaccine remained available until March 2011 for some high-risk individuals. (See the 2011 edition of the <i>Handbook</i> for more information.)
MenACWY	2014	Funded for eligible high-risk groups from 1 July 2014
MenB	2021	Funded for eligible high-risk groups from 1 July 2021
	2023	Introduced to the Schedule at ages 3, 5 and 12 months (alternative 2, 4 and 12 months) 1 March 2023. Catch up for those aged 12–59 months
Adult-dose acellular pertussis (Tdap)	2006	Introduced to the Schedule at age 11 years, combined with IPV as Tdap-IPV, but changed to Tdap only in 2008. This schedule continues in 2017.
	2013	Pregnant women from 28 to 38 weeks' gestation became eligible for the funded vaccine (under the outbreak policy).
	2014	Tdap became available for (re)vaccination of children following immunosuppression.
	2015	Tdap became available for (re)vaccination of patients with certain high-risk conditions. Pregnant women from 28 to 38 weeks' gestation become eligible for the funded vaccine for every pregnancy.
	2019	Tdap eligibility for pregnant women extended to include when given in second or third trimester every pregnancy. It is recommended to be given from 16 weeks' gestation of every pregnancy, preferably in the second trimester.
	2020	Adult Td replaced with Tdap at ages 45 years (if the individual had not previously had 4 doses of tetanus vaccine) and 65 years.
Pneumococcal conjugate vaccine (PCV)	2006	Introduced as PCV7 for high-risk children.
	2008	Introduced to the Schedule in June as PCV7 at ages 6 weeks, 3 months, 5 months and 15 months.
	2011	PCV10 replaced PCV7 on the Schedule. PCV13 replaced PCV7 for high-risk children.
	2014	PCV13 replaced PCV10 on the Schedule.
	2015	PCV13 became available for patients of any age with certain high-risk conditions.
	2017	PCV10 replaced PCV13 on the Schedule. PCV13 continues for high-risk individuals.
	2020	PCV10 recommended as a 2-dose primary schedule plus booster dose given at 6 weeks, 5 months and 12 months. PCV13 remained at 3-dose schedule plus booster for high-risk infants (ie given at ages 6 weeks, 3, 5 and 12 months)
	2022	PCV13 replaced PCV10 on the Schedule in a 2-dose primary plus booster in December. An additional 3-month dose continued for high-risk infants.

*Continued overleaf*

Human papillomavirus vaccine (HPV)	2008	HPV4 was introduced to the Schedule at age 12 years, for females only. There was a catch-up programme for females born from 1990.
	2013	HPV4 was made available in hospitals for transplant patients, and for boys and men under 26 years with confirmed HIV infection.
	2014	Lower age limit for vaccine eligibility changed to age 9 years. Routine immunisation continued for girls aged 12 years, plus a targeted programme for high-risk individuals. Individuals aged under 26 years with HIV infection became eligible for HPV4.
	2015	Funding extended to include other high-risk conditions.
	2017	Funding extended to include all males and females aged 26 years and under. HPV9 replaced HPV4.
Rotavirus	2014	RV5 vaccine was introduced to the Schedule at ages 6 weeks, 3 months and 5 months.
	2017	RV1 replaced RV5, at ages 6 weeks and 3 months.
Varicella (VV)	2014	Two doses of VV were introduced for high-risk individuals.
	2017	One dose of VV was introduced onto the Schedule for children at age 15 months (born on or after 1 April 2016), with a catch-up for previously unvaccinated children turning 11 years old on or after 1 July 2017 who have not previously had a varicella infection.
Herpes zoster (ZV)	2018	From 1 April, ZV was introduced onto the Schedule as a single dose for adults aged 65 years, with a catch-up programme for adults aged 66–80 years inclusive (until 31 December 2021).
	2022	Recombinant ZV (rZV) replaced live ZV on the Schedule at age 65 years.
	2024	rZV funded from 18 years for certain special groups.
COVID-19 vaccines (mRNA-CV, ChAd-CV, rCV)	2021	Available to all in New Zealand from February 2021, mRNA-CV was initially given as part of a prioritised rollout from age 16 years. Age groups widened to 12–17 years from September 2021, 5–11 year-olds in January 2022 and for certain groups ages 6 months – 4 years in February 2023. Alternative vaccines were available: ChAd-CV from age 18 years from December 2021 to September 2022; and rCV from age 18 years in March 2022 and then from age 12 years in September 2022. Additional doses and booster doses, including a bivalent mRNA-CV and Omicron XBB.1.5 mRNA-CV were introduced in stages according to the COVID-19 vaccination programme.

## A1.2 Previous national immunisation schedules

**Table A1.2: March 2023 immunisation schedule**

	DTaP-IPV- HepB/Hib	PCV 13	RV1	MenB	Hib- PRP	MMR	VV	DTaP- IPV	Tdap	HPV9	Influenza	rZV
Pregnancy									•		•	
6 weeks	•	•	•									
3 months	•		•	• <sup>a</sup>								
5 months	•	•		• <sup>a</sup>								
12 months		•		•		•						
15 months					•	•	•					
4 years								•				
11 or 12 years									•	•		
45 years									•			
65 years									•		•	•

a. Alternative MenB schedule approved at age 8 weeks and 4 months.

**Table A1.3: October 2020 immunisation schedule**

	DTaP-IPV- HepB/Hib	PCV10	RV1	Hib- PRP	MMR	VV	DTaP- IPV	Tdap	HPV9	Influenza	ZV
Pregnancy								•		•	
6 weeks	•	•	•								
3 months	•		•								
5 months	•	•									
12 months		•			•						
15 months				•	•	•					
4 years							•				
11 or 12 years								•	•		
45 years								•			
65 years								•		•	•

**Table A1.4: April 2018 immunisation schedule**

	DTaP-IPV- HepB/Hib	PCV10	RV1	Hib- PRP	MMR	VV	DTaP- IPV	Tdap	HPV9	Td	Influenza	ZV
Pregnancy								•			•	
6 weeks	•	•	•									
3 months	•	•	•									
5 months	•	•										
15 months		•		•	•	•						
4 years					•		•					
11 or 12 years								•	•			
45 years										•		
65 years										•	•	•

**Table A1.5: July 2017 immunisation schedule**

	DTaP-IPV- HepB/Hib	PCV10	RV1	Hib- PRP	MMR	VV	DTaP- IPV	Tdap	HPV9	Td	Influenza
Pregnancy								•			•
6 weeks	•	•	•								
3 months	•	•	•								
5 months	•	•									
15 months		•		•	•	•					
4 years					•		•				
11 or 12 years								•	•		
45 years										•	
65 years										•	•

**Table A1.6: July 2014 immunisation schedule**

	DTaP-IPV- HepB/Hib	PCV13	RV5	Hib- PRP	MMR	DTaP- IPV	Tdap	HPV4	Td	Influenza
6 weeks	•	•	•							
3 months	•	•	•							
5 months	•	•	•							
15 months		•		•	•					
4 years					•	•				
11 years							•			
12 years (girls only)								• ×3 doses		
45 years									•	
65 years									•	•



**Table A1.7: July 2011 immunisation schedule**

	DTaP-IPV- HepB/Hib	PCV10	Hib-PRP	MMR	DTaP- IPV	Tdap	HPV4	Td	Influenza
6 weeks	•	•							
3 months	•	•							
5 months	•	•							
15 months		•	•	•					
4 years				•	•				
11 years						•			
12 years (girls only)							• × 3 doses		
45 years								•	
65 years								•	•

**Table A1.8: June 2008 immunisation schedule**

	DTaP-IPV- HepB/Hib	PCV7	Hib- PRP	MMR	DTaP- IPV	Tdap	HPV4	Td	Influenza
6 weeks	•	•							
3 months	•	•							
5 months	•	•							
15 months		•	•	•					
4 years				•	•				
11 years						•			
12 years (girls only)							• × 3 doses		
45 years								•	
65 years								•	•

**Table A1.9: February 2006 immunisation schedule**

	DTaP-IPV	Hib-HepB	Hib-PRP	Tdap-IPV	MMR	MeNZB	Td	Influenza
6 weeks	•	•				•		
3 months	•	•				•		
5 months	•	•				•		
10 months						•		
15 months			•		•			
4 years	•				•			
11 years				•				
45 years							•	
65 years							•	•

**Table A1.10: February 2002 immunisation schedule**

	DTaP-IPV	Hib-HepB	HepB	DTaP/Hib	Polio (IPV)	MMR	Td	Influenza
6 weeks	•	•						
3 months	•	•						
5 months	•		•					
15 months				•		•		
4 years	•					•		
11 years					• <sup>a</sup>		•	
45 years							• <sup>b</sup>	
65 years							• <sup>b</sup>	•

a. For those children who had not received a fourth dose of polio vaccine.

b. With the introduction of Td at ages 45 and 65 years, 10-yearly boosters were no longer recommended.

**Table A1.11: January 2001 immunisation schedule**

	DTaP	Hib-HepB	HepB	DTaP/Hib	Polio (OPV)	MMR	Td	Influenza
6 weeks	•	•			•			
3 months	•	•			•			
5 months	•		•		•			
15 months				•		•		
4–5 years					•	• <sup>a</sup>		
11 years					• <sup>b</sup>		•	
65 years								•

a. MMR was also offered to children aged 5–10 years in a school catch-up programme.

b. For those children who had not received a fourth dose of polio vaccine.

**Table A1.12: August 2000 immunisation schedule**

	DTaP	Hib-HepB	HepB	DTaP/Hib	Polio (OPV)	MMR	Td	Influenza*
6 weeks	•	•			•			
3 months	•	•			•			
5 months	•		•		•			
15 months				•		•		
11 years					•	•	•	
65 years								•

\* Influenza vaccine was introduced for adults aged 65 years and older in 1997 and in 1999 for individuals aged 6 months and older at increased risk of influenza complications.

**Table A1.13: 1996 immunisation schedule**

	DTwPH	HepB	Polio (OPV)	MMR	Td
6 weeks	•	•	•		
3 months	•	•	•		
5 months	•	•	•		
15 months	•			•	
11 years			•	•	•

**Table A1.14: 1994 immunisation schedule**

	DTwPH	HepB <sup>a</sup>	Polio (OPV)	MMR <sup>b</sup>	DT	Hib	Td
6 weeks	•	•					
3 months	•	•	•				
5 months	•		•				
12–15 months		•		•			
18 months			•		•	• <sup>c</sup>	
5 years			•				
11 years				•			
15 years							• <sup>d</sup>

- Hepatitis B was introduced for all neonates, with catch-up for children aged under 5 years in 1988. In 1990 free immunisation was extended to all children aged under 16 years.
- MMR was introduced at 12–15 months in 1990 and at age 11 years in 1992.
- A single dose of Hib was also offered to all children aged under 5 years.
- 10-yearly boosters of Td were recommended.

**Table A1.15: 1984 immunisation schedule**

	DTwP	Polio (OPV)	Measles	DT	Rubella	Tetanus
6 weeks	•					
3 months	•	•				
5 months	•	•				
12–15 months			• <sup>*</sup>			
18 months		•		•		
5 years		•				
11 years (girls only)					•	
15 years						•

- \* Measles vaccine administered at age 12 months was changed to age 12–15 months in 1981.

**Table A1.16: 1980 immunisation schedule**

	DTwP	Polio (OPV)	Measles	DT	Rubella	Tetanus
3 months	•	•				
5 months	•	•				
12 months			• <sup>a</sup>			
18 months		•		•		
5 years		•				
11 years (girls only)					• <sup>b</sup>	
15 years						•

a. Measles vaccine administered at age 10 months was changed to age 12 months in 1974.

b. Rubella vaccine was introduced in 1979.

**Table A1.17: 1971 immunisation schedule**

	DTwP	Polio	Measles	DT	Rubella	Tetanus
3 months	•	•				
5 months	•	•				
10 months			• <sup>a</sup>			
18 months		•		•		
4 years					• <sup>b</sup>	
5 years				•		
15 years						•

a. Measles vaccine was introduced in 1969 for children aged 10 months to 5 years who had not had measles, and for those aged under 10 years at special risk.

b. Rubella vaccine was introduced in 1970 for children at age 4 years, along with a school-based programme for children aged 5–9 years.

**Table A1.18: 1967 immunisation schedule**

	DTwP	Polio <sup>a</sup>	DT
3 months	•	•	
4 months	•	•	
5 months	•	•	
18 months		•	• <sup>b</sup>
5 years			•

a. Between 1961 and 1967 polio vaccine was administered by the Department of Health.

b. The DT booster at age 18 months was introduced in 1964.

**Table A1.19: 1961 immunisation schedule**

	DTwP	DT
3 months	•	
4 months	•	
5 months	•	
5 years		•

## A1.3 History of the Schedule: background information

Note that the following information describes the vaccines which have been, or currently are, on the National Immunisation Schedule. Vaccines which are used for targeted programmes only (ie, hepatitis A, meningococcal) are not discussed. Information about the Meningococcal B Immunisation Programme (an epidemic programme between 2004–2006) can be found in earlier editions of the *Handbook*.

### A1.3.1 Diphtheria-containing vaccines

During the 1920s the Department of Health, at the instigation of individual school medical officers or medical officers of health, began delivering diphtheria immunisations in a few selected schools and orphanages, but there was no national policy. By 1941 diphtheria immunisation was offered routinely to children aged under 7 years through the School Medical Service and the Plunket Society.

From 1960 the Department of Health programme was delivered by GPs using three doses of non-adsorbed triple vaccine (diphtheria, tetanus and whole-cell pertussis vaccine, DTwP) at ages 3, 4 and 5 months, and a dose of double (diphtheria and tetanus, DT) vaccine before school entry at age 5 years. (For the history of the Schedule's diphtheria toxoid-containing vaccine history after 1960, see A1.3.14 'Tetanus-containing vaccines').

### A1.3.2 Hib-containing vaccines

*Haemophilus influenzae* type b (Hib) vaccine was added to the Schedule in January 1994, which meant that diphtheria, tetanus, whole-cell pertussis and Hib (DTwPH) vaccine replaced the diphtheria, tetanus and whole-cell pertussis (DTwP) vaccine given at ages 6 weeks, 3 months and 5 months. A monovalent Hib vaccine was given at age 18 months, and a catch-up programme of a single dose of monovalent Hib vaccine was recommended for all children aged under 5 years (ie, those born from January 1989).

From February 1996 the fourth dose was changed to age 15 months and given as DTwPH to reduce the two immunisation events in the second year to one at age 15 months.

DTwPH led to a more than 90 percent reduction in the number of invasive Hib cases in those aged under 5 years but resulted in an increase in the percentage of Hib cases occurring in those aged under 6 months, some of whom had received age-appropriate vaccination. When a supply issue resulted in a change of vaccine in 2000, the opportunity was taken to change to PRP-OMP (polyribosylribitol phosphate outer membrane protein, as Comvax, Hib-HepB combination), which offers substantial protection after a single dose.

This vaccine was used until 2008, when a hexavalent vaccine containing PRP-T Hib component was introduced. This vaccine induces a minimal first-dose response, with some protection after the second dose. It was acknowledged that there was a risk that the change would result in an increase in cases aged under 6 months, but this risk was outweighed by the benefit of reducing the number of injections at each of the first three visits and the reduction in IPD with the introduction of pneumococcal conjugate vaccine (PCV7).

The Hib component of Infanrix-hexa, PRP-T, requires a primary course of three doses with a booster dose at age 15 months, though some protection is induced after the second dose.

In 2006, Hib-PRP was funded for older children and adults pre- or post-splenectomy. In 2014 funding was extended to include other high-risk conditions.

### A1.3.3 Hepatitis B-containing vaccines

HepB was added to the Schedule gradually, starting in September 1985, when it was offered to newborn babies of HBeAg-positive mothers. Three 10 µg doses of plasma-derived vaccine were given, as recommended by the manufacturer. In March, 1987 the immunisation programme was extended to newborns of all HBsAg-positive mothers and to children born in certain high-risk districts (Northland, Takapuna, Auckland, South Auckland, Rotorua, Napier and Gisborne).

In 1988 a universal infant vaccination programme was introduced using four low doses (2 µg) of the plasma-derived vaccine H-B-Vax. A catch-up campaign for all preschoolers was undertaken in 1989, and household and sexual contacts of HBsAg-positive women identified during antenatal screening were also entitled to free immunisation.

In December 1988 H-B-Vax was replaced by a recombinant vaccine, Engerix-B. This was given at the manufacturer's recommended dose (10 µg) at 6 weeks, 3 months and 15 months of age. Babies of carrier mothers also received a dose of vaccine, plus HBIG at birth. From February 1990 free hepatitis B immunisation was extended to all children aged under 16 years.

In February 1996 the third dose of HepB was brought forward from 15 to 5 months of age to give early protection to infants and to complete the HepB schedule in the first year of life, in the expectation that this would improve vaccine uptake. This schedule continues in 2020, with 10 µg given at ages 6 weeks, 3 months and 5 months as

DTaP-IPV-HepB/Hib (Infanrix-hexa). For infants born to HBsAg-positive mothers, an additional dose of HepB plus HBIG is given at birth.

In 2014, HepB was made available to individuals at high risk of hepatitis B disease or its complications. In 2015, funding was extended to include other high-risk conditions.

### A1.3.4 HPV vaccines

Human papillomavirus (HPV) vaccination, using Gardasil, a quadrivalent vaccine containing virus-like particles (VLPs) derived from HPV types 16, 18, 6 and 11 (HPV4), began in New Zealand on 1 September 2008 and was initially offered only to females born in 1990 and 1991. In 2009 the programme was extended to females born from 1992 onwards. In 2009 and 2010, HPV immunisation was offered through most participating schools to females in school years 8–13.

From 2011 the HPV immunisation was only offered in participating schools to females in school year 8. HPV immunisation was also available through family doctors, local health centres and most Family Planning clinics for females who did not attend a participating school or who did not want to have it at school. In 2013 HPV vaccine was funded (for delivery in hospitals only) for other groups at risk of HPV-related disease; from 2014, high-risk groups have also been able to access HPV vaccine in primary care. In 2015, funding was extended to include other high-risk conditions.

Males became eligible for HPV vaccine in 2017, with funding extended to include all males and females aged 26 years and under. The nine-valent HPV vaccine (HPV9, Gardasil 9) replaced HPV4, and a two-dose schedule was recommended for immunocompetent children aged 9–14 years.

### A1.3.5 Influenza vaccines

Funded influenza immunisation was introduced in 1997 for people aged 65 years and older. From 1999 the vaccine became funded for younger people (aged from 6 months to 64 years) who were at increased risk of influenza complications. In 2010 funded vaccine was extended to pregnant women, and in 2013 to children aged under 5 years who have been hospitalised for respiratory illness or have a history of significant respiratory illness. In 2015, funding was extended to include other high-risk conditions. In 2018, quadrivalent influenza vaccine replaced the previously used trivalent vaccine.

### A1.3.6 Measles-containing vaccines

The measles vaccine was introduced in 1969 for children aged 10 months to 5 years who had not had measles, and for those aged under 10 years at special risk. In 1974 the recommended age for measles vaccine was changed from 10 months to 12 months, and in 1981 it was changed to age 12–15 months. These changes attempted to achieve a balance between too early immunisation, where the vaccine is neutralised by maternally acquired antibody, and the requirement to protect the very young during an epidemic.



MMR (measles, mumps and rubella) vaccine was introduced in 1990 to be given at age 12–15 months in place of the measles vaccine. The dose at age 11 years was introduced in 1992. In 1996 the timing of the first dose of MMR was changed to age 15 months, to be given at the same time as the booster dose of diphtheria, tetanus, whole-cell pertussis and *Haemophilus influenzae* type b (DTwPH) vaccine.

At the start of the 1997 epidemic, the measles immunisation campaign, using MMR, targeted all children aged under 10 years. During the campaign, the recommended time for the first dose was brought forward to age 12 months, and in Auckland a dose was recommended for children aged 6–11 months, to be repeated at age 15 months.

The national coverage achieved in the campaign is not known, but estimates for the school-aged population range from 55 percent for Auckland to 85 percent for the Wellington region.

In 2001 the Schedule was changed to give the first dose of MMR at age 15 months and the second dose at 4 years. There was a school catch-up programme for the second MMR dose for children aged 5–10 years. This schedule of two doses of MMR at 15 months and 4 years continued.

Vaccine-derived maternal antibody levels, which protect young infants, are lower and wane earlier than the antibody levels derived from natural infection. It is likely that in due course the age of the first dose of measles-containing vaccine will be changed to age 12 months.

In 2014, MMR became available for (re)vaccination following immunosuppression (upon specialist advice).

In 2020, the Schedule changed to recommend the first dose of MMR be given at 12 months and the second dose at 15 months.

### A1.3.7 Meningococcal vaccines

In March 2023, the four-component recombinant meningococcal B vaccine was introduced to the routine Schedule at ages 3, 5 and 12 months. An alternative schedule was offered at ages 2, 4 and 12 months. A catch-up programme was available for those aged 12 months – 59 months until 31 August 2025. Targeted meningococcal ACWY and B programmes continued.

