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20 June 2023

s 9(2)(a) [redacted]

[redacted] [redacted]
Ref: H2023025722

Tēnā koe s [redacted]

Response to your request for official information

Thank you for your request under the Official Information Act 1982 (the Act) to Manatū Hauora (the Ministry of Health) on 22 May 2023. Please find a response to each part of your request below:

> *1.a. Please provide confirmation that all persons reporting an Adverse Event Following Immunisation to CARM following COVID-19 immunisation have had an alert linked to their National Health Index numbers (NHI) as per Ministry of Health Medical Warning System (MWS).*
>
> *b. If alerts have not been placed against NHI numbers for persons reporting AEFI's to CARM, please provide reason why this was not done.*
>
> *Medical Warning System*
>
> *The Medical Warning System (MWS) is an alert service linked to National Health Index numbers. It warns health care providers of known risk factors that could be important when making clinical decisions about patient care. This includes drug allergies or medical conditions.*

Not all Adverse Events Following Immunisation (AEFIs) following the COVID-19 vaccine are entered into the Medical Warning System (MWS). Please note, AEFIs are only a *suspected* reaction to the COVID-19 vaccine based on a temporal correlation. They may also include minor medical events following a vaccination.

If these were included by default in the MWS, it would decrease the system's value. The MWS includes information on serious and/or life-threatening adverse reactions to medicines, such as anaphylaxis. It is not intended for minor and/or unproven AEFIs to be monitored. More information on MWS can be found at:
www.medsafe.govt.nz/profs/PUArticles/June2020/Medical-Warning-System.html.

2. Please provide a list of the main health issues/complaints identified through Ministry of Health data collection, causing a hospital admission annually for the past 10 years up to and including the end of year 2022 and number of admissions for each health condition/complaint respectively for each year.

This part of your requested was transferred under section 14(b)(ii) of the Act to Te Whatu Ora 14 June 2023. You can expect a response to this part of your request from Te Whatu Ora in due course.

3. With reference to letter and supporting documentation from Barrister Lisa Hansen dated 20th January 2022, sent on behalf of New Zealand Doctors Speaking out with Science (NZDSOS), and addressed to Minister of Health Andrew Little, Minister of COVID-19 Response Chris Hipkins, Medsafe Chris James, Chief Legal Adviser Minister of Health Phil Knipe (refer to link)

https://nzdsos.com/letter-to-authorities-about-discovery-of-nano-scale-technology-in-the-new-zealand-injections/

a. Please confirm as per Medsafes mission statement "to maximise safety" and in accordance with Medsafes Post marketing surveillance policy which includes "monitoring international literature and other information sources", that the information provided by Barrister Lisa Hansen on behalf of NZDSOS was considered and discussed between the addressee's Minister of Health Andrew Little, Minister of COVID-19 Response Chris Hipkins, Medsafe Chris James, Chief Legal Adviser Minister of Health Phil Knipe, and/or also the Director General of Health and the Prime Minister, MARC, CARM, CV-ISMB, CV-TAG.

b. Please confirm if the information provided by Barrister Lisa Hansen on behalf of NZDSOS outlining concerns around unlisted and potentially harmful contents discovered within Comirnaty vaccine samples analysed in New Zealand and being findings consistent with overseas analysis, was considered a safety signal worthy of further investigation by the Ministry of Health or any of the recipients of the letter.

c. Please provide copies of communications and or advice, decisions or action points discussed between any of the named parties relating specifically to the independent analysis of Comirnaty vaccine by New Zealand scientists, their findings and concerns as highlighted in the letter mentioned.

Where deemed necessary, information received is noted or passed onto relevant teams within Manatū Hauora and Medsafe for their action or consideration.

No communications were generated based on this letter. Therefore, this part of your request is refused under section 18(g)(i) of the Act, as the information requested is not held by Manatū Hauora and there are no grounds for believing it is held by another agency subject to the Act.

4.a. With reference to CV-TAG minutes from meeting Tuesday 29th June 2021 section 2.0, Please provide a copy of the results and conclusions from University of Auckland project estimating background rates of adverse events in New Zealand.

This is published https://gvdn.shinyapps.io/gvdn/

b. Please provide copies of any analysis or reference made by CV-TAG in relation to results of the University of Auckland project mentioned.

Manatū Hauora has identified two documents within the scope of this part of your request. Both documents are itemised in Appendix 1 and copies of the documents are enclosed. Where information is withheld, this is outlined in the Appendix and noted in the document itself. Where information is withheld under section 9 of the Act, I have considered the countervailing public interest in releasing information and consider that it does not outweigh the need to withhold at this time which are released to you in full.

Please note, the PowerPoint provided is in draft form only. Please bear in mind that there may be differences between the draft and final version.

I trust this information fulfils your request. If you wish to discuss any aspect of your request with us, including this decision, please feel free to contact the OIA Services Team on: oiagr@health.govt.nz.

Under section 28(3) of the Act, you have the right to ask the Ombudsman to review any decisions made under this request. The Ombudsman may be contacted by email at: info@ombudsman.parliament.nz or by calling 0800 802 602.

Please note that this response, with your personal details removed, may be published on the Manatū Hauora website at: www.health.govt.nz/about-ministry/information-releases/responses-official-information-act-requests.

Nāku noa, nā

Louise Karageorge
Group Manager, Intelligence, Surveillance and Knowledge
Public Health Agency | Te Pou Hauora Tūmatanui

Appendix 1: List of documents for release

#	Date	Document details	Decision on release
1	6 July 2021	Request for Advice (RfA) – Myocarditis Update for CV TAG	Some information withheld under section 9(2)(g)(ii) of the Act, to protect Ministers, members of organisations, officers, and employees from improper pressure or harassment.
2	20 July 2021	Draft PowerPoint - Background rates of myocarditis and rates post-vaccination	Released in full.

Document 1

SCIENCE & TECHNICAL ADVISORY | RŌPŪ TOHUTOHU I TE PŪTAIAO ME TE HANGARAU

Request for Advice (RfA)

MINISTRY OF HEALTH
MANATŪ HAUORA

- This form contains the details relevant to the questions posed to the Science and Technical Advisory (STA). STA will respond to the request using this form which will also be stored in STA content management system for future reference.
- This form, or parts of it, may also be forwarded to other relevant parties as appropriate.

Title	Myocarditis Update for CV TAG		
Subject	An update on the adverse events of myocarditis and pericarditis in younger populations following administration of Pfizer or Moderna COVID-19 vaccine		
Reference No.	245	**Date Received**	29/06/2021
Requestor	Ministry of Health	**Date Due**	06/07/2021
Advisor	s 9(2)(g)(ii) [redacted]	**Date Completed**	06/07/2021 Last updated 26 July 2021
Peer reviewed by	CV TAG subgroup		
Advice issued to	COVID-19 Vaccine Technical Advisory Group (CV TAG)		
Approved by	Ian Town		
Deliverables	RfA, that will support recommendations from CV TAG		

Request Outline

Background/Context

- Cases of myocarditis and/or pericarditis have been reported following administration of the Pfizer and Moderna mRNA COVID-19 vaccines, internationally and following the Pfizer vaccine in New Zealand.
- On 25 June 2021, myocarditis and pericarditis were added as a warning by the FDA to the Pfizer and Moderna vaccine Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers).[1] Although evidence is still emerging on age-specific incidence, evidence from the US Vaccine Safety Datalink (VSD) active surveillance network supports a causal link to mRNA vaccines.
- This RfA will summarise international data on myocarditis and peridcarditis after vaccination with the Pfizer COVID-19 vaccine, and provide context for Aotearoa New Zealand including background rates, risk factors, and reported events to date.
- The RfA will assist the COVID-19 Vaccine Technical Advisory Group to provide recommendations with regard to providing balanced information on the benefit:risk characterisation for the Pfizer vaccine.

Questions

- What are the background rates for risk of myocarditis in Aotearoa New Zealand - general population, younger population, men/women, and ethnic specific rates?

- What is the risk of myocarditis after Pfizer or Moderna vaccination? What is the risk period for myocarditis after mRNA vaccines?
- What are risk factors for myocarditis after Pfizer/Moderna? E.g., age, sex, ethnicity, prior history of myocarditis.
- How many cases of myocarditis post-vaccination have been recorded in New Zealand and in what interval post vaccination?
- What is the risk of myocarditis after SARS-CoV-2 infection and COVID-19?
- How is myocarditis diagnosed? Is there data on how much mild myocarditis may be missed?
- What is the nature of vaccine readiness or vaccine hesitancy among at risk-populations e.g. young adults aged between 16 and 30? Does this vary by gender and ethnicity? What impact might a potential safety signal have upon vaccine readiness?
- How many young adults aged between groups 1 and 3 have been vaccinated already, and when are most people in this cohort expected to be vaccinated?
- What are possible alternative vaccine schedules for at-risk populations, and how effective are they?
- Are there any recommendations post-vaccination for preventing myocarditis?

Intended application of advice

To inform CV TAG discussion and advice on the risk of myocarditis in New Zealand.

Timeline

Proposed questions and scoping shared with subgroup on Wednesday 30 June

Draft summaries shared with subgroup on Friday 2 July for feedback and review

Revised document to be shared with wider CV TAG on Monday 5 July COB.

CV TAG to discuss and provide advice on Tuesday 6 July.

Document updated 26 July 2021 with new research and advice.

Response to Request for Advice

Executive summary

- Myocarditis is inflammation of the myocardium caused by infectious (viral and non-viral) and non-infectious immune triggers (including autoimmune diseases, hypersensitivity reactions to drugs, and toxic reactions). Pericarditis is the inflammation of the pericardium and has similar aetiologies. Myocarditis and pericarditis may occur separately or together.
- There is limited information on the background rates for myocarditis or pericarditis. In the general population, estimates range from approximately 1-10 cases per 100,000 person-years in the EU and US. Incomplete case ascertainment is likely from routine sources and estimates as high as 59.3 cases per 100,000 have been reported from some settings with more intensive case ascertainment.

