Memo

Update to recommendations on COVID-19 booster vaccinations for pregnant people and immunocompromised: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations

Date:	25 January 2022
To:	Astrid Koornneef, Director, National Immunisation Programme
Copy to:	Dr Ashley Bloomfield, Director-General of Health Allison Bennett, Manager, System Enablers, System Strategy and Policy Dr Caroline McElnay, Director of Public Health
From:	Dr Ian Town, Chief Science Advisor
For your:	Consideration

Purpose of report

1. To summarise the COVID-19 Vaccine Technical Advisory Group's (CV TAG) recommendations about COVID-19 booster vaccinations in pregnant and immunocompromised people.

Background and context

2. On 8 November 2021 Medsafe updated the provisional approval for the Pfizer vaccine to state: "a booster dose of Comirnaty may be administered intramuscularly at least 6 months after completion of the primary course in individuals aged 18 years of age and older."
3. In November 2021, CV TAG made initial recommendations on booster vaccinations in the memo "Priority groups for COVID-19 booster vaccinations: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations", dated 10 November 2021 (Appendix 1).
    a. At this time CV TAG noted "there is insufficient data on the safety profile for booster doses in pregnant people" and therefore the recommendations excluded pregnant people who received a primary course earlier in pregnancy from priority groups, but there was no specific recommendation given about booster vaccination in pregnancy outside of a prioritisation framework.
    b. In this memo, CV TAG also noted that (emphasis added) "Those aged over 18 who are immunocompromised and have received a third primary dose of a COVID-19 vaccine as described in previous CV TAG recommendations, should only receive a booster dose **6 months** after completion of their primary course (i.e., 6 months after their third dose)."
4. In early December 2021, the COVID Vaccine Immunisation Programme (CVIP) asked for further information and clarification on CV TAG's recommendations in specific situations: a) Use of booster doses at less than 6 months after the completion of the primary vaccination course, b) Use

of booster doses for those under the age of 18 years who are at high risk of exposure to SARS-CoV-2, and c) Booster doses for pregnant people.

5. CV TAG issued updated recommendations in the memo "COVID-19 booster vaccinations in specific situations: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations", dated 17 December 2021 (Appendix 2).

    a. CV TAG noted that data was still accumulating about whether early booster doses offer any advantages in protection against the Omicron variant, that there continued to be insufficient data on the safety profile for booster doses in pregnant people, and that Medsafe had authorised boosters only from six months after completion of the primary dose.

    b. CV TAG recommended that a booster be offered to pregnant people who completed their primary vaccination course more than 6 months prior. Those approaching the full-term of their pregnancy 6 months after completing their primary course can choose to receive their booster after the baby is born if preferred. No further recommendation was given on boosters in severely immunocompromised people.

6. The Ministry of Health was requested to provide interim advice over the 2021/22 Christmas and New Year period on these two issues. The Science and Technical Advisory team noted the updated 24.12.21 ATAGI advice (point 15 below) and that of jurisdictions such as the UK and Canada (see below) and recommended that pregnant people and those who are severely immunocompromised be able to access the booster dose at the same dosing interval as the rest of the adult population.

7. As cases of COVID-19 climb globally due to outbreaks of the Omicron variant, some jurisdictions have rolled out fourth doses to their most vulnerable (immunocompromised people, the elderly, and healthcare workers). In light of emerging evidence on the importance of boosters for protection against infection for Omicron, and updates to guidance in other countries, CVIP have requested that CV TAG reconsider recommending that pregnant people can have a booster dose at a shorter interval of four months, even if they have received both two doses of primary vaccination earlier in their pregnancy. They have also requested that CV TAG consider whether severely immunocompromised people who have had three doses in primary vaccination may receive a fourth dose (first booster).

Evidence and international guidance

Timing of a third (booster) dose in pregnant people

Evidence

8. There is limited evidence on the safety of a third (booster) dose in pregnant people. Initial clinical trials did not include pregnant people, but Pfizer is currently recruiting 4,000 pregnant people into a trial.[1] Evidence for safety in pregnant people can be inferred from data from a booster dose of vaccine in non-pregnant populations and the current information regarding the impact of two doses in pregnant people.

