Minutes

MyoPeri-ROC

Date:	1 December 2021
Time:	1:15-2:45 pm
Location:	Ministry of Health & Microsoft Teams
Chair:	Mr Chris James
Attendees:	Saskia Schuitemaker, Professor Ralph Stewart, Professor Chris Frampton, Associate Professor Michael Tatley, Dr Tim Hanlon, Peter Himona
Ministry of Health Attendees:	s 9(2)(g)(ii)
Apologies:	None

	Agenda Item
1.	**Welcome and introductions** • Chris James welcomed all members of the committee and attendees of the meeting in his capacity as Chair of the MyoPeri-ROC. • Opening Karakia was performed. • The members of the ROC and Ministry attendees introduced themselves. • The chair thanked members for completing the COI forms, and noted the scrutiny of the COVID response from the media and the public.
2.	**Overview of committee function** • The Ministry referenced the draft terms of reference which were circulated prior to the meeting. • The Ministry began a discussion which covered the following points: ▪ The purpose the committee is to oversee a follow up study on myocarditis/pericarditis after COVID-19 vaccination. ▪ There is significant scrutiny around the safety signal of myocarditis/pericarditis and the intent is to generate a robust study, with protocols and surveys as tight as they can be to generate high quality data. ▪ The study will be operating under a tight timeframe and will have an equity focus. ▪ There is a goal of creating a valuable study which addresses a knowledge gap. ▪ The Ministry would like the committee to keep the study accountable to the timeline. ▪ The Ministry requested feedback on the terms of reference by the end of the week (Friday the 3rd of December).
3.	**Overview of study**

	• The Ministry stated that the objective of the study is to follow up people who have experienced myocarditis or pericarditis following COVID-19 vaccination in New Zealand and examine long term outcomes for these individuals. • The Ministry acknowledged a similar study being conducted by the CDC in the United States of America. • The Ministry stated that this study will be valuable in as it is occurring in a largely COVID-19 infection free population which will reduce confusion between the cause of myocarditis or pericarditis in reported cases. • There is an expectation that approximately 200 consumers will be surveyed. • The project owners of this study will be Medsafe and CVIP will provide support. • Governance will be provided by this ROC.
4.	**Review of study design and protocol** • The Ministry stated that the study design is an observational study with data collected through both a consumer survey and a healthcare provider survey. • The Ministry went over the study design as written on the draft protocol. • The CBG survey company was identified as the possible choice of surveyor. They currently support COVID-19 case management and NZ Health Surveys and their experience contacting hesitant people was noted. • There was a question raised on whether the study population could be expanded to include a greater number of people who have experienced myocarditis or pericarditis. • The Ministry stated that a diagnosis from any healthcare professional will count as a clinical diagnosis, this is less stringent than the CDC inclusion criteria. • A question was raised as to whether some populations would have underreported to CARM and would then be underrepresented from the study. • A member raised the point that myocarditis or pericarditis cases may be reported to IMAC but may not reported to CARM and thus may be excluded from the study. • It was noted that IMAC should be reporting to CARM if this is the case. • A member asked about contact methods for recruiting participants and whether this could lead to bias about the study participants. • The Ministry discussed the intention to use an experienced survey company who can engage in multiple methods to contact participants including phone interviews, internet surveys, and face to face contact if needed. • The Ministry reiterated their commitment to making access to the survey as accessible and equitable as possible. • The Ministry discussed some of the techniques the survey company can offer, including using nurses as interviewers and ethnicity matching. • It was noted there is the possibility of using the local pharmacist or doctor to contact participants. • A member raised a point around recruitment, response rates and the limitations of the study if response rates are low. They discussed that estimating the true incidence may be helpful to understand the study population and the generalisability of the data obtained from the study, as not all cases will be reported to CARM and some people may choose not to participate in the study. • The Ministry asked for this member to provide expert advice on sample size requirements outside of the meeting. • A member raised a point on the design of the questionnaire and that too long a questionnaire will reduce engagement with the survey. • The Ministry acknowledged this and agreed that ideally the survey will be as short as possible to gather the required information, which may require optimising the currently proposed survey questions. • A member queried the timeframe of the study and whether a stop date should be introduced. This was considered in relation to COVID-19 infection confounding diagnosis, and COVID-19 infection confounding outcomes if case numbers rise in the community. • The Ministry proposed a stop date of the 31st of December, cases diagnosed by this date.

	• It was suggested that a specific start and end date be stated in the study protocol. • A member asked about the data linkage available to the study. • The Ministry confirmed that NHI and vaccination data linkage was available, and that there may be other health information available such as medication prescriptions and hospitalisation data. The Ministry noted that participant consent is required to link health data and this possibility would be explored. • A committee member questioned the value in asking about supplements. • The Ministry answered that it could provide other useful information on the person's health,but agreed to consider if this was essential given the survey length. • The member suggested if survey data could be linked three or four years down the line it would provide truly long-term follow up. • There was agreement in the committee that data linkage would be important. • It was noted by a member that in the vast majority of myocarditis cases the cause is unknown. • A member questioned whether copies of the CARM reports would be provided. • The Ministry stated that use of information in CARM reports in the study would be subject to consumer consent for data linkage but that identifiable information will not be reported on. • The member questioned if individuals making reports to CARM gave permission to be contacted. • The Ministry explained when people make CARM reports there is a statement that says their information can be used for research purposes, but this statement is not considered as explicit consent for the purposes of this study and that ethical approval would still be needed to contact people using the details supplied in a CARM report. It was also noted that not all reports are submitted by consumers. • The Ministry stated that consumers will be asked permission to have their healthcare provider contacted for a survey and also be asked to provide name/contact details for their healthcare provider.
5.	**Outcomes** • The ministry outlined the primary study outcomes as current health, physical functioning, school/university/work attendance, and mental health, and the secondary outcomes as hospitalisations and cardiac recovery. • A member raised a question about economic/financial impacts for consumers. • It was answered that work outcomes can serve as a proxy although no question specifically about finances is currently planned. • The Ministry stated the consumer questionnaire will also include questions confirming the eligibility of participants, the demographics of participants, the vaccination details of the participants, and the contact details of the health care provider.
6.	**Review of study questionnaires** • The Ministry gave the intended questions for each study outcome, starting with current health. • A member noted that questions on syncope were to identify arrhythmia, but that this was uncommon, and the focus on this symptom over others was not necessary. They noted it could be asked in the same format as the other symptom questions. The member also suggested that it may be more helpful to ask about how long symptoms took to resolve (or if they weren't resolved) after diagnosis, rather than just about the last 2 weeks. They noted that the follow-up timepoint after diagnosis may vary between participants. • The Ministry acknowledged this point. The Ministry explained that the proposed questions were based on the survey by the CDC, but that the committee's feedback on wording and priority of questions was needed. • Another member agreed with the rationale behind altering the wording of the survey questions for consumers about their symptoms. • A member questioned if the general health question was helpful information without asking about the baseline.