- In children and adolescents (aged 0-19 years), the overall background rate is approximately 1-2 per 100,000 person-years, but increases substantially in the 12-19 year age group. For example, in a Finnish study of children ≤15 years, the overall rate of myocarditis was 1.95 per 100,000 person-years. However, the rate was highly age-dependent, particularly for boys (see Figure 1). For example, the rate for boys aged 11 and under, was approximately 0-2 per 100,000 person-years, but this increased to approximately 5 for boys aged 12-13 years, and almost 14 per 100,000 person-years for boys aged 14-15 years,
- Myocarditis has been reported after vaccination with both of the currently available mRNA vaccines, Pfizer and Moderna, but elevated rates beyond background have in younger age groups. The rate of myocarditis/pericarditis in 12-39 year-olds within 21 days following the second dose of mRNA COVID-19 vaccines in the US was reported to be 1.26 cases per 100,000 (95%CI, 0.75-1.99); for Pfizer, the corresponding rate was 0.8 per 100,000. These rates compare with background rates of 1-2 per 100,000 *per year* in children.
- Myocarditis after mRNA vaccines is more common in males <30 years old within a few days of the second dose.
- On 25 June 2021, the FDA added myocarditis and pericarditis to the 'Warnings' sections of the Pfizer and Moderna 'Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers)'.[1] However, to date, causality has not been definitively established between the Pfizer or Moderna vaccines and myocarditis.
- Early data on the short-term outcomes of myocarditis after vaccination with mRNA vaccines have been good. The majority of cases reported transient symptoms, with rapid resolution of laboratory abnormalities, and brief hospitalisations [2]. Of the 29 cases in the Vaccine Safety Datalink (VSD) reported in the US, 24 (83%) were hospitalised with a median stay of 1 day (range 0-13 days), including two who were admitted to the ICU. All cases were discharged, and nearly all cases had resolution of symptoms at follow up (number not reported). [3]. However, no long term data is available yet
- In Aotearoa New Zealand, through 01 July 2021, 10 reports of myocarditis or pericarditis events in individuals following vaccination with the Pfizer COVID-19 vaccine have been received and medically assessed. Of those reports, 4 were male, and the ages ranged from 24-63 years.
- It is important to consider for the benefit:risk equation, the incidence of myocarditis following SARS-CoV-2 infection. Acute COVID-19 infection is associated with a range of cardiac complications which include heart failure, myocardial injury and arrythmias. A preliminary analysis reported an incidence of myocarditis of 0 01% after infection. Another study in young college athletes, reported a rates of 0.3-2.3% depending on diagnostic criteria.
- In addition, the US CDC reported that another serious complication associated with COVID-19, multisystem inflammatory syndrome in children (MIS-C), occurs at a rate of approximately 2.1 per 100,000 person-years in children and young adults aged 0-21 years. Rates are somewhat age-dependent, with a rate of 2-3 in children aged ≤14 years, and 0-1.5 in individuals aged 15-20 years.[4] MIS-C occurs in approximately 0.03% of SARS-CoV-2 infections. Approximately, 3.2% have a baseline cardiovascular abnormality and 30.9% have at least one underlying condition (excluding obesity).[5]
- There are limited data on the severity of disease for myocarditis/pericarditis after vaccination. However, early data on acute outcomes have been good.
- With regard to vaccine hesistancy, younger individuals, e.g., under the age of 30, tend to be more vaccine hesitant than older age groups. Vaccine hesitancy appears not be differentially associated with ethnicity in Aotearoa New Zealand, after accounting for age and education. However, systemic barriers to vaccination for ethnic groups still exist. A detailed review of vaccine hesitancy in Aotearoa New Zealand is included as an appendix in this document.

- Latest estimates for the number of vaccinations administered, report that 84,025 individuals aged between 15-34 years have received two doses of Pfizer, of whom 31,365 were male. Four (4) reports of myocarditis/pericarditis have been received by CARM in 15-34 year-olds.
- Data on extended intervals between the first dose and second dose of the Pfizer COVID-19 vaccine is emerging. Researchers at the University of Oxford, University of Liverpool and others, reported that in a study of 503 healthcare workers, that neutralising antibody levels were higher following the second vaccine dose of the Pfizer vaccine after a dosing interval of 6-14 weeks (median 10 weeks) compared to the conventional 3-4 week regimen. The extension of the dosing interval was not associated with an increase or decrease the induction of T cell responses following the second dose. These data suggest that the dosing interval could be extended and still provide the same or even better immune protection.[6]

1. What are the background rates for risk of myocarditis in the general population, younger population, men/women?

General population

- There is limited information on background prevalence and incidence of myocarditis/pericarditis.
- In the US, a literature review of background incidence rates found an overall incidence of myocarditis, from all causes, of between 1-10 cases per 100,000 persons per year. For acute pericarditis, estimates range from 5.7-26 per 100,000 person-years, and for myopericarditis (cases of acute pericarditis that also demonstrate myocarditis) estimates range from 0.95-2.16 per 100,000 population.[7] The authors did not state the proportion hospitalized or identified in an outpatient setting.
- In the UK, the background incidence based on GP records (Clinical Practice Research Datalink, CPRD) was estimated to be approximately 9.4 (95%CI: 8.4-10.4) per 100,000 person-years in 2017, for all ages. In contrast, an estimate based on insurance claims in Germany that include GP, hospital discharge and specialist claims, was much higher: 59.3 (95%CI 52.7-66.6) per 100,000 person-years.
- Background rates for myocarditis in Aotearoa New Zealand are consistent with international data. The rate of myocarditis in the overall population from 2011-2019 was 1.81 per 100,000 person-years (see Table 1). For Māori the rate was 1.95 per 100,000 person-years, and for Pacific Peoples 1.79 per 100 000 person-years. With regards to age, the rates of myocarditis in children and young adults were: 0.20 per 100,000 person-years in 0-9 year-olds, 0.76 per 100,000 person-years in 10-19 year-olds, and 2.13 per 100,000 person-years in 20-29 year-olds. Note that these background rates are for events coded for myocarditis alone; background rates for myocarditis and/or pericarditis for Aotearoa New Zealand are not available.[8]

Table 1. Background rates for myocarditis in Aotearoa New Zealand and internationally

Country	Demographic	Rate per million person-years	Approximate risk over 1 year (to nearest 1000)	Source
New Zealand	Total population	18.1	1 in 55,000	Preliminary results from Dr Helen Petousis-Harris[8]
	Māori	19.5	1 in 51,000	
	Pacific Peoples	17.9	1 in 56,000	
	Males	24.3	1 in 41,000	
	Females	12.1	1 in 83,000	

	0-9 years	2.0	1 in 500,000	
	10-19 years	7.6	1 in 132,000	
	20-19 years	21.3	1 in 47,000	
US	Total population	10-100	1 in 10,000 to 1 in 100,000	Gubernot, D., et al, 2021[7]
UK	0-19 years	20.0	1 in 50,000	ACCESS (based on CPRD GP database)[9]
Italy	0-19 years	8.4	1 in 119,000	ACCESS (based on PediaNET, Italian GP database)[9]
Finland	0-15 years	19.5	1 in 513,000	Arola et al, 2017[10]
	Males, 0-11 years	Approximately 0-20	1 in 50,000 to NE*	
	Males, 12-15 years	Approximately 50-135	1 in 7,400 to 1 in 20,000	
	Females, 0-11 years	Approximately 0-10	1 in 100,000 to NE*	
	Females, 12-15 years	Approximately 10-35	1 in 29,000 to1 in 100,000	

*NE=Not estimable

Background rates in vaccinated individuals (non-COVID vaccines)

- A review from researchers at the FDA evaluating the incidence of myocarditis and pericarditis in persons of all ages after vaccination (type of vaccine not stipulated), reported a wide range of estimates of between 0.24-55 per 100,000 vaccinees.[7]
- Several studies of US military personnel have estimated the rates of myocarditis and related events after vaccination, in the context of the smallpox vaccine. Data on vaccinated military personnel (predominantly male, and younger age groups) estimated rates of myocarditis of between 7.8-16.1 events per 100,000, up to 30 days post-vaccination, compared to 2.1-2.2 per 100,000 for the unvaccinated military population.

Children and younger age groups

- Based on data from GP records in the UK, the rate of myocarditis in the 0-19 year-old age group is estimated to be 2.0 (95%CI 1.6-2.6) per 100,000 person-years. In contrast, the estimate from PediaNET, an Italian GP database, for patients aged 0-19 years was lower, at 0.84 (95%CI 0.27-2.6).
- However, average incidence for 0-19 year olds conceals important differences by age and gender between older and younger people across this wide age range. A Finnish study based on all hospital admissions for myocarditis in patients aged ≤15 years from 2004 to 2014 provides the only national population-based data. The study identified 213 pediatric myocarditis admissions over a 10 year period, for an estimated incidence rate of 1.95 per 100,000 person-years.

