MANATŪ HAUORA
MINISTRY OF HEALTH

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6 March 2023

s 9(2)(a)

By email: s 9(2)(a)
Ref: H2023019062

Tēnā koe s 9(2)(a)

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 6 January 2023 for information regarding myocarditis in COVID-19 patients. Each part of your request is responded to below:

> *I have read in various NZ government Covid information claims that the rate of myocarditis in Covid patients is higher than in those who get mRNA vaccines … Please could you provide copies of whatever information you rely on to support and justify the NZ government claims … Please also provide copies of any internal and/ or external advice about this and/ or how to present this information to the public*
>
> *If you do have any published research on this please provide copies and also Information to show the rates of myocarditis in mRNA vaccinated individuals compared to unvaccinated (ideally comparing each with and without having had Covid).*
>
> *This study shows there is no measurable increase in myocarditis after Covid: www.mdpi.com/2077-0383/11/8/2219"*

Manatū Hauora has identified 14 documents in scope of your request. All documents are itemised in Appendix 1 and copies of the documents are enclosed. 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.

International data shows that myocarditis is more common after COVID-19 infection compared to vaccination. The following studies were referenced in the Medsafe alert communication published in December 2021. Further details can be found here: www.medsafe.govt.nz/safety/Alerts/comirnaty-myocarditis-reminder.htm#references.

- Boehmer TK, Kompaniyets L, Lavery AM, et al. Association Between COVID-19 and Myocarditis Using Hospital-Based Administrative Data — United States, March 2020–January 2021. MMWR Morb Mortal Wkly Rep 2 021;70:1228–1232. DOI:
- Barda N, Dagan,N, Ben-Shlomo Y et al Safety of the BNT162b2 mRNA Covid-19 vaccine in a nationwide setting Aug 25 2021 N Eng J med 385:1078-1090 DOI: 10.1056/NEJMoa2110475

The study quoted above is a large population study from Israel. It is important to note that the study excluded people who had received the COVID-19 vaccine and uses data up to early 2021.

The study compared the rate of myocarditis or pericarditis in those with a positive SARS-CoV-2 PCR test to the rate in those without a positive SARS-CoV-2 PCR test. The overall rate of reported myocarditis was low with a rate of approximately 0.0046% and 0.0056% (or 46 cases per 1,000,000 and 56 cases per 1,000,000) for COVID-19 and non-COVID-19 cases respectively. Again, it is important to note that results obtained in the study excluded data from vaccinated people.

Furthermore, the study has a number of sources of potential bias. Most notably, they did not include information about myocarditis or pericarditis that was recorded between 0 and 10 days after a positive SARS-CoV-2 test. This has the potential to miss myocarditis or pericarditis cases in those with COVID-19 and would artificially lower the rate in those with COVID-19. Unfortunately, the authors do not report information that would allow us to assess how many cases this analysis has missed, and the extent of bias caused.

It is best practice not to rely on the results of a single study, and to assess the potential for bias in each study. Systematic reviews can be useful in this regard. Several systematic reviews are available looking at the risk of myocarditis or pericarditis after COVID-19 vaccination and after SARS-CoV-2 infection. Two examples are available here:

- Cardiovascular safety of COVID-19 vaccines in real-world studies: a systematic review and meta-analysis. Details can be found here: www.tandfonline.com/doi/full/10.1080/14760584.2023.2150169.
- Myocarditis in SARS-CoV-2 infection vs. COVID-19 vaccination: A systematic review and meta-analysis. Details can be found here: www.frontiersin.org/articles/10.3389/fcvm.2022.951314/full.

Both of the systemic reviews mentioned above conclude there is a higher risk of cardiovascular events after infection than after vaccination.

Table One: Data collated from the *Cardiovascular safety of COVID-19 vaccines in real-world studies: a systematic review and meta-analysis study*

Table S5. Incidence of cardiovascular events of unvaccinated, vaccinated and SARS-CoV-2 infection.