### A1.3.8 Mumps-containing vaccines

Mumps vaccine (as MMR) was introduced to the Schedule in 1990 for children aged 12–15 months. (See section A1.3.6.)

### A1.3.9 Pertussis-containing vaccines

A monovalent pertussis vaccine was introduced by the Department of Health in 1945, and from 1953 it was also available combined with the diphtheria and tetanus vaccine. Routine childhood immunisation began in 1960 using the plain (ie, no adjuvant, not adsorbed) diphtheria, tetanus and whole-cell pertussis (DTwP) triple vaccine. Three doses were given, at ages 3, 4 and 5 months.

In 1971 the policy was altered to two doses of adsorbed triple vaccine given at ages 3 and 5 months. It was believed efficacy would be unaltered and the risk of serious reactions would be reduced. Following this schedule change, there was a progressive increase in hospitalisation rates in 1974, 1978 and 1982. Review of the increase in hospitalisations led to the addition, in 1984, of a third dose of DTwP, given at age 6 weeks, to provide earlier protection. From 1994 whole-cell pertussis vaccine was administered as a quadrivalent vaccine with diphtheria and tetanus toxoids and conjugate *Haemophilus influenzae* type b (diphtheria, tetanus, whole cell pertussis and *Haemophilus influenzae* type b – DTwPH).

A fourth dose of pertussis vaccine was added in 1996 (as DTwPH vaccine), given at age 15 months, with the goals of increasing protection in young children and reducing risk of transmission to younger siblings.

Acellular pertussis vaccine was introduced in August 2000, and diphtheria, tetanus and acellular pertussis (DTaP) and DTaP/Hib replaced the whole-cell pertussis vaccines. In February 2002 the vaccine given at ages 6 weeks, 3 months and 5 months was changed to DTaP with inactivated polio vaccine (DTaP-IPV), and a booster dose of DTaP-IPV was introduced and given at age 4 years to protect children during the early school years and to decrease transmission of the infection to younger children.

In 2006 the timing of the booster components of the pertussis schedule was changed to extend vaccine-induced protection into adolescence. Following the three doses of a pertussis-containing vaccine in the first year of life, booster doses are given at ages 4 and 11 years. Since March 2008 the acellular pertussis vaccine has been delivered as DTaP-IPV-HepB/Hib for the primary immunisation series, scheduled at ages 6 weeks, 3 months and 5 months; as DTaP-IPV at age 4 years; and as Tdap at age 11 years. In comparison with DTaP, Tdap contains smaller doses of tetanus and diphtheria toxoids and the pertussis antigens.

Since January 2013 pregnant women have been eligible for a booster dose of Tdap vaccine. Initially, this was under the outbreak policy and became part of high-risk funded vaccine criteria in July 2015. In 2014, pertussis-containing vaccines (as DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap) became available for (re)vaccination of children with certain high-risk conditions. This was extended to high-risk adults (as Tdap) in 2015. In 2019 eligibility for pregnant women was extended to include when given any time in their second or third trimester, with a recommendation it be given from 16 weeks' gestation every pregnancy, preferably in the second trimester.

In 2020, Tdap replaced Td for adult vaccinations at age 45 years and 65 years. Tdap is only offered at age 45 years for those who had not previously had four tetanus containing vaccinations.

### A1.3.10 Pneumococcal vaccines

The 7-valent pneumococcal conjugate vaccine (PCV7, Prevenar 7) and the 23-valent pneumococcal polysaccharide vaccine (23PPV, Pneumovax 23) were introduced in 2006 for high-risk individuals. PCV7 became part of the Schedule in June 2008, with four doses recommended at ages 6 weeks, 3 months, 5 months and 15 months.

In July 2011, the 10-valent pneumococcal conjugate vaccine (PCV10, Synflorix) replaced PCV7 and the 13-valent pneumococcal conjugate vaccine (PCV13, Prevenar 13) was introduced for some high-risk children. PCV13 replaced PCV10 on the Schedule in July 2014. In 2015, PCV13 became available for adults with certain high-risk conditions.

PCV10 replaced PCV13 on the usual childhood schedule in July 2017, with PCV13 and 23PPV continuing for high-risk individuals.

In July 2020, the PCV10 schedule changed to a two-dose primary plus booster given at 6 weeks, 5 months and 12 months. The PCV13 remained at a three-dose primary series plus booster for high-risk individuals, providing an additional dose at age 3 months to the usual Schedule. In December 2022, PCV10 was replaced with PCV13 for all infants as a two-plus-one schedule.

### A1.3.11 Poliomyelitis-containing vaccines

Limited supplies of the Salk vaccine (inactivated polio vaccine, IPV) became available in 1956, and immunisation initially targeted 8- and 9-year-old children. As supplies improved, immunisation was extended to include all 5–10-year-olds, then children aged 11–15 years, with approximately 80 percent coverage. By 1960 immunisation was offered to everyone between 6 months and 21 years of age (with three doses of vaccine).

The Sabin vaccine (oral polio vaccine, OPV) was introduced in August 1961, initially for children up to age 12 months; eight months later it was made available to all school children. On completion of this programme in September 1962 the vaccine was offered to adolescents and adults.

In 1967 OPV was given with diphtheria, tetanus and whole-cell pertussis (DTwP) vaccine at ages 3, 4, 5 and 18 months. The deletion of the DTwP dose at age 4 months in 1971 meant the OPV dose at age 4 months was also removed. An extra dose of polio vaccine was added at age 5 years in 1980, based on serological data, which showed decreased immunity to poliovirus types 1 and 3 in school entrants.

In 1996, as part of the Schedule changes, the third dose of the primary series was moved back to the first year of life, with OPV given at ages 6 weeks, 3 months and 5 months. The booster dose was moved to age 11 years, to be given at the same time as the MMR and adult tetanus and diphtheria (Td) vaccines. In 2001 the Schedule was changed to give the fourth dose of OPV at age 4 years, at the same time as the second dose of MMR. Students aged 5–10 years in 2001 who did not receive the fourth dose of polio vaccine at age 4 years were offered a dose at age 11 years.

IPV replaced OPV in 2002 and was included in three doses of DTaP-IPV in the first year of life, with a booster at age 4 years. Those children who had not received four doses of polio vaccine were offered IPV with Tdap, as Tdap-IPV (Boostrix-IPV) at age 11 years in 2006 and 2007. From 2008, Tdap has been offered at age 11 years, as all children should now have received four doses of polio vaccine by age 4 years.

Combined diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated polio vaccine and *Haemophilus influenzae* type b vaccine (DTaP-IPV-HepB/Hib, Infanrix-hexa) replaced DTaP-IPV (Infanrix-IPV) and Hib-HepB (Comvax) on the Schedule in March 2008.

In 2014, IPV vaccine became available for (re)vaccination following immunosuppression.

### A1.3.12 Rotavirus vaccines

The three-dose pentavalent rotavirus vaccine (RV5, RotaTeq) was introduced to the Schedule in 2014, for infants at ages 6 weeks, 3 months and 5 months. In 2017, the two-dose monovalent vaccine (RV1, Rotarix) replaced RV5 on the Schedule, for infants at ages 6 weeks and 3 months.

### A1.3.13 Rubella-containing vaccines

Immunisation with an attenuated rubella vaccine (Cendehill strain) was first offered to all 4-year-old New Zealand children in 1970, the rationale being to prevent transmission of the wild virus in 5–9-year-old children, who were the main sufferers from clinical disease. At the same time, the Department of Health delivered a school-based programme, which succeeded in immunising 95 percent of children aged 5–9 years. The acceptance rate of the preschool entry dose of rubella was only about 40 percent, and many practitioners did not feel it was appropriate to immunise males.

In 1979 the immunisation policy for rubella was altered to offer the vaccine to girls aged 11 years, in school year 7 (form 1). The aim was to immunise females before they attained childbearing age. In 1990 MMR was introduced at age 12–15 months for all children, and rubella vaccine continued to be offered to girls in school year 7. Since 1992 two doses of rubella vaccine – as measles, mumps and rubella (MMR) vaccine – have been offered to all children, the first dose in the second year of life and the second dose at age 11 years. This was changed in 2001, maintaining the first dose of MMR at age 15 months and changing the second to age 4 years. The aim of this strategy was to prevent rubella epidemics, reduce the background incidence of rubella and continue to protect women before childbearing, therefore eventually eliminating CRS.

In 2001 there was an MMR school catch-up programme throughout the country for all children aged 5–10 years who would no longer receive an MMR dose in school year 7. The rubella schedule continued as two doses of MMR offered at ages 15 months and 4 years.

In 2014, MMR became available for (re)vaccination following immunosuppression (upon specialist advice).

In 2020, the Schedule changed to recommend the first dose of MMR be given at 12 months and the second dose at 15 months (see section A1.3.6).

### A1.3.14 Tetanus-containing vaccines

The history of tetanus vaccine use prior to the 1960 introduction of diphtheria, tetanus and whole-cell pertussis (DTwP) vaccine is not well recorded, but tetanus vaccine was widely used in World War II and subsequently by the armed forces. In New Zealand, universal infant immunisation with tetanus toxoid began in 1960 with the use of three doses of triple vaccine. Anyone born before 1960 is less likely to have received a primary series, unless they were in the armed forces. Older women appear to be at particular risk.

The first scheduled vaccine used for infants (from 1960) was the DTwP vaccine, with three doses at monthly intervals at ages 3, 4 and 5 months, and a diphtheria and tetanus (DT) booster before school entry (at age 5 years). A DT booster at age 18 months was added in 1964, primarily to enhance protection against tetanus. There was a change to a more immunogenic adsorbed vaccine in 1971, and the dose given at age 4 months was dropped.

In 1980 the dose of DT given at age 5 years was replaced by the monovalent tetanus toxoid given at age 15 years, as part of a move from 10-yearly to 20-yearly boosters for tetanus. It was considered that more frequent boosters were unnecessary and the cause of significant local reactions. There was a return to a three-dose primary series of DTwP (by the addition of a 6-weeks-of-age vaccination) in 1984 because two doses had been inadequate to control pertussis. In 1996 the booster of Td, which had been changed from tetanus toxoid in 1994 (see below), and previously given at age 15 years, was changed to age 11 years.

In 2002 the primary schedule for tetanus, given in combination vaccines at ages 6 weeks, 3 months and 5 months, followed by a dose at 15 months, was changed when a further dose was introduced at age 4 years. The Td given at age 11 years continued.

Since 2006 the childhood schedule for tetanus has been given in combination vaccines at ages 6 weeks, 3 months, 5 months (DTaP-IPV-HepB/Hib), 4 years (DTaP-IPV) and 11 years (Tdap).

Td replaced the tetanus toxoid vaccine in 1994, and 10-yearly boosters were recommended. The change was recommended to maintain the adult population's immunity to diphtheria, in response to outbreaks overseas affecting adults and the absence of natural boosting because the disease had become rare. Since 2002 adult boosters have been recommended at ages 45 and 65 years (instead of 10-yearly) as a pragmatic attempt to increase coverage in the adult population.

In 2014, Td became available for (re)vaccination following immunosuppression.

In 2020, Td was discontinued and replaced with Tdap for wound prophylaxis and adult booster doses. A Tdap dose is offered at 45 years, for adults who had not previously received four doses of a tetanus-containing vaccine, and at age 65 years.

### A1.3.15 BCG vaccines

BCG immunisation was first introduced to New Zealand in 1948 and later extended to all adolescents. BCG immunisation of neonates was introduced in 1976, initially in districts with high rates of active TB.

Universal screening and vaccination of 13-year-olds was discontinued in the South Island in 1963, was phased out in regions of the North Island in the 1980s, and had ceased by 1990. It was stopped because TB had declined to a point at which the advantages of universal vaccination were outweighed by the disadvantages (cost, side-effects and reduced diagnostic value of the Mantoux test). BCG vaccine is now only available to neonates and children aged under 5 years at high risk of TB.

### A1.3.16 Varicella vaccines

In 2014 two doses of varicella vaccine (VV, Varilrix) were introduced for individuals at high risk of varicella infection. In 2017 one dose of VV was introduced to the Schedule at age 15 months (for children who were born on or after 1 April 2016). One catch-up VV dose was introduced for previously unvaccinated children turning 11 years old on or after 1 July 2017 who had not previously had a varicella infection.

### A1.3.17 Herpes zoster vaccines

ZV was introduced onto the Schedule on 1 April 2018, as a single dose for adults aged 65 years, with a catch-up programme for adults aged 66–80 years inclusive (the catch-up programme ceased on 31 December 2021). In September 2022, live ZV was discontinued and replaced at the age of 65 years with recombinant zoster vaccine (rZV). Eligibility for rZV vaccination was expanded to those age 18 years and over with certain immunocompromising medical conditions in July 2024.

## References

1. Dow D, Mansoor O. New Zealand immunisation schedule history. *New Zealand Medical Journal*, 1996. 109: : p. 209–12.
2. Reid S. Evolution of the New Zealand childhood immunisation schedule from 1980: A personal view. *New Zealand Medical Journal*, 2006. 119(1236): p. 73–83.
3. Reid S. The further and future evolution of the New Zealand Immunisation Schedule. *New Zealand Medical Journal*, 2012. 125(1354): p. 86–99.



# Appendix 2: Planning immunisation catch-ups

It is essential that vaccinators have a sound understanding of the number of antigens and the most effective spacing of doses required for a primary course and subsequent boosters in order to assess an individual's immunisation requirements. The principles described below will help vaccinators in this process.

Section A2.2 discusses catch-up requirements for children aged under 18 years, and section A2.3 discusses the requirements for adults.

Plan and document your complete catch-up schedule in the patient notes and recall system to ensure continuity of care.

For assistance with planning catch-up schedules, contact your immunisation coordinator, call the IMAC freephone line on 0800 IMMUNE/0800 466 863, or discuss with an experienced colleague.

## A2.1 Eligibility for publicly funded vaccines

The *Health and Disability Services Eligibility Direction 2011* (the Eligibility Direction) issued by the Minister of Health sets out the eligibility criteria for publicly funded health and disability services, including National Immunisation Schedule vaccines, in New Zealand. Only people who meet the eligibility criteria defined in the Eligibility Direction can receive publicly funded health and disability services.

However, regardless of their immigration and citizenship status, all children aged under 18 years are eligible to receive Schedule vaccines, and providers can claim the immunisation benefit for administering the vaccines.

## A2.2 Planning catch-ups for infants, children and adolescents aged under 18 years

When planning a catch-up schedule, start by focusing on the antigens already received and the additional antigens required, not the vaccine combinations available or trade names. There is no need to think in terms of events missed (eg, the 6-week, 3-month,



5-month, 12-month or 15-month vaccination events). It is important to note the age of the child when the antigens were received.

Although catch-up tables are provided in this appendix, children may not fit these unless they are completely unvaccinated, or there is no documented history and they are assumed to be unvaccinated. Trying to fit a child's vaccine requirements to a table can result in too many or not enough antigens being administered.

Use the following principles to establish what antigens the infant, child or adolescent requires.

### A2.2.1 Principles of catch-up for infants and children aged under 10 years

1. If the immunisation status of a child is uncertain or unknown, plan the catch-up schedule assuming the vaccines have not been given.
2. Administer catch-up immunisations as per the New Zealand Schedule, not an overseas immunisation schedule.
3. The best approach is to ascertain the antigens required for the child's current age, subtract any already given and then develop the individual's catch-up schedule.
4. There is considerable flexibility when planning catch-up schedules. To offer the best protection in the shortest time possible, most vaccines can be given at the same visit, and the catch-up schedule shortened to four-weekly intervals to ensure the required number of doses are administered.
5. If the schedule has been interrupted, do not repeat prior doses regardless of how long ago the previous doses were given. Exceptions to this principle are the following vaccines given to children aged under 12 months: MMR or measles-containing vaccine (see point 10 below), Hib vaccine (see point 11), PCV (see point 12), and varicella vaccine (see point 13).
6. If a child infrequently attends general practice and failure to return for future immunisation is a concern, it is prudent to administer as many antigens as possible at every visit.
7. For infants and children aged under 10 years, use DTaP-IPV-HepB/Hib or DTaP-IPV for primary immunisation. Tdap may be used as an alternative for primary immunisation of children aged 7 to under 18 years (note that Tdap (Boostrix) is not registered for primary immunisation, but there is no evidence of safety concerns).
8. Where the combination vaccine DTaP-IPV-HepB/Hib is used, there are no safety concerns around receiving extra doses of Hib or HepB. If there is parental concern, then separate DTaP-IPV and Hep B or Hib can be used but would require an extra injection. If single antigen HepB is used, give as 0-1-6-month schedule.

9. The first dose of rotavirus vaccine (RV1, Rotarix) should be given before age 15 weeks (ie, the latest age is 14 weeks and 6 days), and the second dose administered a minimum of four weeks later. An infant who has not had the first dose before age 15 weeks will not be eligible to commence the rotavirus course. Where the first dose is inadvertently given at age 15 weeks or older, the remaining dose should be given, but both doses should be given before age 25 weeks (ie, by age 24 weeks and 6 days).
10. The first dose of MMR is scheduled at 12 months and the second dose of MMR at 15 months, or at least four weeks after the first MMR. MMR or any single-antigen measles vaccine given before age 12 months is not counted as part of the two-dose MMR schedule.
11. A single dose of Hib-PRP is required for all children aged 12 months to under 5 years regardless of the number of doses given in their first year. Children who receive catch-up DTaP-IPV-HepB/Hib between ages 12 months to under 5 years do not require a single antigen Hib vaccine (Hib-PRP) as this is covered by the combination vaccine. Healthy children aged 5 years and older do not need Hib vaccination.
12. For healthy infants commencing PCV vaccination under 12 months of age, a primary course is two doses with a minimum of eight weeks between doses. A booster dose is given eight weeks after the completion of the primary course from age 12 months. To get them back on schedule, if the booster dose is not given after 8 weeks, it can be given at the 15-months event. Unimmunised healthy children aged 12 months to under 5 years require two PCV doses given at least eight weeks apart. For a child who did not complete their primary course when under 12 months of age, do not count doses given prior to age 12 months when determining the number of PCV catch-up doses required– give two doses as for unvaccinated healthy children. Healthy children aged 5 years and older do not need PCV. See chapter 17 'Pneumococcal disease' for PCV13 schedules for high-risk children.
13. All children eligible for meningococcal B catch-up should be vaccinated at the earliest opportunity (see Table 13.4). If MenB was started before the age 5 years, then the funded course can be completed. The recommended number (two or three doses) is based on the age at which the child receives their first dose.
  - For children aged under 12 months at the time of first dose, give two doses eight weeks apart, followed by a booster from 12 months of age or a minimum of six months after the second dose, whichever is later.
  - For children aged 12 months to under 24 months at time of first dose, give two doses eight weeks apart followed by a booster dose given 12–23 months after dose two. The spacing between dose one and two can be reduced to six weeks if indicated, with a prescription.
  - For children aged 24 months or over, give just two doses eight weeks apart (see Table A2.7). This can be reduced to four weeks if clinically indicated.
14. One dose of varicella vaccine is funded at age 15 months for children who were born on or after 1 April 2016. A child who has received a non-funded varicella vaccine prior to age 12 months is still eligible to receive the 15-month funded vaccine. A child who has had varicella disease does not require the varicella vaccine.

15. Remember to check whether the infant/child has any specific health conditions that may make them eligible for additional vaccines or additional doses of vaccine (see chapter 4 'Immunisation of special groups').
16. Once the child has received the appropriate vaccines for their age, they should continue with the Schedule as usual.