	• The Ministry answered that one of the questions in the current health section, and one in the mental health section were questions from the NZ Health Survey and this would allow a comparison with the general NZ population, however agreed that it would be useful to establish the baseline too. • The committee acknowledged the possible value in being able to compare this information. • The Ministry provided the proposed questions around physical functioning. The Ministry noted that the wording will be slightly different between adults and children. • A member noted that questions on current levels of activity may not very helpful if it there is no comparison to the person's baseline level of activity before the myocarditis. • The member discussed that the psychological impact of the health advice not to exercise could have an impact on people's activity levels or perceived ability and queried whether this could be captured in the survey. • The Ministry acknowledged this point. • A member expressed the importance of capturing patient perception of their condition, but that it would be helpful to know if this was in line with objective evidence that would be captured in the healthcare professional survey. • The Ministry provided the proposed questions relating to school, work, and university. • Members queried the wording of questions related to school and university. • It was acknowledged that as with the symptom questions it may not be helpful to ask only about the last 2 weeks. • The Ministry provided the proposed question relating to mental health. • A member raised a point on the interpretation of this question and its usefulness without a baseline established. • The Ministry provided the proposed questions relating to the secondary outcome hospitalisation. • A member questioned if data linkage could be used to more effectively capture this information • The Ministry raised the point that some people may not consent to data linkage and that this could be useful in providing patient perception of events. The Ministry acknowledged that most of this information should be accessible through data linkage and this will be explored. • The Ministry provided the sample questions relating to medications. • A member proposed that some of the questions be rephrased to provide more useful information regarding the timeframe of their pharmaceutical use, and do not necessarily need to list specific medications. • The Ministry acknowledged the proposed changes and suggested a more in-depth review of the medication question with relevant committee members. • The Ministry provided the proposed questions relating to investigation results. • A member provided an opinion that these questions could be rephrased to be more accessible to consumers rather than just health care professionals, for example, asking if any of the tests they had showed damage to the heart. • The Ministry acknowledged these suggestions. • A member questioned whether all consumer study participants would have a healthcare professional to answer the corresponding survey. • The Ministry stated that the GP or diagnosing clinician should be able to provide answers to several parts of the survey for all participants but there would be some limitations for consumers who had not engaged with health services beyond their initial diagnosis. • A member suggested that questions about hospitalisation be expanded to include outpatient cardiology appointments and GP appointments. • The Ministry provided the proposed questions relating to medical history. • A member proposed an open response option instead of selected options for past medical history, as some of the conditions listed are very rare and are unlikely to have a high hit rate.

	• The Ministry acknowledged the possible benefits of this approach. • A member noted that it is unlikely that most people require ongoing cardiac medications, and that many will only require anti-inflammatory medications or colchicine in the initial phases, therefore it may be helpful to ask about medications when they were first diagnosed and how long they were needed for. • The Ministry outlined proposed aetiology questions for the healthcare professional survey. • The Ministry responded that a question on this is currently included in the healthcare provider's survey and stated that the possibility of including this in the consumer survey would be explored. • The Ministry speaker opened the floor to questions and feedback. • A member provided feedback suggesting the survey be shortened. • A member stated that there may be difficulty convincing healthcare professionals to complete a long survey. • The Ministry acknowledged the benefits of shortening the survey. • There was discussion on what the key focus of the study should be, for example what is essential to know and what is just interesting to know. There was agreement that there may need to be some pragmatic decisions about what is and isn't included in order to ensure the survey is a manageable length for consumers. • A member raised the point that people who have experienced significant events are prepared to share their information and that it is likely that many would like the opportunity to speak. • A member raised the possibility of a pilot study first used to guide revisions to the survey. • A member raised a question about whether incentives would be used to encourage participation. • The Ministry agreed to explore the possibility of using incentives if needed.
7.	AOB • The Ministry proposed a Teams channel to be used by members of the committee. • The Ministry stated that they would make adjustments to the survey questions and provide the revised survey to committee members for review. • The Ministry stated that they were in the process of applying for ethics approval and that a finalised survey was a requirement for ethics approval. • The Ministry stated that there was no scheduled date for the next meeting of the committee but indicated a second meeting could be in late January or in February near the study start. Payments discussed for eligible members.
8.	Closing • The Ministry thanked the committee for their attendance and contributions to the meeting. • The Chair thanked the committee attendees for their feedback. • There was a closing karakia. • The meeting closed at 2:50pm.

Agenda

MyoPeri-ROC

Date:	21 March 2022
Time:	10:00-11:00 am
Location:	Ministry of Health & Microsoft Teams
Chair:	Mr Chris James
Attendees:	Saskia Schuitemaker, Professor Ralph Stewart, Professor Chris Frampton, Dr Tim Hanlon, Peter Himona
Ministry of Health Attendees:	s 9(2)(g)(ii)
Apologies:	Associate Professor Michael Tatley

Agenda item
Welcome & Karakia *The Chair welcomed attendees to the second MyoPeri-ROC.* *The meeting was opened with the Ministry of Health's (the Ministry) karakia.*
The Ministry study team provided an update about the key study parameters. - Target group is adults and children over 12 years of age with a clinical diagnosis of myopericarditis after dose 1 or dose 2. - Target group identified by adverse event reports to the Centre for Adverse Events Monitoring (CARM). - Participants must have had a minimum of three month between onset of myocarditis/pericarditis and participation in the survey. - The study aim is to capture their current mental and physical health, their physical functioning, their ability to attend daily life, their disease severity, and the aetiology of their disease.
The Ministry study team provided a status update on the current stage of the research study. - Ethics approval has been obtained. - The study protocol has been registered. - The Ministry's communications approach has begun. A Ministry of Health webpage has been created and targeted communications to the health sector have begun with the goal of building awareness about the study. - Participant information letters have begun to be sent out. - A study email inbox has been set up to correspond with participants and members of the public that have questions. - The first interviews are due to start on 28 March 2022.