	Studies, No.	Incidence rate (95% confidence interval), per million or per 10,000 persons	Heterogeneity, I^2
Myocarditis		per million persons	
unvaccinated	6	11.55(5.59–17.52)	99.2%
vaccinated	29	14.80(12.96–16.65)	99.6%
SARS-CoV-2 infection	2	107.88(61.80–153.96)	48.7%
Myocardial infarction		per 10,000 persons	
unvaccinated	2	2.13(-0.73–4.99)	99.8%
vaccinated	11	1.73(1.63–1.82)	100.0%
SARS-CoV-2 infection	2	9.81(-3.52–23.23)	99.9%
Arrhythmia		per 10,000 persons	
unvaccinated	3	2.52(-0.73–5.77)	99.4%
vaccinated	4	9.62(-4.31–23.55)	100.0%
SARS-CoV-2 infection	1	20.21(18.07–22.35)	0.0%

The following documents have been identified as pertinent to your request for internal/external advice regarding myocarditis and COVID-19 vaccines.

- Booster doses after myocarditis/pericarditis: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations available here: www.health.govt.nz/system/files/documents/pages/cv_tag_boosters_after_myocarditis_and_pericarditis.pdf.

- Myocarditis following vaccination: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations on the use of the Pfizer vaccine available here: www.health.govt.nz/system/files/documents/pages/20210721_-_cv_tag_myocarditis_following_vaccination.pdf.

Memos produced by Manatū Hauora related to COVID-19 are also publicly available online here: www.health.govt.nz/about-ministry/leadership-ministry/expert-groups/covid-19-vaccine-technical-advisory-group-cv-tag.

I trust this information fulfils your request. 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

Dr Andrew Old
Deputy Director-General
Public Health Agency | Te Pou Hauora Tūmatanui

Appendix 1: List of documents for release

#	Date	Document details	Decision on release
1	2 June 2021	Vaccine Associated Myocarditis – Myocarditis after COVID-19 Vaccination	Released in full.
2	29 June 2021	Minutes: COVID-19 Vaccine Technical Advisory Group	Excerpt released under section 16(1)(e) of the Act. Some information withheld under the following sections of the Act: • Section 9(2)(g)(ii) to maintain the effective conduct of public affairs through the protection of Ministers, members of organisations, officers, and employees from improper pressure or harassment, and • Section 9(2)(k) to prevent the disclosure or use of official information for improper gain or advantage.
3	6 July 2021	Minutes: COVID-19 Vaccine Technical Advisory Group	
4	13 July 2021	Minutes: COVID-19 Vaccine Technical Advisory Group	
5	20 July 2021	Minutes: COVID-19 Vaccine Technical Advisory Group	
6	26 July 2021	Request for Advice (RfA) – Myocarditis update for CV TAG	Some information withheld under section 9(2)(g)(ii) of the Act.
7	27 July 2021	Minutes: COVID-19 Vaccine Technical Advisory Group	Excerpt released under section 16(1)(e) of the Act. Some information withheld under the following sections of the Act: • Section 9(2)(g)(ii), and • Section 9(2)(k).
8	19 October 2021	Request for Advice (RfA) – Update on Myocarditis following COVID-19 Vaccination	Some information withheld under section 9(2)(g)(ii) of the Act.
9	19 October 2021	Minutes: COVID-19 Vaccine Technical Advisory Group	Excerpt released under section 16(1)(e) of the Act. Some information withheld under the following sections of the Act:

#	Date	Document details	Decision on release
			• Section 9(2)(g)(ii), and • Section 9(2)(k).
10	20 January 2022	Minutes: COVID-19 Vaccine Technical Advisory Group	
11	8 March 2022	Request for Advice (RfA) – Myocarditis risk with boosters	Some information withheld under section 9(2)(g)(ii) of the Act.
12	8 March 2022	Minutes: COVID-19 Vaccine Technical Advisory Group	Excerpt released under section 16(1)(e) of the Act. Some information withheld under the following sections of the Act: • Section 9(2)(g)(ii), and • Section 9(2)(k).
13	13 September 2022	Minutes: COVID-19 Vaccine Technical Advisory Group	
14	6 December 2022	Minutes: COVID-19 Vaccine Technical Advisory Group	