9. There is no evidence to date to suggest that vaccination with an mRNA vaccine has any adverse effect in pregnancy. Multiple studies have investigated large datasets which collectively account for hundreds of thousands of pregnancies.[2-5] Studies to date have not detected safety signals in pregnant or lactating people. Studies using US registry (V-safe) data when around 150,000 pregnant people had been vaccinated, mainly with mRNA vaccines including Pfizer-BioNTech and Moderna, showed no safety concerns being raised,[6] with one study of 35,691 pregnant people in

V-safe stating "the proportions of adverse pregnancy and neonatal outcomes…among participants with completed pregnancies…appear to be similar to the published incidences in pregnant populations studied before the COVID-19 pandemic".[2] Data from 2,456 people enrolled in the V-safe Pregnancy Registry suggest that receipt of a mRNA COVID-19 vaccine pre-conception or during pregnancy is not associated with an increased risk of spontaneous abortion when compared to the expected range in recognised pregnancies.[7] In a further study, no foetal growth restriction was seen in infants delivered by people vaccinated with mRNA vaccines (n=13, to date only data from those vaccinated in late stages of pregnancy).[8] There is also a small amount of (non-peer-reviewed) data from lactating people showing that mRNA from the Pfizer vaccine is not found in breastmilk after vaccination.[9]

10. The risks associated with acute COVID-19 in pregnancy have been well demonstrated.[10] In a multinational cohort study of 2130 pregnant people in 18 countries, pregnant people with COVID-19 diagnosis were at increased risk of a composite maternal morbidity and mortality index. Newborns of people with COVID-19 diagnosis had significantly higher severe neonatal morbidity index and severe perinatal morbidity and mortality index compared with newborns of people without COVID-19 diagnosis.[11]

11. Due to waning of immunity, a booster dose of vaccine is associated with a decrease in the risk of infection. Some early data from cohort studies of primary vaccination suggests vaccination in pregnancy is effective. Immunogenicity in pregnant and lactating people vaccinated with the Pfizer vaccine was found to be comparable to non-pregnant people, and neutralising antibodies (but not vaccine mRNA) can be detected in both umbilical cord blood and breastmilk.[8, 12-14]

12. The relative risk:benefit ratio for Omicron infection in pregnancy in individuals who have received a primary course of Pfizer vaccine is not known. However, the current evidence indicates that vaccine effectiveness against symptomatic infection has substantially waned by four months after the last primary dose. This evidence forms the primary indication for decreasing the booster interval from six to four months in non-pregnant people. As the current recommendation is for pregnant people to receive a booster dose at six months, the issue in question is not whether an additional dose is given during pregnancy but the interval at which it is given.

    Therefore, the decision to use boosters in pregnancy can be framed in three ways:

    a. That a booster in pregnancy in individuals who have already received a primary course in pregnancy is not recommended until safety of a booster in pregnancy can be established by evidence from trials in pregnant people.

    b. That pregnant people who have already received a primary course of vaccination in pregnancy should not be denied the opportunity to receive a booster.

    c. That a booster is recommended for all pregnant people at least four months after a primary course of vaccine, irrespective of the time at which the primary course occurred.

Advice from other jurisdictions

13. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) states that "a booster dose can be considered if you are 18 years or older and had your initial COVID-19 vaccine course (called the primary course) ≥ 6 months ago. Pfizer is the preferred brand for booster doses for all people, including in pregnancy, regardless of the brand used initially". RANZCOG argue "mRNA vaccines are safe and effective for those trying to conceive, pregnant and breastfeeding women. Booster doses have not yet been studied in those who are pregnant but

have been shown to be safe and effective in non-pregnant adults. We do know that COVID-19 infection in pregnancy poses a significant risk for mothers and their babies, and RANZCOG recommends that pregnant women receive booster vaccinations in line with the recommendations for the non-pregnant adult population".[15]

14. Given the novelty of the mRNA vaccine platform, the World Health Organization advised a risk-based strategy until further data are available whereby pregnant women may receive the vaccine if the benefit of vaccinating outweighs the potential vaccine risks.[16]
15. ATAGI (Australia) advises that pregnant people aged 18 or older who received their primary COVID-19 vaccination course ≥ 4 months ago are recommended to have a booster dose. When practical and in line with the broader community, this interval should be brought forward to 3 months.[17]
16. The CDC (US) advises that if an individual became pregnant after receiving their first dose of a COVID-19 vaccine that requires two doses (i.e., Pfizer-BioNTech COVID-19 vaccine or Moderna COVID-19 vaccine), the advice is to receive the second dose to get as much protection as possible. People who are pregnant may receive a COVID-19 vaccine shot. The time interval not specified.[18]
17. RCOG (UK) advise all adults including pregnant people to book a COVID-19 booster vaccine (third dose) three months after their second dose. The UK's JCVI advised on 16 April 2021 that pregnant women should be offered COVID-19 vaccination at the same time as the rest of the population, based on their age and clinical risk group.[19]
18. In Canada (Ontario), people who are pregnant can book a COVID-19 booster vaccine if it has been three months after their second vaccine dose.[20]