**Table A2.1: Minimum number of antigens required, by age at time of presentation, for infants and children aged <10 years**

<12 months	12 months to <5 years	5 years to <10 years
3 DTaP <sup>a</sup>	3 or 4 DTaP <sup>a</sup>	4 DTaP <sup>a</sup>
3 IPV <sup>a,e</sup>	3 or 4 IPV <sup>a,e</sup>	3 or 4 IPV <sup>e</sup>
3 HepB <sup>a,b</sup>	3 HepB <sup>a,b</sup>	3 HepB <sup>a,b</sup>
2 or 3 Hib-PRP <sup>a</sup>	1 Hib-PRP <sup>f</sup>	2 MMR
2 PCV <sup>c</sup>	2 PCV <sup>c</sup>	1 VV <sup>h</sup>
2 RV <sup>d</sup>	2 MMR <sup>g</sup>	
2 MenB <sup>i</sup>	1 VV <sup>h</sup> 2 or 3 MenB <sup>i</sup>	

- a. Use DTaP-IPV-HepB/Hib (or DTaP-IPV) for the 3-dose primary series (at a minimum of 4-weekly intervals), then continue with the usual childhood schedule with a booster dose of DTaP-IPV-HepB/Hib given at age 4 years to ensure longer term HepB protection. (Note, if there is at least a 5-month gap between doses two and three, DTaP-IPV can be used for the 4-year-old vaccination event). If the child commences immunisation at age 4 years or older, give the booster dose at least 6 months after the third dose of the primary series. A fourth DTP given earlier than 3 years of age on an overseas schedule is not counted as the 4-year dose. For infants requiring Hib-PRP only, the primary series consists of 3 doses for those starting under 6 months of age; for those starting from age 6 months and over, 2 primary doses are required.
- b. If the child received HepB at birth, they require a total of four HepB doses as the birth dose does not count as part of the primary course. Infants born to HBsAg-positive mothers require serological testing at age 9 months – see section 9.5.2.
- c. For healthy infants commencing PCV vaccination under 12 months of age, a primary course is 2 doses with a minimum of 8 weeks between doses. A booster dose is given 8 weeks after the completion of the primary course from age 12 months. To get them back on schedule, if the booster dose is not given after 8 weeks, it can be given at the 15-months event. Infants who commenced vaccination with PCV10 can complete the course with PCV13. For healthy children aged 12 months to under 5 years who are commencing immunisation or with an incomplete course, give 2 doses of PCV13 at least 8 weeks apart. (See chapter 17 'Pneumococcal disease' for PCV13 schedules for high-risk children.)
- d. The first dose of rotavirus vaccine should be given before age 15 weeks (ie, the latest is 14 weeks and 6 days) and the second dose given a minimum of 4 weeks later. Both doses must be given before age 25 weeks (ie, the latest is 24 weeks and 6 days). Where the first dose is inadvertently given at age 15 weeks or older, the second dose should be given, but both doses must be given before age 25 weeks (ie, latest age 24 weeks and 6 days).
- e. A minimum of 3 polio doses are required for the primary series (at a minimum of 4-weekly intervals) for children aged under 10 years, but 4 doses may be given when combination vaccines are used (eg, DTaP-IPV-HepB/Hib or DTaP-IPV). For all infants and children who have had OPV (ie, either OPV or bOPV) a further dose of IPV should be administered even if they have completed a full OPV/bOPV course. Those who received a dose of OPV at birth require a minimum of 3 further doses of polio vaccine – do not count the birth dose.
- f. A single dose of Hib-PRP is required for all children from age 12 months to under 5 years, regardless of the number of doses given before age 12 months. Children who receive catch-up DTaP-IPV-HepB/Hib between 12 months to under 5 years do not require a single antigen Hib-PRP vaccine as this is covered by the combination vaccine.

- g. Children commencing immunisation at age 12 months or older require 1 dose of MMR, then continue the usual childhood schedule with a second dose of MMR given at age 15 months, or at least 4 weeks after the first MMR dose.
- h. One dose of varicella vaccine is funded for children at 15 months born on or after 1 April 2016. Children who received a non-funded varicella vaccine prior to age 12 months are still eligible to receive the funded 15-month varicella vaccine. A child who has had varicella disease does not require the varicella vaccine.
- i. Three doses of MenB are funded for all infants up to age 12 months (inclusive). A catch-up programme is available until 31 August 2025 for children aged under 5 years. If MenB was started before age 5 years, then the funded course can be completed.

The required number (two or three) of doses is based on the age at which the child receives their first dose:

- For children aged under 12 months at the time of first dose, give two doses eight weeks apart, followed by a booster from 12 months of age or a minimum of six months after the second dose, whichever is later.
- For children aged 12 months to under 24 months at time of first dose, give two doses eight weeks apart followed by a booster dose given 12–23 months after dose two. The spacing between doses one and two can be reduced to six weeks if indicated, with a prescription.
- For children aged 24 months or over, give just two doses eight weeks apart. This can be reduced to four weeks if clinically indicated. See also Table A2.7.

## A2.2.2 Principles of catch-up for children and adolescents aged 10 to under 18 years

1. The best approach is to ascertain the antigens required for current age, subtract any already given and then develop the individual's catch-up schedule.
2. There is considerable flexibility when planning catch-up schedules. To offer the best protection in the shortest time possible, most vaccines can be given at the same visit and the catch-up schedule shortened to four-weekly intervals to ensure the required number of doses are administered.
3. If the Schedule has been interrupted, do not repeat prior doses regardless of how long ago the previous doses were given.
4. If the immunisation status of an individual is uncertain or unknown, plan the catch-up schedule assuming the vaccine has not been given.
5. If an individual infrequently attends general practice and failure to return for future immunisation is a concern, it is prudent to administer as many antigens as possible at every visit. MMR should be recommended at the first visit.
6. For individuals aged 10 years to under 18 years, Tdap is recommended and funded for primary and booster immunisation. While Tdap is not approved for use (registered) as a primary course, no safety concerns are expected when using Tdap for primary immunisation in individuals aged 10 to under 18 years.
7. For individuals aged 10 years to under 18 years, give HepB (Engerix B 20µg) at 0, 1 and 6 months. An alternative two-dose HepB catch-up schedule may be considered for individuals aged 10–15 years with the second dose given six months after the first.
8. A two-dose schedule of HPV at least 6–12 months apart is recommended for individuals who receive their first dose before their 15th birthday, even if they are

15 years or older at the time of the second dose. Individuals who start their HPV schedule from age 15 years and older receive three doses of HPV at 0, 2 and 6 months. If required, a shortened schedule of three doses can be given with a minimum of four weeks between doses one and two, and the third dose given at least 12 weeks after dose two. Non-residents who were under age 18 years when they commenced HPV vaccination are currently funded to complete the course, even if they are aged 18 years or older when they complete it. See Table A2.10 for HPV catch-up schedules.

9. One dose of varicella vaccine is funded for children turning age 11 years on or after 1 July 2017, who have not previously had varicella vaccination or infection. The appropriate varicella schedule for those aged 13 years or older when starting is two doses with a minimum of a four-week gap; however, only one dose is currently funded for those turning 11 years on or after 1 July 2017.
10. Remember to also check whether the individual has any specific health conditions that may make them eligible for additional vaccines or additional doses of vaccine (see chapter 4 'Immunisation of special groups').
11. Once the individual has received the appropriate vaccines for their age, they should continue with the Schedule as usual.

**Table A2.2: Minimum number of antigens required by individuals aged 10 to under 18 years at the time of presentation**

10 years to <18 years
4 Tdap <sup>a</sup>
3 IPV <sup>b</sup>
3 HepB for children aged 10 to <18 years; or alternatively 2 HepB doses for children aged 10–15 years <sup>c</sup>
2 MMR
2 HPV <sup>d, e, f</sup> for those aged 11–14 years, or 3 HPV <sup>d, g</sup> for those aged 15 years and older
1 VV <sup>h</sup>

- a. If aged 10 years to under 18 years, use Tdap for the primary series and the booster dose, with a minimum interval of 6 months between doses 3 and 4 (the primary series and the booster dose).
- b. A minimum of 3 polio doses are required for the primary series (at a minimum of 4-weekly intervals).
- c. If aged 10 years to under 18 years, 3 doses of HepB are required at 0, 1 and 6 months. An alternative 2-dose schedule may be used for children aged 10–15 years with the second dose given 6 months after the first.
- d. Individuals who started with HPV4 may complete their remaining doses with HPV9.
- e. For those aged 11–14 years, the second HPV dose is preferably given at least 6 months after the first. If the second dose is given earlier than 5 months after the first, a third HPV dose is recommended and funded — give the third dose at least 5 months after the first dose.
- f. A two-dose schedule of HPV at least 6–12 months apart is recommended for individuals who receive the first dose before their 15th birthday, even if they are 15 years or older at the time of the second dose.
- g. For those aged 15 years and older, give a 3-dose HPV course at 0, 2 and 6 months. If a shortened schedule is required for these older individuals, the three doses can be given with a minimum of 4 weeks between doses one and two, and the third dose given at least 12 weeks after dose two.
- h. One dose of varicella vaccine is funded for children turning 11 on or after 1 July 2017, who have not previously had varicella vaccination or infection.

## A2.2.3 National Immunisation Schedule catch-up guides for infants, children and adolescents aged under 18 years

Note: the following tables are guides only, and the principles described in sections A2.2.1 and A2.2.2 should be followed. The vaccinator must subtract any previous doses given. It is important to note the age at which the antigens have been given.

**Table A2.3: Age at presentation: 3–6 months**

Note: Subtract previous doses given.

Dose	Vaccines			
First dose*	DTaP-IPV-HepB/Hib	PCV <sup>a</sup>	RV <sup>b</sup>	MenB
4 weeks later	DTaP-IPV-HepB/Hib		RV <sup>b</sup>	
4 weeks later	DTaP-IPV-HepB/Hib	PCV <sup>a</sup>		MenB <sup>c</sup>

Once the child has received the appropriate vaccines for their age, continue with the Schedule as usual.

- See chapter 17 'Pneumococcal disease' for PCV13 schedules for high risk children.
- Only eligible for RV if the first dose is given before age 15 weeks (ie, 14 weeks and 6 days). The second dose must be given before age 25 weeks (ie, 24 weeks and 6 days).
- Infants commencing Men B immunisation aged under 12 months require 2 doses separated by 8 weeks plus a booster dose at from age 12 months or a minimum of 6 months after second dose, whichever is later.

**Table A2.4: Age at presentation: 7–11 months**

Note: Subtract previous doses given.

Dose	Vaccines		
First dose	DTaP-IPV-HepB/Hib	PCV <sup>a</sup>	MenB
4 weeks later	DTaP-IPV-HepB/Hib		
4 weeks later	DTaP-IPV-HepB/Hib	PCV	MenB <sup>b</sup>

Once the infant has received the appropriate vaccines for their age, continue with the Schedule as usual.

- See chapter 17 'Pneumococcal disease' for PCV13 schedules for high-risk children.
- Infants commencing Men B immunisation aged under 12 months require 2 doses separated by 8 weeks plus a booster dose at from age 12 months or a minimum of 6 months after second dose, whichever is later. See also Table A2.7.

**Table A2.5: Age at presentation: 12–23 months**

Note: Subtract previous doses given.

Dose	Vaccines				
First dose	DTaP-IPV- HepB/Hib <sup>a</sup>	PCV <sup>b</sup>	MMR <sup>c</sup>	VV <sup>d</sup>	MenB
4 weeks later	DTaP-IPV- HepB/Hib <sup>e</sup>		MMR <sup>c</sup>		
4 weeks later or at age 15 months, whichever is applicable	DTaP-IPV- HepB/Hib <sup>e</sup>	PCV <sup>b</sup>			MenB
Booster dose given 12–24 months later <sup>f</sup>					MenB <sup>f</sup>
Once the child has received the appropriate vaccines for their age, continue with the Schedule as usual. <sup>g</sup>					

- a. One dose of Hib-PRP is required from age 12 months to under 5 years regardless of previous doses. Children who receive DTaP-IPV-HepB/Hib between 12 months to under 5 years do not require a single antigen Hib-PRP as this is covered by the combination vaccine.
- b. Healthy children commencing immunisation at age 12–23 months require 2 PCV doses, with a minimum interval of 8 weeks between doses. If the child did not complete a primary course of PCV when under 12 months of age, do not count the previously given doses when determining the number of PCV catch-up doses required. If the child completed a primary course of PCV before age 12 months, give a booster dose from 12 months of age, at least 8 weeks after the completion of the primary course. Children who commenced vaccinations with PCV10 should complete the course with PCV13, as appropriate. (See chapter 17 'Pneumococcal disease' for PCV13 schedules for high-risk children.)
- c. The first dose of MMR is scheduled at age 12 months, with a second dose given at 15 months or at least 4 weeks after the first dose.
- d. One dose of varicella vaccine is funded for children born on or after 1 April 2016 at 15 months. Children who received a non-funded varicella vaccine prior to 12 months are still eligible to receive the 15-month varicella vaccine.
- e. Parents/guardians should be informed that their child will receive extra doses of Hib but there are no safety concerns with these extra doses. If the parents/guardians prefer, vaccinators may administer the DTaP-IPV and HepB vaccines as 2 separate injections instead of the combination DTaP-IPV-HepB/Hib vaccine.
- f. Dependent on age of first dose. Infants who commenced MenB immunisation aged under 12 months require 2 doses separated by 8 weeks plus a booster dose at age 12 months or a minimum of 6 months after second dose, whichever is later. Children who start from age 12 to 23 months should receive 2 doses separated by 8 weeks and a booster dose is given 12–24 months after second dose. See also Table A2.7.
- g. If there is a less than 5-month gap between the second and third doses of primary series of DTaP-IPV-HepB/Hib, then a DTaP-IPV-HepB/Hib should be given at age 4 years instead of DTaP-IPV.



**Table A2.6: Age at presentation: 2 years to under 5 years**

Note: Subtract previous doses given.

Dose	Vaccines			
First dose	DTaP-IPV-HepB/Hib <sup>a</sup>	PCV <sup>b</sup>	MMR	MenB
4 weeks later	DTaP-IPV-HepB/Hib <sup>d</sup>		MMR <sup>e</sup>	VV <sup>c</sup>
4 weeks later	DTaP-IPV-HepB/Hib <sup>d</sup>	PCV <sup>b</sup>		MenB <sup>g</sup>
6 months later, or at age 4 years, whichever is later	DTaP-IPV <sup>f</sup>			

Once the child has received the appropriate vaccines for their age, continue with the Schedule as usual.

- One dose of Hib-PRP is required from age 12 months to under 5 years regardless of previous doses. Children who receive DTaP-IPV-HepB/Hib between 12 months to under 5 years do not require a single antigen Hib-PRP as this is covered by the combination vaccine.
- A healthy child who presents at age 2 years to under 5 years: if previously unvaccinated, requires 2 PCV doses at least 8 weeks apart. If they completed a primary PCV course before age 12 months, give 1 PCV dose. If they started but did not complete a primary PCV course before age 12 months, give 2 PCV doses at least 8 weeks apart (this is the exception to the principle of counting previous doses given). Children who commenced vaccination with PCV10 should complete their immunisations as appropriate with PCV13. (See chapter 17 'Pneumococcal disease' for PCV13 schedules for high-risk children.)
- One dose of varicella vaccine is funded for children who were born on or after 1 April 2016. Children who received a non-funded varicella vaccine prior to 12 months are still eligible to receive the 15-month varicella vaccine. A child who has had clinician-confirmed varicella disease does not require the varicella vaccine.
- Parents/guardians should be informed that their child will receive extra doses of Hib, but there are no safety concerns with these extra doses. If the parents/guardians prefer, vaccinators may administer the DTaP-IPV and HepB vaccines as 2 separate injections instead of the combination DTaP-IPV-HepB/Hib vaccine.
- Administer the second MMR dose a minimum of 4 weeks after the first dose.
- At age 4 years, administer DTaP-IPV-HepB/Hib a minimum of 6 months after the third DTaP-IPV-HepB/Hib dose, if there is a less than 5-month gap between doses two and three in the primary series of DTaP-IPV-HepB/Hib. If the child is aged 4 years or older at presentation, administer DTaP-IPV-HepB/Hib a minimum of 6 months after the third DTaP-IPV-HepB/Hib dose. A fourth DTP given earlier than 3 years of age overseas is not counted as the 4-year-old dose.
- Children who start the course at age 24 months or over require just two doses, separated by 8 weeks, this can be reduced to 4 weeks if clinically necessary (see Table A2.7). Children previously vaccinated with MenB aged 23 or under months will also be eligible for a booster dose. See Table 13.4 for timing and eligibility.

**Table A2.7: Age at presentation: 8 weeks to 59 months – MenB only**

Note: Subtract previous doses given. Three doses of MenB are funded for all infants up to age 12 months (inclusive). A catch-up programme is available for those aged under 5 years until 31 August 2025. If MenB was started before age 5 years, then the funded course can be completed.

Dose	Vaccine
<b>Infants ≥8 weeks to ≤ 12 months, at presentation</b>	
First dose	MenB
8 weeks later	MenB
<hr/>	
≥12 months or a minimum of 6 months after second dose, whichever is later.	MenB
<hr/>	
<b>Infants ≥12 to ≤23 months at presentation</b>	
First dose	MenB
8 weeks later <sup>a</sup>	MenB
12–24 months after second dose	MenB
<hr/>	
<b>Children ≥24 to 59 months (for first dose)</b>	
First dose	MenB
8 weeks later <sup>b</sup>	MenB

- a. This can be reduced to 6 weeks if clinically necessary, with a prescription.  
 b. This can be reduced to 4 weeks if necessary (no prescription required).

**Table A2.8: Age at presentation: 5 years to under 10 years**

Note: Subtract previous doses given.

Dose	Vaccines
First dose	DTaP-IPV-HepB/Hib <sup>a,b</sup> MMR      VV <sup>d</sup>
4 weeks later	DTaP-IPV-HepB/Hib <sup>a,b,c</sup> MMR
4 weeks later	DTaP-IPV-HepB/Hib <sup>a,b,c</sup>
6 months later	DTaP-IPV-HepB/Hib <sup>b,c</sup>
Once the child has received the appropriate vaccines for their age, continue with the Schedule as usual.	

- a. Healthy children aged 5 years and older do not need Hib-PRP. However, DTaP-IPV-HepB/Hib should be offered to reduce the number of injections at each visit. Parents/guardians should be informed that their child will receive extra doses of Hib-PRP but there are no safety concerns with these extra doses.  
 b. If the parents/guardians prefer, vaccinators may administer DTaP-IPV and HepB vaccines as 2 separate injections instead of the combination DTaP-IPV-HepB/Hib vaccine. If a single antigen HepB is requested, then HepB (Engerix B 10µg) is used as 0-1-6 months schedule (Engerix 20µg can be used if no paediatric 10µg vaccine is available).  
 c. If a child turns 10 years old before completing their catch-up programme, they should continue on the '10 years to under 18 years' catch-up schedule (see Table A2.9).  
 d. One dose of varicella vaccine is funded for children who were born on or after 1 April 2016. Children who received a non-funded varicella vaccine prior to 12 months are still eligible to receive the 15-month varicella vaccine. A child who has had clinician-confirmed varicella disease does not require VV.

**Table A2.9: Age at presentation: 10 years to under 18 years – excluding HPV**

Note: Subtract previous doses given.

Dose	Vaccines			
First dose	Tdap <sup>a</sup>	IPV <sup>b</sup>	HepB <sup>c</sup>	MMR
4 weeks later	Tdap <sup>a</sup>	IPV <sup>b</sup>	HepB	MMR
4 weeks later	Tdap <sup>a</sup>	IPV <sup>b</sup>		
6 months later, or at age 11 years, whichever is later	Tdap		HepB	
At age ≥11 years				VV <sup>d</sup>

- Use Tdap for the primary series and the booster dose, with a 6-month interval between the completion of the primary series and the booster (doses 3 and 4).
- A minimum of 3 IPV doses are required for the primary series (at a minimum of 4-weekly intervals).
- If aged 10 years to under 18 years, 3 doses of HepB are required. An alternative 2-dose schedule of HepB may be used for children aged 10–15 years with the second dose given 6 months after the first.
- One dose of varicella vaccine is funded for children turning 11 years on or after 1 July 2017, who have not previously had varicella vaccination or infection.

**Table A2.10: Age at presentation: 11 years to under 18 years – HPV only**

Note: Subtract previous doses given.

Dose	Vaccine
<b>Age 11–14 years<sup>a,b</sup> at presentation</b>	
First dose	HPV
6–12 months later <sup>c,d</sup>	HPV
<b>Age 15 years or older<sup>b,e</sup> at presentation</b>	
First dose	HPV
2 months later	HPV
4 months later	HPV

- Although the usual schedule is at age 11 or 12 years (school year 7 or 8), HPV vaccine may be given from age 9 years.
- Individuals who started with HPV4 may complete their remaining doses with HPV9.
- For those aged 11–14 years, the second dose is preferably given at least 6 months after the first. However, if the second dose is given less than 5 months after the first, a third HPV dose is recommended and funded — give the third dose at least 5 months after the first dose.
- A two-dose schedule at least 6–12 months apart is recommended for individuals who receive the first dose before their 15th birthday, even if they are 15 years or older at the time of the second dose.
- If a shortened schedule is required for those aged 15 years or older, three doses can be given with a minimum of 4 weeks between doses one and two, and the third dose given at least 12 weeks after dose two.

## A2.3 Immunisation catch-up for eligible adults aged 18 years and older

When seen at general practice or by vaccination providers, adults should be checked to see that they have received protection against the following diseases and have received a primary immunisation course as in Table A2.11 below. Adults are eligible for age-appropriate catch-up immunisations if they are New Zealand residents, citizens, former refugees or hold a visa which makes them eligible for health care in New Zealand.