Myocarditis after COVID-19 Vaccination

Executive Summary

1. There have been reports of myocarditis reported after vaccination using Pfizer (Comirnaty) but these reports are primarily case reports and reports from the media.
2. The reported cases of myocarditis after vaccination usually resolve spontaneously.
3. There is no "signal" for myocarditis because at this time, there is no evidence that these events are more common after vaccination than would have occurred in the absence of vaccination.
4. Myocarditis has been reported after vaccination with influenza and other vaccines.
5. The rate of myocarditis after non-COVID vaccines is unknown, but is very rare and generally limited to case reports.
6. Should there be a link between myocarditis and Pfizer vaccination, this is most likely to be due to the non-specific acute inflammatory response induced by the vaccination, but may be due to vaccine-induced antibodies acting on a specific, as yet unrecognised cardiac target
7. There is no current evidence to support a pathophysiological link between myocarditis occurring as a result of acute COVID-19 infection and myocarditis occurring after vaccination.
8. The accurate identification of the incidence of myocarditis after vaccination may be difficult to establish.

Introduction

There have been a number of reports of myocarditis occurring after COVID-19 vaccination. However, as yet there is insufficient evidence on which to determine the mechanism of this complication. The possible mechanisms can broadly be divided into the possibility that the immunisation mimics infection or vaccination induces inflammatory or immune responses which causes myocardial damage.

Myocarditis after Vaccination with BNT162b2 (Comirnaty Pfizer)

The current evidence for an association between myocarditis associated with BNT162b2 is from three main sources. These are case reports in the medical and grey literature, a media report from a leaked Health Ministry document in Israel and some media reports from vaccination of armed forces personal in the United States.

A search (MEDLINE Epub daily version May 20th, 2021) identified only one case report of myocarditis after Pfizer vaccination (16).

The leaked report from the Israel Health Ministry has reported 62 cases of myocarditis after the Pfizer vaccine, mostly after the second dose. There were 2 deaths reported in that group in a 22-

year-old woman and a 35-year-old man. The remainder were discharged well. At the time, more than 5 million individuals had been vaccinated. Pfizer has stated that there were not similar reports from other countries in which the vaccine was being used but they would examine the data.

The Pharmacovigilance Risk Assessment committee (PRAC) of the European Medicine Agency (EMA) reported in early May that it had received reports of myocarditis after the Pfizer vaccine, and reported that "There is no indication at the moment that these cases are due to the vaccine," (17).

The CDC has also stated that it has not observed any evidence to link cases of myocarditis with COVID-19 vaccination despite actively looking for a signal (1). News reports have claimed that a small number (14) of individuals in the armed forces have developed myocarditis in addition to 45 cases reported through VAERS since January.

Myocarditis after other COVID-19 vaccines

To date there have been no credible reports of myocarditis after any other vaccines.

Cardiac events after non-COVID-19 vaccination

Case reports of post-vaccination myocarditis has been reported after vaccination with influenza (2) (3), tetanus (4) and small pox (5). These events have been reported to be associated with the adjuvant used for the purpose of enhancing the immune response to the primary antigen. Autoimmune manifestations due to vaccine adjuvants has been named Autoimmune Syndrome Induced by Adjuvants (ASIA) or by the eponymous name of Shoenfield's Syndrome (6). The five cases reported after the smallpox vaccination included two young men in the armed forces with no underlying cardiac disease (5).

The Relationship between myocarditis and cardiac arrythmias.

Cardiac arrythmias are a recognised complication of myocarditis (7) but may also be caused by hypoxia, myocardial ischaemia, electrolyte imbalances, volume imbalances and drug side effects (8). A detailed review of cardiac rhythm disturbances and myocarditis is not possible in this brief review. Instead the review will concentrate on the known mechanisms whereby vaccination may cause myocarditis.

Myocarditis after COVID-19 Infection

Acute COVID-19 infection is associated with a range of cardiac complications which includes heart failure, myocardial injury and arrythmias (9). A population study of 259, 352 patients reported an incidence of myocarditis of 0.01% after SARS-CoV-2 infection (10). In addition, a case-controlled study of individuals with mild COVID-19 compared to individuals without COVID-19 did not demonstrate myocardial dysfunction at 6 months after infection using detailed cardiovascular magnetic resonance and biomarkers.

There have been multiple proposed mechanisms responsible for the cardiac manifestations of acute COVID-19. Many of these mechanisms are the result of severe sepsis, but direct cardiotoxicity has also been demonstrated to occur (11). Viral myocarditis is a well-recognised complication of many infectious agents including poliomyelitis (12), mumps (13), measles (14) and Coxsackievirus (15). 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.