A fourth dose (first booster) in the immunocompromised

Evidence

19. Preliminary results from the UK Octave Duo study has reported that around half of the patients who had no antibody response after two doses had some response after three doses, however, a quarter of immunosuppressed patients still had no response after three doses and therefore there is a continuing need for protection in this population.[21] Among a sample of kidney transplant patients in France, antibody response and cellular immunity were measured at one month and six months, and demonstrates that protection from the third dose does wane (see Table 1).[22]

Table 1: Immunogenicity (IgG and T cell response) status one and six months after the third dose of after third dose SARS-Cov-2 mRNA BNT162b2 vaccine in 39 kidney transplant recipients

	Immunogenicity at 1 month	Immunogenicity at 6 months	p
IgG response and T-cell response - n(%)	33/39 (84.6)	19/39 (48.7)	0.001
T-cell response only - n(%)	6/39 (15.4)	9/39 (23.1)	NS
IgG response only - n(%)	0/39 (0.0)	10/39 (25.6)	0.001
Neither T-cell response nor IgG response - n(%)	0/39 (0.0)	1/39 (2.6)	NS

20. While there is limited data on the efficacy of a fourth dose used as a booster in immunocompromised people, a study of 67 kidney transplant recipients (who had had a weak antibody response to three doses) measured neutralising antibody responses before and after a fourth dose of an mRNA vaccine. While only 16% of patients demonstrated a response before the fourth dose, this increased to 66% afterwards. Neutralising antibody titres also increased significantly from <7.5 (IQR : <7.5−15.1) to 47.1 (IQR <7.5−284.2), however the study was done during Delta's dominant and responses may be lower for Omicron.[23]
21. The significant waning of immunity within 6 months post-third dose for those with good immune responses (particularly in the context of Omicron) further support the need for a fourth dose in the immunosuppressed. Results from the study conducted at Kaiser Permanente Southern California found vaccine efficacy of Moderna against Omicron infection was significantly lower among immunocompromised people (11.5%, 95%CI 0.01%-66.5%) compared to boosted immunocompetent individuals (62.5%, 95%CI 56.2%-67.9%) or immunocompetent people with two doses (30.4%, 95%CI, 5.0%-49.0%).[24]
22. In Israel, initial news reports of a fourth Pfizer dose (second booster) trial in 154 immunocompetent medical personnel have noted minor side effects only and no safety signals. The fourth dose was given 4-5 months after the third dose, and preliminary findings in the media have reported a fivefold increase in the level of antibodies. An additional 25,000 people over 60 years (some of whom are immunocompromised) have now had a fourth Pfizer dose.(link)
23. There are however significant limitations to the evidence, namely: 1) thresholds for detection vary between studies; 2) a lack of detectable response is not necessarily reflective of lack of protection; 3) immunocompromised individuals received a third dose earlier and as such lower vaccine efficacy may partly reflect waning immunity and 4) studies relate to small populations.

International guidance

24. Several countries have approved the use of fourth doses in certain populations, particularly for immunocompromised people. Some countries have also extended the approval and recommendations to include high-risk populations such as the elderly and healthcare workers, and for these populations the fourth doses function as a second booster dose.

Country	Vaccine	4th Dose Policy	Time interval (after 3rd dose)	Announcement date
Israel	Pfizer-BioNTech	Immunocompromised, health-care workers and people over 60 years old	4 months	22-Dec-21
US	Pfizer-BioNTech, Moderna	Immunocompromised	5 months	24-Dec-21
UK	Pfizer-BioNTech, Moderna	Immunocompromised	No information available	24-Dec-21
Thailand	No information available	Immunocompromised, frontliners, health-care workers and people over 60 years old*	3 months	4-Jan-21
Chile	Pfizer-BioNTech, AstraZeneca, Sinovac	12 years of age and older immunocompromised people, who received their first booster dose until September 12. From 7-February, people over 55 years old are eligible for the second booster shot.	4 months (immunocompromised) 6 months (over 55)	10-Jan-22
Australia	No information available	Highly vulnerable people (severely immunocompromised)	4 months	15-Jan-22
Greece	No information available	Immunocompromised and those who suffer from serious chronic diseases	3 to 6 months	11-Jan-22
Hungary	No information available	Voluntary	No information available	12-Jan-22
Denmark	No information available	Highly vulnerable people	No information available	12-Jan-22
Spain	No information available	Highly vulnerable people (immunocompromised)	No information available	14-Jan-22
Ontario (Canada)	No information available	Immunocompromised	No information available	14-Jan-22

Recommendations

25. CV TAG met on 25 January 2022 and recommended:

a. That pregnant people aged 18 and older can receive the Pfizer booster vaccine at any stage of pregnancy, at least 4 months after the second dose, and are encouraged to discuss the timing of their booster with their midwife, obstetrician or general practitioner.

b. That immunocompromised people who have received three primary doses should have a booster dose in line with the timing for the general population i.e., currently a 4-month interval from their primary course (three doses).