1. If the requisite number of doses have not been received, catch-up vaccination is recommended. There is flexibility when planning catch-up schedules. To offer the best protection in the shortest time possible, most vaccines may be given at the same visit and the catch-up schedule shortened to four-weekly intervals to ensure the required number of doses are administered.
2. Do not repeat prior doses regardless of how long ago the previous doses were given.
3. Adults should be reminded of the necessity for age-appropriate boosters for tetanus, diphtheria and pertussis at 45 years of age if they have not previously received four tetanus vaccines in their lifetime, and for all adults at 65 years of age.
4. Pertussis (Tdap; given from 16 weeks' gestation) and influenza vaccines are recommended and funded in every pregnancy. A single dose of unfunded Tdap and influenza vaccines may be considered for adults requesting pertussis and influenza protection, especially for those in close contact with young babies.
5. Women of childbearing age should know whether they are immune to rubella, and are considered immune if have two documented doses of MMR after 12 months of age. If the patient does not have documented evidence of immunity (see section 12.8.3), two doses of funded MMR should be offered four weeks apart (MMR cannot be given in pregnancy and pregnancy should be avoided for four weeks following vaccination). If they have received one documented dose of MMR, a second dose should be administered.
6. Previously unvaccinated males and females aged 15 years to 26 years inclusive may receive three doses of HPV vaccine. Those who started with HPV4 may complete their remaining doses with HPV9. Those who were aged under 27 years when they commenced but did not complete HPV vaccination are funded to complete the three-dose course even if they are aged 27 years or older when they complete it. Non-residents who were under the age of 18 years when they commenced HPV vaccination are funded to complete the course, even if they are aged 18 years or older when they complete it.
7. Two doses of rZV are funded for adults aged 65 years. The second dose is given 2–6 months after the first dose. The second dose is funded and can be given if the individual turns age 66 years after their first dose. There is no catch-up programme currently.

8. Check whether the individual has any additional immunisation requirements, such as specific health conditions or occupational risk (see chapter 4 'Immunisation of special groups').

**Table A2.11: Primary immunisation requirements for adults**

**Antigens and number of doses required**

3 Tdap<sup>a</sup>

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3 polio (IPV)<sup>b</sup>

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2 MMR<sup>c</sup>

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3 HPV<sup>d,e</sup> (aged 26 years and under)

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- a. A primary course of 3 doses of Tdap vaccines (at a minimum of 4-weekly intervals) is recommended and funded for unimmunised or partially immunised adults. At age 45 years, the Tdap is recommended for those adults who have not previously received four tetanus containing vaccines in their lifetime, and for all adults at age 65 years.
- b. A primary course of 3 polio (IPV) doses (at a minimum of 4-weekly intervals) is recommended and funded for unimmunised or partially immunised adults.
- c. Two doses of MMR (given a minimum of 4 weeks apart) are recommended and funded for unimmunised adults who are susceptible to any one of the three diseases. Those born in New Zealand before 1969 are considered immune to measles and those born prior to 1980 are considered to be immune to mumps.
- d. HPV9 vaccine is recommended and funded for individuals aged up to 26 years inclusive. Give the 3-dose course at 0, 2 and 6 months. If a shortened schedule is required, the 3 doses can be given with a minimum of 4 weeks between the doses one and two, and third dose given at least 12 weeks after dose two.
- e. Those who were under age 27 years when they commenced HPV vaccination are currently funded to complete the 3-dose course, even if they are aged 27 years or older when they complete it. Non-residents who were under age 18 years when they commenced HPV vaccination are currently funded to complete the course, even if they are aged 18 years or older when they complete it.

# Appendix 3:

## Immunisation standards for vaccinators and guidelines for organisations offering immunisation services

### A3.1 Purpose

The 'Immunisation standards for vaccinators' (see section A3.3) are quality levels all vaccinators should achieve to ensure they can competently deliver safe and effective immunisation services.

The 'Immunisation standards for vaccinators' and the 'Guidelines for organisations storing vaccines and/or offering immunisation services' (see section A3.4) apply to all vaccinators, including those delivering National Immunisation Schedule vaccines, vaccines on an authorised programme or privately purchased vaccines including travel vaccines.

The Schedule aims to protect children and adults against 16 serious vaccine-preventable diseases and offers publicly funded immunisation to individuals at risk of COVID-19, hepatitis A, influenza, varicella, TB, meningococcal and/or pneumococcal disease.

Note: The term 'vaccinator' used throughout these standards applies to *any* health professional offering a vaccinator service, including registered nurse vaccinators, authorised vaccinators, pharmacist vaccinators, GPs and midwives. For the purposes of this appendix the term pharmacist vaccinator refers to both registered pharmacist and registered intern pharmacist who have met the educational and clinical requirements: although the scope of vaccines they can administer is different, the process they undergo to gain vaccinator status is the same. These standards apply to fully authorised, pharmacist and provisional vaccinators. For vaccinating health workers, see section A4.3.

## A3.2 Health and Disability Commissioner (Code of Health and Disability Services Consumers' Rights) Regulations 1996

It is expected that all organisations and providers offering immunisation services practise in accordance with the Health and Disability Commissioner (Code of Health and Disability Services Consumers' Rights) Regulations 1996. The Regulations establish the rights of consumers and the obligations and duties of providers to comply with the Code of Rights made pursuant to the Health and Disability Commissioner Act 1994.

The obligation under the Regulations is to take 'reasonable actions in the circumstances to give effect to the rights and comply with the duties' in the Code of Rights. The Code of Rights is as follows.

- Right 1: Right to be treated with respect
- Right 2: Right to freedom from discrimination, coercion, harassment and exploitation
- Right 3: Right to dignity and independence
- Right 4: Right to services of an appropriate standard
- Right 5: Right to effective communication
- Right 6: Right to be fully informed
- Right 7: Right to make an informed choice and give informed consent
- Right 8: Right to support
- Right 9: Rights in respect of teaching or research
- Right 10: Right to complain

For more detailed information on the Code of Health and Disability Services Consumers' Rights, refer to the Health and Disability Commissioner's website ([hdc.org.nz](http://hdc.org.nz)).

## A3.3 Immunisation standards for vaccinators

These standards apply to fully authorised, pharmacist and provisional vaccinators. For vaccinating health workers, see section A4.3.

**Standard 1: The vaccinator is competent in all aspects of the immunisation technique and has the appropriate knowledge and skills for the task**

### Required characteristics of the vaccinator

- 1.1 The vaccinator completes an appropriate training programme approved by the Ministry of Health. If a vaccinator is working as a fully authorised vaccinator, pharmacist or provisional vaccinator, they will also have undertaken a clinical assessment and vaccinate in accordance with their Scope of Practice (see A3.6).



- 1.2 Vaccinators are required to have a summary<sup>1</sup> of their immunisation practice over the past 12 months.
- 1.3 The vaccinator remains current with developments in immunisation theory, practice, cultural competency, and policy. At least every two years the vaccinator is required to retrain having completed a vaccinator update course that meets the current *Vaccinator Update Course Standards* (published by IMAC) and have evidence of completion. See authorisation requirements outlined in A3.6.
- 1.4 The vaccinator maintains linkages with other providers associated with immunisation delivery; for example, immunisation coordinators, outreach immunisation providers, Māori and Pacific health providers, and their local district AIR team.
- 1.5 Vaccinators are recommended to carry indemnity insurance for their personal/professional protection.

## Standard 2: The vaccinator obtains informed consent to immunise

### Required characteristics of the vaccinator

- 2.1 The vaccinator is able to assess the knowledge of the individual/parent/guardian regarding vaccine-preventable diseases and the process of immunity, and has the knowledge of the relevant diseases and vaccines to be able to provide evidence-based information to enable individuals/parent/guardian to make an informed choice and give informed consent.
- 2.2 The vaccinator communicates in a form, language and culturally appropriate way that enables the individual/parent/guardian to understand the information provided. Communication should be supported by evidence-based health information material (see section 2.1.2).
- 2.3 The vaccinator allows time to answer questions and obtains feedback indicating that the individual/parent/guardian understands which vaccine is being recommended and why.
- 2.4 The vaccinator informs the individual/parent/guardian about the AIR, including information on the use and disclosure of the information held on the AIR, how the information is stored, and that all vaccinations given will be recorded on the AIR.
- 2.5 The AIR is maintained by Health NZ | Te Whatu Ora. Information about a consumer's immunisation history in AIR is normally shared with their enrolled General Practice and is available to other health care practitioners as required for the consumer's health care. Health NZ | Te Whatu Ora will also use information in AIR for planning, statistical and research purposes. For more information about a consumer's privacy in relation to AIR, including their rights to control access to and use of their information, they can be referred to <https://www.tewhatauora.govt.nz/AIR-Privacy>
- 2.6

<sup>1</sup> The summary should include type of immunisation practice as a vaccinator (eg, general practice, occupational health, pharmacy, etc); types of vaccinations given (eg, intramuscular, subcutaneous, intradermal); and other responsibilities related to immunisation (eg, cold chain-designated person, etc).

- 2.7 Consent does not need to be given in writing (except for school-based immunisation programmes and BCG vaccination), but the vaccinator must document in the clinical notes a summary of the discussion and note that verbal consent was obtained.
- 2.8 The vaccinator obtains consent for each immunisation episode and documents that the individual/parent/guardian has been made aware of the benefits and risks of the disease and the vaccine in order to make an informed choice about immunisation and the immunisation programme, including the AIR (see section 2.3.5).
- 2.9 If the individual/parent/guardian declines to be immunised/to immunise their child, the vaccinator provides information about keeping themselves and others healthy. The individual/parent/guardian should be advised that they can reconsider their decision at any time, and the declined immunisation will be offered again by their health provider.

### Standard 3: The vaccinator provides safe immunisation

#### Required characteristics of the vaccinator and immunisation setting

- 3.1 The venue provides privacy and is appropriate for the individual/parent/guardian/whānau. Facilities are available for assessment and management of adverse events, including anaphylaxis (see section 2.3.3).
- 3.2 If the venue is a non-clinical setting (eg, in a home, workplace, marae or school) then a minimum of two immunisation team members must be present for vaccination; one of whom must be an authorised vaccinator or pharmacist vaccinator, the other must be a competent adult who is able to call for emergency support and has a current basic life support certificate.
- 3.3 The vaccinator can manage AEFIs, including anaphylaxis, ensures that they have onsite access to the minimum set of emergency equipment (see Table 2.12 in chapter 2), and has a contingency plan for seeking emergency assistance.
- 3.4 Because of the potential for anaphylactic reactions, vaccine recipient (with their parents/guardians if applicable) are required to remain under observation for a minimum of 20 minutes after immunisation.
- 3.5 The vaccinator ensures continuity of the cold chain and adheres to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* and the practice/clinic cold chain management policy. The vaccinator ensures the practice/clinic achieves Cold Chain Accreditation.<sup>2</sup>
- 3.6 Before vaccinating, the vaccinator undertakes an appropriate clinical assessment (pre-vaccination screen) (see section 2.1.3).
- 3.7 The vaccinator uses clean techniques in the preparation and administration of all vaccines (see section 2.1 and Appendix 7), visually checks the vaccine, checks expiry date, prepares vaccine as appropriate and uses vaccines within the recommended period after preparation.

<sup>2</sup> Refer to Cold chain standards for vaccines (available at <https://www.tewhātuora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines/>).

- 3.8 The vaccinator provides verbal and written information that is evidence based and follows best practice principles about care after immunisation (see sections 2.1.2 and 2.3.1).

#### Standard 4: The vaccinator documents information on the vaccine(s) administered, and maintains patient confidentiality

##### Required characteristics of the vaccinator

- 4.1 The vaccinator has had training in the correct use of their PMS, the SBVS, the AIR manual forms to enable them to correctly enter an individual's information on the AIR (if applicable) and to claim an immunisation benefit (if applicable).
- 4.2 The vaccinator documents the individual's personal details, including NHI number, name, date of birth, ethnicity, address, contact telephone number, next of kin details and primary health care provider (if the vaccinator is not the usual primary health care provider).
- 4.3 Having chosen the appropriate immunisation schedule, the vaccinator documents the following details:
- consent obtained
  - date vaccine administered
  - vaccine type and number in the series
  - batch number and expiry date
  - injection site (eg, 'right deltoid' not 'upper arm')
  - needle length
  - that the patient was observed for 20 minutes post-vaccination
  - if the vaccine was given by a non-standard route (the reasons must be documented)
  - the immunisation event in the child's *Well Child Tamariki Ora My Health Book* (if applicable)
  - the date for the next immunisation in the child's *Well Child Tamariki Ora My Health Book* (if applicable)
  - advice and resources given.
- 4.4 The vaccinator ensures the immunisation information is sent to the AIR (ie, electronically or manually) where applicable.
- 4.5 The vaccinator ensures the immunisation certificate (see Appendix 5) is accurately completed following the 15-month and 4-year immunisation events.
- 4.6 If the practice/clinic is not the usual primary health care provider, then the individual's primary health care provider is informed by the vaccinator or by AIR notification within five working days of giving the vaccine, unless the individual declines for this to occur.
- 4.7 All clinical documentation is appropriately managed and stored to maintain confidentiality, and is made available to the individual/parent/guardian on request.

Standard 5: The vaccinator administers all vaccine doses for which the vaccine recipient is due at each visit and only follows true contraindications

Required characteristics of the vaccinator

- 5.1 The vaccinator adheres to the National Immunisation Schedule or approved immunisation programme and delivers all the immunisations recommended for that visit, unless the individual/parent/guardian does not consent to this.
- 5.2 When catch-up immunisation is required, this is planned with the minimum number of visits/injections and in conjunction with the individual/parent/guardian.
- 5.3 A dose of vaccine is deferred or avoided only when contraindicated or the individual/parent/guardian has chosen to defer/avoid it. The reason for deferral or avoidance must be documented (see section 2.1.4 and the specific disease chapters).

Standard 6: The vaccinator reports AEFIs promptly, accurately and completely

Required characteristics of the vaccinator

- 6.1 All serious or unexpected AEFIs are reported by the vaccinator to the Medical Assessor, CARM (see section 1.6.3 for the adverse event reporting process) and to the individual's primary health care provider (if the vaccinator is another person). If the individual/parent/guardian does not consent to being identified, the report should be made without personal identification.
- 6.2 The vaccinator informs the individual/parent/guardian that if an adverse event occurs, they can also report it to CARM.
- 6.3 When a CARM report is received, and further doses of the vaccine have been contraindicated, the vaccinator advises the local district AIR Administrator so that an appropriate AEFI code is recorded in the individual's AIR record.
- 6.4 The vaccinator seeks specialist (eg, GP, paediatrician, infectious diseases physician or medical officer of health) opinion if uncertain about the safety of further doses, and referral is made to secondary care if required.
- 6.5 The vaccinator ensures the adverse event, and any subsequent decisions relating to the event, are effectively communicated to the individual/parent/guardian and clearly documented in the child's *Well Child Tamariki Ora My Health Book* (if applicable) and in the patient records, and appropriate follow-up is carried out.

## **A3.4 Guidelines for organisations storing vaccines and/or offering immunisation services**

These guidelines apply to all organisations that store vaccines and/or offer immunisation services, including (but not limited to) general practices, public health

units, community pharmacies, travel clinics, occupational health clinics, emergency medical services, research units and hospital wards/clinics/departments/pharmacies.

## The organisation that employs vaccinators to offer immunisation services has links to primary health care and to Well Child Tamariki Ora providers

### Required characteristics

Immunisation is not delivered in isolation, but as an integrated part of primary health care services, including Well Child Tamariki Ora for children.

If possible, at the time of immunisation, the organisation undertakes other health promotion and/or disease prevention activities as applicable, such as the Well Child National Schedule or Care Plus.

Immunisation events, childhood and adult, are well communicated to other health services linked to the individual (eg, primary health care, outreach immunisation services, pharmacies, occupational health).

## The organisation achieves high immunisation coverage of its population

### Required characteristics

The organisation has an effective, secure, NHI-based system for recording and reporting immunisations and identifying individuals requiring immunisation.

Respecting the individual's/parent's/guardian's rights to make an informed choice, the organisation takes all steps to ensure that an individual's immunisation schedule commences on time and that subsequent events are administered on the due date.

The organisation has electronic linkage to the AIR for registration and immunisation event notification, and the AIR is used to assist with follow-up. If electronic linking is not available, manual processes must be used.

The organisation has a robust reminder (pre-call) system which encourages the delivery of on-time immunisation and timely follow-up for overdue immunisation.

The organisation has an effective communication strategy to target high-needs population groups.

Attendance at the practice/organisation is used as an opportunity to remind individuals/parents/guardians of the importance of immunisation and, if appropriate, to check and offer to bring up to date the individual's immunisation status.

Those who do not respond to recall and who have not declined to take part are referred to the outreach immunisation service, as per local protocol.

## The organisation supports vaccinators and AIR administrators

### Required characteristics

The organisation has comprehensive immunisation-related policies based on best practice, informed consent, the vaccination process and management of adverse events.

The organisation uses a pharmaceutical refrigerator to store vaccines, has a vaccine cold chain policy in place and meets the requirements outlined in the *National Standard for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)*<sup>3</sup> for all areas within the organisation storing vaccines.

The organisation provides training and support workers (eg, kaiāwhina, community health workers) for vaccinators working in the community.

The organisation supports the need for vaccinators to have access to ongoing education and training on all aspects of immunisation at least every two years and when there are changes to the Schedule.

The organisation provides initial and ongoing training and support specific to the AIR, PMS, and/or the SBVS (if applicable).

## The service is readily available, with no barriers to access

### Required characteristics

No fee is charged to the individual/guardian for the immunisations that are on the Schedule or high-risk programmes (or for completing the child's immunisation certificate). Regardless of their immigration and citizenship status, all children aged under 18 years are eligible to receive funded Schedule vaccines, and providers may claim the immunisation benefit for these children. Non-residents who were under age 18 years when they commenced HPV vaccination in New Zealand are currently funded to complete the course, even if they are aged 18 years or older when they complete it. Further information on eligibility can be found on the Health New Zealand | Te Whatu Ora website ([www.tewhatora.govt.nz/for-health-providers/publicly-funded-health-and-disability-services/](http://www.tewhatora.govt.nz/for-health-providers/publicly-funded-health-and-disability-services/)).

Immunisations are provided to both enrolled and casual patients, at all times when the organisation or service is open.

A person's immunisation status is checked at each visit to the service.

The organisation is culturally appropriate (ie, all health workers are assessed as culturally competent, reflect the populations they serve and offer a range of health information resources<sup>4</sup> in different languages).

<sup>3</sup> Refer to the National Immunisation Programme cold chain management (available at [www.tewhatora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhatora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).

<sup>4</sup> Ministry of Health immunisation resources are available in English and a variety of languages from the HealthEd website ([healthed.govt.nz](http://healthed.govt.nz)) or from the local health education authorised provider.

## A3.5 Recommended resources

- The current Immunisation Handbook
- The current National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 2nd Edition (available at [www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines))
- Cold Chain Management Policy Template (available at [www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines))
- Cold Chain Accreditation Provider Self-Assessment Form (available at [www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines))
- Cold Chain Accreditation Provider Reviewer Form (available at [www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines))
- Kōrero Mārama: Health Literacy and Māori – Results from the 2006 Adult Literacy and Life Skills Survey, February 2010 ([www.health.govt.nz/publications/korero-marama-health-literacy-and-maori-results-from-the-2006-adult-literacy-and-life-skills-survey](http://www.health.govt.nz/publications/korero-marama-health-literacy-and-maori-results-from-the-2006-adult-literacy-and-life-skills-survey))
- Whakamaua: Māori Health Action Plan 2020–2025, July 2020 ([www.health.govt.nz/publications/whakamaua-maori-health-action-plan-2020-2025](http://www.health.govt.nz/publications/whakamaua-maori-health-action-plan-2020-2025))
- Pae Ora (Healthy Futures) Act (available at [www.health.govt.nz/about-us/new-zealands-health-system/overview-and-statutory-framework/pae-ora-healthy-futures-act](http://www.health.govt.nz/about-us/new-zealands-health-system/overview-and-statutory-framework/pae-ora-healthy-futures-act))
- New Zealand’s health system (available at [www.health.govt.nz/about-us/new-zealands-health-system/overview-and-statutory-framework/pae-ora-healthy-futures-act](http://www.health.govt.nz/about-us/new-zealands-health-system/overview-and-statutory-framework/pae-ora-healthy-futures-act))

## A3.6 Relevant legislation and regulations

See [www.legislation.govt.nz](http://www.legislation.govt.nz).

- Health (Immunisation) Regulations 1995
- Medicines Act 1981
- Medicines Regulations 1984
- Health (Infectious and Notifiable Diseases) Regulations 1966, Amendment No. 2, regulation 44A
- Health Act 1956, section 22F
- Health Information Privacy Code 2020



- Health and Disability Commissioner Act 1994: Code of Health and Disability Services Consumers' Rights 1996 (see [hdc.org.nz](http://hdc.org.nz))
- Health Practitioners Competence Assurance Act 2003
- Privacy Act 1993
- The Children's Act 2014
- Accident Compensation Act 2001
- Health and Safety at Work Act 2015
- Resource Management Act 1991
- Primary Maternity Services Notice 2007 (see <https://www.health.govt.nz/publications/primary-maternity-services-notice-2007>) pursuant to section 88 of the New Zealand Public Health and Disability Act 2000
- Therapeutic Products Act 2023

### Immunisation Advisory Centre ([immune.org.nz](http://immune.org.nz))

- Vaccinator Foundation Course Standards
- Vaccinator Update Course Standards

# Appendix 4: Authorisation and criteria of vaccinators

This section provides details around the authorisation of vaccinators. There are three main categories of authorisation: fully authorised, provisionally authorised and supervised vaccinators. Pharmacists can vaccinate, having met certain criteria, as either fully authorised or provisionally authorised vaccinators. See Table A4.1 (Full authorisation), Table A4.2 (Pharmacist vaccinators), Table A4.3 (Provisional vaccinators), and Table A4.4 (supervised vaccinators) for details of the criteria and authorisation of each group.