Diagnosis of Myocarditis

Myocarditis is defined as inflammation of the myocardium that is not due 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 (11).

A diagnosis of myocarditis may be prompted 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 associate 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 (16).

The gold standard for the diagnosis of myocarditis is by histologic examination of the heart which is seldom undertaken in living patients. Cardiovascular magnetic resonance (CMR) is the gold standard non-invasive method for assessing myocardial inflammation (17). Criteria for the non-invasive diagnosis of non-ischaemic cardiomyopathy ("Lake Louise Criteria") have been published (18).

These criteria propose 3 diagnostic targets 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%) (19).

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.

Relationship between COVID-19 infection and Vaccination

COVID-19 vaccination is not a "mild case" of COVID-19 infection although the similarity of the vaccine and the disease will depend upon the type of vaccine used. Whereas the original vaccinations for smallpox used a small inoculum of the natural virus to provide immunity, the mRNA vaccines introduce a small segment of RNA which codes for a specific viral protein.

Apart from vaccination and COVID-19 both producing an acute inflammatory response, the vaccination will also produce antibodies against the spike protein of SARS-CoV-2. There is no evidence that the antibody has a functional cardiac target, i.e. acts as an autoantibody, although this is a possibility. In addition, as the spike protein can bind to the ACE2 receptor, it is possible that binding of the spike protein could induce downregulation of the ACE2 receptor, causing imbalance of the renin-angiotensin system and diminishing the protective and anti-inflammatory effects of angiotensin. However, if the vaccine produces a limited amount of spike protein in the peripheral circulation the ability to induce ACE2 downregulation is likely to be very limited.

UPDATE: 2 June 2021

Israel Cases

The Israel Health Ministry reported that 275 cases of myocarditis have been reported in mostly young men after Pfizer vaccination. Most cases spent no more than 4 days in hospital. Current information remains limited to multiple media reports. The report does not appear to be available on the Ministry of Health Website.

Diagnosis of Myocarditis

A recent report assessed the risk of myocarditis after COID-19 infection in competitive athletes diagnosed by symptomatology and cardiac MRI (20). In this report which involved 1597 athletes with COVID-19 infection, the prevalence of myocarditis based on symptom-based screening was 0.31% but increased to 2.3% after screening using cardiac MRI. Persistence of MRI abnormalities for more than 3 months occurred in approximately one half of the athletes. The implication is that the rate of identification of myocarditis will depend heavily upon the methods used for diagnosis and this factor must be taken into account when attempting to compare rates after vaccination with background rates. In addition, the possibility of myocarditis occurring after SARS-CoV-2 infection, unrelated to the vaccination should also be considered.

Further assessment of possible mechanisms of vaccine induced complications

A report (pre-print) has reported that in vector-based vaccines, transcription of wildtype and codon-optimised Spike open reading frames enables alternative splice events that lead to C-terminal truncated, soluble Spike protein variants. These soluble variants may initiate severe side effects by binding to the ACE-2 expressing endothelial cells and cause complications in a similar manner to the SARS-CoV-2 virus. Although this mechanism has not been identified for mRNA vaccines, the possibility of spike protein-induced complications remain a possibility.

References

1. Shimabukuro T. COVID-19 vaccine safety update, Advisory Committee on Immunization Practices (ACIP), March 1, 2021: CDC; 2021 [Available from: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-02/28-03-01/05-covid-Shimabukuro.pdf.
2. Cheng MP, Kozoriz MG, Ahmadi AA, Kelsall J, Paquette K, Onrot JM. Post-vaccination myositis and myocarditis in a previously healthy male. Allergy Asthma Clin Immunol. 2016;12:6-.
3. Kim Y-J, Bae J-I, Ryoo SM, Kim WY. Acute Fulminant Myocarditis Following Influenza Vaccination Requiring Extracorporeal Membrane Oxygenation. Acute Crit Care. 2019;34(2):165-9.
4. Dilber E, Karagöz T, Aytemir K, Özer S, Alehan D, Oto A, et al. Acute Myocarditis Associated With Tetanus Vaccination. Mayo Clinic Proceedings. 2003;78(11):1431-3.
5. Roos R. Link between smallpox vaccine and myocarditis looks more likely 2003 [updated Mar 27, 2003. Available from: https://www.cidrap.umn.edu/news-perspective/2003/03/link-between-smallpox-vaccine-and-myocarditis-looks-more-likely.
6. Perricone C, Colafrancesco S, Mazor RD, Soriano A, Agmon-Levin N, Shoenfeld Y. Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) 2013: Unveiling the pathogenic, clinical and diagnostic aspects. Journal of Autoimmunity. 2013;47:1-16.
7. Peretto G, Sala S, Rizzo S, De Luca G, Campochiaro C, Sartorelli S, et al. Arrhythmias in myocarditis: State of the art. Heart Rhythm. 2019;16(5):793-801.