- Healthcare professional surveys are being finalised and will start at a later time point. These surveys will be delivered electronically.
- Data collection is expected to complete by late May or early June.

The Ministry study team outlined the changes in the study design since the last meeting.

- It was noted that in the last committee meeting there was a discussion about data-linking with the Ministry's COVID-19 records to ensure high data quality.
- CBG Health Research has been contracted to carry out the study, which has provided additional data-linking through Conporto, which is an integrated primary health care record that provides patient summaries. Patient's will now be asked during the call if they consent to the surveyors accessing their data through Conporto, to facilitate and prompt their memory in the small details of their timeline and diagnosis.
- It is hoped that Conporto will ensure high data quality by reducing the level of health literacy required by the participant and result in a quicker and improved survey experience for participants.
- It was noted that some questions will utilise the patient's described experience only.
- It was highlighted that privacy is the top priority. Participants will need to consent for Conporto to be used and only relevant information will be used.
- It was noted that there are some limitations with Conporto, namely it may not be available for all participants as Conporto only covers about 70% and 80% of general practices and pharmacies nationally. Importantly, some geographical areas are not covered, such as central Christchurch and the Waikato. Traditional data linking will still be used to validate vaccination dates, COVID-19 test results, pharmacy and hospitalisation data, with consent.

The Ministry study team provided an update on the current New Zealand myocarditis and/or pericarditis CARM data.

- The age distribution of clinically confirmed myocarditis and pericarditis continues to see the same pattern, with the 20-29- and 30-39-year age groups seeing the highest case numbers.
- There have been a small number of reports following booster doses so far, but the booster campaign is still underway.
- There are no confirmed reports of myocarditis or pericarditis in children under 12.
- Distribution of time to onset data is unchanged, with most cases occurring within the first few days following vaccination.
- The Ministry did an analysis of the number of myocarditis cases being captured by passive reporting to CARM. This was done by comparing the number of cases of clinically confirmed myocarditis reported to CARM who were hospitalised with a discharge diagnosis code of myocarditis, to all cases in the National Minimum Data Set (NMDS) database with a discharge diagnosis code of myocarditis. The NMDS data was limited to people who had been vaccinated up to 6 months prior to the relevant hospitalisation.
- 47% of cases in the NMDS were reported to CARM. When limiting the data to hospitalisations occurring up to 30 days after vaccination which are more likely to be related to the vaccine, this percentage increased to 69%.
- It was acknowledged that while this reporting rate is high, it could be higher, and part of the comms approach is to encourage retrospective reporting.
- This analysis will be expanded to include pericarditis and all other non-clinically validated reports to CARM, as well as a more detailed analysis of the NMDS data.
- It was further noted that through Conporto, there is a possible opportunity to explore primary care data to understand rate of reporting of cases that did not go to hospital.

The Ministry study team provided an update of the international research, namely the CDC long-term follow up of myocarditis survey.

- Preliminary results from the CDC study were presented at an ACIP meeting in February.
    - This preliminary analysis focused on people 12-29 years of age with myocarditis meeting CDC case definition.
    - 56% of consumers completed the survey and 59% of healthcare professionals completed the survey.
    - The average time from diagnosis to interview was approximately 5 months for consumers and approximately 6 months for healthcare professionals.

- Key figures were discussed:
  - 83% had no previous medical history
  - 4% were readmitted to hospital since their diagnosis
  - 49% experienced at least one symptom two weeks prior to interview
  - 8% and 5% reported missing school or work respectively in the two weeks prior to interview, but not all absences were attributed to the myocarditis.
  - 45% reported problems with anxiousness and depression
  - In the healthcare professional survey it was found that 83% of participants had exercise restrictions at time of diagnosis and 39% had ongoing restrictions at follow-up.
  - 66% of healthcare professionals indicated their patient had 'fully recovered', and a further 15% indicated their patient had 'probably fully recovered' but are waiting further information.
- The CDC is planning to do the same follow-up in children aged 5-11 years of age.

- It was noted that the German medicines regulator is planning a 12-month prospective follow up study for all suspected cases of myocarditis in children and adolescents occurring after the COVID-19 vaccine.

The Committee engaged in a discussion about the study design and data analysis.

- A member of the committee commented that one of the challenges in data of this nature is interpreting a what a normal rate versus an increased rate is when there is no control group. It was discussed whether an appropriate control group existed for this study population, for example people with myocarditis or pericarditis for other reasons, or people with other conditions reported to CARM.
- The committee member also noted that people who have been diagnosed with a heart problem can become hyper-aware of the symptoms.
- The Ministry study team agreed there will be some limitations in the interpretation of the study data without a comparison. It was noted that for some of the questions on general health and mental health, it may be possible to make a comparison with data collected from the NZ Health Survey. In addition question wording has been carefully chosen to be as helpful as possible, for example establishing the burden of persistent symptoms rather than just the persistence or absence of.
- A member of the committee noted that any control group will focus the study in a specific direction, and therefore it may be more beneficial for the study to remain a descriptive one. In addition, he noted there would be significant challenges in surveying control groups.
- The Ministry noted that there would be regular engagement with CBG Health Research throughout the recruitment and data collection phase of the study, which will include feedback on how recruitment is progressing, and if there are any specific issues or challenges that need to be addressed.
- The committee were asked if they had any advice on timing for conducting provisional analysis of survey data.
- The committee agreed that an early review of study data was strongly recommended to ensure that the data quality was good (for example the first 10-20 surveys), and that the survey was performing as expected.
- A committee member noted that a big challenge will be engagement and a loss of engagement in any group could result in the results being skewed.
- The Ministry study team asked if there were particular outcomes that should be focused on for any provisional analysis.
- A committee member commented that there was not a particular outcome to focus on, and that data analysis will be descriptive. They noted that data quality was very important.
- **The Ministry agreed to provide a status update to the committee on recruitment and data collection, once enough information has been gathered, and noted that any specific issues noted will be flagged to the committee. [action]**
- It was noted by the Ministry that from a National Immunisation Programme (the Programme) perspective the earlier an update is provided the better as there is a Ministry interest in providing public confidence through this study if the results support this.