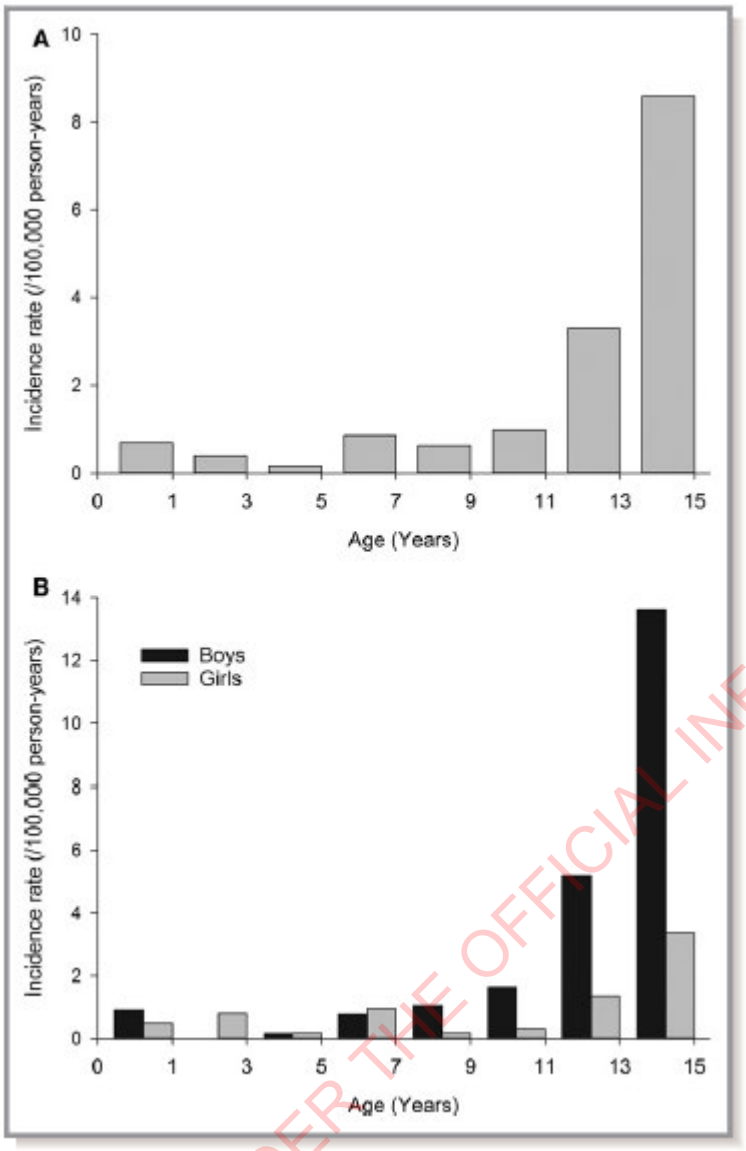

Figure 1 Age-specific Incidence rates of myocarditis in children aged 15 years or younger in Finland, overall and by sex (per 100,000 person-years) (Arola et al, 2017)

- The majority of cases were boys (77%), but no gender differential appeared until the age of 10, after which myocarditis admissions drove steadily increasing incidence reaching a peak in 15-year-old boys of 18.1/100 000 person-years (see Figure 1). Although viral infection was recorded as the cause of myocarditis in 11% of cases, it was rarely documented, with influenza infection (4 cases) the single most common virus identified.

2. What is the risk of myocarditis after administration of Pfizer or Moderna COVID-19 vaccine?

- From 23-25 June 2021, the US COVID-19 Vaccine Safety Technical workgroup (VaST), a working group of the US Advisory Committee on Immunisation Practicses (ACIP), met to discuss emerging evidence on the risk of myocarditis after mRNA vaccination. It concluded that a causal association between between myocarditis with mRNA vaccines is likely.[2]

- In response, the Food and Drug Administration (FDA) have added a statemtent in the 'Warnings' section of the patient and provider vaccine data sheets for Pfizer and Moderna COVID-19 vaccines, stating that "*The decision to administer the Pfizer-BioNTech COVID-19 Vaccine to an individual with a history of myocarditis or pericarditis should take into account the individual's clinical circumstances*".[1]
- Data from the passive adverse event reporting system in the US, Vaccine Adverse Event Reporting System (VAERS), to 11 June 2021 shows that, after approximately 300 million mRNA doses administered, there have been a total of 1,226 reports of myocarditis or pericarditis (see Table 2). Of these, 827 (67.5%) were reported to be after the second dose of either the Pfizer or Moderna vaccine.

Table 2: Reports in the passive reporting system VAERS of myocarditis or pericarditis after administration of the Pfizer or Moderna COVID-19 vaccines in the US up to 11 June 2021 (presented at ACIP 23-25 June 2021).Note: 'unknown' dose indicates that the whether the adverse event occurred after the first or second dose was not reported.

Manufacturer	Reports after dose 1	Reports after dose 2	Reports after unknown dose
Pfizer-BioNTech (n=791)	150	563	78
Moderna (n=435)	117	264	54
Total (N=1,226)	**267**	**827**	**132**

- Symptom onset clusters within the week following vaccination, with most cases occurring within 5 days of the second vaccine dose. Observed cases are higher than expected reports, particularly after the second dose for males. For example, observed number of cases for males aged 12-17 years and 18-24 years are approximately 10-100 times greater than expected. [3].
- For VAERS, the incidence after the second dose for 12-29 year old males was approximately 1 in 25,000, and for 12-29 year old women it was approximately 1 in 240,000. For people aged over 30 years, the incidence was approximately 1 in 420,000 for males, and 1 in 1,000,000 for females. While the risk for females is lower than for males, it is still greater overall for younger people.[11, 12] In addition, lower rates of myocarditis could in part be due to under-diagnosis in women.[13]
- The Vaccine Safety Datalink (VSD) is a well-established system of active surveillance of healthcare records of approximately 12 million people of all ages enrolled in a network of US managed health organisations where funding arrangements dictate that all presentations are captured . An analysis of VSD data for events of myocarditis and pericarditis (confirmed via chart review) in 12-39 year olds up to 21 days after vaccination, tended to report higher rates for Moderna (compared to Pfizer) and after the second dose (compared to the first dose). See Table 3. For example:
    - Incidence of 1.26 cases per 100,000 (95%CI, 0.75-1.99) after 2nd dose of any mRNA vaccine.
    - Incidence of 0.80 cases per 100,000 (95%CI, 0.32-1.65) after 2nd dose of Pfizer.
    - Incidence of 1.98 cases per 100,000 (95%CI 0.99-3.55) after 2nd dose of Moderna.
    - Incidence of 0.26 cases per 100,000 (95%CI, 0.05-0.77) with the 1st dose of Pfizer.[12]

Table 3 Incidence of myocarditis/pericarditis in chart-confirmed data in VSD, 21-days after vaccination in 12-39 year-olds (ACIP presentation, T Shimabukuro, 23 June 2021). Note: incidence presented per million in table, not per 100,000 person-years as is used in other sources and throughout the rest of this document.

Myocarditis/pericarditis chart confirmed rates in VSD in 21-day risk interval, 12–39-year-olds

(thru Jun 5, 2021)

Vaccine(s) (dose #)	Cases	Doses admin	Rate per million doses (95% CI)
mRNA (both doses)	26	3,418,443	8 (5.3–11.8)
mRNA (dose 1)	8	1,879,585	4.4 (1.9–8.8)
mRNA (dose 2)	18	1,538,858	12.6 (7.5–19.9)
Pfizer-BioNTech (dose 1)	3	1,211,080	2.6 (0.5–7.7)
Pfizer-BioNTech (dose 2)	7	958,721	8.0 (3.2–16.5)
Moderna (dose 1)	5	668,505	7.5 (2.4–17.6)
Moderna (dose 2)	11	580,137	19.8 (9.9–35.5)

- These rates compare with background rates of 1-2 per 100,000 *per year* in children.
- The majority of cases reported transient symptoms, with rapid resolution of laboratory abnormalities (further details not provided), and brief hospitalisations [2]. Of the 29 cases in VSD, 24 (83%) were hospitalised with a median stay of 1 day (range 0-13 days), including 2 admitted to the ICU. All cases were discharged, and '*nearly all follow-up visit notes indicated resolution of symptoms at the time of follow-up*' [slide 40]. No data on long term effects are yet available [3]. No deaths have been reported associated with the reports of myocarditis or pericarditis. In the presentation to ACIP, the US CDC also reported incidence rate ratios relative to vaccinated comparators on the same calendar days.[12] The analysis was based on VSD chart-confirmed events, in 12-39 year-olds in the 21 days following vaccination (see Table 4). In general, there was not enough evidence to conclude elevated incidence for Pfizer (i.e., confidence interval for the incidence rate ratio included 1) based on this data alone, but there was evidence for increased incidence for mRNA vaccines combined after the second dose (95% CI IRR 1.1-15.7) and for Moderna alone after the second dose (95%CI IRR 2.4-not estimable).

Table 4 Chart-confirmed VSD incidence rate ratios (IRRs) for ages 12-39, 21 days after vaccination, compared to other vaccinated comparators. An IRR>1 indicates increased incidence of myocarditis/pericarditis for the COVID-19 vaccine compared to other vaccines.

VSD age-stratified analysis: Chart confirmed myocarditis/pericarditis events in 12–39-year-olds in the 21-day risk interval compared with events in vaccinated comparators on the same calendar days

(thru Jun 5, 2021)

Vaccine (dose #)	Events in risk interval	Adj Rate ratio*	95% CI
Any mRNA (both doses)	26	3.5	1.1–15.0
Any mRNA (dose 1)	8	3.7	0.8–23.4
Any mRNA (dose 2)	18	3.6	1.1–15.7
Pfizer-BioNTech (both doses)	10	1.2	0.3–6.2
Pfizer-BioNTech (dose 1)	3	1.6	0.2–12.6
Pfizer-BioNTech (dose 2)	7	1.5	0.3–7.7
Moderna (both doses)†	16	.	2.4–ne‡
Moderna (dose 1)	5	.	0.8–ne‡
Moderna (dose 2)	11	.	2.4–ne‡

*Adjusted for VSD site, 5-year age group and then the single year of age for 12-19 year olds, sex, race/ethnicity, and calendar date
†Moderna COVID-19 Vaccine is not authorized in persons aged <18 years
‡ne=not estimable, no events in comparison interval (22–42 days after final dose)

- The majority of cases reported transient symptoms, with rapid resolution of laboratory abnormalities, and brief hospitalisations [2]. Of the 29 cases in VSD, 24 (83%) were hospitalised with a median stay of 1 day (range 0-13 days), including two who were admitted to the ICU. All cases were discharged, and nearly all cases had resolution of symptoms at follow up (number not reported). No data on long term effects are yet available [3].
- There have been reports of myocarditis outside the USA. For example, in a press release, Israel's Ministry of Health reported 275 cases between December 2020 and May 2021, of which 148 occurred within 30 days of the administration of the mRNA vaccine.[14] Little detail on the cases was included in the media release. There were 27 cases among approximately 5.4 million first doses and 121 cases among approximately 5 million second doses. Most cases were men aged 16-30 years, and 95% were considered 'mild'. The authors estimated that between 1 in 3000 and 1 in 6000 men aged 16 to 24 who received the vaccine developed myocarditis, an incidence of 17-33 events per 100,000. These estimates are consistant with the estimates from the US VSD data.
- Myocarditis cases were not reported following vaccination in clinical trials of current COVID-19 vaccines. Adverse cardiac events of any kind were reported in less than 0.1% of trial participants, and were not higher in recipients of vaccine compared with placebo. However, numbers in the relevant age groups in clinical trials were below 20,000 making it difficult to identify rare adverse events.
- On 09 July 2021, the European Medicines Agency's (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) recommended adding myocarditis and pericarditis as side effects for the Pfizer and Moderna vaccines, and adding a warning. In their discussion, the PRAC reviewed of 145 cases of myocarditis in the European Economic Area (EEA) among people who received Comirnaty (Pfizer) and 19 cases among people who received Spikevax (Moderna). PRAC also reviewed reports of 138 cases of pericarditis following the use of

Comirnaty and 19 cases following the use of Spikevax. As of 04 July 2021, approximately 276 million doses of Pfizer and 20 million doses of Moderna had been administered in the European Union/EEA.[15].