Dr Ian Town

Chief Science Advisor and

Chair of the COVID-19 Vaccine Technical Advisory Group

Appendix 1: Priority groups for COVID-19 booster vaccinations: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations

Memo

MINISTRY OF HEALTH
MANATŪ HAUORA

Date:	10 November 2021
To:	Joanne Gibbs, Director of National Operations, COVID Vaccine Immunisation Programme
Copy:	Dr Ashley Bloomfield, Director-General of Health Allison Bennett, Manager, System Enablers, System Strategy and Policy Dr Caroline McElnay, Director of Public Health
From:	Dr Ian Town, Chief Science Advisor
Subject:	Priority groups for COVID-19 booster vaccinations: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations
For your:	Consideration

Purpose

26. To summarise the COVID-19 Vaccine Technical Advisory Group's (CV TAG) recommendations about COVID-19 booster vaccinations.

Context

27. Current evidence shows that antibody levels against SARS-CoV-2 wane over time following the second Pfizer COVID-19 vaccine dose, and that there is a reduction in protection against infection, particularly from 6 months after a primary vaccination course.[25-27] The reduction in protection is similar for Delta and other virus variants.[26, 28] Protection against transmission from vaccinated individuals who are infected also appears to wane over time.[29] However, evidence suggests that protection against severe disease remains high, including for the Delta variant, though follow-up times varied between studies.[25-28, 30-32]

28. Booster doses are now being given in several countries, including but not limited to the United Kingdom, the United States, Germany, Israel, Singapore, and Malaysia.

29. Medsafe has assessed an application submitted by Pfizer for the use of booster vaccines within New Zealand. On 8 November 2021 Medsafe updated the provisional approval for the Pfizer vaccine to state "a booster dose of Comirnaty may be administered intramuscularly at least 6 months after completion of the primary course in individuals aged 18 years of age and older".

30. *Reactogenicity of a Pfizer booster dose:* Amongst 306 participants aged 18-55 years old receiving a third dose in Pfizer's phase III trial, reactogenicity was largely in line with findings after the second dose, with the exception of lymphadenopathy which occurred at a rate of 5.2% compared to 0.4% post-second dose.[33] Other studies also suggest that the common mild and transient side effects after booster doses are comparable to those following primary vaccine doses.[34-38]

31. *Safety of a Pfizer booster dose:* Data from Israel shows that after more than 2.8 million administered third doses, 19 serious adverse events have been reported, of which 2 have been confirmed as linked, though there is likely underreporting in this data.[39] Only one case of myocarditis has been reported and is under investigation, in a male older than 30 years, however most younger individuals have had limited follow up time.[39] Israeli data suggests that the risk of myocarditis with the booster dose is not increased when compared with the risk after second doses of vaccine.[40] However, there remain limited data on the incidence of myocarditis after second doses of the mRNA vaccines in younger people.[40-46]

32. *Immunogenicity and effectiveness of a Pfizer booster dose:* A COVID-19 vaccine booster dose administered at 6 months or more after completion of the primary vaccine course has been demonstrated to boost the immune response and is expected to increase protection against infection and disease, particularly in older people where waning appears more marked.[33-36] Data from Israel, where booster doses have been administered to large numbers of people, show reductions in all eligible age groups in the rate of infection, as well as severe disease in those aged ≥40 years, and deaths in those ≥60 years, after the booster dose.[40, 47, 48]

33. *AstraZeneca booster dose:* A small study suggests that AstraZeneca, when used as a booster following a full primary course of Pfizer or Moderna, augments humoral and T cell immune responses, and is well tolerated.[31]

34. *Prioritisation:* The UK's Joint Committee on Immunisation (JCVI) advised on 14 September 2021 that booster vaccines be offered to those more at risk from serious disease, and who were vaccinated during Phase 1 of the vaccine programme (priority groups 1 to 9). This was seen as needed in order to maintain a high level of protection against hospitalisation or death from the virus through winter 2021/2 (while acknowledging that insufficient time has passed to know what levels of protection might be expected 6 to 12 months after the primary course). Those to be offered boosters in the UK include:

    a) those living in residential care homes for older adults
    b) all adults aged 50 years or over
    c) frontline health and social care workers
    d) all those aged 16 to 49 years with underlying health conditions that put them at higher risk of severe COVID-19, and adult carers
    e) adult household contacts of immunosuppressed individuals

    The JCVI advised that the booster vaccine dose is offered no earlier than 6 months after completion of the primary vaccine course, in the same order as during Phase 1. They also indicated a preference for the Pfizer vaccine for the booster programme, regardless of which vaccine brand someone received for their primary doses.