- A committee member commented that in terms of publishing results and instilling confidence, it may be helpful to perform some secondary analysis to highlight if there are any differences between cases where there was objective evidence of myocarditis or not.
- The Ministry study team noted that a classification system (such as the Brighton classification) will be used in the analysis if sufficient data is available.
- A committee member expressed interest in understanding if, based on NMDS data, it would be possible to discern the severity of reported cases or non-reported cases.
- The Ministry study team noted that it seems plausible that cases that are hospitalised may be the more severe cases, as opposed to cases that are diagnosed in primary care for example. Therefore, based on this assumption, an analysis into the hospitalised cases may give us some insight into reporting rates for more severe cases.
- It was agreed by the committee that due to current Omicron outbreak that COVID status will need to be captured by the study.
- The Ministry study team noted that the survey asks for consent in linking the Ministry's COVID-19 databases to fully understand if there is previous COVID-19 infection in participants, and that participants are also asked this question directly in the survey.
- A member of the committee asked a question around what is being done to actively recruit Maori and Pasifika participants. It was further noted that the reporting rate to CARM for Māori and Pasifika is of concern and how is this being addressed by the study.
- The Ministry study team agreed that the low reporting rate for any adverse event is an issue, particularly for Pasifika peoples. At the moment there are a small number of Māori and Pasifika people who have been identified as eligible for the study from a CARM report; therefore there are any difficulties in recruiting these individuals, the recruitment strategy will need to be reviewed. It was noted that part of the comms plan is to encourage retrospective reporting to capture any cases that have not yet been reported.
- It was agreed that recruitment/response rates of Māori and Pasifika individuals will need to be monitored.
- A member of the committee highlighted that given the low numbers of Māori and Pasifika participants, the first engagement attempt may be the best chance to engage the person, so it is key to utilise the resources correctly from the start.
- The committee agreed strongly to this point.
- The Ministry study team noted that CBG has indicated that ethnicity matching of interviewers can be done, and that they have the capacity to do face-to-face recruitment and interviewing (COVID-19 permitting). It was also noted that CBG has Māori and Pasifika advisors that can provide support if needed, in addition to the Ministry's Māori Health team.
- A member of the committee noted that given that we cannot oversample Māori and Pasifika due to the nature of the study, it is key that recruitment is closely monitored.
- **The Ministry agreed to feedback the committee's recommendations on ethnicity matching to CBG. [action]**
- A member of the committee asked if there is a protocol if concerning issues arise as a result of the interview.
- The Ministry study team answered that CBG have a protocol in place. The interviewers are nurses and are able to contact a CBG provided general practitioner for advice. The team conducting the interviews have had experience conducting interviewers in the COVID-19 case management space.
- A member of the committee asked to see the latest surveys.
- **The Ministry agreed to share the latest versions of the survey via the Teams channel, noting that the consumer survey was now finalised, and that minor edits could still be made to the health care professional survey. [action]**
  A member of the committee asked if there was data regarding incidence of myocarditis by age and ethnicity prior to the vaccine roll-out.
- The Ministry study team replied that they believe that the age distribution follows a similar pattern, but will share that data with the committee.
- Another member of the committee agreed that myocarditis does tend to affect younger males more regardless of vaccination, so the predisposition is clear.
- **The Ministry agreed to share data regarding myocarditis/pericarditis incidence by age and ethnicity prior to the vaccine roll-out with the committee. [action]**

The Chair thanked everyone for attending the second Research Oversight Committee meeting for the myocarditis and pericarditis follow-up study.

The meeting was closed with the Ministry's Karakia.

Minutes

MyoPeri-ROC

Date:	25 May 2022
Time:	10:00-11:30 am
Location:	Ministry of Health & Microsoft Teams
Chair:	Mr Chris James
Attendees:	Saskia Schuitemaker, Professor Michael Tatley, Professor Chris Frampton, Dr Tim Hanlon, Peter Himona
Ministry of Health Attendees:	s 9(2)(g)(ii)
Guests:	s 9(2)(g)(ii)
Apologies:	Professor Ralph Stewart

Agenda item
Welcome & Karakia *The Chair welcomed attendees to the third MyoPeri-ROC.* *The meeting was opened with a karakia.*

The Ministry study team provided a status update on the current stage of the research study.
- The first consumer was enrolled 28 March 2022.
- The first health care professional (HCP) surveys were sent out the week of the 11th of April.
- Consumer surveys are due to be completed at the end of May which is on track.
- Response rates from consumers have been good; in the last week they dropped just below 70%.
- CBG Health Research (CBG) has stated that for some people this is an invalid contact detail issue and that other consumers are not picking up the phone.
- A process has been started whereby after 5 unanswered calls, if it is a valid number, CBG will text message the consumer ahead of the next call attempt to inform them of who will be calling and why, as some people may be hesitant to pick up a call where they don't recognise the caller.
- A number of consumers have been marked as ineligible after contact from CBG.
  o This includes some people who had a prior history of myocarditis/pericarditis (prior to vaccination) and had a flare up following vaccination. These people should have been included and will be re-contacted by CBG.
  o A small proportion of people appear to have had a diagnosis from their health care provider based on a report submitted to CARM, but when contacted said they did not have a diagnosis. This is potentially a health literacy issue. The plan for these

consumers is to go back to the reporter, usually a health care provider, and get more details, and then potentially contact the consumer again.
    - Question 3 of the consumer survey (which asks if the consumer had been told that they had myocarditis, pericarditis or myopericarditis) may need to be rephrased.
- The HCP survey does not have as high a completion rate as the consumer survey. This will be discussed during the presentation of a separate memo.

The Ministry study team presented a memo about expanding the key study parameters to include third and subsequent doses (referred to using the general term 'booster').