- In Australia, to 08 July 2021, the Therapeutic Goods Administration (TGA) has received reports of 38 cases of suspected myocarditis or pericarditis. Approximately 3.2 million doses have been administered in Australia: *"…13 reports were in men and 25 were in women. Of the men, five were aged 17–23 years, while the others were aged 41–72 years The women were aged 22–65 years old with the most aged in their 20s and 30s. At the time of reporting, the majority of individuals had recovered or were recovering*". TGA has sought advice on this issue from the Australian Technical Advisory Group on Immunisation (ATAGI), who are closely monitoring this issue.[16]
- The TGA states that it will be adding a warning to the Product Information for Comirnaty (Pfizer's COVID-19 vaccine). They also added a statement referring to the cardiovascular and risks from COVID-19 disease, and a statement on the potential symptoms after vaccination: "*We know that myocarditis and pericarditis are much more common with COVID-19 infection and the risks to the heart can be more severe in this context. The benefits of protection against COVID-19 far outweigh these rare and generally mild side effects. We encourage people to seek medical attention if they experience symptoms that could suggest myocarditis or pericarditis such as of chest pain, shortness of breath and palpitations. Typically these have occurred within seven days of vaccination, and more commonly after the second dose of Comirnaty.*"[16, 17]

- In Canada, up to 09 July 2021, 111 cases of myocarditis and/or pericarditis have been reported to the Public Health Agency of Canada (PHAC) or Health Canada following administration of the Pfizer COVID-19 vaccine. Of those, 26 cases followed the second dose.[18] Through 10 July 2021, approximately 7.8 million second doses of the Pfizer COVID-19 vaccine have been administered in Canada.[19] This corresponds to an approximate rate for myocarditis and/or pericarditis of 3.3 per million second doses, or 1 in 303,000. Of note, in Canada the immunisation schedule for the Pfizer COVID-19 vaccine allows an interval of up to 16 weeks (4 months).
  - On 09 July 2021 the COVID-19 subcommittee of the WHO Global Advisory Committee on Vaccine Safety (GACVS) reported that a 'strong' signal had been reported in the US with regard to myocarditis/pericarditis. The GACVS also noted that the PRAC found that there was a 'plausible' causal connection.[20]
  - There is limited information on the long-term effects of myocarditis after vaccination and it is yet unknown whether the risk may vary by ethnicity. Overall, the USA ACIP recommended that the benefits of using mRNA COVID-19 vaccines such as Pfizer and Moderna clearly outweighed the risks in all populations, including adolescents and young adults for the USA population, **in the context of an ongoing pandemic in the USA.**

Table 5. Risk of myocarditis after administration of the second dose of Pfizer and/or Moderna mRNA COVID-19 vaccines

Country	Demographic, follow-up time, dose, vaccine type	Incidence per million second doses	Approximate risk within 7 days of dose 2 (to nearest 1000)	Source
US	Males, 12-29 years, within 7 days post dose 2 of mRNA vaccine	40.6	1 in 25,000	Gargano et al, 2021[11] based on confirmed and unconfirmed cases after administration of an mRNA COVID-19 vaccine (Pfizer or
	Males, 30 years and over, within 7 days post	2.4	1 in 417,000	

	dose 2 of mRNA vaccine			Moderna), reported to VAERS.
	Females, 12-29 years, within 7 days post dose 2 of mRNA vaccine	4.2	1 in 238,000	
	Females, 30 years and over, within 7 days post dose 2 of mRNA	1.0	1 in 1,000,000	
	12-39 year-olds, within 21 days following dose 2 of an mRNA vaccine	12.6	1 in 79,000	Chart confirmed cases following dose 2 of Pfizer, reported to Vaccine Safety Datalink (VSD), US CDC ACIP, 23 June 2021[12]
	12-39 year-olds, within 21 days following dose 2 of Pfizer COVID-19 vaccine	8.0	1 in 125,000	
	Males, 12-39 years, within 21 days post dose 2 of Pfizer COVID-19 vaccine	23.0	1 in 43,000	ICD-10 coded cases following dose 2 of Pfizer, reported to Vaccine Safety Datalink (VSD), US CDC ACIP, 23 June 2021[12]
	Females, 12-39 years, within 21 days post dose 2 of Pfizer COVID-19 vaccine	NE*	NE	

*NE=not estimable

3. What are risk factors for myocarditis after administration of mRNA vaccines?

- Preliminary VAERS analysis suggests that the risk is higher among young adults and adolescents, males, and higher after the second dose, as outlined in Table 6 andTable 7, below. Following the second dose, observed rates in young men were approximately 10-100 times higher than expected.
- No international data on cases has been broken down by ethnicity thus far.

Table 6 Myocarditis/pericarditis reports to VAERS following the second dose of mRNA COVID-19 vaccines (presented at ACIP 23-25 June 2021). Note: yellow highlighting is part of the original presentation.

Table **Preliminary myocarditis/pericarditis reports to VAERS following dose 1 mRNA COVID-19 vaccination, Exp. vs. Obs. using 21-day risk window (data thru Jun 11, 2021)** *7*

	Females			Male		
Age groups	Doses admin	Expected*,†	Observed*	Doses admin	Expected*,†	Observed*
12–17 yrs	3,777,097	1–13	4	3,569,239	2–21	32
18–24 yrs	6,830,706	2–23	9	5,863,268	3–34	47
25–29 yrs	5,198,356	2–18	3	4,685,036	3–27	18
30–39 yrs	11,505,068	7–66	15	10,391,499	6–60	17
40–49 yrs	11,996,507	7–69	9	10,513,258	6–60	8
50–64 yrs	21,957,007	13–126	22	19,270,825	11–111	18
65+ yrs	24,795,212	14–143	13	20,473,779	12–118	15
Not reported	—	—	2	—	—	4

Myocarditis/pericarditis reports to VAERS following the first dose of mRNA COVID-19 vaccines (presented at ACIP 23-25 June 2021)

- Similar trends are seen in the VSD data in the US, where cases are confirmed via chart review, for myocarditis and pericarditis in 12-39 year-olds, 21 days after vaccination:
- There are more cases after mRNA COVID-19 vaccination with 2nd dose, with a rate of 2.3 (95%CI, 11.0-42.3) per 100,000 after 2 doses and 0.18 (95%CI, 0.0-10.0) after 1 dose of Pfizer per 100,000. (Note that estimates presented at ACIP are per million).

Preliminary myocarditis/pericarditis reports to VAERS following dose 2 mRNA COVID-19 vaccination, Exp. vs. Obs. using 21-day risk window (data thru Jun 11, 2021)

	Females			Males		
Age groups	Doses admin	Expected*,†	Observed*	Doses admin	Expected*,†	Observed*
12–17 yrs	2,189,726	1–7	20	2,039,871	1–12	132
18–24 yrs	5,237,262	2–18	27	4,337,287	2–25	233
25–29 yrs	4,151,975	1–15	11	3,625,574	2–21	69
30–39 yrs	9,356,296	5–54	14	8,311,301	5–48	71
40–49 yrs	9,927,773	6–57	23	8,577,766	5–49	40
50–64 yrs	18,696,450	11–108	25	16,255,927	9–94	34
65+ yrs	21,708,975	12–125	17	18,041,547	10–104	16
Not reported	—	—	1	—	—	9

- Rates appear higher in males (0.47 versus 3.2 events per 100,000 in females and males, respectively, after the second dose).

Table 8 Rates of myocarditis/pericarditis in 12-39 year-olds, reported in VSD within 21 days after vaccination with mRNA COVID-19 vaccines in the US, by dose and sex

Product (dose)	Female cases	Female rates per million doses (95% CI)	Male cases	Male rates per million doses (95% CI)
Any mRNA (both doses)	6	3.2 (1.2–6.9)	26	16.9 (11.0–24.8)
Any mRNA (dose 1)	2	1.9 (0.2–7.0)	4	4.7 (1.3–12.0)
Any mRNA (dose 2)	4	4.7 (1.3–12.0)	22	32.0 (20.1–48.5)
Pfizer-BioNTech (both doses)	1	0.8 (0.0–4.7)	11	11.1 (5.5–19.8)
Pfizer-BioNTech (dose 1)	1	1.5 (0.0–8.5)	1	1.8 (0.0–10.0)
Pfizer-BioNTech (dose 2)	0	. (. – .)	10	23.0 (11.0–42.3)
Moderna (both doses)	5	7.1 (2.3–16.6)	15	27.5 (15.4–45.4)
Moderna (dose 1)	1	2.7 (0.1–14.9)	3	10.2 (2.1–29.9)
Moderna (dose 2)	4	12.2 (3.3–31.2)	12	47.7 (24.6–83.3)

- In VAERS, of 323 cases aged 29 years or younger were assessed as meeting the case definition of myocarditis or pericarditis or both, and 148 are still under review (and are therefore possible cases). Of the 323 confirmed cases, 309 were hospitalized, 218 (79%) are known to have recovered, and 9 were still hospitalised (2 in ICU).

4. How many cases of myocarditis post-vaccination have been recorded in Aotearoa New Zealand?

- As of 01 July 2021, 10 reports of myocarditis or pericarditis events in individuals following vaccination with the Pfizer COVID-19 vaccine have been received by CARM. Of those cases, 4 were male, and the ages of the individuals ranged from 24-63 years. Reported time from vaccination to onset ranged from approximately 6 hours to up to 18 days, with 2 cases occurring after the first dose and 8 after the second dose. An additional 3 are as yet unconfirmed myocarditis or pericarditis. All cases have been medically assessed and follow up information sought if needed. See 9 for further details.