- All vaccinators should complete Health New Zealand | Te Whatu Ora approved vaccinator course(s) relevant to their authorisation type.
- All authorised vaccinators must complete an immunisation update every two years to maintain their status and to apply for re-authorisation.
- All vaccinators are required to meet resuscitation requirements as detailed in section A4.4.

## A4.1 Protocols for full authorisation of vaccinators and pharmacist vaccinators

### A4.1.1 Authority for fully authorised vaccinators<sup>5</sup> and pharmacist vaccinators

A person may be authorised under regulation 44A(2) of the Medicines Regulations 1984 by the Director-General of Health or the National Medical Officer of Health to administer a vaccine for the purposes of an approved immunisation programme.<sup>6</sup> Regulation 44A(2) stipulates that the person seeking approval must apply in writing to the Director-General or a medical officer of health and provide documentary evidence that they:

- can carry out basic emergency techniques including resuscitation and the treatment of anaphylaxis
- have knowledge of the safe and effective handling of immunisation products and equipment
- can demonstrate clinical interpersonal skills
- have knowledge of the relevant diseases and vaccines to be able to explain the vaccination to the individual, parent or guardian who is to consent to the

<sup>5</sup> Fully authorised vaccinators were previously called 'authorised independent vaccinators'.

<sup>6</sup> See the Ministry of Health document *Definition of an Approved Immunisation Programme* (available for download from [www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/about-immunisation-in-new-zealand/immunisation-policy-statements/](http://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/about-immunisation-in-new-zealand/immunisation-policy-statements/)).

vaccination on behalf of the individual, to ensure that the individual or parent or guardian of the individual can give informed consent to the vaccination.

The usual protocol requires fully authorised vaccinator applications to be submitted to a medical officer of health in the applicant’s local region. Authorisation given under Regulation 44A(2) is valid for a period of two years from the date of authorisation and is subject to such conditions as the Director-General or the National Medical Officer of Health thinks fit. During the early stages of the COVID-19 response, the Director of Public Health, in their capacity as a National Medical Officer of Health, authorised all authorised vaccinators and provisional authorised vaccinators to provide National Immunisation Schedule and funded vaccinations (as noted in their authorisation) for those at increased risk of vaccine-preventable disease (as identified in this Immunisation Handbook). This meant they did not need to apply for authorisation in different PHU areas. This remains in effect until 1 June 2024. See Section A4.1.5 *Process when a vaccinator is new to the health district in which they intend to practise*.

Successful applicants will be authorised to administer either all or specific vaccines depending on the training they have completed (see Table A4.1). Details of the training they must complete is set out in section A4.1.2.

**Table A4.1: Fully authorised vaccinators**

Note: All vaccinators are required to meet resuscitation requirements (see section A4.4).

Vaccinator type	Authorisation requirements	Profession	Vaccines they may be able to administer	Age groups <sup>a</sup>	Sites for injection	Authority to obtain informed consent
<b>Fully authorised vaccinator</b>	Director-General or Medical Officer of Health (under reg 44A of the Medicines Regulations 1984)	Health professionals with current annual practicing certificate <sup>b</sup>	Vaccines on the National Immunisation Schedule and any other vaccines part of an approved immunisation programme (approved by the Director-General or Medical Officer of Health)	All ages	Vastus lateralis Deltoid	Yes

a. Restrictions may apply depending on scope of authorisation, vaccine reclassification and/or district funding to age groups that vaccinator can administer vaccines to. It is the vaccinators responsibility to understand and adhere to these restrictions.

b. Practitioners without a New Zealand practicing certificate may be unable to get indemnity insurance.

## Authority for pharmacist vaccinators

A number of vaccines have been reclassified by the Medicines Classification Committee from prescription medicines to prescription medicine except when administered by pharmacists or registered intern pharmacists who have successfully completed the *Vaccinator Foundation Course* (or any equivalent training course approved by the Ministry of Health, but excluding vaccinators who have completed the *Provisional*

Vaccinator Foundation Course) and who comply with the immunisation standards of the Ministry of Health.

The reclassification means that pharmacists and pharmacist interns can administer specific vaccines once they have: successfully completed a Ministry of Health-approved VFC (including the open-book assessment); and are complying with the immunisation standards as described in Appendix 3 of this Handbook. Pharmacist and intern pharmacist vaccinators are expected to be aware of which vaccines have been reclassified for their scope (see Table A4.2).

Due to these classifications, pharmacist vaccinators are not required to apply to a medical officer of health for authorised vaccinator status to be able to administer vaccines that have been reclassified. However, the expectation is they notify Pharmaceutical Society of New Zealand (PSNZ) when they have completed the requirements specified above, including the course completion date (see Completion of authorisation).

Like all vaccinators, pharmacists and pharmacist interns must attend an approved vaccinator update every two years to be able to continue to administer vaccines. The training required for pharmacists and intern pharmacists is detailed in section A4.1.3.

**Table A4.2: Pharmacist vaccinators**

Note: All vaccinators are required to meet resuscitation requirements (see section A4.4).

Vaccinator type	Authorisation requirements	Profession	Vaccines they may be able to administer	Age groups <sup>a</sup>	Sites for injection	Authority to obtain informed consent
<b>Pharmacist vaccinator</b>	Enabled to vaccinate pursuant to the Medicines Regulations classifications on completion of full vaccinator training. It is then recommended that they inform the Pharmaceutical Society of New Zealand to be added to the vaccinator database.	Registered Pharmacists	Influenza MMR COVID-19 <sup>b</sup> HPV Meningococcal Tdap Zoster	Ages 3 years and over All ages All ages Ages 9 years and over Ages 16 years and over Ages 18 years and over. Pregnant women aged 13 years and over Ages 50 years and over	Primarily deltoid <sup>c</sup>	Yes

*Continued overleaf*

Vaccinator type	Authorisation requirements	Profession	Vaccines they may be able to administer	Age groups <sup>a</sup>	Sites for injection	Authority to obtain informed consent
<b>Intern Pharmacist Vaccinators</b>	Enabled to vaccinate pursuant to the Medicines Regulations classifications on completion of full vaccinator training. It is then recommended that they inform the Pharmaceutical Society of New Zealand to be added to the vaccinator database.	Registered Pharmacist interns	Influenza MMR COVID-19 <sup>b</sup> HPV	Ages 3 years and over All ages All ages Ages 9 years and over	Primarily deltoid <sup>c</sup>	Yes
<b>Provisional pharmacist vaccinator<sup>d</sup> MMR, Influenza and COVID 19</b>	Director-General or Medical Officer of Health (under reg 44A of the Medicines Regulations 1984)	Registered Pharmacists and Pharmacist interns	Influenza MMR COVID-19 <sup>b,d</sup>	Ages 3 years and over or 13 years and over <sup>e</sup> Ages 16 and over Ages 3 years and over on completion of Ministry approved COVID-19 training	Deltoid only	Yes

- Restrictions may apply depending on scope of authorisation, clinical assessment undertaken, vaccine reclassification and/or district funding to age groups that vaccinator can administer vaccines to. It is the vaccinators responsibility to understand and adhere to these restrictions.
- Upon completion of appropriate COVID-19 vaccine education course.
- Vastus lateralis can be used when deltoid is not appropriate, and the vaccinator is confident in the use of the site.
- See section A4.2.
- Ages 3 years and over if re/authorised after 19 April 2022, otherwise approved age is 13 years and over.

## A4.1.2 Process for full authorisation for vaccinators and pharmacist vaccinators

### Assessment requirements

To become a fully authorised vaccinator or pharmacist/intern pharmacist vaccinator, all applicants must first meet the following HNZ | TWO requirements.

- Demonstrate that within the preceding 24 months they have attended, completed and passed a Vaccine Foundation Course (VFC) and have received the

associated certificate. The VFC must meet the current *Vaccinator Foundation Course Standards* (published by IMAC) and the course should consist of:

- a. a minimum of 16 hours' educational input
  - b. a written open-book assessment (minimum one-hour duration), which may be oral at the facilitator's discretion.
2. Undergo an independent clinical assessment by an immunisation coordinator or an approved assessor (as agreed by the Medical Officer of Health).<sup>7</sup> Information about the practice environment, including cold chain and emergency management processes, will be collected at the time of the clinical assessment. When a vaccinator is expecting to provide vaccines to infants and young children under 3 years of age, their clinical assessment must include the vaccination of at least one child aged under 2 years using the vastus lateralis injection site.
  3. Have evidence that they hold a current practising certificate from their registration authority (eg, Nursing Council of New Zealand, Pharmacy Council of New Zealand, Paramedic Council).
  4. Have a current cardiopulmonary resuscitation (CPR) certificate (see section A4.4 for details).

## Completion of authorisation

### Fully authorised vaccinator applicants

Authorised vaccinator applicants<sup>8</sup> who have successfully completed their clinical assessment will then need to apply for authorisation under Regulation 44A(2) by submitting an application, including the documentation described above, to a medical officer of health. Generally, this will be their local Medical Officer of Health, but in some instances, this authorisation may be given by a national Medical Officer of Health.

### Pharmacist vaccinator applicants

Pharmacists and intern pharmacists who have met the assessment requirements detailed above and should notify the Pharmaceutical Society (PSNZ) by an email containing the following information:

1. full name
2. membership number
3. name of the pharmacy or pharmacies which vaccinations will be provided from, or if the pharmacist is a locum
4. date of the course (or update course)
5. date of their clinical assessment.

<sup>7</sup> If it has been more than 12 months but less than 24 months since the applicant completed a full VFC, they should complete an online update prior to the clinical assessment.

<sup>8</sup> Fully authorised vaccinators will not be able to vaccinate without a prescription or standing order until they have completed all the required processes and have received their authorisation letter.

Copies of the vaccination certificate or resuscitation certificates are not required. Emails should be sent to [p.society@psnz.org.nz](mailto:p.society@psnz.org.nz) and need to include 'pharmacist vaccinator' in the subject line.

For audit purposes, it is recommended that all pharmacist vaccinators keep a copy of the record of their vaccinator training and other relevant documentation in a file at their current place of work.

### A4.1.3 Process for renewal of vaccinator status for fully authorised vaccinators and pharmacist vaccinators

Authorisation of fully authorised vaccinators is valid for two years from the date of the authorisation approval letter from the Medical Officer of Health. To maintain status as an authorised vaccinator, authorisation must be renewed two yearly. To be authorised, the vaccinator must meet the requirements specified below.

To renew their vaccinator status, vaccinators are required to:

1. during the past two years or within a month of expiry of status, have completed a vaccinator update course that meets the current *Vaccinator Update Course Standards*<sup>9</sup>
2. have a summary of their immunisation practice over the past 12 months. The summary should include type of immunisation practice as a vaccinator (eg, general practice, occupational health, pharmacy etc); types of vaccinations given (eg, intramuscular, subcutaneous, intradermal); and other responsibilities related to immunisation (eg, cold chain-designated person, etc)
3. have evidence of a current practising certificate
4. have evidence of a current CPR certificate (see section A4.4 for details).

#### Fully authorised vaccinators

To continue vaccinating, fully authorised vaccinators need to apply for renewal of their authorisation to their local Medical Officer of Health and submit all relevant documentation (ie, immunisation update, CPR certificates and immunisation summary), prior to the expiry of their authorised vaccinator status.

#### Pharmacist vaccinators and intern pharmacist vaccinators

Prior to the expiry of their pharmacist vaccinator status (two-yearly, on the anniversary of their vaccinator foundation course), pharmacist vaccinators should notify PSNZ when they have completed the HNZ | TWO requirements specified above.

<sup>9</sup> Authorised vaccinators will not be able to vaccinate without a prescription or standing order until they have completed all the required processes.



#### A4.1.4 Process when fully authorised vaccinator status has not been maintained or has not been achieved

If it is less than five years since the vaccinator attended and completed an approved vaccinator course (ie, initial VFC or subsequent approved vaccinator update)

When a vaccinator has not achieved or maintained their vaccinator status, they must:

1. have a clinical assessment by an immunisation coordinator or approved assessor, completed within three months prior to application for authorisation/reauthorisation. If vaccinator status expired by less than one month, a clinical assessment is not required
2. have completed a vaccinator update course that meets the current *Vaccinator Update Course Standards* in the last two years
3. have a summary of their immunisation practice over the past 12 months or intended area of practice. The summary should include type of immunisation practice as a vaccinator (eg, general practice, occupational health, pharmacy, etc); types of vaccinations given (eg, intramuscular, subcutaneous, intradermal); and other responsibilities related to immunisation (eg, cold chain-designated person)
4. have evidence of a current practising certificate
5. have evidence of a current CPR certificate (see section A4.4 for details).

#### If it is five or more years since the applicant completed an approved vaccinator training and they have not achieved or maintained their vaccinator status

If it is more than five years since the applicant completed their initial VFC or subsequent approved vaccinator update, they will be required to attend and pass another VFC. This is because there will have been significant developments in vaccination delivery in the intervening interval.

See section A4.1.2 *Process for full authorisation for vaccinators and pharmacist vaccinators*.

#### A4.1.5 Process when a vaccinator is new to the health district in which they intend to practise

Currently in place is provision for fully authorised vaccinators to be covered to work nationally until 1 June 2024. However, if a fully authorised vaccinator wishes to practise outside of the health district and/or public health area they were initially authorised for, they must advise the local Medical Officer of Health for the new area, and send through a copy of their current authorisation.

Pharmacist and intern pharmacist vaccinators are required to advise the local immunisation coordinator of their intention to set up a new pharmacist vaccinator service; this is to ensure that the coordinator is aware of which pharmacies require three-yearly spatial logging of the refrigerator. Where a vaccination service is already being offered this is not required.

#### A4.1.6 Additional endorsement process for BCG vaccinators

All BCG vaccinators are fully authorised vaccinators with BCG endorsement. They are authorised by the local Medical Officer of Health as described below.

#### New BCG vaccinators and gazetted BCG vaccinators seeking regional BCG endorsement

To be endorsed as a BCG vaccinator, the applicant needs to:

1. complete an approved VFC
2. be nominated by their employer to become a BCG vaccinator
3. successfully complete a Ministry of Health-approved online BCG vaccination course
4. complete under clinical supervision a minimum of five BCG vaccinations (using a standing order or prescription)
5. successfully complete a BCG clinical assessment by an approved BCG assessor
6. apply to the Medical Officer of Health for BCG endorsement approval, providing documented evidence of these requirements.

If a BCG vaccinator needs to administer additional Schedule vaccines, they will need to undertake a clinical assessment appropriate for the age group they will be vaccinating. Standing orders or prescriptions are required for the clinical assessment process.

For more information, see the Health New Zealand | Te Whatu Ora webpage *BCG vaccine and vaccinator endorsement* (available at <https://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/bcg-vaccine-and-vaccinator-endorsement/>).

#### Process for two-yearly renewal of BCG vaccinator status

To renew BCG endorsement, vaccinators must apply to their local Medical Officer of Health prior to the expiry date and provide documented evidence that they:

1. are a current authorised vaccinator, and
2. have completed an online vaccination course that includes an update on BCG.
3. A BCG vaccinator who also holds full authorisation will need to complete a standard vaccinator update course, in addition the BCG update.

Note: BCG vaccinators must complete a *BCG Vaccinator Update* course every two years. This online course is available as part of IMAC education (available at [www.immune.org.nz](http://www.immune.org.nz)).

## A4.2 Protocols for provisional authorised vaccinators and provisional pharmacist vaccinators

In April 2020, as part of the New Zealand COVID-19 response, a pathway to provisional authorisation for vaccinators (PAV) was developed. This pathway was a short-term measure alongside the *Provisional Vaccinator Foundation Course* available from IMAC. This pathway was discontinued on 30 September 2022.

### A4.2.1 Authority for provisional authorised vaccinators and provision authorised pharmacist vaccinators

Provisional authorised vaccinators and provisional authorised pharmacist vaccinators, like fully authorised vaccinators, are authorised under regulation 44A(2). Regulation 44A(2) stipulates that the person seeking approval must apply in writing to the Director-General or the national Medical Officer of Health and provide documentary evidence that they:

1. can carry out basic emergency techniques, resuscitation, and the treatment of anaphylaxis
2. have knowledge of the safe and effective handling of immunisation products and equipment
3. can demonstrate clinical interpersonal skills
4. have knowledge of the relevant diseases and vaccines to be able to explain the vaccination to the individual, parent or guardian of the individual who is to consent to the vaccination on behalf of the individual, to ensure that the individual or parent or guardian of the individual can give informed consent to the vaccination.

Provisional authorised vaccinators and provisional authorised pharmacist vaccinators are only able to be authorised to administer influenza, MMR and COVID-19 vaccines (these are the only vaccines covered by the *Provisional Vaccination Foundation Course* and the *COVID-19 Vaccine Education Course* that these vaccinators complete). See Table A4.3.

**Table A4.3: Provisional authorised vaccinators**

Note: All vaccinators are required to meet resuscitation requirements (see section A4.4).

Vaccinator type	Authorisation requirements	Profession	Vaccines they may be able to administer	Age groups <sup>a</sup>	Sites for injection	Authority to obtain informed consent
<b>Provisional Vaccinator MMR, Influenza and COVID 19</b>	Director-General or national Medical Officer of Health (under reg 44A of the Medicines Regulations 1984)	Health professionals with current annual practicing certificate <sup>b</sup>	Influenza MMR COVID-19	Ages 3 years and over Ages 3 years and over Ages 3 years and over on completion of Ministry approved COVID-19 training	Primarily deltoid <sup>c</sup>	Yes
<b>Provisional pharmacist vaccinator MMR, Influenza and COVID 19</b>	Director-General or national Medical Officer of Health (under reg 44A of the Medicines Regulations 1984)	Registered Pharmacists and Pharmacist interns	Influenza MMR COVID-19	Ages 3 years and over <sup>d</sup> Ages 16 and over Ages 3 years and over, on completion of Ministry approved COVID-19 training		

- Restrictions may apply depending on scope of authorisation, vaccine reclassification and/or district funding to age groups that vaccinator can administer vaccines to. It is the vaccinators responsibility to understand and adhere to these restrictions.
- Practitioners without a New Zealand practicing certificate may be unable to get indemnity insurance.
- Vastus lateralis can be used when deltoid is not appropriate, and the vaccinator is confident in the use of the site.
- Ages 3 years and over if re/authorised after 19 April 2022, otherwise approved age is 13 years and over.

## A4.2.2 Process for provisional authorised vaccinators

To achieve provisional authorised vaccinator or provisional authorised pharmacist vaccinator status, HNZ | TWO requires vaccinators to:

- complete the online *Provisional Vaccinator Foundation Course* (including learning assessment and webinar)
- successfully complete a peer assessment of clinical practice
- hold a current *New Zealand Annual Practising Certificate*
- final year students completing a degree within a relevant field of study to provide proof of enrolment and student identification
- have evidence of current CPR certificate (see section A4.4 for details)

6. submitted a completed application for authorisation as a provisional authorised vaccinator to the Ministry of Health
7. on receipt of written authorisation from a medical officer of health, provisional authorised vaccinators send copy of authorisation and peer assessment to the local immunisation coordinator.

Provisional authorised vaccinators who wish to continue to vaccinate after expiration of their authorisation will be required to transition to become a fully authorised vaccinator or pharmacist vaccinator. More information is available from the IMAC education website ([www.immune.org.nz](http://www.immune.org.nz)).

## A4.3 Protocols for Vaccinating Health Workers

In May 2022 a new vaccinating health worker (VHW) role was created under section 44AA of the Medicines Regulations 1984 (see Table A4.4). Authority for already approved COVID-19 vaccinators (working under supervision) (CVWUS) expired on 1 June 2023.

**Table A4.4: Vaccinating health workers (VHW)**

Note: All vaccinators are required to meet resuscitation requirements (see section A4.4). Anaphylaxis training is part of the IMAC course for VHW.

Vaccinator type	Authorisation requirements	Profession	Vaccines they may be able to administer	Age groups	Sites for injection	Authority to obtain informed consent
<b>Vaccinating Health Worker: Stage one</b>	Director-General or National Medical Officer of Health (under reg 44AA of the Medicines Regulations 1984)	Person working under clinical supervision and direction of a suitably qualified health practitioner	mRNA-CV (30 µg) <sup>a</sup>	Ages 12 years and over	Deltoid only	<b>No</b>
			Influenza, administration only <sup>a</sup>	Ages 12 years and over		
			Tdap, administration only <sup>b</sup>	Ages 11 years and over		
			HPV9, administration only <sup>b</sup>	Ages 11 years and over		

*Continued overleaf*

<b>Vaccinating Health Worker: Stage two</b>	Director-General or National Medical Officer of Health (under regulation 44AA of the Medicines Regulations 1984)	Person working under clinical supervision and direction of a suitably qualified health practitioner	mRNA-CV (30 µg), administer <sup>a,c</sup>	Ages 12 years and over	Deltoid only	<b>No</b>
			mRNA-CV (10 µg) administer <sup>a,c</sup>	Ages 5 to 11 years		
			Influenza, prepare and administer <sup>a,c,d</sup>	Ages 5 years and over		
			Tdap, prepare and administer <sup>b,c,d</sup>	Ages 11 years and over		
			HPV, prepare and administer <sup>b,c,d</sup>	Ages 11 years and over		
		MMR, prepare and administer <sup>c,d</sup>	Ages 5 years and over			
		Prepare mRNA-CV multidose vials <sup>c,d</sup>				

- Upon completion of appropriate Stage One core course plus influenza and COVID-19 vaccine specific course.
- Upon completion of appropriate Stage One core course plus Tdap/HPV9 vaccine education course.
- Upon completion of appropriate Stage Two vaccine administration course.
- Upon completion of appropriate Stage Two vaccine preparation training.