- The current study population is adults and children aged 12 and older:
    - with a clinical diagnosis of myocarditis and/or pericarditis after dose 1 or 2; and
    - The diagnosis made on or before 31 December 2022; and
    - At least 3 months post diagnosis at the time of the survey.
- Boosters are not currently included in the study design.
- The approved interval for the Comirnaty (Pfizer) booster is 6 months or more after the primary course.
- Boosters were initially excluded as the study was due to begin at the start of 2022 and very few people would have been eligible.
- On 04 Feb 2022 the booster gap interval was shortened to three months.
- 2,040,241 people received a booster between 1 Jan 2022 and 28 Feb 2022, compared to just 332,959 in 2021.
- Including boosters and moving the time of diagnosis cut-off to the end of February (28 February 2022) would increase the study population by approximately 100 people based on records held in COVID-CARM.
- The Ministry study team believes that extending the study population would:
    - Enhance the utility of the study, by increasing the study population and making study results more generalisable.
    - Help reduce equity issues by including people who might be more likely to be vaccinated later or people who experienced a delay in diagnosis.
    - Require minimal updates to the current processes and documentation.
    - Increase the length of time required for data capture by around 4 weeks.
    - Possibly need an amendment for ethics.
- The Ministry recommended that:
    - The study population be extended to include people with a diagnosis of myocarditis and/or pericarditis after any dose.
    - The time of diagnosis cut-off be extended to 28 February 2022.

The Committee engaged in a discussion about the recommendations.

- A member of the committee asked why the end of February chosen for the extension to the diagnosis date cut-off.
- The Ministry responded that the end of May, when the meeting was taking place, was three months after the end of February, meaning any person diagnosed on or before 28 February would be eligible for recruitment immediately.
- The member asked what level of vaccine coverage there was in February.
- The Ministry responded that the majority of boosters were given by the end of February 2022 but did not have the exact numbers to hand.
- The member commented that the consumer response rates for the survey were impressive, and that in previous surveys they had been involved in 70% response rates had been celebrated.
- Another member of the committee endorsed previous comments that the consumer and general practitioner participation rates are good.
- A member of the committee asked about participation in children, given the requirement for child surveys to require both parent and child consent.
- The Ministry responded that the overall numbers of eligible children was very low (about 12 children under 16). Two surveys were not completed because the children did not consent. It was noted that for ethical reasons, due to the nature of the survey, children had to be given the opportunity to decline to have their personal information shared, independent of their parent's decision.

- A member of the committee referred to question 3 of the consumer survey, which asks about diagnosis, and stated that, from looking at consumer adverse event reports, some people are quite confused about which diagnosis they have. They suggested that potentially that question could be tweaked.
- The Ministry responded that they are looking at altering the way the question is phrased, but they are very keen not to exclude anyone unnecessarily, e.g. due to lack of understanding of the diagnosis. Anyone where it becomes clear they do not have the diagnosis can be excluded from the final analysis.
- A guest general practitioner (GP) commented that from their professional experience diagnoses are often not communicated well to patients.
- The Chair took a vote:
    - There was unanimous agreement to extend study population to include boosters.
    - There was unanimous agreement to extend the study dates for diagnoses up to and including 28 February 2022.

The Ministry study team presented a memo on HCP engagement with the survey. The committee was invited to comment through the presentation.

- The response rate was 32% for HCP (compared to 67% for consumers).
- The Ministry asked the committee what the minimum response rate needed for the data to be useful is and what response rate should be aimed for.
- A committee member commented that the current response was good considering current circumstances where HCPs are experiencing very high workloads.
- Another member of the committee stated that the consumer response rate is very acceptable and for the HCP, 32% is pretty good. The member commented that some published papers have very low response rates, as low as 5%. The member gave their opinion that everything should be done to get the response rate as high as possible but at a certain point you just have to use the data you get.
- A member of the committee noted that although it may initially appear to be a low response rate, you are looking for the information you can get out of it and that quality is important.
- A member of the committee asked if the number would provide adequate power for the study.
- Another member responded that power is not really the issue in this type of study, and that there are only so many people who are eligible to be in the study. The HCP survey already has approximately 50 responses, though it is likely that this a biased set of HCPs. This a point for discussion in the study. The responses you get are what you have to work with, taking into account the limitations.
- The Ministry explained the survey process. The consumer survey is done over the phone as an interview. The HCP survey is completed online. Initially CBG was phoning the practice in order to invite the HCP to participate, but this had a very low uptake as they could not get through to GPs. The process now is to send an email and invitation letter, with a link to the survey in the email body. After at least 3 days a second email is sent, and then after 3 further days a telephone call is made to the practice (practice manager, if possible) as a further reminder. After another week, if there is no acknowledgement, these HCPs are referred back to the Ministry; the follow-up process from this point is still to be finalised pending advice from the committee.
- The Ministry highlighted that the initial two email contacts come from a CBG email address, and it is possible that an email from a Ministry of Health email address may be more attention grabbing and could increase the likelihood of the email being read.
- The Ministry presented the findings of the literature review regarding methods of increasing survey engagement in HCPs. The methods presented were in two segments, survey delivery and incentives.
- The Ministry stated that email reminders were shown to improve response rates, had a low cost to implement, and could use official branding. The drawbacks were that email reminders were already implemented through CBG so further reminders may have diminishing returns. In addition, too many reminders risked irritating HCPs.
- The Ministry stated that postal surveys were a popular method of survey delivery. In a 2011 study of Australian GPs, 81.1% of GPs said they preferred postal surveys. Postal surveys have higher completion rates compared to telephone or email surveys and increase completion when included in mixed delivery models. Paper survey can include official

branding. Drawbacks include additional time required for completion and return, that responses must be inputted into the system, and that additional costs are incurred.