8. Dherange P, Lang J, Qian P, Oberfeld B, Sauer WH, Koplan B, et al. Arrhythmias and COVID-19: A Review. JACC Clinical electrophysiology. 2020;6(9):1193-204.
9. Kunutsor SK, Laukkanen JA. Cardiovascular complications in COVID-19: A systematic review and meta-analysis. Journal of Infection. 2020;81(2):e139-e41.
10. F. Annie HA, A. Nanjundappa, A. Elashery. Association Between Myocarditis and Mortality in SARS-CoV-2 Patients in a Large Registry. The Lancet. 2021.
11. Knowlton KU. Pathogenesis of SARS-CoV-2 induced cardiac injury from the perspective of the virus. Journal of molecular and cellular cardiology. 2020;147:12-7.
12. Spain DM, Bradess VA, Parsonnet V. Myocarditis in poliomyelitis. Am Heart J. 1950;40(3):336-44.
13. Bengtsson E, ÖRndahl G. Complications of Mumps with Special Reference to the Incidence of Myocarditis. Acta Medica Scandinavica. 2009;149:381-8.
14. Lucke B. Postmortem findings in measles-bronchopneumonia and other acute infections. Journal of the American Medical Association. 1918;70(26):2006-11.
15. Dalldorf G. The Coxsackie Viruses. Annual Review of Microbiology. 1955;9(1):277-96.
16. Howlett JG, McKelvie RS, Arnold JM, Costigan J, Dorian P, Ducharme A, et al. Canadian Cardiovascular Society Consensus Conference guidelines on heart failure, update 2009: diagnosis and management of right-sided heart failure, myocarditis, device therapy and recent important clinical trials. Can J Cardiol. 2009;25(2):85-105.
17. Catapano F, Marchitelli L, Cundari G, Cilia F, Mancuso G, Pambianchi G, et al. Role of advanced imaging in COVID-19 cardiovascular complications. Insights into Imaging. 2021;12(1).
18. Ferreira VM, Schulz-Menger J, Holmvang G, Kramer CM, Carbone I, Sechtem U, et al. Cardiovascular Magnetic Resonance in Nonischemic Myocardial Inflammation: Expert Recommendations. J Am Coll Cardiol. 2018;72(24):3158-76.
19. Ferreira VM, Schulz-Menger J, Holmvang G, Kramer CM, Carbone I, Sechtem U, et al. Cardiovascular Magnetic Resonance in Nonischemic Myocardial Inflammation. J Am Coll Cardiol. 2018;72(24):3158-76.
20. Daniels CJ, Rajpal S, Greenshields JT, Rosenthal GL, Chung EH, Terrin M, et al. Prevalence of Clinical and Subclinical Myocarditis in Competitive Athletes With Recent SARS-CoV-2 Infection: Results From the Big Ten COVID-19 Cardiac Registry. JAMA Cardiology. 2021.

Document 2

MINUTES: COVID-19 Vaccine Technical Advisory Group

Date:	Tuesday 29 June 2021
Time:	11:00am to 12:00pm
Location:	Teams: s 9(2)(k) [redacted]
Chair:	Ian Town
Members:	Andi Shirtcliffe, David Murdoch, Edwin Reynolds, Elizabeth Wilson, Helen Petousis-Harris, Ian Frazer, James Ussher, Nikki Moreland, Nikki Turner, Peter McIntyre, Pippa Scott, Sean Hanna, Sue Crengle, Tony Walls
Ministry of Health Attendees:	s 9(2)(g)(ii) [redacted]
Guests:	
Apologies:	