### A4.3.1 Authority for vaccinating health workers

A person may be authorised by the Director-General of Health or a National Medical Officer of Health to prepare and administer a vaccine without a prescription. An authorised vaccinating health worker must, at all times while performing the tasks authorised under regulation 44AA, work under the clinical supervision and direction of a suitably qualified health practitioner.

Regulation 44AA(3) stipulates that the person must apply to the Director-General of Health or a National Medical Officer of Health and provide documentary evidence that they:

- have successfully completed training as approved by the Director-General
- can carry out basic emergency techniques, including resuscitation and the treatment of anaphylaxis and
- have knowledge of the safe handling of immunisation products and equipment.

## A4.3.2 Process for authorisation for vaccinating health worker

The VHW role is authorised in stages.

- Stage One vaccinators can administer specific vaccines to a limited age range:
  - mRNA-CV (30 µg) and influenza vaccine to those aged 12 and over
  - and/or Tdap and HPV9 to those aged 11 and over.
- Stage Two vaccinators can prepare and administer influenza and MMR vaccine, and administer prepared mRNA-CV (10 µg) to children from age 5 years. There is an optional extension of training to allow them to prepare multidose vials of mRNA-CV.

Further detail is provided at [tewhatauora.govt.nz/for-the-health-sector/vaccinating-workforce/](https://www.tewhatauora.govt.nz/for-the-health-sector/vaccinating-workforce/)

### Stage One

Vaccinating health workers are not required to be registered health care professionals, but to complete Stage One authorisation they are required to apply to the Health New Zealand | Te Whatu Ora VHW authorisation portal

([workforcerequest.powerappsportals.com](https://workforcerequest.powerappsportals.com)) and provide the following evidence:

1. course completion certificate(s) for Vaccinating Health Worker Stage 1 core course and vaccines specific course(s)
2. completed practical assessment from the IMAC Training and Competency Workbook
3. a current CPR certificate in basic life support (anaphylaxis management is covered through Ministry-approved IMAC training for all vaccinators).

Once authorisation is accepted a letter will be issued stipulating which vaccines they can administer under supervision.

### Stage Two

For further authorisation as a Stage Two Vaccinating Health Worker, all applicants must meet the following Ministry of Health requirements for stage two. Stage Two VHWs may prepare and administer certain vaccines to children aged from 5 years under the clinical supervision and direction of a qualified health professional. There is the option to extend skills by completing then mRNA-CV multidose vial preparation training and authorisation.

To be granted Vaccinating Health Worker Stage 2 status, it is expected all applicants have completed core in-house training for Stage 1 and have completed at least 25 vaccination events over the previous 8 weeks and have been authorised for VHW Stage One – four vaccines. Applicants are required to apply to Health New Zealand | Te Whatu Ora VHW authorisation portal ([workforcerequest.powerappsportals.com](https://workforcerequest.powerappsportals.com)) and provide the following evidence:

1. Vaccinating Health Worker Stage 2 course certificate



2. Completed practical assessment from the IMAC Training and Competency Workbook. Only the completed checklists and signed declaration are required to be submitted, The workbook should be retained by the applicant.
3. To apply for authorisation for preparation of Covid-19 multi-dose vials the signed checklists for mRNA-CV (30 µg), mRNA-CV (15/15 µg), mRNA-CV (10 µg) must be submitted along with the completed declaration.
4. The second-checker course certificate
5. A current CPR certificate in basic life support (anaphylaxis management is covered through Ministry-approved training for all vaccinators) is required for each application for authorisation.

Note: VHW Stage 2 preparation training is not required for pharmacy technicians as this is already covered in their scope of practice.

### A4.3.3 Process for renewal of vaccinator status for vaccinating health workers

Authorisation of a vaccinating health worker (VHW) is valid for two years from the date of the authorisation from the National Medical Officer of Health. To maintain status as an authorised VHW, authorisation must be renewed two yearly and the vaccinator must meet the requirements specified below.

To renew their vaccinator status, vaccinators are required:

1. during the past two years or within a month of expiry date on authorisation letter, have completed a Vaccinating Health Worker update course that meets the current *Vaccinator Update Course Standards*<sup>10</sup>
2. to provide a summary of their immunisation practice over the past 12 months. The summary should include type of immunisation practice as a vaccinator (eg, general practice, pharmacy etc); and other responsibilities related to immunisation (eg, cold chain-designated person, etc)
3. to have evidence of a current CPR certificate (see section A4.4 for details).
4. to submit this evidence to receive updated authorisation letter.

## A4.4 Resuscitation requirements for all vaccinators

All vaccinators, by virtue of their occupation, need to be able to resuscitate patients and therefore need to achieve and maintain the following resuscitation skills:

1. infant, child and adult CPR including mouth-to-mouth

<sup>10</sup> Authorised vaccinators will not be able to vaccinate without a prescription or standing order until they have completed all the required processes.

2. administration of IM adrenaline for treatment of anaphylaxis
3. use of an automated external defibrillator
4. one- and two-person bag valve mask ventilation and mouth-to-mask technique.

Resuscitation training for vaccinators should cover the specific skills outlined above. The use of oxygen, sizing of airways, insertion of intravenous lines and the preparation of emergency medications (except for intramuscular adrenaline) are not skills specifically required of a vaccinator.

**All** vaccinators must maintain their current resuscitation certification, typically, this is required every two years. (Note: employer protocols may require this more frequently.)

**All** vaccinators, except vaccinating health workers, need to be able to administer intramuscular adrenaline in the event of an anaphylactic reaction to an immunisation event (see section 2.3.3).

Vaccinating health workers must be aware of the signs of anaphylaxis and have the knowledge to treat it but are not expected to administer adrenaline in practice.

**All** vaccinators must meet the emergency equipment and management requirements, regardless of the immunisation setting (eg, in general practice and in non-clinical settings, such as homes, schools, rest homes, workplaces and pharmacies), as listed in section 2.3.3.

**All** vaccinators are expected to keep up to date with any guidance changes, including infection control and requirements for PPE.

## A4.5 Local immunisation programmes

Medical Officers of Health may approve additional vaccinations (funded or unfunded) for authorised vaccinators to administer either as part of the standard authorisation process or as part of a local immunisation programme. Public health units (PHUs) need to maintain a register of the authorised vaccinators in their region. Temporary authorised vaccinators can be added to approved local immunisation programmes by Medical Officers of Health.

## A4.6 Minimum staff and equipment requirements for vaccination services

All vaccinators providing immunisation services need to have a minimum of two people present, one of whom must be an authorised vaccinator or pharmacist vaccinator; the other must be a competent adult who is able to call for emergency support and has a basic life support certificate.

Vaccinating health workers must work at all times under clinical supervision and direction of a suitably qualified health practitioner.

The following check list contains the emergency equipment that is required when vaccinating offsite.

Check list of Emergency Equipment required for off-site vaccinations	Office use only
<p>1. Equipment</p> <p>The following should be available:</p> <ul style="list-style-type: none"> <li>• Emergency kit containing:               <ul style="list-style-type: none"> <li>– adrenaline 1:1000 (minimum of 3 ampoules)</li> <li>– syringes (1 mL), 25 mm needles for IM injection (minimum of six)</li> <li>– adrenaline IM dose chart (ideally laminated)</li> <li>– cotton wool balls, gauze                   <ul style="list-style-type: none"> <li>• cell-phone or phone access</li> <li>• sharps box</li> <li>• bag valve mask resuscitator (eg, Ambu bag) suitable for the population being vaccinated</li> <li>• pen and paper for emergency use</li> <li>• appropriately sized syringes and needles for specific vaccine programme</li> <li>• cotton wool balls, gauze, surgical tape or plasters</li> <li>• vaccines</li> <li>• cold chain equipment as required by the National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition) (see link in note below)<sup>a</sup></li> <li>• data logger with a probe, external display and alarm<sup>1</sup></li> <li>• vomit bowl</li> <li>• tissues</li> <li>• gloves</li> <li>• appropriate surface cleaner</li> <li>• approved biohazard bag</li> </ul> </li> </ul> </li> </ul>	<p>Yes / No</p>

*Continued overleaf*

Check list of Emergency Equipment required for off-site vaccinations	Office use only
2. Optional additional emergency equipment <ul style="list-style-type: none"> <li>• an oxygen cylinder, flow meter, tubing and paediatric/adult masks</li> <li>• airways – infant through to adult</li> <li>• blood pressure monitoring equipment</li> <li>• thermometer</li> <li>• Intravenous cannula and administration sets:</li> <li>• intravenous fluids</li> <li>• hydrocortisone for injection</li> <li>• saline flush</li> </ul>	Yes / No
<hr/> a. Consider using a secondary back-up device in case the data logger gets damaged. See the <i>National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)</i> (available at <a href="http://www.tewhatuora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines">www.tewhatuora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines</a> ).	

# Appendix 5:

## Immunisation certificate

### A5.1 Introduction

The Health (Immunisation) Regulations 1995 require parents/guardians of children born from 1 January 1995 to show their child's immunisation certificate when these children start at an early childhood service and on entry to primary school (school year 1). The immunisation certificate shows whether a child is fully immunised or not. Information must be recorded at age 15 months when the early childhood vaccinations are complete, and after the immunisations at age 4 years. For those parents/guardians who decline to have their child vaccinated, the immunisation certificate may be completed at any time, but the completed immunisation certificate must still be shown when the child starts at an early childhood service or primary school.

### A5.2 Parent/guardian responsibilities

Parents or guardians can choose whether to vaccinate their child, but they must show the immunisation certificate when their child starts at an early childhood service and on school entry, regardless of the child's immunisation status.

### A5.3 Vaccinator responsibilities

When completing and signing the immunisation certificate, vaccinators should be confident that a child is fully vaccinated. The primary concern is the child's protection. If the previous vaccination history is uncertain and parents/guardians do not wish their child to be vaccinated, the child should be certified as 'not fully immunised'. Children who have not received the necessary doses of a vaccine or have no evidence of laboratory-proven disease should be recorded as 'not fully immunised'.

The immunisation certificate is included in the *Well Child Tamariki Ora My Health Book*. This book also contains the record of the child's vaccinations. Vaccinators should ensure they record vaccination and other relevant health information in this book. This becomes particularly important if the child sees different health professionals. If the child's book is lost, it should be replaced. Copies of the *Well Child Tamariki Ora My Health Book* and immunisation certificate pads can be obtained from the authorised provider of health education materials, usually the local public health service, or ordered from the HealthEd website ([www.healthed.govt.nz](http://www.healthed.govt.nz)).

## A5.4 Early childhood services and school responsibilities

All early childhood services and primary schools, including kōhanga reo, independent schools and kura kaupapa Māori, must keep an immunisation register for children born from 1 January 1995. The register is a tool to help reduce the spread of vaccine-preventable diseases in early childhood services and schools, as well as in the wider community. Registers are available from the authorised provider of health education materials or from the HealthEd website ([www.healthed.govt.nz/](http://www.healthed.govt.nz/)).

The early childhood service or school has the responsibility to:

- advise the child's parent/guardian that an immunisation certificate is required
- ensure the parent or guardian is asked to provide the immunisation certificate
- record the information from the immunisation certificate (or the fact that it was not shown) on the register
- advise the parent/guardian that a GP, practice nurse or public health nurse can help them to get an immunisation certificate if they do not have one.

# Appendix 6: Passive immunisation

## A6.1 Introduction

Passive immunisation involves administering pre-formed antibody as human immunoglobulin to a recipient who is thought to have either no natural immunity to one or more infections, or who has impaired antibody production. CSL Behring Australia is the primary manufacturer of immunoglobulin products for the New Zealand Blood Service (NZBS). These products are prepared by fractionating large pools of plasma collected from blood donors.

The immunoglobulin products available in New Zealand are usually derived from voluntary, unpaid New Zealand donors who are in good health and who do not have any conditions identifiable by the standard questionnaire that all blood donors complete or by the mandatory testing for HIV/AIDS, hepatitis B, hepatitis C and syphilis on each donation. Blood donations are only used if the tests show no evidence that these infections are present. Similar screening standards apply to the manufacture of other specialist immunoglobulin products which are obtained from an overseas sources. Some of these commercial products may be derived from remunerated, voluntary donors.

## A6.2 Preparations available in New Zealand

Immunoglobulin products available in New Zealand include human normal immunoglobulin for intramuscular (IM) use, specific immunoglobulins for intramuscular use, human normal immunoglobulin for intravenous use (IVIG) and human normal immunoglobulin for subcutaneous use (SCIG). All these products have an excellent safety record in both Australia and New Zealand.

### A6.2.1 Human normal immunoglobulin for intramuscular use

Human normal immunoglobulin for intramuscular use (available as Normal Immunoglobulin-VF) is a sterile, preservative-free, pasteurised solution containing 160 mg/mL human plasma proteins and 22.5 mg/mL glycine. The solution has a pH of 6.6. At least 98 percent of the protein comprises immunoglobulins, mainly immunoglobulin G (IgG). Normal Immunoglobulin-VF is intended for IM injection and is available in 5 mL preservative-free vials. It is prepared by Cohn cold ethanol fractionation of human plasma. The manufacturing process involves specific viral removal steps to reduce the possibility of virus transmission, and includes pasteurisation for viral inactivation and nanofiltration for virus removal.



## A6.2.2 Specific immunoglobulin for intramuscular use

Specific human immunoglobulin preparations for IM use are available, including those for tetanus, hepatitis B, varicella zoster and anti-D. These are manufactured from plasma pools containing donations from individuals known to have high levels of the appropriate antibody. These preparations are available in single vials containing the specific antibody. The volume of the product will be determined by the potency for the appropriate antibody. In unusual circumstances, when supplies of specific immunoglobulin products manufactured from New Zealand plasma are not available, commercial products from alternative donor sources may be supplied by NZBS.

RIG is imported from a commercial source and is held at NZBS sites in Auckland, Christchurch and Wellington. The product is not registered as a medicine in New Zealand. It may be accessed and supplied under section 29 of the Medicines Act 1981 after discussion with an NZBS medical officer.

## A6.2.3 Human normal immunoglobulin for intravenous use

For information about the current human normal immunoglobulins for intravenous use in New Zealand refer to immunoglobulin preparations section in the **Transfusion Medicine Handbook**. Further queries regarding usage and dosage of IVIG can be directed to the New Zealand Blood Service transfusion medicine specialists via the district blood bank.

## A6.2.4 Human normal immunoglobulin for subcutaneous use

Human normal immunoglobulin for subcutaneous use (Evogam) is produced by CSL Behring, Australia, from NZBS New Zealand-sourced plasma. It is a sterile solution containing 16 g per 100 mL of human immunoglobulin with a purity of at least 98 percent immunoglobulin G (IgG). At least 85 percent consists of monomers and dimers (typically >90 percent), and less than 10 percent of the IgG is aggregates. The distribution of the IgG subclasses closely resembles that found in normal human plasma.

The pH value of the solution is 6.6. It contains 2.25 g/100 mL of glycine as a stabiliser. It does not contain a carbohydrate stabiliser (eg, sucrose, maltose) and contains no preservative. Evogam contains only trace amounts of IgA, typically <0.025 mg/mL.

Evogam is produced by chromatographic fractionation of large pools of human plasma obtained from New Zealand's voluntary blood donors. The manufacturing process involves special steps to reduce the possibility of virus transmission, including pasteurisation (heating at 60°C for 10 hours) and nanofiltration.

## A6.2.5 Accessing immunoglobulin or contacting NZBS for advice

NZBS operates a 24-hour on-call service for medical advice and access to these products. Details of the medical officer on call can be obtained from any district hospital blood bank in New Zealand.

Product can be requested using the NZBS request form. This can be accessed online ([www.nzblood.co.nz/Clinical-information/Transfusion-medicine/Information-for-Health-Professionals/Request-forms](http://www.nzblood.co.nz/Clinical-information/Transfusion-medicine/Information-for-Health-Professionals/Request-forms)), by contacting your local blood bank or writing to:

New Zealand Blood Service  
Private Bag 92071  
Victoria Street West  
Auckland 1142

email: [info@nzblood.co.nz](mailto:info@nzblood.co.nz)  
telephone (during normal office hours): 09 523 5744.

## A6.3 Indications for use

### A6.3.1 Passive immunisation

For advice on the use of immunoglobulin products and specific dosages of these products, please contact a medical officer at NZBS. Copies of the product data sheet are available on the NZBS website ([www.nzblood.co.nz/Clinical-information/Transfusion-medicine/Health-professionals-medicine-datasheets/Immunoglobulins](http://www.nzblood.co.nz/Clinical-information/Transfusion-medicine/Health-professionals-medicine-datasheets/Immunoglobulins)).

Normal Immunoglobulin-VF is available for passive immunisation (pre- or post-exposure prophylaxis) against measles (see section 12.8.2) and hepatitis A (see section 8.8) where active vaccination is not appropriate or is contraindicated. It is not recommended for the prevention of rubella or mumps. Guidance on the use of specific preparations is provided in other sections of this *Handbook*: for pre- or post-exposure prophylaxis against hepatitis B (section 9.5.2 and section 9.8.1), tetanus (section 22.5.5) and varicella zoster (section 24.8.2).

### A6.3.2 Management of primary and acquired immune deficiency

Recurrent infections can occur in individuals who have low or absent levels of circulating immunoglobulins – so-called humoral immune deficiency. This can arise as a congenital disorder, or it can be acquired as a consequence of a number of diseases. Humoral immune deficiency can exist alone or as part of a wider immune deficiency syndrome. Immunoglobulin products can be used to prevent recurrent infections in these patients.

Until recently, IVIG was the product of choice for managing these patients. A subcutaneous IgG product (Evogam) is also now available, which can be infused by patients at home. This avoids the need for outpatient or day-case admission for

infusion of IVIG and is preferred by some patients. The subcutaneous preparation is not suitable for use in prophylaxis against hepatitis A or measles infection.

For replacement therapy in antibody deficiency disorders, monthly administration of IVIG is given, usually at a dosage of 0.2 to 0.6 g/kg of body weight.<sup>1</sup> Subcutaneous product is administered one to two times per week, with the overall monthly dosage similar to that of IVIG. For both types of product, the dosage and frequency of infusion should be based on the effectiveness in the individual patient. In general, however, the aim of treatment should be to maintain the serum IgG at or above a level of 5 g/L.

## A6.4 Storage and administration

Immunoglobulin products must be stored at +2°C to +8°C and must not be frozen. They should also be protected from light. If the product appears turbid or contains sediment, it must not be used. Always check and observe the manufacturer's expiry date before injecting the product. The product does not contain an antimicrobial preservative and must be used immediately after opening the vial; any unused portions should be discarded. Information on the batch number and dose injected must be kept in the recipient's records.

The intramuscular and subcutaneous forms of normal immunoglobulin should be brought to room temperature before use. They *must not* be given intravenously because of the possible reactions discussed in section A6.7.<sup>1</sup>

The intramuscular product, Normal Immunoglobulin-VF, should be given slowly by deep IM injection, using a needle of appropriate gauge and length. If a large volume (more than 5 mL) is required, administration in divided doses at different sites is recommended.

The subcutaneous product, Evogam, is normally given using an infusion pump. Information on infusion rates is provided in the medicine's data sheet.

### A6.4.1 Interactions with other drugs

Immunoglobulin should not be mixed with other pharmaceutical products, except as indicated by the manufacturer.

**Passively acquired antibody can interfere with the response to live attenuated virus vaccines.** Live virus vaccines should be given at least two weeks before, or deferred for up to 11 months after, doses of human normal immunoglobulin or other blood products.<sup>2</sup> The interval will be determined by the blood product and dose received (see Table A6.1).

Table A6.1 gives the current recommendations for deferment of live parenteral vaccines, MMR and VV, after receipt of blood products. Note that the live vaccines will not cause harm if given earlier than this, but the immune response may be suboptimal, leaving a patient at risk for the relevant disease(s). In an outbreak situation (e.g.

measles) immunisation may be given at any time as the benefit could outweigh the potential impaired response. If given earlier, then subsequent serological testing or repeating live vaccine dose at an appropriate time interval can be done.

**Table A6.1: Suggested intervals between immunoglobulin and blood product administration or blood transfusion and MMR or varicella vaccination**

Note that these live vaccines will not cause harm if given earlier than these intervals, but the immune response could be suboptimal, leaving a patient at risk for the relevant disease(s). In an outbreak situation (e.g. measles) immunisation may be given at any time as the benefit could outweigh the potential impaired response.