35. The Australian Technical Advisory Group on Immunisation (ATAGI) advised on 27 October 2021 that the highest priority groups to receive booster doses should be those with risk factors for severe COVID-19 and/or those at increased occupational risk of COVID-19, notably:

    a) People at greater risk of severe COVID-19: individuals aged 50 years and older, those with underlying medical conditions, residents of aged care and disability facilities, and Aboriginal and Torres Strait Islander adults. In these groups the benefit of a booster dose is primarily to reduce the risk of severe COVID-19.

b) People at increased occupational risk of COVID-19: a booster dose for individuals in this group is expected to reduce their likelihood of SARS-CoV-2 infection and associated occupation-related impacts, acknowledging that infection will be mostly mild in these individuals due to prior vaccination and younger age. Booster doses may also reduce the potential for infected individuals to transmit SARS-CoV-2, although evidence for this is currently limited.

36. ATAGI supports the use of a single booster dose for those who completed their primary COVID-19 vaccine course ≥6 months ago. This will initially include, but not be limited to, the groups who were prioritised in the rollout of the vaccine programme from early 2021. This recommendation will be reviewed by ATAGI in January 2022, as groups other than the high-risk groups listed above will become eligible in larger numbers. Pfizer is recommended as a single booster dose, irrespective of the primary COVID-19 vaccine used. Although not preferred, ATAGI recommended that AstraZeneca can also be used as a booster dose in the following situations:

    a) For individuals who have received AstraZeneca for their first two doses if there are no contraindications or precautions for use.

    b) If a significant adverse reaction has occurred after a previous mRNA vaccine dose which contraindicates further doses of mRNA vaccine (e.g., anaphylaxis, myocarditis).

37. ATAGI does not currently recommended boosters for those aged <18 years. In this age group, severe COVID-19 is uncommon, and the primary course of COVID-19 vaccines generates a strong immune response, and therefore the benefit from additional doses of vaccine is thought to be to be small. In addition, there are currently only very limited data on the safety of repeated mRNA vaccine doses in this age group.

38. The Ministry of Health's Policy team requested CV TAG's clinical guidance on which groups should be prioritised for booster vaccines, and when these vaccinations should start.

Recommendations

39. CV TAG met on 2 and 9 November 2021 to consider recommendations regarding priority groups for COVID-19 booster vaccinations.

40. **CV TAG noted that:**

    a) Data are still accumulating about waning of protective vaccination effects after primary vaccination and the benefits of a booster dose.

    b) The goal of offering booster doses in New Zealand is to prevent severe disease caused by SARS-CoV-2, to reduce burden on hospitals and other healthcare providers, and to protect those at high occupational risk of exposure.

    c) The current situation in New Zealand is different to the situation at the start of vaccine roll-out (starting in late February 2021, priority groups listed in Appendix 1). There is now greater availability of Pfizer vaccine and effective infrastructure for administering the vaccine, but there is also a higher risk of healthcare workers being exposed to SARS-CoV-2 with the virus now in the community in New Zealand, especially in Auckland.

    d) There is limited data on the safety profile for booster doses in people younger than 30 years of age from the published trials. Concern was noted around vaccine mandates requiring booster doses in this age group before further data are available

    e) There is insufficient data on the safety profile for booster doses in pregnant people.

f) Māori and Pacific People are at an increased risk of severe disease and hospitalisation,[49] and therefore having a universal age-criteria for prioritisation is inequitable. A lower age band for Māori and Pacific People would be needed to provide equitable protection.

g) It is now approximately 8 months since the first doses of COVID-19 vaccine were administered in New Zealand.