Table 9 Cases of myocarditis/pericarditis after Comirnaty vaccine reported to CARM (up to 01 Jul 2021).

No.	Myocarditis /Pericarditis	Time to onset (hh:mm)	Gender	Ethnic group	Age	Dose nb	Seriousness	Reported severity
1	Myocarditis	06:00	M	NZ European	28	2	Non-serious	Moderate
2	Myocarditis	14:15	F	NZ European	47	2	Non-serious	Severe
3	Myo/peri	25:39	M	Middle Eastern	36	1		Moderate
4	Myo/peri	67:38	F	NZ European	49	2	Serious	Moderate

5	Pericarditis	291:32	M	European or other	53	2	Non-serious	Moderate
6	Myocarditis	50:56	F	European or other	31	2	Serious	Moderate
7	Myocarditis	452:27	F	European or other	34	1	-	-
8	Pericarditis	5:45	F	-	24	2	-	-
9	Myocarditis	24:19	F	European or other	44	2	Serious	Severe
10	Pericarditis	119:42	M	European or other	63	2	Not serious/ Serious	Moderate

- In Aotearoa New Zealand, Medsafe has been monitoring this emerging signal for some time with data provided by CARM and regulators internationally. Medsafe has briefed the Independent Safety Monitoring Board (ISMB) frequently with updates on data and received advice including the need to communicate early to consumers and healthcare professionals. Medsafe issued a monitoring communication on 9 June 2021 to highlight this potential adverse reaction of myocarditis and seeking further information from healthcare professionals to help with our assessment of the signal. Whilst the New Zealand data do not currently indicate an association between the Pfizer COVID-19 vaccine (Comirnaty) and myocarditis, the international data does. Therefore, Medsafe has confirmed that Pfizer will update the data sheet for the Pfizer COVID-19 vaccine. The wording will be similar to the recent United Kingdom update: There have been very rare reports of myocarditis and pericarditis occurring after vaccination with Comirnaty often in younger men and shortly after the second dose of the vaccine. These are typically mild cases and individuals tend to recover within a short time following standard treatment and rest. Health care professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinated individuals should also seek immediate medical attention should they experience new onset of chest pain, shortness of breath, palpitations or arrythmias.
- In Aotearoa New Zealand, Medsafe intends to publish an updated communication on myocarditis/pericarditis associated with Comirnaty. The communication is an update to the June communication and will provide the proposed wording above, with advice to healthcare professionals and consumers. The communication confirms that, after assessing the data currently available on myocarditis, the benefits of vaccination with Comirnaty continue to outweigh the risk of experiencing a side effect for people of all ages in the approved indication. The communication has been shared for comment with the ISMB, the CVTAG, and Medicines Adverse Reactions Committee (MARC). Medsafe will publish this information to ensure advice based on the current evidence is avai able to healthcare professionals and the public.
- Medsafe has discussed the signal of myocarditis with its international regulatory partners on a number of occasions, most recently on 21 July 2021. All regulatory partners who were present on 21 July 2021 (US FDA, Health Canada, Singapore, Australia, Israel, European Medicines Agency) agree that the product information should be updated in line with the wording above (or similar). All agree that the benefits of vaccination with Comirnaty continue to outweigh the risks for people of all ages in the approved indication and no changes to the dosing schedule have been put in place or recommended. Medsafe will continue to monitor local and international reports of myocarditis and/or pericarditis with support from CARM and the ISMB. Medsafe will also be taking a review of myocarditis and/or pericarditis reports associated with Comirnaty to the next meeting of the Medicines Adverse Reactions Committee (MARC). The MARC is an independent, Ministerial appointed, expert advisory committee who provides expert advice to Medsafe on the regulation of medicines.

5. What is the risk of myocarditis after SARS-CoV-2 infection and COVID-19?

- Evidence is emerging on the risk of myocarditis after SARS-CoV-2 infection. Acute COVID-19 infection is associated with a range of cardiac complications which include heart failure, myocardial injury and arrythmias [21]. A preliminary analysis of a large multi-national registry of approximately 170,000 individuals with prior SARS-CoV-2 infection that was reported between January and October 2020, reported an incidence of myocarditis of 0.01% [22].
- COVID-19 itself is associated with a range of cardiac complications, the most common of which are heart failure, myocardial injury and arrhythmias.[23] A study of 1597 college athletes (60.4% men) with prior history COVID-19 (assessed via positive PCR) in the US, found that, after cardiovascular screening, 37 (2.3%) had clinical or subclinical myocarditis. If cardiac testing were based on symptoms alone, is was estimated that only 5 (0.31%) would have been detected.[24]

Other risks from SARS-CoV-2 infection in children: MIS-C

- Generally, children experience mild symptoms or are asymptomatic after SARS-CoV-2 infection, but some children do experience severe disease, including multisystem inflammatory syndrome in children, or MIS-C. The US CDC reported that MIS-C occurs in approximately 1 in 3,200 SARS-CoV-2 infections (0.03%); and at a rate of approximately 2.1 per 100,000 person-years in children and young adults aged 0-21 years. Rates are somewhat age-dependent, with a rate of 2-3 in children aged ≤14 years, and 0-1.5 per 100,000 person-years in individuals aged 15-20 years.[4] MIS-C occurs in approximately 0.03% of SARS-CoV-2 infections. Approximately, 3.2% have a baseline cardiovascular abnormality and 30.9% have at least one underlying condition (excluding obesity).[5] Most cases occur in children under 12, but about a third (36%) of cases occur in older children and young adults (ages 12–20 years), who are eligible or potentially eligible to be vaccinated. There is a potential equity issue, in that the majority of cases of MIS-C (62%) have occurred in children who are Hispanic/Latino or Black.
- A retrospective review of cases of acute myocarditis in children treated at a single center included 7 cases that had prior SARS-CoV-2 infection. Ultimately, 6 out of 7 of those cases of acute myocarditis were diagnosed with MIS-C.

Possible mechanisms responsible for the cardiac manifestations of acute COVID-19

- There have been multiple proposed mechanisms responsible for the cardiac manifestations of acute COVID-19. Some are related to the consequences of severe sepsis, but direct cardiotoxicity has also been demonstrated[25]. Myocarditis could also be a consequence of inflammation. Viral myocarditis is a well-recognised complication of many infectious agents including poliomyelitis [26], mumps [27], measles [28] and Coxsackievirus [29]. SARS-CoV-2 gains entry into the cardiac myocyte through the ACE-2 receptor. The subsequent mechanism of cardiac damage will depend on the response to viral infection.[25]

6. How is myocarditis diagnosed? Is there data on how much mild myocarditis may be missed?

- The CDC case definitions for identifying cases of acute myocarditis (probable and confirmed, adults and infants and children) are shown in Table 10.

Table 10 CDC working case defintion for acute myocarditis

Acute Myocarditis

Clinical myocarditis

Probable Case

Presence of ≥ 1 new or worsening of the following clinical symptoms:

- chest pain/pressure/discomfort
- dyspnea/shortness of breath/pain with breathing
- palpitations
- syncope

OR, infants and children <12 years of age may instead present with ≥ 2 of:

- irritability
- vomiting
- poor feeding
- tachypnea
- lethargy

AND

≥ 1 new finding of:

- troponin level above upper limit of normal (any type of troponin)
- abnormal electrocardiogram (ECG or EKG) or rhythm monitoring findings consistent with myocarditis*
- abnormal cardiac function or wall motion abnormalities on echocardiogram
- cMRI findings consistent with myocarditis†

AND

- No other identifiable cause of the symptoms and findings

Confirmed Case

Presence of ≥ 1 new or worsening of the following clinical symptoms:

- chest pain/pressure/discomfort
- dyspnea/shortness of breath/pain with breathing
- palpitations
- syncope

OR, infants and children <12 years of age may instead present with ≥ 2 of:

- irritability
- vomiting
- poor feeding
- tachypnea
- lethargy

AND

- Histopathologic confirmation of myocarditis§

OR

- Troponin level above upper limit of normal (any type of troponin), **AND**
- cMRI findings consistent with myocarditis†

AND

- No other identifiable cause of the symptoms and findings

*To meet the ECG or rhythm monitoring criterion, must include at least one of:

- ST-segment or T-wave abnormalities
- Paroxysmal or sustained atrial, supraventricular, or ventricular arrhythmias
- AV nodal conduction delays or intraventricular conduction defects

†Using either the original or the revised Lake Louise criteria (Ferreira et al. *J Am Coll Cardiol.* 2018;72:3158-76)
§Using the Dallas criteria (Aretz et al. *Am J Cardiovasc Pathol.* 1987;1:3-14)

Notes:
1. Autopsy cases may be classified as confirmed clinical myocarditis on the basis of meeting histopathologic criteria if no other identifiable cause
2. Cases with individuals who lack the listed symptoms but who meet other criteria may be classified as subclinical myocarditis (probable or confirmed)

- The Brighton Collaboration have also reported their draft case definitions for myocarditis as of 30 May 2021. See Figure 2. For more detail see: https://brightoncollaboration.us/myocarditis-case-definition-update/