Product or indication	Route	Dose	Interval (months) <sup>a</sup>
Tetanus immunoglobulin (250 IU/vial)	IM	250 IU if <24h 500 IU if >24h or gross contamination or burns	3
Hepatitis A prophylaxis (with human normal immunoglobulin)			
• Contact and short-term travel (<3 months prophylaxis)	IM	0.03 mL/kg	3
• International travel (>3 months) <sup>b</sup> , other requirement for long-term prophylaxis – repeated 6monthly	IM	0.06 mL/kg	3
Hepatitis B immunoglobulin (a different low-volume product is provided for neonatal use)	IM	Adults 400 IU Neonates 100 IU	3
Rabies immunoglobulin	IM	20 IU/kg	4
Varicella prophylaxis (with zoster immunoglobulin, 200 IU/vial)	IM	125 IU/10 kg (max 625 IU) 0–10 kg: 1 vial 10.1–30 kg: 2 vials >30 kg: 3 vials	5
Measles prophylaxis (with human normal immunoglobulin)			
• immunocompromised contact	IM	0.6 mL/kg	6
Blood transfusion:			
• washed red blood cells	IV	10 mL/kg	0
• red blood cells resuspended, adenine saline added	IV	10 mL/kg	3
• whole blood, allogeneic	IV	10 mL/kg	6
• platelets in PAS	IV	1 unit	5
• plasma	IV	10 mL/kg	7
Cytomegalovirus immunoglobulin <sup>c</sup>	IV	Contact NZBS MO to discuss product and dose	6
Replacement (or therapy) of immune deficiencies (with IVIG)	IV	0.3–0.4 g/kg occasionally higher	8

*Continued overleaf*

Product or indication	Route	Dose	Interval (months) <sup>a</sup>
IVIg therapy for autoimmune or inflammatory disorders, including idiopathic thrombocytopenic purpura and Kawasaki's disease	IV	0.4 g/kg	8
		1–1.5 g/kg	10
		1.6–2 g/kg	11
Rh (D) immunoglobulin (anti-D)	IM	na	0
Monoclonal antibody (as palivizumab) <sup>d</sup> to respiratory syncytial virus	IM	15 mg/kg	0
Berinert, Riastap and Biosate <sup>e</sup>	IV	na	0

Key: IM = intramuscular; IU = international units; IV = intravenous; IVIG = intravenous immunoglobulin; NZBS MO = New Zealand Blood Service medical officer; PAS = platelet additive solution; RBCs = red blood cells; na = not applicable.

#### Notes

- Unvaccinated persons might not be protected fully against measles during the entire recommended interval, and additional doses of immunoglobulin or measles vaccine might be indicated after measles exposure.
- Immunoglobulin is not normally available or recommended in New Zealand for pre-travel use.
- Cytomegalovirus immunoglobulin is not available in New Zealand. Contact NZBS MO to discuss access to an alternative product.
- Palivizumab contains antibody only to respiratory syncytial virus and does not interfere with the immune response to live or inactivated vaccines. For further information, see Starship guidelines [starship.org.nz/guidelines/palivizumab-synagis-r-immunisation-for-respiratory-syncytial-virus-rsv](http://starship.org.nz/guidelines/palivizumab-synagis-r-immunisation-for-respiratory-syncytial-virus-rsv)
- Other fractionated blood products may contain traces of immunoglobulin. Contact a transfusion medicine specialist to discuss potential impact on vaccination.

Adapted from: Centers for Disease Control and Prevention. 2011. General recommendations on immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morbidity and Mortality Weekly Report* 60(RR2): 1–61. Table 5. Deferral interval for vaccination after blood components and products calculated from NZBS data.

Note: These intervals do not apply to BCG vaccines and rotavirus vaccines in infants, nor to zoster vaccine for individuals  $\geq 50$  years of age, the efficacy of which is unaffected by the presence of passive immunoglobulin.

Inactivated vaccines may be administered concurrently with passive antibody (although in separate syringes) to induce active immunity, as is done for some tetanus-prone wounds and for babies born to HBsAg-positive mothers.

## A6.4.2 Passive transfer of antibodies and interference with serological testing

Serological testing after the administration of immunoglobulin may detect transfused antibodies for several months after administration. Serological testing for any infection after immunoglobulin should therefore be discussed with an expert.

## A6.5 Duration of effect

- The estimated half-life of **intramuscular** human normal immunoglobulin is  $27 \pm 7$  days (mean  $\pm$  standard deviation [SD]).<sup>1</sup> The duration of effect is linked to the initial dosage.
- The estimated half-life of **intravenous** human normal immunoglobulin is  $40 \pm 8$  days (mean  $\pm$  SD).<sup>1</sup>
- The estimated half-life of **subcutaneous** human normal immunoglobulin is 55 days (range 14–165 days).<sup>1</sup>

## A6.6 Contraindications and precautions

### A6.6.1 Contraindications

Immunoglobulin products intended for subcutaneous and intramuscular injection must not be administered intravenously because of the potential for anaphylactic reactions.

Health professionals should check the package insert for the immunoglobulin product to be administered.

Skin tests should not be conducted with immunoglobulin preparations. Intradermal injection of any concentrated immunoglobulin product may cause a local inflammatory reaction, which can be misinterpreted as a positive allergic reaction. Allergic responses to normal immunoglobulin given in the prescribed IM route are extremely rare, but may occur in those with complete immunoglobulin A (IgA) deficiency in whom anti-IgA is present.

Intramuscular injection of immunoglobulin products should be avoided in patients with a low platelet count or with any coagulation disorder that would contraindicate IM injections. In these circumstances, the injection may be given subcutaneously, with a lightly applied pressure pad if prone to bruising; for example, if thrombocytopenia or von Willebrand disease is present.<sup>3</sup>

### A6.6.2 Precautions

Injections of Normal Immunoglobulin-VF must be IM, and care should be taken to draw back on the plunger of the syringe before injection to be certain that the needle is not in a blood vessel (see section 2.2.3).

As with any injection, there is a risk of anaphylaxis. Adrenaline and other means of treating acute reactions should therefore be immediately available (see section 2.3.3).

## A6.7 Potential responses and adverse events following passive immunisation

Clinicians in New Zealand are requested to notify all adverse reactions arising from, or in association with, the use of blood products. Reactions to any immunoglobulin product should be reported on a form obtainable from NZBS or any local district hospital blood bank.

Local tenderness, erythema and muscle stiffness occasionally occur at the site of injection and may persist for several hours after intramuscular injection. An occasional recipient may react more strongly, with a low-grade fever. Systemic reactions, including nausea, urticaria and generalised hypersensitivity reactions, may occur.<sup>1, 3</sup>

Reactions to IVIG tend to be related to the infusion rate and are most likely to occur during the first hour of the infusion. However, delayed reactions can occur, and include nausea, vomiting, chest pains, rigors, dizziness and aching legs. Systemic and local reactions are more common in those being treated for hypogammaglobulinaemia than in those with normal gammaglobulin levels who are being treated with immunoglobulin preparations for autoimmune conditions.

Occasional reports exist of renal failure following infusion of IVIG. These largely relate to sucrose-containing products. The IVIG products available in New Zealand, do not contain sucrose, but patients should be adequately hydrated prior to their administration. Renal function should be monitored in patients considered to be at increased risk.

Aseptic meningitis has been reported following treatment with IVIG. This may present up to two days following treatment. Anaphylactic reactions, although rare, have been reported following injection of immunoglobulin products, although anaphylaxis is more likely to occur following intravenous infusion. Other significant adverse events that have been observed in New Zealand and are mostly associated with large or ongoing treatment with high-dose IVIG or SCIG include: haemolysis, rashes, febrile events, pain or hypotension.

Immunoglobulin products may interfere with the immune response to live virus vaccines. In general, live vaccines should be given at least two weeks before or up to 11 months after the immunoglobulin preparation (see Table A6.1). This does not apply to the yellow fever vaccine, because New Zealand blood donors are very unlikely to have antibodies to this virus. For travellers abroad, the necessary interval may not be possible. No evidence of adverse interaction with rotavirus vaccine has been reported.

See section 1.6.3 for further information about adverse events and reporting.



# References

1. NZ Blood. 2017 *Immunoglobulins: CSL Product Data Sheets*. New Zealand Blood Service; 2017 [updated 07 March 2017]; URL: <https://www.nzblood.co.nz/Clinical-information/Transfusion-medicine/Health-professionals-medicine-datasheets/Immunoglobulins>. (accessed 3 July 2020)
2. Freedman M ,Kroger A. 2023. General immunization practices. in *Plotkin's Vaccines: Eighth edition*, Orenstein W (eds). Philadelphia, US. p. 113-144.e6. (accessed 25 May 2023)
3. NZ Blood. 2016. *Transfusion Medicine Handbook Third Edition, 2016: A guide to the clinical use of blood components, blood products and blood transfusion procedures in New Zealand* (ed.), Epsom, Auckland: New Zealand Blood Service. URL: <https://www.nzblood.co.nz/assets/Transfusion-Medicine/PDFs/111G122.pdf> (accessed 3 July 2020)

# Appendix 7: Vaccine presentation, preparation, disposal, and needle-stick recommendations

## A7.1 Presentation of vaccines

Most of the vaccines in current use are supplied in prefilled syringes or vials. The exceptions to this are the rotavirus vaccine, which is supplied as a syringe-style oral applicator, and the BCG vaccine, which is supplied as a multi-dose vial.

A vial is a glass container with a rubber seal on the top, protected by a metal or plastic cap until it is ready for use. Assume the rubber seal is latex unless stated 'latex-free'. Vials contain either liquid or powder (freeze-dried or pellet/cake) preparations.

Vaccines should not be mixed in the same syringe, unless the manufacturer's data sheet specifically states it is permitted (eg, the DTaP-IPV-HepB vaccine is mixed with the Hib-PRP pellet for the Infanrix-hexa vaccine).

## A7.2 Preparation and administration of vaccines

To minimise the risk of spread of infection and needle-stick injury, vaccinators should observe standard occupational health and safety guidelines.

- Ensure proper hygiene is maintained (ie, regularly wash hands for at least 20 seconds and dry them for 20 seconds, or regularly use an alcohol-based hand rub if hands are not visibly soiled).
- Prepare the appropriate injection equipment for the vaccines to be administered (see section 2.2).
- Ensure the refrigerator temperature is within the required range of +2°C to +8°C before removing the vaccines (refer to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)*, available at [www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines](http://www.tewhatauora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines)).
- Ensure the correct vaccine is taken from the refrigerator and that it is within the expiry date.

- Vaccines should only be drawn up after informed consent has been obtained and the vaccine requirements determined. This should include an AIR status query (if applicable) if there is uncertainty about previous doses. Any vaccines drawn up and not used should be discarded unless otherwise stated.

Vaccines in vials require one needle to draw the vaccine into the syringe, and then a new needle to administer the vaccine. The passage of needles through rubber seals causes blunting, resulting in increased tissue trauma if that needle is used to administer the injection. Also, a new needle prevents tracking the vaccine through the skin and subcutaneous tissue, thereby reducing the risk of local reactions. Do not expel the air contained in the new needle – it is sterile and minute in quantity (see chapter 2, Table 2.7). These recommendations differ for COVID-19 vaccine (see section 5.4.5 for specific information about mRNA-CV).

### A7.2.1 Preparing vaccines supplied as a liquid preparation

- Where applicable, remove the detachable portion of the label from the vial or syringe and place it on (or with) the appropriate documentation. If there is no detachable label, note the batch number and expiry date.
- Inspect the vaccine for any foreign particulate matter and/or variation in the physical appearance described by the manufacturer – if either is observed, do not use.
- Shake the vial: Most inactivated vaccines contain an adjuvant, and to obtain a uniform suspension they must be shaken vigorously prior to being drawn up.
- Flip the plastic cap off the vial, taking care not to touch the rubber seal.
- With the vial upright, insert the tip of the needle through the centre of the rubber seal, where it is thinner and easier to penetrate.
- Invert the vial and draw up the entire volume into the syringe.
- Withdraw the needle from the vial.
- Change the needle, choosing the appropriate gauge and length for administration.
- Administer the vaccine.
- Dispose of the empty vials, used syringes and needles into the sharps container.
- Complete the required documentation (eg, in the PMS).

### A7.2.2 Preparing vaccines supplied as powder/pellet vaccines

Some vaccines are presented as a prefilled syringe and freeze-dried (lyophilised) combination vaccines where:

- the pellet or powder preparation is reconstituted with the diluent (vial or prefilled syringe) supplied by the manufacturer (eg, MMR or Hib-PRP), or
- the pellet or powder preparation is reconstituted with a prefilled syringe containing vaccine (eg, DTaP-IPV-HepB/Hib).

The method for reconstituting the vaccine varies depending upon whether vials or prefilled syringes are used, as follows.

## Reconstituting vaccines where the diluent is in a vial

- Where applicable, remove the detachable portion of the label from the diluent and/or vaccine (powder/pellet) vials and place these on (or with) the appropriate documentation. If there are no detachable labels, note the batch number and expiry date for both vaccine and diluent.
- Inspect the vaccine (powder/pellet) and diluent vials for any foreign particulate matter and/or variation in the physical appearance described by the manufacturer – if either is observed, do not use.
- Flip the plastic cap off the diluent vial, taking care not to touch the rubber seal.
- With the diluent vial upright, insert the needle tip through the centre of the rubber seal, where it is thinner and easier to penetrate.
- Invert the vial and draw up the entire volume of diluent into the syringe.
- Flip the plastic cap off the powder/pellet vial, and slowly, to avoid frothing, empty the contents of the syringe (diluent) into the powder/pellet vial, using the vial entry technique mentioned above.
- Swirl the vial gently to dissolve the powder/pellet. The needle and syringe may be removed or left in place.
- After reconstitution, the vaccine should be checked to see that the colour compares with the information supplied by the manufacturer on the data sheet and that there is no particulate matter present. If the colour does not match the manufacturer's information, do not use.
- Withdraw the entire volume of the reconstituted vaccine into the syringe.
- Withdraw the needle from the vial.
- Change the needle, choosing the appropriate gauge and length for administration.
- Once reconstituted, the vaccine must be used within the manufacturer's recommended period. See the respective vaccine data sheets for more information.
- Administer the vaccine.
- Dispose of the empty vials, used syringes and needles into the sharps container.
- Complete the required documentation (eg, in the PMS).

## Reconstituting vaccines where the vaccine or diluent is in a prefilled syringe

- Where applicable, remove the detachable portion of the label from the prefilled syringe and/or vaccine (powder/pellet) vial and place these on (or with) the appropriate documentation. If there are no detachable labels, note the batch number and expiry date for both the prefilled syringe and the vaccine (powder/pellet) vial.
- Inspect the prefilled syringe and vaccine (powder/pellet) vial for any foreign particulate matter and/or variation in the physical appearance described by the manufacturer – if either is observed, do not use.
- Flip the plastic cap off the powder/pellet vial, and with the vial upright, insert the prefilled syringe needle tip through the centre of the rubber seal, where it is thinner and easier to penetrate.

- Slowly, to avoid frothing, empty the contents of the prefilled syringe into the vial.
- Swirl the vial gently to dissolve the powder/pellet. The needle and syringe may be removed or left in place.
- After reconstitution, the vaccine should be checked to see that the colour compares with the information supplied by the manufacturer on the data sheet and that there is no particulate matter present. If the colour or presentation does not match the manufacturer's information, do not use.
- Withdraw the entire volume of the reconstituted vaccine into the syringe.
- Withdraw the needle from the vial.
- Change the needle, choosing the appropriate gauge and length for administration.
- Once reconstituted, the vaccine must be used within the manufacturer's recommended period. See the respective vaccine data sheets for more information.
- Administer the vaccine.
- Dispose of the empty vials, used syringes and needles into the sharps container.
- Complete the required documentation (eg, in the PMS).

### A7.2.3 Preparing vaccines supplied as prefilled syringes

- Where applicable, remove the detachable portion of the label from the prefilled syringe and place it on (or with) the appropriate documentation. If there is no detachable label, note the batch number and expiry date.
- Inspect the vaccine for any foreign particulate matter and/or variation in the physical appearance described by the manufacturer – if either is observed, do not use.
- Shake the syringe: Most inactivated vaccines contain an adjuvant, and to obtain a uniform suspension they must be shaken vigorously prior to being administered.
- Do not expel air if the needle is fixed (eg, with an influenza vaccine). This prevents tracking the vaccine through the skin and subcutaneous tissue, thereby reducing the risk of local reactions.
- When the needle is not fixed, attach an appropriate administration needle. Do not expel the air.
- Administer the vaccine.
- Dispose of the used syringe and needle into the sharps container.
- Complete the required documentation (eg, in the PMS).

### A7.2.4 Preparing the rotavirus vaccine

The rotavirus vaccine is administered orally. It is available as a syringe-type applicator with a plunger stopper.

- Remove the detachable portion of the label (which includes the batch number but not the expiry date) and place it on (or with) the appropriate documentation. Note the expiry date.

- Inspect the vaccine for any foreign particulate matter and/or variation in the physical appearance described by the manufacturer – if either is observed, do not use.
- Remove the protective tip cap from the oral applicator.
- Administer the entire contents of the oral applicator into the infant’s mouth, towards the inner cheek.
- Discard the empty applicator and cap into the sharps container.

For more information, refer to the manufacturer’s data sheet (available on the Medsafe website, [medsafe.govt.nz](https://www.medsafe.govt.nz)).

### A7.2.5 Preparing vaccines supplied as multi-dose vials<sup>1</sup>

Note: These processes differ for the COVID-19 vaccine (see section 5.4.5 for specific information about mRNA-CV).

- The vial should be marked with the date and time of opening and the vaccinator’s initials.
- Shake the vial before use and before drawing up subsequent vaccine doses.
- Inspect the vaccine for any foreign particulate matter and/or variation in the physical appearance described by the manufacturer – if either is observed, do not use.
- To ensure optimal vial dosage and minimal vaccine wastage, use a 1 mL syringe.
- Flip the plastic cap off the vial, taking care not to touch the rubber seal.
- Inspect the rubber seal. If there is any doubt about the integrity of the seal (eg, the vial leaks when turned upside down), do not use.
- Ideally, draw up all doses of the vaccine at the same time; this allows the drawing-up needle to remain in the vial and avoids the need for alcohol swabbing (of the rubber seal).
- Alcohol swabs should be used with caution. There is an increased risk of alcohol contamination when the swabbed rubber seal is repeatedly pierced. If an alcohol swab is used, allow 30 seconds for the alcohol to completely dry before inserting the needle into the rubber seal.
- Use each vial in one session of vaccinating and discard the vial four hours after first opening (or follow the manufacturer’s instructions), even if the vaccine has not been used.

<sup>1</sup> Sources: WHO. 2014. *WHO Policy Statement: Multi-dose Vial Policy (MDVP) – Handling of multi-dose vaccine vials after opening*. Geneva: World Health Organisation URL: [https://apps.who.int/iris/bitstream/handle/10665/135972/WHO\\_IVB\\_14.07\\_eng.pdf](https://apps.who.int/iris/bitstream/handle/10665/135972/WHO_IVB_14.07_eng.pdf) (accessed 06 May 2022); the Australian Technical Advisory Group on Immunisation and the National Centre for Immunisation Research and Surveillance.

## A7.3 Disposal of needles, syringes and vaccine vials

Note: For information about returning vaccines for destruction (such as in the event of a cold chain excursion or failure), see the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)*, available at <https://www.tewhātuora.govt.nz/health-services-and-programmes/vaccine-information/vaccine-service-delivery/cold-chain-standards-for-vaccines>.

- Do not separate needles from syringes or recap needles, unless a recapping device is used.
- All needles plus empty or partly used vials, syringes, dosing tubes and caps should be discarded into the sharps container for crush incineration.

### A7.3.1 Sharps containers

- Sharps containers should be made of rigid, leak- and puncture-proof material. They must be fitted with a carrying handle and have an opening that is wide enough to allow disposable materials to be dropped into the container with one hand while still preventing removal of the contents.
- Sharps containers should be situated out of children's reach and available in every area where vaccinations take place.
- Sharps containers should be filled only to the indicated line, then sealed and given to an approved hazardous waste disposal person for incineration (as per the Resource Management Act 1991).

### A7.3.2 Spillages

- In the event of blood or vaccine splashes on the skin, thoroughly wash the area under cold running water, then wash with soap and water or the hand wash that vaccinators have available.
- In the event of spills on work surfaces, put on gloves and treat the spill by wiping the area with a disposable pad soaked in 0.5 percent hypochlorite (household bleach diluted 1 to 9 parts water). Repeat with the hypochlorite solution and a fresh pad, then clean up with water or a commercial detergent. Alternatively, granular hypochlorite can be used for liquid spills, by applying sufficient granules to absorb the spilt fluid and then cleaning up after 10 minutes' contact time. Carefully seal all contaminated material in an approved biohazard bag for incineration by an approved hazardous waste disposal person.
- Contaminated linen is adequately treated by a routine hot wash cycle (60–70°C) using an ordinary bleach concentration.