- The Ministry invited the committee to comment.
- The guest GP gave their opinion that engaging practice managers is a good way to get buy-in. They noted that there is a deluge of digital administrative tasks that GPs are expected to do, and this is why analogue tasks can get special attention. They noted that the study team could also ask practice managers to print out the task and deliver it to the GP's desk. In their opinion, this would make a big difference to commitment to filling in a survey. They noted that it is a little sad that HCPs aren't engaging in these important surveys but that it also speaks to the number of demands on GP's time.
- The guest GP asked who has to fill in the survey and whether nurses or other employees could make a start and hand over the survey to the GP for review. They noted that other employees may have more flexibility to complete the survey.
- The chair thanked the guest GP.
- The Ministry thanked the GP for their 'lived experience view,' and noted that it is very easy to come up with a theoretical view but valuable to hear a GP's point of view.
- It was asked whether it is made clear to the practice that this is in relation to a patient on their books, not a general enquiry about adverse reactions. This might be material in getting HCPs to prioritise the survey.
- The Ministry stated that there have been recent adjustments to communications to emphasise this.
- A member of the committee stated that GPs are receiving several surveys a week, each claiming to be only a few minutes of their time, and this contributes to a lack of engagement. The member stated that it is important to raise awareness that this is a targeted study. The member suggested raising awareness through the Royal College of GPs and also try GP Facebook groups.
- A member of the committee suggested an article in NZ Doctor.
- A member of the committee suggested that it could increase perceived credibility if the survey comes from the Ministry and/or CARM, as well as emphasising that is relates to a specific patient. They agreed a paper-based method could be useful.
- A member of the committee seconded the earlier comment for an article in NZ Doctor and also suggested using ePulse, a newsletter sent to GPs.
- The Ministry commented that they were currently trying to get an article in a GP newsletter.
- The guest GP reiterated their point about nurses doing the survey.
- The Ministry stated that they were open to nurses doing the survey but that perhaps this had not been well communicated to HCPs and was not as easy to do with the online survey method. The Ministry suggested a postal survey could also help as the nurse could physically hand it over to the GP for review.
- The guest GP agreed and stated that nurses could do any of the administrative sections in particular.
- The Ministry agreed, noting especially as parts of the survey are likely to need information from health records, for example test results or medicines.
- The guest GP stated that getting HCP to start is half the battle, and that once they start the survey it is more likely to be finished.
- The Ministry then gave a presentation on offering incentives, specifically monetary incentives, gifts, and Continuing Professional Development (CPD) credits.
- The Ministry noted that offering any incentive would require an ethics amendment. Any incentives would need to be retrospectively applied to HCPs who have already completed the survey. The Ministry noted the need to factor in how quickly an incentive could be operationalised, given the expected end date for the study.
- The benefits of monetary incentives presented were that some studies found increased completion rates, they were faster to arrange than non-monetary gifts, they were relatively cheap at less than a quarter of the cost of a face-to-face interview, and that there is a possibility of using the framework already established that allows patients to see their GP for free regarding suspected adverse reactions. The drawbacks were that the literature review showed mixed results, prize draws were not as effective as guaranteed rewards, larger rewards were more effective, this would add an additional cost and additional time, and that ethics approval would be required.

- The benefits of non-monetary gifts presented were that some studies found increased completion rates and that gifts were more effective than lottery incentives. The drawbacks presented were that many studies found that although the groups sent gifts had higher response rates, these were not actually statistically significant; it would take time and money to find and post the gifts; there is a small risk that any gift sent is inadvertently offensive or otherwise unwanted and therefore a waste; and ethics approval would be required.
- The benefits of CPD credits were that GPs are required to completed 150 CPD credits every three years, therefore this may be an attractive incentive for completing the survey, and that this incentive would have a low financial cost. The drawbacks were that there was a lack of literature on effectiveness, this would take additional time to operationalise, it would be up to the GP College to determine if it was an appropriate CPD activity, and would require ethics approval.
- The Chair asked the committee if paying GPs would increase survey completion.
- The guest GP stated that from their personal experience, ease of access is more important. If you are not the practice owner, the financial incentive may not make a difference.
- The Chair noted that CPD requirements have been reduced this year, and therefore offering CPD credits as an incentive may not be a big drawcard.
- The guest GP noted that the entering an activity in the CPD credit system can be a time-consuming administrative task in itself, which may put GPs off.
- A member commented that they do not like the idea of gifts and thought it better to make the survey part of the workflow. From discussion, they felt it may be better to pay a consultation charge for completion of the survey and add it to the workflow. However, this would be difficult to implement retrospectively.
- The guest GP noted they were very keen on the idea of the survey being able to take up a 15-minute consultation slot. They gave their opinion that a dedicated piece of time appeals over a financial incentive.
- A member of the committee said that, from their understanding of the presentation, sending written questionnaires leads to a better response; providing financial incentives does not necessarily make much difference. Therefore they would be happy to not offer incentives but to send out a postal survey, noting some of it could be completed by the nurses.
- Another member said that they appreciated previous comments on time. They recommended emphasising that the scientific attraction of this study is that it covers a time period where COVID was not spreading widely, with an uncontaminated study population.
- The Ministry acknowledged the committee's valuable insights.

The Ministry study team provided the exploratory data analysis (EDA) of the consumer survey.

- 28 consumers declined to participate, 3 in advance and 25 when telephoned.
- Reasons provided included: no interest in the survey; unhappiness with the way they were treated by the Ministry or health system; too busy; privacy or personal safety concerns; or no concern expressed/no reason given.
- A small number of consumers were deemed ineligible to participate after contact. The reasons for this were if the consumer stated that they were not diagnosed with myocarditis/pericarditis; myocarditis/pericarditis occurred before the vaccine; or myocarditis/pericarditis occurred after the booster dose.
- The Ministry is currently investigating the list of consumers who could not be contacted after ten attempts.
- The diagnosis was most commonly pericarditis and the 35–44-year-old age category was the largest age group affected.
- A member of the committee noted that it would be helpful to see a figure showing the number with myocarditis/pericarditis cases compared with the number of people who received the vaccine.
- The Ministry acknowledged this.
- The age trend of participants was similar to that seen for all reported myocarditis/pericarditis cases. Ethnicity was mostly New Zealand European with small numbers of Māori, Samoan, and other ethnicities. There were more males than females. Most consumers reported that the vaccine was the cause of their myocarditis/pericarditis. Slightly more events occurred after the second dose than the first dose.