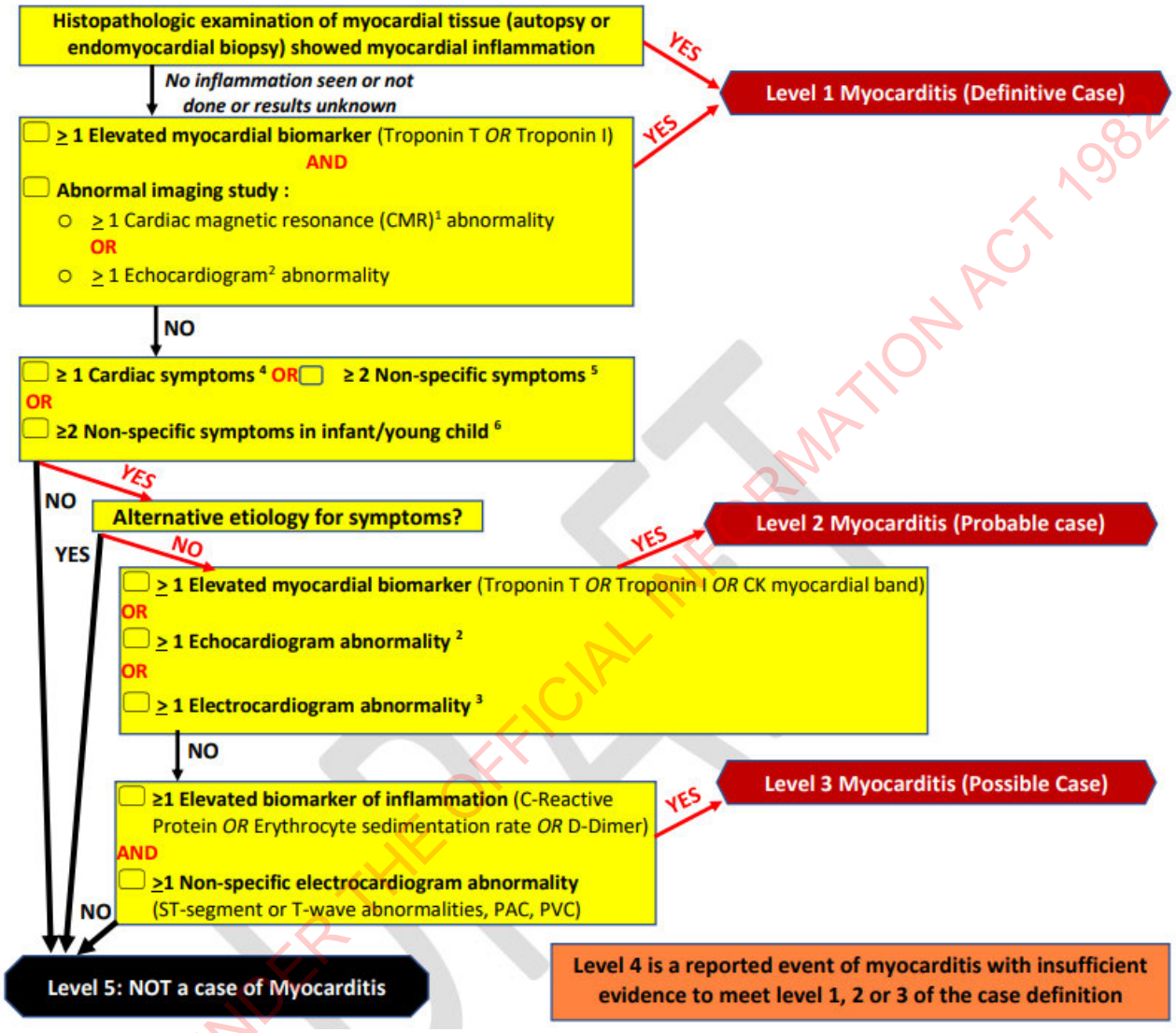

Figure 2 Brighton Collaboration draft case definition for myocarditis, as of 30 May 2021

- Myocarditis is defined as inflammation of the myocardium that is not due to coronary artery disease. Viral myocarditis may occur due to the cytopathic effect of viral infection of the cardiac myocyte, which is not necessarily associated with an inflammatory myocardial infiltrate or due to immune mediated myocardial damage [25].
- A diagnosis of myocarditis may be suggested by a range of symptoms, primarily chest pain, worsening dyspnoea, and new onset arrythmias. The diagnostic protocol emphasises the "need for speed" in diagnosing acute coronary syndrome. Initial testing will include ECG, cardiac biomarkers and chest X-ray. Cardiac biomarkers such as troponin are usually elevated in acute myocarditis. ECG changes usually reflect acute myocardial injury but is also used to exclude alternative causes of cardiac symptoms and to characterise any associated rhythm abnormalities. Myocarditis should be suspected in patients with a rise in cardiac biomarkers, ECG changes suggestive of acute myocardial injury, arrythmia or abnormalities in left ventricular systolic function, particularly in an individual with a low risk of underlying coronary artery disease [30].

- The gold standard for the diagnosis of myocarditis is by histologic examination by endomyocardial biopsy. Biopsy is not typically performed for the clinical diagnosis, and reserved for selected cases when the diagnosis is likely to influence treatment or prognosis of patients.
- Cardiovascular magnetic resonance (CMR) is the gold standard non-invasive method for assessing myocardial inflammation. Criteria for the non-invasive diagnosis of non-ischaemic cardiomyopathy ("Lake Louise Criteria") have been published [31].
- These criteria propose 3 diagnostic features in myocardial tissue. These are oedema, hyperaemia and necrosis or scar and are derived from signal intensity assessment in T-2 weighted, early and late gadolinium enhancement CMR images. A recent meta-analysis reported that the Lake Louise Criteria have a diagnostic accuracy of 83% (sensitivity-80%, specificity 87%).
- Due to the difficulties in diagnosis and the transitory nature of the condition, it may be difficult to establish an accurate assessment of the incidence of myocarditis after vaccination. In children <12 years old, it is unlikely we would meet the US CDC case definition of confirmed myocarditis, as CMR usually requires a general anaesthetic in this group of patients.

7. What is the nature of vaccine readiness or vaccine hesitancy among at risk-populations e.g. young adults aged between 16 and 30? Does this vary by gender and ethnicity?

- Vaccine hesitancy has been found to be more prevalent in the under 30-year age group in several Aotearoa New Zealand studies in late 2020 and early 2021, mirroring overseas predictions and actual uptake figures. Massey University research found the demographic characteristics of the 24% vaccine hesitant group include being more likely to belong to be younger (18-25 years) or middle-aged (36-45 years) compared to other age groups, have low (no qualification) to moderate education and income levels, slightly more likely to be female, and more likely to be Māori compared to other ethnicities.
- These findings were supported more recently in 2021 by Victoria University researchers who found 70% intention to get a COVID-19 vaccine with one of the key findings that young people and those with less education were less likely to say they would take the vaccine. An important finding in this study is that identifying as Māori or Pacific ethnicity was not statistically associated with vaccine hesitancy, rather it was the population characteristics of these ethnic subgroups of being younger and less educated that accounted for the bivariate associations.
- In other vaccine-based research, young people aged 15-24 have been identified as high risk for missing out on routine vaccinations. This age group are least likely to be enrolled in a Primary Health Organisation (PHO). In 2020, 6% of the population were not enrolled with a PHO provider.

Equity considerations

- A review commissioned in 2019 by the Ministry of Health examined causes of childhood under-immunisation, and found that systemic barriers (including socio-economic, rurality, parental difficulties) were the leading causes of under-immunisation. researched reasons for the decrease in Māori tamariki immunisation rates, concluding that the combination of individual, provider, systemic, policy and environmental factors all have a role to play in the current situation.

- The Hauora Waitangi Tribunal report (2019) showed the need for increased cultural competency by practitioners, providers and systems, to address persisting Māori health inequities in Aotearoa New Zealand, [32] and this finding is strongly supported by leading Māori health experts and researchers [33, 34].

What impact might a potential safety signal have upon vaccine readiness?

- In the countries with the highest vaccine coverage so far, US, UK, Chile and Israel, uptake is showing signs of levelling off at 50-60% coverage. Younger people are over represented in the unvaccinated population in US based research. By May 22, 2021, the US coverage was lowest among persons aged 18–29 years (38.3%). Vaccination coverage was lower among younger age groups in all states, regardless of timing of expanded vaccine eligibility to all adults (Supplementary Table, https://stacks.cdc.gov/view/cdc/107123). Higher social vulnerabilities or higher percentages of the population who are uninsured, living in poverty, lacking access to a computer, and lacking access to a computer with Internet made it less likely for younger people to be vaccinated.

8. How many young adults aged between groups 1 and 3 have been vaccinated already, and when are most people in this cohort expected to be vaccinated?

- In Aotearoa New Zealand, based on estimates reported 01 July 2021, approximately, 84,025 individuals aged 15-34 have received two doses of the Pfizer vaccinPe, with approximately 31,365 of these being male.
- Two doses have been administered to approximately 7,487 Māori, 5,526 Pacific Peoples, 25,702 Asian, and 44,299 European/Other.
- For a further breakdown of doses administered, see Table 11.

Table 11 Number of New Zealanders who have recieved the Pfizer COVID-19 vaccine by ethnicity, age, gender, and group

			Ethnicity									
			Asian		European or other		Māori		Pacific Peoples		Unknown	
Age group	**Group**	**Gender**	First Dose	Second Dose	First Dose	Second Dose	First Dose	Second Dose	First Dose	Second Dose	First Dose	Second Dose
15 to 19	Group 1	Female	168	151	703	615	166	143	138	114	6	<5
		Male	218	190	721	628	164	139	144	115	7	<5
		Unknown/Other	<5		<5	<5						
	Group 2	Female	618	351	2009	1382	477	284	297	138	16	10
		Male	435	238	977	716	286	178	239	96	8	5
		Unknown/Other	<5	<5								
	Group 3	Female	38	14	171	55	87	30	50	20		
		Male	43	9	133	46	86	33	55	13	<5	
		Unknown/Other			<5				<5			
20 to 24	Group 1	Female	479	423	1495	1331	340	292	329	282	21	18
		Male	681	605	1530	1365	341	302	302	253	26	22
		Unknown/Other	13	10	<5	<5			<5	<5	<5	<5
	Group 2	Female	3110	2441	8330	6852	1471	1103	1025	656	54	37
		Male	1673	1154	3191	2578	707	531	473	273	50	37
		Unknown/Other	14	11	7	7			10	<5	10	7
	Group 3	Female	59	21	289	97	121	44	59	24		
		Male	72	17	225	73	137	34	130	28	6	<5
		Unknown/Other	<5						22	<5	<5	<5
25 to 29	Group 1	Female	762	701	1690	1540	272	241	309	274	25	22
		Male	1044	949	1975	1783	281	247	302	263	52	47
		Unknown/Other	18	15	6	6	<5	<5			8	7
	Group 2	Female	5372	4350	9449	8022	1539	1164	1191	857	229	193
		Male	2831	2073	4563	3734	809	615	568	371	147	113
		Unknown/Other	40	26	12	9			6	<5	30	23
	Group 3	Female	103	41	334	140	109	39	68	12	6	<5
		Male	117	48	294	114	147	40	132	20	9	
		Unknown/Other	<5		<5	<5			18	5	<5	
30 to 34	Group 1	Female	698	648	1198	1086	189	160	263	233	18	13
		Male	1038	968	1730	1591	211	179	276	251	52	43
		Unknown/Other	13	13	5	5			<5	<5	6	5
	Group 2	Female	8112	6616	8109	6749	1475	1094	1159	813	270	199
		Male	4464	3448	4441	3515	679	510	563	369	213	167
		Unknown/Other	48	37	16	14			5	<5	49	43
	Group 3	Female	168	82	377	132	137	42	67	26	5	<5
		Male	153	52	319	114	144	43	112	20	8	<5
		Unknown/Other	<5	5					18	<5	8	<5

- The groups are characterised as follows:
  - Group 1: Border workers and their household contacts
  - Group 2: Frontline health workers. Emergency Response Services, Facility Worker or Resident, Unknown, Other, Early Vaccine Access. Individuals vaccinated at NZDF sites who identify as Border Workers or Household contacts. Individuals over 65 and with underlying health conditions in Counties Manukau.
  - Group 3: People at greatest risk of serious illness which includes over 65s and those with underlying health conditions. Health and social services.