41. **CV TAG recommends that:**

a) Increasing the vaccination coverage of first and second doses, particularly for Māori and Pacific People, should remain the first priority of the COVID-19 vaccination programme in New Zealand.

b) The Pfizer vaccine is recommended as a single booster dose.

c) COVID-19 vaccine booster doses should be offered to those 18 years of age and older, who have completed their full primary vaccination course 6 or more months prior.

d) Those aged over 18 who are immunocompromised and have received a third primary dose of a COVID-19 vaccine as described in previous CV TAG recommendations, should only receive a booster dose 6 months after completion of their primary course (i.e., 6 months after their third dose).

e) Any future vaccine mandates should not require booster doses in younger age groups (<30 years) until further data are available.

f) When considering prioritisation, priority groups for a booster dose (at least 6 months after completion of the primary course) are those most at risk of exposure to SARS-CoV-2, and those most at risk from serious COVID-19 disease. In particular, these are:

i. Frontline healthcare workers, particularly in regions where there is COVID-19 in the community (or regions that are at high risk of further spread of COVID-19),

ii. All those who are aged 65 years or over,

iii. Māori and Pacific People aged 50 years and over,

iv. Anyone over the age of 18 with comorbidities, as specified in Group 3 in Appendix 1, with the exception of pregnant people, who completed a full primary course of vaccination in early pregnancy.

g) AstraZeneca can also be used as a booster dose if available for specific situations including if an individual has had a significant adverse reaction after a previous Pfizer vaccine dose (e.g., anaphylaxis, myocarditis), and if AstraZeneca is not contraindicated.

42. CV TAG will continue to monitor all relevant information (including vaccine efficacy data against emerging variants of concern and emerging evidence on the duration of immunity) and will update their recommendations as further evidence becomes available.

Ian G Town

Dr Ian Town

Chief Science Advisor

Chair, CV TAG

Appendix 2: COVID-19 booster vaccinations in specific situations: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations

Memo

MINISTRY OF HEALTH
MANATŪ HAUORA

Date:	17 December 2021
To:	Dr Ashley Bloomfield, Director-General of Health
Copy:	Astrid Koornneef, Director of National Immunisation Programme Allison Bennett, Manager, System Enablers, System Strategy and Policy Dr Caroline McElnay, Director of Public Health
From:	Dr Ian Town, Chief Science Advisor
Subject:	COVID-19 booster vaccinations in specific situations: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations
For your:	Consideration

Purpose

43. To summarise the COVID-19 Vaccine Technical Advisory Group's (CV TAG) recommendations about booster doses of the Pfizer vaccine.

Context

44. On 8 November 2021 Medsafe updated the provisional approval for the Pfizer vaccine to state: ***"a booster dose of Comirnaty may be administered intramuscularly at least 6 months after completion of the primary course in individuals aged 18 years of age and older".***

45. CV TAG has previously made recommendation about booster vaccinations in the memo "Priority groups for COVID-19 booster vaccinations: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations", dated 10 November 2021 (Appendix 1).

46. The COVID Vaccine Immunisation Programme (CVIP) has asked for further information and clarification on CV TAG's recommendations in specific situations:

    a) Use of booster doses at less than 6 months after the completion of the primary vaccination course.

    b) Use of booster doses for those under the age of 18 years who are at high risk of exposure to SARS-CoV-2.

    c) Booster doses for pregnant people.

47. *Antibody waning:* Current evidence shows that antibody levels against SARS-CoV-2 wane over time following the second dose of the Pfizer COVID-19 vaccine. There is a reduction in protection against infection, particularly from 6 months after a primary vaccination course.[25-27] The reduction in protection is similar for Delta and other virus variants.[26, 28] Protection against transmission from vaccinated individuals who are infected also appears to wane over time.[29]

However, evidence suggests that protection against severe disease remains high, including for the Delta variant, though follow-up times varied between studies.[25-28, 30-32]

48. *Reactogenicity of a Pfizer booster dose:* Amongst 306 participants aged 18-55 years old receiving a third dose in Pfizer's phase III trial, reactogenicity was largely in line with findings after the second dose, with the exception of lymphadenopathy which occurred at a rate of 5.2% compared to 0.4% post-second dose.[33] Other studies also suggest that the common mild and transient side effects after booster doses are comparable to those following primary vaccine doses.[34-38]

49. *Safety of a Pfizer booster dose:* Data from Israel shows that after more than 2.8 million administered third doses, 19 serious adverse events have been reported, of which 2 have been confirmed as linked, though there is likely underreporting in this data.[39] Only one case of myocarditis has been reported and is under investigation, in a male older than 30 years, however most younger individuals have had limited follow up time.[39] Israeli data suggests that the risk of myocarditis with the booster dose is not increased when compared with the risk after second doses of vaccine.[40] However, there remain limited data on the incidence of myocarditis after second doses of the mRNA vaccines in younger people.[40-46]

50. *Immunogenicity and effectiveness of a Pfizer booster dose:* A COVID-19 vaccine booster dose administered at 6 months or more after completion of the primary vaccine course has been demonstrated to boost the immune response (e.g. neutralising antibody) and is expected to increase protection against infection and disease, particularly in older people where waning appears more marked.[33-36] Data from Israel, where Pfizer booster doses have been administered to large numbers of people, show reductions in all eligible age groups in the rate of infection, as well as severe disease in those aged ≥40 years, and deaths in those ≥60 years, after the booster dose.[40, 47, 48]

Use of booster doses at less than 6 months after the completion of the primary vaccination course

51. Potential reasons to consider early booster doses include:

    a) to provide potentially higher protection against COVID-19 caused by new variants

    b) to protect people who are close to 6 months post-primary vaccination course who are at risk of severe COVID-19 and/or SARS-CoV-2 exposure.