2.0	**Myocarditis after Pfizer Vaccination** • Advice on the Decision to Use Pfizer for 12-15-year-olds was issued to Cabinet, however a decision has been deferred pending advice from CV TAG on myocarditis. • The FDA have added a warning for myocarditis and pericarditis to the Pfizer and Moderna vaccine data sheets, after observing a series of cases following vaccination. It is seen most predominantly in adolescent and young adults, particularly males aged <30 years, and after the second dose. CV TAG discussed the current evidence and risks. Key points of discussion: • The University of Auckland is leading a project estimating background rates of adverse events in New Zealand, including myocarditis, and is expected to report findings within the next 7-10 days. Data on the ethnic breakdown of cases was requested to be included. • CV TAG noted concern about the potential risk of myocarditis has grown and a sense of urgency to develop options, e.g., for alternative vaccine schedules, and advice.

- While evidence is still emerging, IMAC clinicians are already fielding requests on myocarditis. It was noted that because the issue is relatively rare, the true risk may not be known for some time until the vaccine rollout internationally has progressed further.
- There is a need to communicate safety information to inform the public and present a balanced assessment of the risk and benefits. Science communicators who can appeal to a range of different ethnicities will be important.
- Further information is needed on vaccine hesitancy among young adults and men <30 and how this may be impacted by a potential safety signal, to inform how the commentary would be managed.
- Possible options raised by CV TAG included:
    - Considering using only a single dose among people who are at higher risk (e.g. young males <30, people with a history of myocarditis) until further evidence is available. It was noted that Israel is actively considering this option.
    - Heterologous vaccine schedules (e.g., offering Janssen or another vaccine – when available - as a second dose).
    - Considering the ongoing use of Pfizer in young males <30 until further evidence emerges. It was noted that many within this population would have been captured under groups 1-3. Data on the numbers in each of these groups, as well as when they are expected to be vaccinated, is needed from CVIP.

It was agreed that a subgroup would be convened to draft advice which will be presented to the CV TAG next week (06 July) to inform recommendations around using the Pfizer vaccine in younger people.

Document 3

MINUTES: COVID-19 Vaccine Technical Advisory Group

Date:	Tuesday 06 July 2021
Time:	11:00am to 12:00pm
Location:	Teams: s 9(2)(k) [redacted]
Chair:	Ian Town
Members:	David Murdoch, Elizabeth Wilson, Helen Petousis-Harris, James Ussher, Nikki Moreland, Peter McIntyre, Pippa Scott, Tony Walls
Ministry of Health Attendees:	s 9(2)(g)(ii) [redacted]
Guests:	
Apologies:	

6.0 **Myocarditis after Pfizer Vaccination**

CV TAG discussed advice provided by the STA and a subgroup of CV TAG, on the current evidence on events of myocarditis/pericarditis post vaccination, and related questions.

Key points:

- Previous studies of US military personnel, that evaluated the risk of myocarditis following the smallpox vaccine, indicated that myocarditis was a potential safety issue, with cases usually occurring within a few days of vaccination.
- Events of myocarditis tend to be associated with the second dose of mRNA COVID-19 vaccines, although some cases occur after the first dose. The rate of myocarditis tends to be higher in males and younger age groups, particularly in males aged 16-30.
- There is limited information, to date, on the long-term outcomes and severity of myocarditis following vaccination. 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.
- Overall, emerging evidence suggests that myocarditis is a largely self-limiting and rare event following mRNA vaccination, with the rate for Pfizer in the US being approximately 0.8 per 100,000 in 12-39 year-olds within 21 days following the second dose.
- CV TAG discussed possibility of alternative vaccination schedules that might mitigate the risk in younger age groups. However, any change in dosing schedule will require Medsafe approval.
- CV TAG discussed potential recommendations, including advice for those with rheumatic heart disease, those with a previous history of myocarditis, or those who develop myocarditis following the first dose.

A subgroup of the CVTAG will meet 08 July to draft recommendations. The recommendations will be finalised by the end of week and discussed at the next CV TAG full meeting.