9. What are possible alternative vaccine schedules for at-risk populations, and how effective are they?

- Alternative vaccine schedules may lower risk of myocarditis following Pfizer vaccination but are unproven. These include the administration of the second dose as a different vaccine (heterologous schedule), administration of only one dose, delaying the second dose, or delaying the rollout in the at-risk group altogether, until more data becomes available to better understand the risk of myocarditis.
- **Heterologous schedules:** The strategy of mixing vaccines has been used internationally in response to a range of issues, including safety concerns and unpredictable supplies. Data is emerging on heterologous schedules and multiple preliminary studies have shown that administering the Pfizer vaccine as a second dose, in those who received the AstraZeneca

vaccine as their first dose, triggers antibody responses that are at least as robust as a homologous Pfizer schedule.[35-38]

- On the other hand, administering AstraZeneca as the second dose after Pfizer as the first dose, induces lower antibody responses than a homologous Pfizer schedule.[35]
- The heterologous schedules also seem to have an acceptable safety profile, with no serious adverse events reported in any of the studies. However, it is not known how the level of immune response from a heterologous schedule translates to vaccine effectiveness, and no data on whether this impacts on the risk of myo/pericarditis. In Aotearoa New Zealand, only the Pfizer vaccine has been approved for use, so a heterologous schedule cannot be administered at this stage. However, the Janssen COVID-19 vaccine is expected to become available in Aotearoa New Zealand towards the end of 2021.
- **Administration of one dose and delaying the second dose:** Multiple studies have reported on the vaccine effectiveness of the Pfizer vaccine after one dose, with point estimates varying from 44-80% against lab-confirmed infection. While the vaccine effectiveness can vary depending on age, time after the first dose, and SARS-CoV-2 variants, all studies show statistically significant, measurable protection after one dose. However, a second dose is required for higher vaccine effectiveness. There is limited information on the impact of delaying a second dose of the Pfizer vaccine. However, given the general improvement in immunogenicity it seems likely that effectiveness would be higher following a delayed dose.
- Data on extended intervals between the first dose and second dose of the Pfizer COVID-19 vaccine is emerging. Researchers at the University of Oxford, University of Liverpool and others, reported that in a study of 503 healthcare workers, that neutralising antibody levels were higher following the second vaccine dose of the Pfizer vaccine after a dosing interval of 6-14 weeks (median 10 weeks) compared to the conventional 3-4 week regimen. The extension of the dosing interval was not associated with an increase or decrease the induction of T cell responses following the second dose. These data suggest that the dosing interval could be extended and still provide the same or even better immune protection.[6]

10. Are there any recommendations post-vaccination for preventing myocarditis? E.g., against exercise post-vaccination

- There is currently no literature detailing recommendations for preventing myocarditis post-vaccination, including abstaining from exercise. In trained athletes with confirmed myocarditis, physical exertion as part of a regular exercise program has been found to be associated with arrhythmias and sudden cardiac death. Exercise restrictions are therefore seen as critical in the management of myocarditis in athletes during the initial inflammatory period.[23]

Glossary

Abbreviation	Definition
ACIP	Advisory Committee on Immunisation Practices
CPRD	Clinical Practice Research Datalink
IRR	Incidence rate ratio
MIS-C	Multisystem Inflammatory System in Children
US CDC	United States Centers for Disease Control
US FDA	United States Food and Drug Administration
VAERS	Vaccine Adverse Event Reporting System
VSD	Vaccine Safety Datalink

Appendix 1: Vaccine hesitancy review

- Prepared by Dr Mary Silcock, Intelligence and Surveillance, COVID-19 Science and Insights

Vaccine hesitancy has been found to be more prevalent in the under 30-year age group in several Aotearoa New Zealand studies, mirroring overseas predictions and actual uptake figures. Massey University research found the demographic characteristics of the 24% vaccine hesitant group more likely to belong to be either younger (18-25 years) or middle-aged (36-45 years) groups (compared to other age groups), have low (no qualification) to moderate education levels (certification or diploma), and lower income levels. They are slightly more likely to be female compared to male, and more likely to be Māori compared to other ethnicities. The informational sources this group are more likely to trust was social media. Respondents were found less likely to trust mass media, scientists, and family and friends as sources of accurate information. They are more likely to trust information on social media on COVID-19 and less likely to report that the information they saw on social media about COVID-19 was fake.

These findings were supported more recently by Victoria University researchers who found 70% intention to get a COVID-19 vaccine with one of the key findings that young people and those with less education were less likely to say they would take the vaccine . An important finding in this study is that identifying as Māori or Pacific ethnicity was no longer statistically associated with vaccine hesitancy, rather it is the population characteristics of these ethnic subgroups of being younger and less educated accounting for the bivariate associations.

In other vaccine-based research young people aged 15-24 have been identified as high risk for missing out on routine vaccinations. This age group are least likely to be enrolled in a PHO, making them more likely to miss out on vaccinations. In 2020, 6% of the population were not enrolled with a Primary Health Organisation (PHO) provider [39, 40]. Furthermore, a pre-print by Iruzun-Lopez et al (2020) indicated that Māori have lower PHO enrolment than European/Other, and Auckland DHB has the lowest enrolment rates [40]. The risk of unenrolled people missing out on vaccination was also raised as an issue in the recent evaluation of the 2020 Māori Influenza Vaccination Programme (MIVP) as providers were unable to pro-actively find individuals and their whānau through medical records and data sets [41].

Table 12: Ethnic differences in New Zealand childhood immunisation coverage in 2020 [42]

Ethnicity	European	Māori	Pacific	Asian	Other
Percentage of the population fully vaccinated	90.3%	80.4%	88.6%	92.0%	78.3%

A review commissioned in 2019 by the Ministry of Health examined causes of childhood under-immunisation, and found that systemic barriers (including socio-economic, rurality, parental difficulties) were the leading causes of under-immunisation [43] Other research has demonstrated that the regions with the highest childhood immunisation coverage were in areas with a high proportion of the population who identified as European ethnicity Immunisation coverage was lower in minor urban areas (small towns). Vaccination rates in the northern South Island, central–southern North Island, around Auckland and in Northland had the strongest negative effect of area-level deprivation, indicating these regions vaccine uptake rates were impacted more by their location and may require more intensive support and resourcing for vaccination provision .

researched reasons for the decrease in Māori tamariki immunisation rates, concluding that the combination of individual, provider, systemic, policy and environmental factors all have a role to play in the current situation. The Hauora Waitangi Tribunal report (2019) showed the need for increased cultural competency by practitioners, providers and systems, to address persisting Māori health inequities in

Aotearoa New Zealand, and this finding is strongly supported by leading Māori health experts and researchers

The standout success of the Māori Influenza Vaccine Programme (MIVP) and the Māori response over the lockdown in 2020 [44-46] are examples of how kaupapa Māori services can address these systemic barriers. As an example of a vaccination strategy that may also be effective for young people is how one provider proactively addressing culturally unsafe practice by using a voucher system for eligible Māori, to "ensure others in the health system did not interpret the eligibility criteria differently and turn them away. They aimed to ensure that whānau were not embarrassed or hesitant to present for vaccination" [41]. Tākiri Mai Te Ata Whānau Ora collective responded over the COVID-19 lockdown to a multitude of health needs such including catch up vaccinations and influenza vaccinations whilst delivering food parcels or carrying out welfare checks which also may be an effective strategy to reach young people.

There are nuances in vaccination uptake in other population groups, including minority ethnic and socio-cultural groups, although there is very limited research in this area. Low uptake rates of childhood vaccinations was identified among migrant and refugee children in an analysis of National Immunisation Register records [47]. New Zealanders of Asian descent have been noted to have high rates of vaccine uptake but as with the overall population based research young people who have left school are an at-risk group for not accessing vaccinations. Information used in immunisation campaigns involving young adults needs to resonate and become real to the target group, while also targeting the support people in their lives who may be involved in influencing decisions about vaccination.

What impact might a potential safety signal have upon vaccine readiness?

There is little research yet to show any change in uptake of COVID vaccines directly attributed to safety signals however, the Janssen vaccine pause in mid-April due to blood clotting safety concerns has resulted in observable decline in uptake in the American roll-out with 21 million doses reportedly unused. Demand for all vaccines has slowed since mid-April, but the drop has been significantly steeper for the Janssen vaccine. Pharmacists report that older people who are at lower risk for the clotting issue are still willing to take the Janssen vaccine.

In the countries with the highest vaccine coverage so far, US, UK, Chile and Israel, uptake is showing signs of levelling off at 50-60% coverage. Younger people are more represented in the unvaccinated population in US based research. By May 22 2021, the US coverage was lowest among persons aged 18–29 years (38.3%). Vaccination coverage was lower among younger age groups in all states, regardless of timing of expanded vaccine eligibility to all adults (Supplementary Table, https://stacks.cdc.gov/view/cdc/107123). Higher social vulnerabilities or higher percentages of the population who are uninsured, living in poverty, lacking access to a computer, and lacking access to a computer with Internet made it less likely for younger people to be vaccinated.