- The guest GP asked if anyone got myocarditis/pericarditis after the first dose and went on to develop myocarditis/pericarditis after a subsequent dose.
- The Ministry responded that 63 consumers went on to get a further COVID vaccine (including some people receiving a further Pfizer vaccine) after their diagnosis. The survey did not include a specific question about what happened after that dose. Possibly a short follow up survey could be offered to these consumers if we require information over and above what will be gathered in this survey.
- Medsafe commented that we do know they have not submitted another CARM report.
- The Ministry stated that most people who did not go on to have further vaccines did so on the advice of an HCP.
- Of the symptoms, chest pain was the most common symptom, but the other symptoms asked about (except fainting) were also very commonly reported. Most people reported more than one symptom. For each symptom, each person was asked how long they had that symptom. Approximately 50% of the study population reported ongoing symptoms at the time of the interview.
- A member of the committee asked how long the symptoms had been ongoing for.
- The Ministry replied at least three months. The minimum time from diagnosis to participate in the survey is three months but for many consumers it is more than that. Analysis of this time since myocarditis/pericarditis onset to survey completion has not yet been performed.
- When it came to current health, most consumers said their current health was good (the middle option). When asked to compare, most consumers said their current health was a little worse or a lot worse compared to prior to their diagnosis. When asked if that change was due to the myocarditis/pericarditis, most consumers said yes.
- A member of the committee asked if there was analysis with myocarditis cases compared to pericarditis cases.
- The Ministry said this analysis had not yet been done but was planned for the final analysis. The current analysis is both diagnoses grouped together.
- About half of consumers indicated some form of anxiety or depression symptoms. For physical functioning, most said they were still unable to do the same level of physical functioning. The reason given for this was most commonly due to still experiencing symptoms, and a number of people were also told to limit activities by a HCP, and some still felt worried about increasing their activity.
- When it came to school/university attendance, the most common response was no change but some had to reduce their attendance or were less productive. For paid work, the most common response was no change, the second most common was reduced hours and/or less productivity. For unpaid work, most had to reduce the numbers of unpaid working house and/or were less productive.
- The Ministry noted that some survey questions had not been analysed yet and asked the committee for feedback on the analysis.
- A member of the committee stated that the EDA looked good so far. They stated that they had some ideas for ethnicity analysis that they would email later.
- The Ministry presented the plans for sub-group analysis. Diagnostic criteria, age, gender, and time to onset were pre-specified in the study plan. Other possible subgroups that were not pre-specified were illness severity, dose interval, past medical history, people who had another Comirnaty dose after myocarditis/pericarditis. The Ministry asked for comments from the committee.
- A member of the committee commented that in terms of individual question summaries, it was their opinion that the study team had to do them for every question for the whole group. They commented that if you keep splitting subgroups, due to the low sample size, there may be issues. If you keep splitting, for example by diagnosis, age, and sex, it will get too small.
- A member of the committee commented that subgroup analysis is important up to a point, for example by splitting myocarditis and pericarditis. Source data shows that some cases classed as myocarditis or pericarditis do not fit the criteria exactly so analysis of severity or diagnostic certainty (e.g. Brighton criteria) should be useful. They acknowledged that continuing to split would lead to issues.
- The Ministry asked the committee about the most valuable way to analyse HCP and consumer survey data: linked, independent, or mixed? Are there any analyses that would

involve linking that would be particularly helpful? They noted that they are aware that as the HCP survey uptake is relatively low it may limit usefulness.

- A member suggested investigating if the linked consumer surveys were representative of the whole group. If they were, it would give some guidance about the representativeness of HCP survey responses. Their opinion was that the study team should do both linked and independent analysis.
- Another member commented that some ideas will evolve as the data is analysed.
- A member seconded this point and stated the study team should not be too rigid about analysis plans.
- The guest GP stated that they thought this was a fascinating piece of work. They noted that many participants had reported symptoms many months after vaccination. They also noted the numbers who had their work impacted months after vaccination. They stated it would be good to understand if these are consumers who had co-morbidities to start with and this tipped them over the edge. They commented that in the future it would be good to be able to see risk factors.
- The guest GP commented that it would be good to find ways to link to what the CDC is doing with their myocarditis/pericarditis study, and that this would be a good way to provide international comparison.
- The guest GP stated that getting this diagnosis can be a significant event for a consumer. They commented that it raises the question of what we can do to help these people.
- The Ministry stated that they want the study to be meaningful and incite change if it finds change is needed.
- The guest GP noted that a lot of people get disenfranchised from healthcare, and that this impacts on their future health.
- Another committee member stated that myocarditis/pericarditis is an ACC claimable event. ACC looks at a point in time, if a consumer has a prolonged experience, this study may help provide evidence for ACC.
- A member asked what support is available for participants. They noted that there are ethical obligations, for example if someone identifies that they have worries, what support is being provided to them?
- The Ministry replied that interviewers are directing people to helpful resources, and the feedback from CBG has been that consumers are finding this helpful.

The Chair noted that due to time, any other business would be covered via email.

- The reporting rates analysis update will be emailed to the committee.

The Chair thanked everyone for attending the third Research Oversight Committee meeting for the myocarditis and pericarditis follow-up study.

The meeting was closed with a Karakia at 11:34 am.

Te Whatu Ora
Health New Zealand

Minutes

Myo-peri Research Oversight Committee

Date:	28 November 2022		
Start Time:	2:00 pm	**Finish Time:**	3:00 pm
Location:	133 Molesworth Street, Wellington & Microsoft Teams		

Members: Chris James (Chair), Professor Chris Frampton, Professor Michael Tatley, Dr Tim Hanlon, Peter Himona, Professor Ralph Stewart

Medsafe and Te Whatu Ora attendees: s 9(2)(g)(ii)

Apologies: Saskia Schuitemaker

1. Welcome

- Meeting was opened at 2:02 pm by the Chair
- A karakia was performed

2. Update on current literature

The study team provided an update on similar international studies

- Two studies on vaccine-induced myocarditis highlighted to the Committee
- CDC published results of a study in the Lancet in September 2022. The study population was US consumers aged 12-29 years old who experienced myocarditis after mRNA COVID-19 vaccination.
- Study participants had a median age of 17 years and 88% were male. All cases included met the CDC definition of myocarditis.
- After at least 90 days since onset of myocarditis, 81% of people were considered recovered by their health care provider (HCP).
- AusVaxSafety currently recruiting for a long term follow study on mRNA vaccine induced myocarditis. Propose to follow up participants up to 18 months post diagnosis.

Discussion

- The Chair asked if there were any timeframes for the AusVaxSafety study.
- Answered that this is in the early stage of recruitment, and it is unclear how data will be released.
- The Committee noted from the Lancet paper that 33% of study participants were unable to be followed up.

3. Overview of data analysis

The study team provided an overview of the approach taken in the analysis conducted to date

- Data predominantly comes from surveys (quantitative outcomes).
- Child and adult data have been combined, due to only 10 child surveys being completed.
- Analysis of each study question by gender, ethnicity, diagnosis, and Brighton classification (BC).
- Chi-Square tests routinely performed to determine if there was a statistically significant difference based on gender, ethnicity, diagnosis, or BC.
- Fisher's exact test was performed when there were too few values to perform the Chi-Square test.
- P-value ≤ 0.05 considered statistically significant.