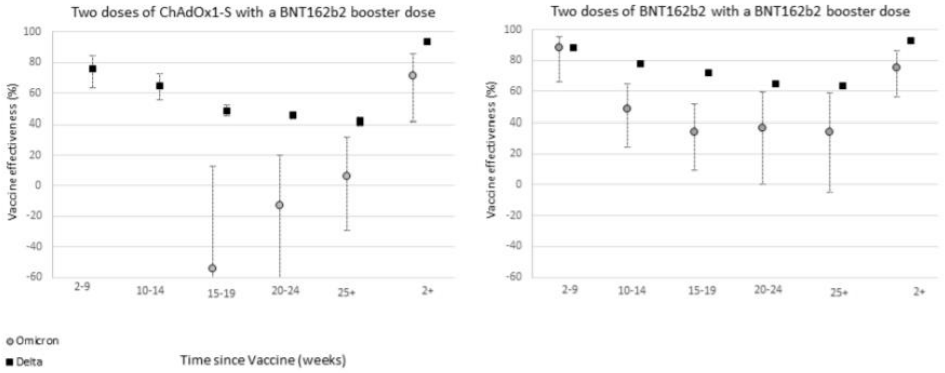
52. It is not yet clear if Omicron can evade vaccine-induced immunity. The laboratory data on Omicron from antibody neutralisation studies to date is very limited and preliminary [50-52], and cannot be used to infer an impact on vaccine protection in real world settings at this stage. Additional information about these studies is presented in Appendix 2.

53. Very early data about vaccine effectiveness (VE) against **symptomatic** disease caused by Omicron and Delta variants was released by the UK Health Security Agency (UKHSA) on 10th December 2021.[53] This analysis included data from 56,439 Delta cases including 581 Omicron cases. Results are shown in Figure 1 (Figure 7 in original document), below. Data about VE of a Pfizer primary series (weeks "2-9" to "25+") and booster dose (week "2+") against Delta and Omicron variants are shown in the right-hand panel of Figure 1. Confidence intervals for VE estimates for Omicron are extremely wide. However, they do not appear to overlap with confidence intervals for Delta at any point from 9 weeks after the primary course (including after the booster dose). This suggests a lower VE for Omicron than for Delta, but it remains unclear to what extent. The point estimate for VE against Omicron increased to ~76% at >2 weeks after a Pfizer booster dose, from ~35% at 15 to >25 weeks after the Pfizer primary course.

Figure 1: Early UKHSA data on vaccine effectiveness for Delta and Omicron (right panel show Pfizer primary course and booster, with lower effectiveness against Omicron)

Figure 7: Vaccine effectiveness against symptomatic diseases by period after dose 1 and dose 2 for Delta (black squares) and Omicron (grey circles) for (A) recipients of 2 doses of AstraZeneca vaccine as the primary course and a Pfizer as a booster[1] and (B) recipients of 2 doses of Pfizer vaccine as the primary course and a Pfizer as a booster

Supplementary data are not available for this figure.



[1] The early observations for 2 doses of AstraZeneca are particularly likely to be unreliable as they are based on relative small numbers and are likely to reflect an older population and a population with more co-morbidities than those given the Pfizer vaccine, and this may explain the negative point estimates.

54. A press release with data from South Africa during the Omicron wave states that two doses of Pfizer has a VE of **70% against hospitalisation**, and **33% against COVID-19 infection,** though the data does not mention time since vaccination.[54]

55. Other data from South Africa shows that the risk of reinfection has increased in the era of Omicron. [55] This suggests that Omicron could have increased evasion of immunity following prior infection.

56. The Australian Technical Advisory Group on Immunisation (ATAGI) advised on 3rd December 2021 in a statement about SARS-CoV-2 Omicron variant and COVID-19 booster doses, that at that time there was no evidence to suggest that earlier booster doses of current COVID-19 vaccines will augment protection against the Omicron variant. However, ATAGI also said in this statement that in certain circumstances, the routine six-month interval for booster doses may be shortened to five months for logistical reasons, for example:

    a) for patients with a greater risk of severe COVID-19 in outbreak settings;

    b) if an individual is travelling overseas and will be away when their booster dose is due; or

    c) in outreach vaccination programs where access is limited.