In a recent study Canadian study with young people aged 14 to 17 years old willingness to get a COVID-19 vaccine was 65.4%. Willingness did not differ by age, sex, or mental health conditions, but did differ for other sociodemographic characteristics, physical health conditions, COVID-19 knowledge, practicing social/physical distancing, **and adversity history**. Similar to older people the most common reasons for not wanting a vaccine were related to safety, knowledge, and effectiveness, however adversity history is associated with being younger. Male sex were more likely to be not concerned about getting vaccinated, whereas female sex were more likely to stated they did not know enough to decide .

Similar results have been seen in a recent CDC publication that pooled findings from two representative surveys of U.S. adults aged 18–39 years . Only one half (51.8%) reported that they had been or were planning to be vaccinated, whereas 24.9% reported that they probably or definitely would not be vaccinated, and 23.2% reported that they would probably be vaccinated or were unsure if they would be vaccinated. Respondents who were reluctant or unsure about vaccination reported concerns about vaccine side effects, distrust of COVID-19 vaccines, a plan to wait and see whether the vaccine was safe and to

possibly get vaccinated later, thinking that others needed a vaccine more than they did, and the belief that they did not need the vaccine.

Misinformation fuelling the hesitancy from safety signals:

In the two most recent Virality Project Weekly Briefings June 22 - June 29, 2021 safety concern stories were prominent across social media platforms this week, including concerns around blood clots while others emphasized ongoing concerns of myocarditis in young people. Prominient American and UK public figures have referred to the vaccination of children as "a sacrifice to save older adults,"; and have equated pharmaceutical companies with paedophiles "these pharma-philes also want to fiddle with our children." There are also rumours spreading among young people, on Tik Tok that the vaccine makes you sterile. Child safety concerns are at the forefront of the anti-vaccine community's discussions this week with parents focussing on the limited number of myocarditis cases to spread vaccine hesitancy sentiment. Claims about myocarditis, some based on real adverse reactions and others blended with unrelated or conspiratorial claims, have spread across languages as well as platforms, potentially reflecting significant ongoing public concern.

These safety concerns appear to have leveraged off the recent US Advisory Committee on Immunization Practices meeting to discuss myocarditis and pericarditis and COVID vaccination; a cabinet minister in the UK announcing that vaccination experts in the nation are not planning to recommend vaccines to children aged 12-17; and the WHO's June 22 release of its updated guidance, wh ch included information on not prioritising vaccination for children. These differences in official guidelines for vaccinating 12-17-year olds are being used to undermine public health institutions' expertise and ferry parents towards alternative wellness influencers. Campaigns against vaccine mandates continue to gain significant traction online, particularly among right-leaning communities.

Aotearoa New Zealand implications

In the past vaccine campaigns, there were many findings that can be built on in relation to the elements of vaccine hesitancy, safety signals, misinformation, parental influence and access to vaccination outlined above. A limitation to these is that less information and evidence about young men and boys' attitudes and uptake to vaccination was identified in this rapid review. The Aotearoa HPV vaccination roll-out only involved girls/young women so there is a gender bias in the evidence from this campaign and the Measles and Meningococcal B campaigns did not provide commentary on gender differences. Young men and boys may have gender specific risks associated with less proactive health seeking behaviours, not wanting to be seen going to seek health care and greater beliefs in their own immune response that may need to be considered.

Some key findings from the Aotearoa HPV vaccination rollout were:

- 80% of 18+ young women received the vaccination at Primary Care providers not schools, but uptake was much lower than targets, indicating this was not the best site for vaccination.
- School-based delivery met targets and resulted in faster uptake and has better completion rates for a three-dose vaccine.
- Young women's reasons for declining vaccination included a lack of awareness about the vaccine, particularly for young Māori women; not getting round to having it especially for young Pākehā women; a false perception that only those who are sexually promiscuous need it; a fear of needles; and concerns about efficacy and side effects
- Uptake decision for young Māori and Pacific women based on trust, sense of protection from cancer, family history of cancer or social desirability (i.e. vaccinated to please parent, doctor or others).
- Across all ethnicities, the reasons to vaccinate were similar: protection from cervical cancer, whānau exposure to cervical and other cancers, the sense of 'doing the right thing' and the vaccine is free

- Mothers and the wider whānau had a strong influence particularly for Māori and Pacific young women's vaccine decision-making. Parental and whānau fears maybe impacting hesitancy for young people.
- Pākehā parents tended to be confident in their ability to make a decision either for or against having the vaccine. In contrast, Māori and particularly Pacific parents tended to follow advice received from a trusted source with less consideration of written information (i.e. the consent form)
- Health professions support (or lack of support) influenced decision-making and vaccine uptake for young people
- Health workforce needs to be prepared to ensure those delivering the vaccine and the wider health sector are aware of the disease (e.g. HPV and cervical cancer), the vaccine and its benefits as well as risks and contraindications. Their support (or not) influenced the target groups' decision.
- Clear resources of layered information is required for health workforce to enable informed consent and support appropriate communication due to varied health literacy within the young peoples age group. Information needs to be layered:
- Level 1 - the need and key vaccine benefits together with reassurances the vaccine is safe and works; Level 2 - key information needed to inform a decision to act or not, e.g. vaccine efficacy, side effects, duration of protection; Level 3 - detailed information with links to relevant and credible researc
- Parents reasons for declining the HPV vaccine were concerns about the link between the vaccine and sexual activity, efficacy and side-effects, vaccination fatigue, their daughters' fear of needles and inconsistency with religious beliefs
- Young people did not generally consider Meningococcal B a threat, and therefore did not think they were at risk from contracting it
- Some young people do not want to be seen to actively seek vaccination, and/or go to the GP
- Vaccination offered at sports events or concerts are unlikely to be effective – youth don't like being approached for vaccination when they have gone to an event for quite a different purpose
- Young people thought that it would be acceptable for Meningococcal B providers to create fun events for the specific purposes of providing vaccinations
- Opportunities for group vaccination should be explored, and incentives such as free coffee, competitions or vouchers should be considered
- Many providers emphasised that vaccination should be available at community awareness events
- Community Outreach was most effective when targeted to children and families known to still require vaccination. Door knocking and providing clinics to non-specific families contained within an area of lower coverage did not result in a higher number of vaccinations.
- The venue for community clinics is important and should be culturally appropriate and easily accessible. Opening times should recognise that many children are in working families.
- Future vaccination campaigns should consider providing multiple vaccination opportunities for young people including at youth centres, work sites, tertiary education and other training sites and at community venues such as parks and shopping malls.
- Larger DHBs are likely to face greater difficulty in achieving high coverage rates for Māori and need to devote extra resources to reaching urban Māori

Next Steps	Share with CV TAG for feedback and to inform advice.

In the development of this advice, the following parties have been consulted with:	CV TAG
What are the implications and considerations of this advice on Te Tiriti o Waitangi and equity?	Equity and Te Tiriti are relevant to assessing who is at risk of infection and severe disease, and who is at greater risk and more vulnerable. It is important to establish whether there has been an increased burden for in any ethnicities overseas and within New Zealand. There is limited data on cases in New Zealand but breaking these down by ethnicity will be important to establish who is more at risk, and to ensure these populations are informed, protected and empowered. International evidence will be broken down by ethnicity to provide a baseline of potential risk and how this could play out in the New Zealand setting.

Resources used:		
Ministry of Health Policies and Procedures	Yes No	
External Health Scientific organisations	Yes No	
Existing database of RFAs	Yes No	
Internal MH Advice	Yes No	
External Expert Advice	Yes No	
Literature Review	Yes No	

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Background rates of myocarditis and rates post-vaccination - DRAFT

20 July 2021

Document 2

Background rates for myocarditis, all causes

Country	Demographic	Rate per million person-years	Approximate risk over 1 year (to nearest 1000)	Source
Aotearoa New Zealand	Total population	18.1	1 in 55,000	Preliminary results courtesy of research team led by Dr Helen Petousis-Harris
	Māori	19.5	1 in 51,000	
	Pacific Peoples	17.9	1 in 56,000	
	Males	24.3	1 in 41,000	
	Females	12.1	1 in 83,000	
	0-9 years	2.0	1 in 500,000	
	10-19 years	7.6	1 in 132,000	
	20-19 years	21.3	1 in 47,000	
US	Total population	10-100	1 in 10,000 to 1 in 100,000	Gubernot, D., et al, 2021[1]
UK	0-19 years	20.0	1 in 50,000	ACCESS (based on CPRD GP database)[2]
Italy	0-19 years	8.4	1 in 119,000	ACCESS (based on PediaNET, Italian GP database)[2]
Finland	0-15 years	19.5	1 in 513,000	Arola et al, 2017[3]
	Males, 0-11 years	Approximately 0-20	1 in 50,000 to NE	
	Males, 12-15 years	Approximately 50-135	1 in 7,400 to 1 in 20,000	
	Females, 0-11 years	Approximately 0-10	1 in 100,000 to NE	
	Females, 12-15 years	Approximately 10-35	1 in 29,000 to 1 in 100,000	

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NE=Not estimable

Document 2

Rate of myocarditis after vaccination with Pfizer/BioNTech mRNA COVID-19 vaccine

Country	Demographic	Incidence per million second doses	Approximate risk within 7 days of dose 2 (to nearest 1000)	Source
US	Males, 12-29 years, within 7 days post dose 2	40.6	1 in 25,000	Gargano et al, 2021[4]
	Males, 30 years and over, within 7 days post dose 2	2.4	1 in 417,000	
	Females, 12-29 years, within 7 days post dose 2	4.2	1 in 238,000	
	Females, 30 years and over, within 7 days post dose 2	1.0	1 in 1,000,000	
NZ	Total population, post dose 2	13 per 564,789 dose 2, ~ 23 per million second doses*		
	Total population, all doses	18 per 1,404,343 doses ~ 13 per million doses*		

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*Approximate rates. Numerator based on number of cases received by CARM 19 July 2021; denominator based on doses administered in NZ as of 13 July 2021, https://www.health.govt.nz/our-work/diseases-and-conditions/covid-19-novel-coronavirus/covid-19-vaccines