### A7.3.3 Recommendations following a needle-stick injury

In the event of a needle-stick injury, follow the guidelines below.

- The vaccinator should stop what they are doing and attend to the injury.
- Wounds and skin sites should be washed with soap and water. There is no evidence that encouraging bleeding or applying antiseptic reduces the risk of infection, but these actions are not contraindicated.
- The injury should be immediately reported to the medical advisor or employer, who should consider what immediate action is advisable.
- When the needle-stick injury involves exposure to an individual's blood, serological testing of that source individual should be sought and undertaken as soon as possible.
- Blood should be withdrawn from the affected vaccinator within a few days after the injury and counselling arranged. Testing for hepatitis B, hepatitis C and HIV serology should be undertaken.
- Depending on the infection status of the individual and the immune status of the injured vaccinator, it may be appropriate to start anti-HIV medications within the next few hours or to administer HBIG within the next few days.
- The blood-borne viruses of main concern in needle-stick injuries are hepatitis B, hepatitis C and HIV. All vaccinators should be immunised against hepatitis B and their antibody status known. Currently in New Zealand most HIV-infected individuals (or their parents/guardians) are likely to know their status at the time of immunisation, so HIV testing in case of needle-stick injuries is not routinely advocated. If there is a possibility that the individual could be HIV infected, the informed consent of the individual/parent/guardian is required before blood is drawn for testing.
- Blood-borne virus exposures after vaccination are rarely of high risk: because of the small needle size there is seldom visible blood, and there is a low risk of blood-borne viruses in the community.

For more information, see also section 9.5.7 for serological testing guidelines for hepatitis B, the *Starship Clinical Guidelines for Community Needle-stick Injuries* (available at <https://www.starship.org.nz/guidelines/community-needlestick-injuries/>) (for needle-stick injuries from needles discarded in the community) or your local district guidelines (if available).

# Appendix 8: Websites and other online resources

## A8.1 New Zealand-based websites

### **health.govt.nz**

The official website for the Manatū Hauora Ministry of Health.

### **tewhātuora.govt.nz**

The official website for Health New Zealand | Te Whatu Ora

### **www.healthpathwayscommunity.org**

HealthPathways Community

### Immunisation

#### **info.health.nz/immunisations/**

#### **www.tewhātuora.govt.nz/health-services-and-programmes/vaccine-information/**

Health New Zealand | Te Whatu Ora information about immunisation in New Zealand, including vaccination laws and practices, information for parents/guardians, young people and health professionals about the vaccines and the disease they protect against, immunisation coverage, and links to other reputable national and international websites. Electronic versions of the *Handbook* (pdf, html and ebook) are also available.

### COVID-19 vaccines

#### **info.health.nz/immunisations/vaccines-aotearoa/covid-19-vaccines/**

Health New Zealand | Te Whatu Ora information about getting a COVID-19 vaccine, the safety and approval process, types of vaccine and the vaccine rollout plan, including updates for the health sector.

### Pregnancy and kids

#### **info.health.nz/pregnancy-children/**

Health New Zealand | Te Whatu Ora information for parents, guardians and whānau about pregnancy, labour and birth, and caring for children during their first five years.

### Communicable Disease Control Manual

#### **www.tewhātuora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/**

National guidelines to support public health professionals with the prevention and control of notifiable diseases.

## Pharmaceutical Management Agency (PHARMAC) | Te Pātaka Whaioranga

### **pharmac.govt.nz**

Information about the medicines (including vaccines) and related products which are funded on the Pharmaceutical Schedule for use in the community and public hospitals. Electronic versions of the Pharmaceutical Schedule and updates (pdf and html) are published on the PHARMAC website ([pharmac.govt.nz/tools-resources/pharmaceutical-schedule](https://pharmac.govt.nz/tools-resources/pharmaceutical-schedule) and [schedule.pharmac.govt.nz/ScheduleOnline.php](https://schedule.pharmac.govt.nz/ScheduleOnline.php)).

## Medsafe – New Zealand Medicines and Medical Devices Safety Authority

### **medsafe.govt.nz**

Information on the regulation of medicines and medical devices in New Zealand and the safe use of medicines, including medicine data sheets for health professionals and consumer medicine information for consumers.

## Institute of Environmental Science and Research Ltd (ESR)

### **esr.cri.nz**

A source of New Zealand infectious disease epidemiology, including regular surveillance reports for a number of diseases.

## HealthEd

### **healthed.govt.nz**

A source of public health education resources, including immunisation and communicable diseases, for health professionals and the public. Resources can be viewed, downloaded and/or ordered from this site.

## Immunisation Advisory Centre (IMAC)

### **immune.org.nz**

Information for parents and clinicians, including newsletters for providers of immunisation services in New Zealand.

## KidsHealth

### **kidshealth.org.nz**

A joint initiative between the Paediatric Society of New Zealand Inc and the Starship Foundation. The KidsHealth website provides accurate and reliable information about children's health for New Zealand parents and caregivers, the wider family and whānau, and health professionals working with parents.

## Health Promotion Agency (HPA) | Te Hiringa Hauora

[www.hpa.org.nz](http://www.hpa.org.nz)

The HPA works closely with the Ministry of Health and Health New Zealand | Te Whatu Ora to deliver immunisation messages to the general public.

## A8.2 International websites

### World Health Organization (WHO)

[www.who.int/teams/immunization-vaccines-and-biologicals](http://www.who.int/teams/immunization-vaccines-and-biologicals)

Sources of statistics, graphs and maps for immunisation profiles, by country. Useful for the practitioner planning vaccination of an immigrant child based on the current Schedule.

### The Global Health Observatory

[www.who.int/data/gho](http://www.who.int/data/gho)

Provides access to a range of data sets and dashboards, including immunisation data and vaccine-preventable disease, including the **Immunization dashboard**.

### Centers for Disease Control and Prevention (CDC)

[cdc.gov/vaccines/](http://cdc.gov/vaccines/)

This site includes sections on the vaccines recommended (in the US) by age and for specific groups of people, and also includes safety factsheets for individual vaccines.

### Immunize.org (formerly Immunization Action Coalition)

[immunize.org](http://immunize.org)

Educational information for both clinicians and parents. This site includes an 'Unprotected people stories' section and has its own search facility.

### Healthychildren.org – American Academy of Pediatrics

[www.healthychildren.org](http://www.healthychildren.org)

Information for parents and clinicians, which includes colourful (and graphic) pictures ([www.healthychildren.org/immunizations](http://www.healthychildren.org/immunizations)). Useful articles include 'Why immunize your child?' and 'Vaccine safety: examine the evidence'.

### Raising Children Network

[raisingchildren.net.au](http://raisingchildren.net.au)

Parenting videos, articles and apps backed by Australian experts.

## Institute for Vaccine Safety

[www.vaccinesafety.edu](http://www.vaccinesafety.edu)

Information on the safety of recommended vaccines and current vaccine issues in the media. Based at Johns Hopkins University, Baltimore, USA.

## The Vaccine Page

[www.vaccines.org](http://www.vaccines.org)

The latest information and news about vaccines for adults, parents, practitioners and researchers. This site also has links to journals and other vaccine-related sites.

## National Centre for Immunisation Research & Surveillance (NCIRS)

[www.ncirs.org.au](http://www.ncirs.org.au)

An Australian-based research organisation that provides independent expert advice on all aspects of vaccine-preventable diseases, vaccine safety, communication and social and other issues related to immunisation.

## Sharing Knowledge About Immunisation (SKAI)

[ncirs.org.au/our-work/sharing-knowledge-about-immunisation](http://ncirs.org.au/our-work/sharing-knowledge-about-immunisation)

An Australian website containing a package of communication strategies and tools to assist in conversations between health providers and families around immunisation. It includes an e-learning module for health providers and a website with information accessible by parents ([talkingaboutimmunisation.org.au/](http://talkingaboutimmunisation.org.au/)) to help inform consent.

## A8.3 Influenza-related websites

### National Influenza Immunisation Programme

[www.immune.org.nz/immunisation/programmes/influenza](http://www.immune.org.nz/immunisation/programmes/influenza)

Influenza immunisation programme for health professionals. Information for consumers is available on the Ministry of Health website at [info.health.nz/immunisations/vaccines-aotearoa/flu-influenza-vaccine/](http://info.health.nz/immunisations/vaccines-aotearoa/flu-influenza-vaccine/)

### Ministry of Health – Pandemic planning and response

[www.health.govt.nz/strategies-initiatives/programmes-and-initiatives/emergency-management/pandemics](http://www.health.govt.nz/strategies-initiatives/programmes-and-initiatives/emergency-management/pandemics)

Pandemic planning and response information, including the current pandemic influenza alert status and pandemic plans, policies and other guidance for the health sector.

## FluTracking

<https://info.flutracking.net/>

Online surveillance system used to detect the potential spread of influenza, influenza-like respiratory illnesses and COVID-19 within Australia and New Zealand.

## Institute of Environmental Science and Research Ltd

Virological surveillance

[www.esr.cri.nz/digital-library/respiratory-illness-dashboard/](http://www.esr.cri.nz/digital-library/respiratory-illness-dashboard/)

Monthly updated respiratory illness dashboard.

## WHO – Global Influenza Programme

[www.who.int/teams/global-influenza-programme/surveillance-and-monitoring/](http://www.who.int/teams/global-influenza-programme/surveillance-and-monitoring/)

Information on national influenza centres and vaccine manufacturers around the world, as well as global surveillance data and links to reports of the *Weekly Epidemiological Record*. It also includes the WHO's geographical information system for monitoring global influenza activity. Recent activity is featured in a series of animated maps and news reports, and listings of participating centres, influenza vaccine manufacturers and related websites are provided and shared through FluNet and FluID.

## CDC – Influenza (Flu)

[www.cdc.gov/flu/index.htm](http://www.cdc.gov/flu/index.htm)

Information for the public and health professionals on influenza viruses, vaccines, and antiviral agents, and on the clinical features and natural history of human influenza.

## A8.4 Travel-related websites

### Health New Zealand | Te Whatu Ora – Travelling

[www.tewhatauora.govt.nz/keeping-well/travelling](http://www.tewhatauora.govt.nz/keeping-well/travelling)

Information to help travellers manage risk and stay well. Includes links to other New Zealand-based travel websites.

### Ministry of Foreign Affairs and Trade – Safe Travel

[safetravel.govt.nz](http://safetravel.govt.nz)

Official advice for New Zealanders living and travelling overseas.

### WHO – International travel and health

[who.int/travel-advice](http://who.int/travel-advice)

Immunisation and disease information for travellers.

## CDC – Travellers' health

**[wwwnc.cdc.gov/travel](http://wwwnc.cdc.gov/travel)**

US-based information for travellers and health professionals, including updates on national and international disease outbreaks.

## Fit for travel

**[fitfortravel.nhs.uk](http://fitfortravel.nhs.uk)**

Travel health information for people travelling abroad from the UK, including updates on national and international disease outbreaks.



# Main sources

## Books

American Academy of Pediatrics. 2018. *Red Book: 2018 Report of the Committee on Infectious Diseases*. Kimberlin D, Brady M, Jackson M, et al. (eds.) American Academy of Pediatrics. Elk Grove Village, IL. URL: <https://redbook.solutions.aap.org/redbook.aspx>

Australian Technical Advisory Group on Immunisation (ATAGI). 2018. *Australian Immunisation Handbook* [Internet] Canberra: Australian Government Department of Health. URL: <https://immunisationhandbook.health.gov.au>

Health New Zealand | Te Whatu Ora. 2024 *Communicable Disease Control Manual*. Wellington: Health NZ URL: <https://www.tewhatauora.govt.nz/for-the-health-sector/health-sector-guidance/communicable-disease-control-manual/>

Plotkin S, Orenstein W, Offit P, et al (eds). 2018. *Plotkin's Vaccines (7th edition)*. Philadelphia: Elsevier.

## New Zealand epidemiology data

Information on New Zealand epidemiology is sourced from data collated by the Institute of Environmental Science and Research (ESR), on behalf of the Ministry of Health, or from Analytical Services, Ministry of Health.


For the most up-to-date epidemiological data, see the ESR Public Health Surveillance ([www.esr.cri.nz/expertise/public-health/](http://www.esr.cri.nz/expertise/public-health/)) and Ministry of Health ([www.health.govt.nz/statistics-research](http://www.health.govt.nz/statistics-research)) websites.

# Commonly used abbreviations

Ad26-CV	adenovirus (Ad26) viral vector COVID-19 vaccine
AEFI	adverse event following immunisation
AFP	acute flaccid paralysis
AIDS	acquired immunodeficiency syndrome
AIR	Aotearoa Immunisation Register
AOM	acute otitis media
BCG	bacillus Calmette–Guérin vaccine
CARM	Centre for Adverse Reactions Monitoring
CDC	Centers for Disease Control and Prevention
ChAd-CV	adenovirus (ChAdOx1) viral vector COVID-19 vaccine
CHD	congenital heart disease
COVID-19	coronavirus disease 2019
CPR	cardiopulmonary resuscitation
CRS	congenital rubella syndrome
cVDPV	circulating vaccine-derived polio virus
CVWUS	COVID-19 vaccinators working under supervision
DNA	deoxyribonucleic acid
DT	diphtheria tetanus vaccine
DTaP	diphtheria, tetanus and acellular pertussis vaccine
DTaP-IPV	diphtheria, tetanus, acellular pertussis and inactivated polio vaccine
DTaP-IPV-HepB/Hib	diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and <i>Haemophilus influenzae</i> type b vaccine
DTwP	diphtheria, tetanus and whole-cell pertussis vaccine
DTwPH	diphtheria, tetanus, whole-cell pertussis and <i>Haemophilus influenzae</i> type b vaccine
ESR	Institute of Environmental Science and Research
GBS	Guillain–Barré syndrome
GP	general practitioner
GSK	Formerly GlaxoSmithKline (New Zealand)
HAV	hepatitis A virus
HBcAg	hepatitis B core antigen
HBeAg	hepatitis B e antigen
HBIG	hepatitis B immunoglobulin
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus

HepA	hepatitis A vaccine
HepB	hepatitis B vaccine
Hib	<i>Haemophilus influenzae</i> type b
Hib-PRP	<i>Haemophilus influenzae</i> type b polyribosylribitol phosphate vaccine conjugated with tetanus toxoid
HIV	human immunodeficiency virus
HPV	human papillomavirus
HSCT	haematopoietic stem cell transplant
ICD	International Classification of Diseases
IFNAR	interferon alpha receptor
IG	immunoglobulin
IgG	immunoglobulin G
IM	intramuscular
IMAC	Immunisation Advisory Centre
IMID	immune-mediated inflammatory disease
IPD	invasive pneumococcal disease
IPV	inactivated polio vaccine
ISRR	immunisation stress-related response
irAE	immunisation-related adverse events
ITP	idiopathic thrombocytopenic purpura (also known as immune thrombocytopenia)
IV	intravenous
IVIG	intravenous immunoglobulin
LAIV	live attenuated influenza vaccine
Medsafe	New Zealand Medicines and Medical Devices Safety Authority
MenACWY	quadrivalent meningococcal conjugate vaccine
MenB	Four-component recombinant meningococcal B vaccine
MenB-fHbp	Two component recombinant meningococcal B vaccine
MenC	meningococcal C conjugate vaccine
MeNZB	New Zealand epidemic meningococcal B vaccine
MMR	measles, mumps and rubella vaccine
MMRV	measles, mumps, rubella and varicella vaccine
mRNA	messenger ribonucleic acid
mRNA-CV	messenger RNA COVID-19 vaccine
MSD	Merck Sharp & Dohme (New Zealand)
NHI	National Health Index
NIP	National Immunisation Programme
NIR	National Immunisation Register
NTHi	non-typeable <i>Haemophilus influenzae</i>
NZBS	New Zealand Blood Service
OPV	oral polio vaccine

PAV	provisional authorised vaccinator
PCR	polymerase chain reaction
PCV7	7-valent pneumococcal conjugate vaccine
PCV10	10-valent pneumococcal conjugate vaccine
PCV13	13-valent pneumococcal conjugate vaccine
23PPV	23-valent pneumococcal polysaccharide vaccine
PFU	plaque-forming unit
PHARMAC	Pharmaceutical Management Agency
PIMS-TS	paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2
PMS	practice management system (also known as patient management system)
PPE	personal protective equipment
PRP	polyribosylribitol phosphate
PSNZ	Pharmaceutical Society of New Zealand
PTAC	Pharmacology and Therapeutics Advisory Committee
QIV	quadrivalent influenza vaccine
RIG	rabies immunoglobulin
RNA	ribonucleic acid
rCV	recombinant spike protein COVID-19 vaccine, adjuvanted
RSV	respiratory syncytial virus
RSVpreF	respiratory syncytial virus prefusion F protein vaccine
RV1	rotavirus vaccine (monovalent)
RV5	rotavirus vaccine (pentavalent)
rZV	recombinant zoster vaccine, adjuvanted
SARS-CoV-2	serious acute respiratory syndrome coronavirus 2
SBVS	school-based vaccination system
SC	subcutaneous
SCID	severe combined immune deficiency
STI	sexually transmitted infection
SUDI	sudden unexpected death in infancy
TB	tuberculosis
Td	adult tetanus and diphtheria vaccine (formerly ADT-Booster)
Tdap	adult tetanus, diphtheria and acellular pertussis vaccine
TIG	tetanus immunoglobulin
TIV	trivalent influenza vaccine
UK	United Kingdom
US	United States of America
VAERS	vaccine adverse event reporting system (US)
VAPP	vaccine-associated paralytic poliomyelitis
VFC	vaccinator foundation course
VHW	vaccinating health workers



VLP	virus-like particle
VV	varicella vaccine
VZV	varicella zoster virus
WHO	World Health Organization
ZIG	zoster immunoglobulin
ZV	zoster vaccine

# Glossary of vaccine brand names and abbreviations

Generic abbreviation	Vaccine trade name	Sponsor	Target antigens or disease
<b>Schedule and funded vaccines</b>			
BCG	BCG Vaccine SSI	Serum Institute India	tuberculosis (TB)
DTaP-IPV	Infanrix-IPV	GlaxoSmithKline (GSK)	diphtheria, tetanus, acellular pertussis, inactivated poliovirus
DTaP-IPV-HepB/Hib	Infanrix-Hexa	GSK	diphtheria, tetanus, acellular pertussis, inactivated poliovirus, hepatitis B and <i>Haemophilus influenzae</i> type b
HepA	Havrix 1440	GSK	hepatitis A
HepB	Engerix-B	GSK	hepatitis B
Hib-PRP	Act-HIB	sanofi-aventis	<i>Haemophilus influenzae</i> type b conjugated with tetanus toxoid
HPV9	Gardasil 9	MSD	human papillomavirus (9-valent)
IPV	I POL	sanofi-aventis	inactivated poliovirus
QIV	Influvac	Viatrix	influenza – quadrivalent
MenACWY	MenQuadfi	sanofi-aventis	quadrivalent meningococcal vaccine conjugated with tetanus toxoid
MenACWY	Nimenrix	Pfizer	quadrivalent meningococcal vaccine conjugated with tetanus toxoid
MenB	Bexsero	GSK	group B recombinant meningococcal vaccine
MMR	Priorix	GSK	measles, mumps, rubella
mRNA-CV	Comirnaty	Pfizer/BioNTech	COVID-19
PCV13	Prevenar 13	Pfizer	pneumococcal conjugate vaccine (13-valent)
23PPV	Pneumovax 23	Merck Sharp and Dohme (MSD)	pneumococcal polysaccharide vaccine (23-valent)
rCV	Nuvaxovid	Bioclect (for Novavax)	COVID-19
RV1	Rotarix	GSK	rotavirus
rZV	Shingrix	GSK	zoster (shingles; varicella-zoster virus)
Tdap	Boostrix	GSK	tetanus, diphtheria and acellular pertussis
Tdap-IPV	Boostrix IPV	GSK	tetanus, diphtheria, acellular pertussis and inactivated poliovirus
VV	Varilrix	GSK	varicella (chickenpox; varicella-zoster virus)
<b>Other available vaccines (excluding travel vaccines)</b>			
HepA	Avaxim	sanofi-aventis	hepatitis A

<b>Generic abbreviation</b>	<b>Vaccine trade name</b>	<b>Sponsor</b>	<b>Target antigens or disease</b>
HepA-typhoid	Vivaxim	sanofi-aventis	hepatitis A and <i>Salmonella typhi</i>
HepB-HepA	Twinrix / Twinrix Junior	GSK	hepatitis A and B
MMR	M-M-R-II	MSD	measles mumps rubella
RSVpreF	Arexvy	GSK	respiratory syncytial virus
Tdap	Adacel	sanofi-aventis	tetanus, diphtheria and acellular pertussis
Tdap-IPV	Adacel-Polio	sanofi-aventis	tetanus, diphtheria, acellular pertussis and inactivated poliovirus
VV	Varivax	MSD	varicella (varicella-zoster virus)