57. **On 12th December, ATAGI updated their statement to recommend COVID-19 booster vaccination for anyone aged 18 and older who completed their primary course of COVID-19 vaccination 5 or more months ago.**

58. The UK's Joint Committee on Vaccination and Immunisation (JCVI) have reduced the minimum interval between completion of the primary course and the booster to 3 months, stating that "it may be that higher levels of antibody induced by vaccines directed at the original 'wild type' variant will provide better protection against the Omicron variant, as has been demonstrated in laboratory studies with respect to other variants", and "additional data regarding the Omicron

variant will take some time to accrue. Waiting for such data before taking some actions risks a suboptimal delayed response".

Use of booster doses in those under the age of 18 years who are at high risk of exposure to SARS-CoV-2

59. In those under 18 years of age, severe COVID-19 is uncommon, and the primary course of COVID-19 vaccines generates a strong immune response. Therefore, the benefit from additional doses of vaccine is thought to be to be small. In addition, there are currently only very limited data on the safety of repeated mRNA vaccine doses in this age group.

60. On 9th December 2021, the U.S. Food and Drug Administration (FDA) amended the emergency use authorization for the Pfizer vaccine, allowing the use of a booster in individuals 16 and 17 years of age at least six months after completion of primary vaccination with Pfizer vaccine.

61. ATAGI does not currently recommended boosters for those aged <18 years.

Booster doses for pregnant people

62. CV TAG recommendations from 10th November (Appendix 1) excluded pregnant people who received a primary course earlier in pregnancy from priority groups, but there was no specific recommendation given about booster vaccination in pregnancy outside of a prioritisation framework. Specifically, there is concern that messaging that those vaccinated in early pregnancy should not receive a booster dose while still pregnant is raising unintended concerns about the safety of vaccination with COVID-19 vaccines while pregnant (both primary and booster doses).

63. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) states that "a booster dose can be considered if you are 18 years or older and had your initial COVID-19 vaccine course (called the primary course) ≥ 6 months ago. Pfizer is the preferred brand for booster doses for all people, including in pregnancy, regardless of the brand used initially". RANZCOG argue "mRNA vaccines are safe and effective for those trying to conceive, pregnant and breastfeeding women. Booster doses have not yet been studied in those who are pregnant but have been shown to be safe and effective in non-pregnant adults. We do know that COVID-19 infection in pregnancy poses a significant risk for mothers and their babies, and RANZCOG recommends that pregnant women receive booster vaccinations in line with the recommendations for the non-pregnant adult population".[15]

Recommendations

64. CV TAG met on 14 December 2021 to consider recommendations regarding COVID-19 booster vaccinations in specific situations.

65. **CV TAG noted that:**

    a) Data are still accumulating about whether early booster doses offer any advantages in protection against the Omicron variant.

    b) There are no long term data available about the safety of early booster doses but short term side effects appear to be modest.

    c) There is insufficient data on the safety profile for booster doses in pregnant people.

    d) Medsafe has authorised boosters only from six months after completion of the primary dose.

66. **CV TAG recommends that:**

a) A Pfizer booster dose should be offered to adults 18 years or over, 5 months after the completion of the primary vaccination course.

b) Priority should be given to those at high risk of severe disease or exposure to SARS-CoV-2, including:

   i. those aged 65 years and over

   ii. those with comorbidities that put them at higher risk of severe COVID-19

   iii. Māori and Pacific peoples

   iv. health care workers and workers in other settings at high-risk of SARS-CoV-2 exposure eg Border Workers and MIQ staff.

c) The COVID-19 Vaccine and Immunisation Programme (CVIP) of the Ministry of Health will need to work with Medsafe to manage access to boosters for the shorter 5-month interval.

d) Booster doses for 16- and 17-year-olds are not currently recommended (including for those working in settings that place them at higher risk of exposure to SARS-CoV-2), in line with the Medsafe authorisation of booster doses.

e) Boosters can be offered to pregnant people who completed their primary vaccination course more than 6 months prior. Those approaching the full-term of their pregnancy 6 months after completing their primary course can choose to receive their booster after the baby is born if preferred.

67. CV TAG will continue to monitor all relevant information (including vaccine efficacy data against emerging variants of concern and emerging evidence on the duration of immunity) and will update their recommendations as further evidence becomes available.

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