Document 4

MINUTES: COVID-19 Vaccine Technical Advisory Group

Date:	Tuesday 13 July 2021
Time:	11:00am to 12:00pm
Location:	Teams: s 9(2)(k) [redacted]
Chair:	Ian Town
Members:	David Murdoch, Elizabeth Wilson, Helen Petousis-Harris, James Ussher, Nikki Moreland, Peter McIntyre, Pippa Scott, Sue Crengle,
Ministry of Health Attendees:	s 9(2)(g)(ii) [redacted]
Guests:	
Apologies:	

4.0	**Myocarditis Recommendations** • Draft recommendations on the risk of myocarditis after mRNA vaccination were presented to CV TAG. • It was noted that, this is a developing issue, and there are still several uncertainties in the data. • Based on preliminary US data, the risk of myocarditis after Pfizer vaccination is approximately 1 in 25,000 for males 12-29 years, and 1 in 240,000 for females 12-29 years. For individuals 30 and over, the corresponding risks decrease to approximately 1 in 400,000 for males, and 1 in a million for females. While the risk for females is lower than for males, it is still greater for younger people, and therefore any recommendation should be applied to all people aged under 30.

- The New Zealand context of having no community transmission is important to consider, as the risk of COVID-19 is currently low and this effects the benefit:risk assessment.
- CV TAG noted that cardiac-related events after vaccination are being reported to CARM, and the Independent Safety Monitoring Board (ISMB) is reviewing reported cases.
- Emerging evidence suggests one dose of the vaccine appears to be highly immunogenic, and provides greater protection in younger compared to older age groups, and therefore may provide sufficient protection in the interim, until further evidence emerges on second dose options.
- CV TAG progressed to summarise an initial draft of the approach:
    - The second dose of Pfizer vaccination could be deferred in individuals aged 29 years and under until further information is available about the risk, long-term outcomes of myocarditis and/or pericarditis, and protection offered by one dose for this age group.
    - People 29 years of age and younger who require regular clinical review by a cardiologist are advised to discuss the risks and benefits of the first dose of COVID-19 vaccine for their specific situation with their healthcare team.
    - People aged 30 years and over should still receive two doses of the vaccine, 21 days apart as the risk of myocarditis and/or pericarditis post vaccination is less than 1 in 400,000 and risks of severe disease and sequelae due to COVID-19, including myocarditis, are substantially higher in this age group compared to people aged 29 years and under.
    - Anyone who develops confirmed myocarditis and/or pericarditis after the first dose should not receive a second dose of the Pfizer COVID-19 vaccine. CV TAG will consider alternative options for a second dose of COVID-19 vaccination in this group at a future date as evidence emerges from overseas safety monitoring.
    - CV TAG will continue to monitor all relevant effectiveness and safety data closely and advise on the need and options for the second dose for individuals aged 29 years and under at a future date. Options for the second dose may include: 1) proceeding with the second dose of the Pfizer COVID-19 vaccine after a longer interval between doses; 2) not administering a second dose; 3) administering a second dose of an alternative COVID-19 vaccine.
- A memo with these recommendations is being prepared and will be shared with CV TAG for feedback. Public-facing communications will be drafted for CVIP Communications. Options will need to remain agile as further evidence emerges.
- Cardiac-related events associated with alternative vaccine schedules will be explored by the Science and Technical Advisory team, as will the use of other options.
- Given that vaccinating the whānau together is a key approach for delivering the vaccine to Māori, further discussion will be needed on the equity implications of these recommendations.
- The Director-General will need to be consulted about the options and the CVIP team will need to consider the implications for the programme.

Document 5

MINUTES: COVID-19 Vaccine Technical Advisory Group

Date:	Tuesday 20 July 2021
Time:	11:00am to 12:00pm
Location:	Teams: s 9(2)(k) [redacted]
Chair:	Ian Town
Members:	David Murdoch, Elizabeth Wilson, Ian Frazer, Nikki Turner, Peter McIntyre, Pippa Scott, Sean Hanna, Sue Crengle, Tony Walls
Ministry of Health Attendees:	s 9(2)(g)(ii) [redacted]
Guests:	
Apologies:	