- BC assessment provides indication of level of certainty of diagnosis, is not a reflection of severity (Level 1 = definite, Level 2 = probable, Level 3 = possible, Level 4 = reported event without evidence to support higher level, Level 5 = not a case/clear alternate explanation).
- All cases assigned a BC level based on information provided in CARM report, no Level 5 cases were invited to participate in study.
- Any cases initially assessed as Level 4 have been reassessed using survey response data.

Discussion

- The Committee asked about the decision to report BC 1-3 together, gradation by some levels of certainty. Noted that they felt comfortable combining Levels 1 and 2, however Level 3 are more likely to be an intermediate probability of diagnosis.
- Answered that presenting separately, may make numbers too small for analysis.
- The Committee commented that the evidence is based on the availability of the information, rather than the diagnosis.
- The Committee further noted that objective levels of disease may be likely to have ongoing symptoms etc.

4. Presentation and discussion of results and analysis

The study team provided an overview of the preliminary study results

- Total of 929 reports to CARM for myocarditis and pericarditis up to 31 July 2022; 495 people were considered potentially eligible for the study.
- 312 people completed the consumer survey during the study period.
- 299 people consented to their HCP being contacted; 163 completed the survey.
- 1 consumer excluded from analysis due to systematic don't know answers.
- 2 further consumers excluded due to unclear diagnosis, but this decision is not final.

Overview of participants (n=309)

- 62% male, 90% non-Māori, 65% pericarditis, even spread between BC.
- Average of 191 days between completion of survey and reported diagnosis date for participants.
- Average of 29 days between vaccination and reported diagnosis. Noted that the survey asked about diagnosis date rather than onset of symptoms.

Discussion

Analysis - Diagnosis

- All myopericarditis analysed as myocarditis (for BC analysis myocarditis level used).
- A small number of HCPs answered, 'none of these', n=7 and 'don't know', n=8 for diagnosis, and these answers terminated the survey. Question for the committee if these people should be excluded from the consumer survey analysis?
- The committee answered that these people should remain within the study population. Comment that there is a heap of people in consumer survey, however, don't have the same level of data for the HCP survey.
- Question for the committee, where response for diagnosis differ between the consumer and HCP survey (or assigned BC when no HCP survey), is there one which should override?
- The committee answered where there is a discrepancy the CARM report should override as this is how people have entered the study. Comment that it would be interesting to see a comparison of these people where there is a discrepancy to see what people thought they had.
- Question for the committee, pericarditis was reported by HCP (survey and discharge), troponin quite elevated, 100. Would this be consistent with myocarditis, or do we stick with diagnosis?
- The committee answered that a troponin of 100 would be consistent with myocardial injury. Noted that there is a need to be consistent with the sources of data used. Recommendation to stick with the diagnosis, however if there is clear objective evidence to suggest otherwise it seems reasonable to use this.

- The study team noted there were discrepancies for approximately 20 cases, additional information providing the objective evidence that would upgrade the case from pericarditis to myocarditis or change the BC level.
- The committee commented that for major analysis the diagnosis is important rather than the BC.
- Action for study team to connect with Professor Stewart directly where there is any uncertainty around how specific cases should be included in the analysis.

Analysis - Aetiology

- Question for the committee, if aetiology was said to be something other than the vaccine; do we include or exclude them?
- The committee answered that these people should be included, noting they experienced myocarditis or pericarditis after the vaccine, but it could be due to a different cause.

Results example

Example provided of current health overall to illustrate analysis conducted

- Question to the committee, if we should continue to report results overall in population or continue to present by diagnosis?
- The committee noted that Wilcoxon rank sum nonparametric test will improve power. Suggested that totals are included at the bottom or top of tables.
- Comment from the committee about data for comparison in current health (ie, control population), and whether the New Zealand Health Surveys population could be used. The committee further commented that there could be difficulty with data matching with age etc.
- Comment from that committee that current health is at 'x time' after the diagnosis, this needs to be made clear as part of the analysis.
- The study team suggested that a range and/or standard deviation could be provided for the time.
- Medsafe noted that participants weren't asked if anything else had happened to them since their diagnosis that could have impacted their health.
- The study team noted that for certain questions people were asked they thought change was due to the myocarditis/pericarditis or something else.
- The study team noted that a number of people had reported ongoing symptoms, with a high number also reporting anxiety/depression related symptoms.
- The committee commented that cardiologists are missing subjective symptoms if this is correct. Noted that people with pericarditis generally return to normal within 2-3 weeks. Similar with myocarditis, mild-moderate symptoms, most people recover well. Difference between objective and subjective symptoms.
- The committee commented about reflecting differences in the consumer's response and objective data provided.
- The committee further commented that the focus is often on the objective evidence of disease. Noted that most specialist's once objective markers clear up, they move on from this and where doses this leave the person.
- Comment from the committee that the objective verse subjective differences could perhaps be explored as part of further follow up work.
- The committee commented that using the number of weeks persisting was too granular for symptoms, this would be better presented as resolved/not resolved.
- The study team noted that there hasn't been any analysis conducted based on age. Is this needed and if so, how should these be grouped?
- The committee recommended that the study team use the source data to work out actual ages of participants as this will provide a lot more power and ability to conduct analysis.

5. Publication and dissemination of findings

- The goal is to have the study written up into publication, need to consider:
  - key results to include
  - presentation of data (tables verse figures)
  - potential points of difference verse CDC work
- In addition, results will be disseminated through various channels

- internal report
- lay summary to send to participants
- overview of results published on Te Whatu Ora/Medsafe websites

Discussion

- The committee commented that this is descriptive data with internal groups. Perhaps consideration could be given to having three groups (definite, possible and no supporting information). There is a disconnect between the objective and subjective reporting of disease.
- The committee further noted that there is a high burden of ongoing symptoms, and it would be of interest to know if there is a difference between those that you have objective supporting evidence for and those without.
- Comment from the committee that a breakdown of BC could be provided initially and then grouped together moving forward.
- The committee suggested that Level 3 BC could be considered separately. Including these with Level 1-2 cases would likely muddy the waters. Noted that classification is the key to get right, and this will drive everything else.
- The study team commented that analysis of each variable has been done independently (e.g. BC or ethnicity separately, not ethnicity and BC together). Question to the committee, whether this should this be further broken down?
- The committee commented that a multivariate analysis could be conducted.
- Comment from the committee that there needs to be an analysis of the CDC work to understand what the point of difference is.

Meeting Closed: 3:03 pm with a karakia