5.0	**Myocarditis Recommendations Update**

- A Medsafe alert on myocarditis will be published later this week. The draft communication was shared with CV TAG, and feedback will be collated by the Secretariat to share back to Medsafe.
- CV TAG discussed the background rates of myocarditis, and rates post-Pfizer vaccination, internationally and in Aotearoa New Zealand.
    - It was agreed that the US rates provided the best available baseline for comparisons with Aotearoa New Zealand.
    - The US data is broken down further by gender, age group and follow-up time, and notes a risk of 1 in 25,000 for males aged 12-29 within 7 days of the second dose, and 1 in 238,000 for females aged 12-29 within 7 days of the second dose, for mRNA vaccines.
    - Severity measures should also be incorporated into the presentation of the data, for example hospitalisation and/or ICU admission rates, if data are available.
- Draft recommendations on the risk of myocarditis after Pfizer vaccination were discussed.
    - CV TAG noted that there is some evidence that young people aged 16 to 29 years have a strong immune response after one dose, however that two doses provide the best protection. A delayed schedule for the second dose was discussed. Whether this potentially reduces the risk of myocarditis, in addition to the severity of other adverse events, is unknown.
    - CV TAG recommended that for people aged 16 to 29 years the second dose be administered at least 8 weeks after the first.
    - It was noted that this would have practical implications for the booking system, planning mass vaccination events, and public risk communications.
- A memo with these recommendations will be updated and provided to the Director-General and CVIP.

Document 6

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.

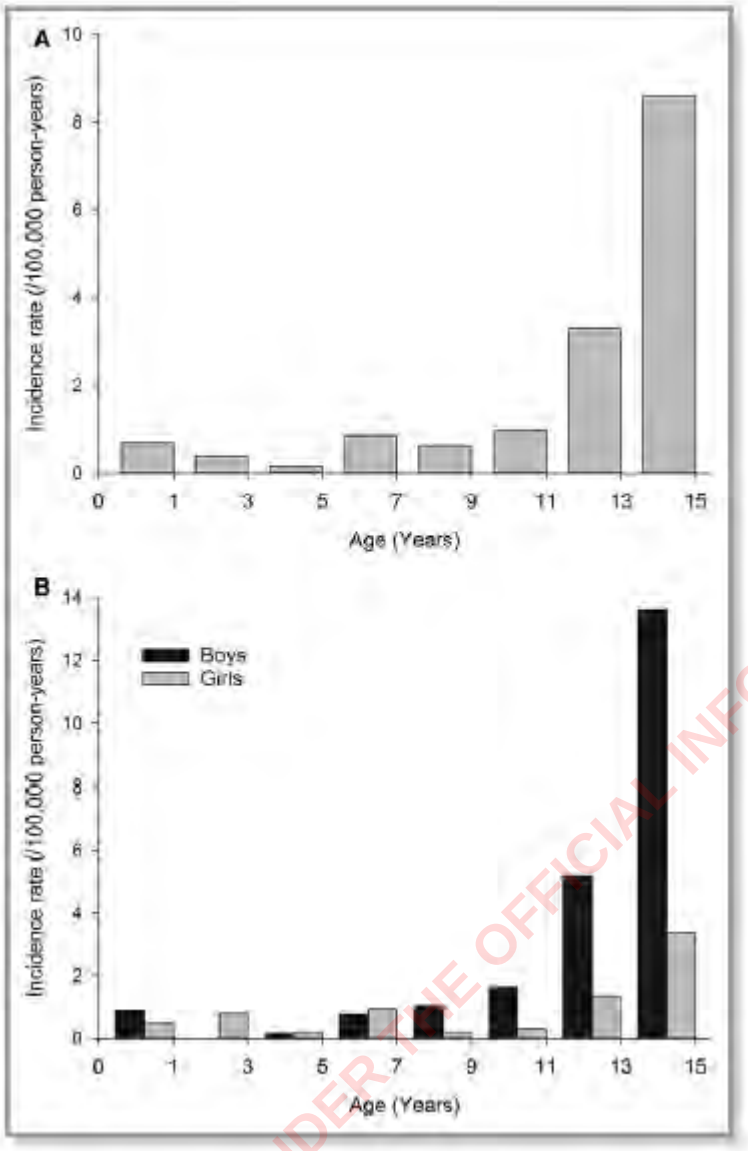

Figure 1 Age-specific Incidence rates of myocarditis in children aged 15 years or younger in Finland, overall and by sex (per 100,000 person-years) (Arola et al, 2017)

- 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*

Age groups	Females			Male		
	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)

Age groups	Females			Males		
	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 available 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/

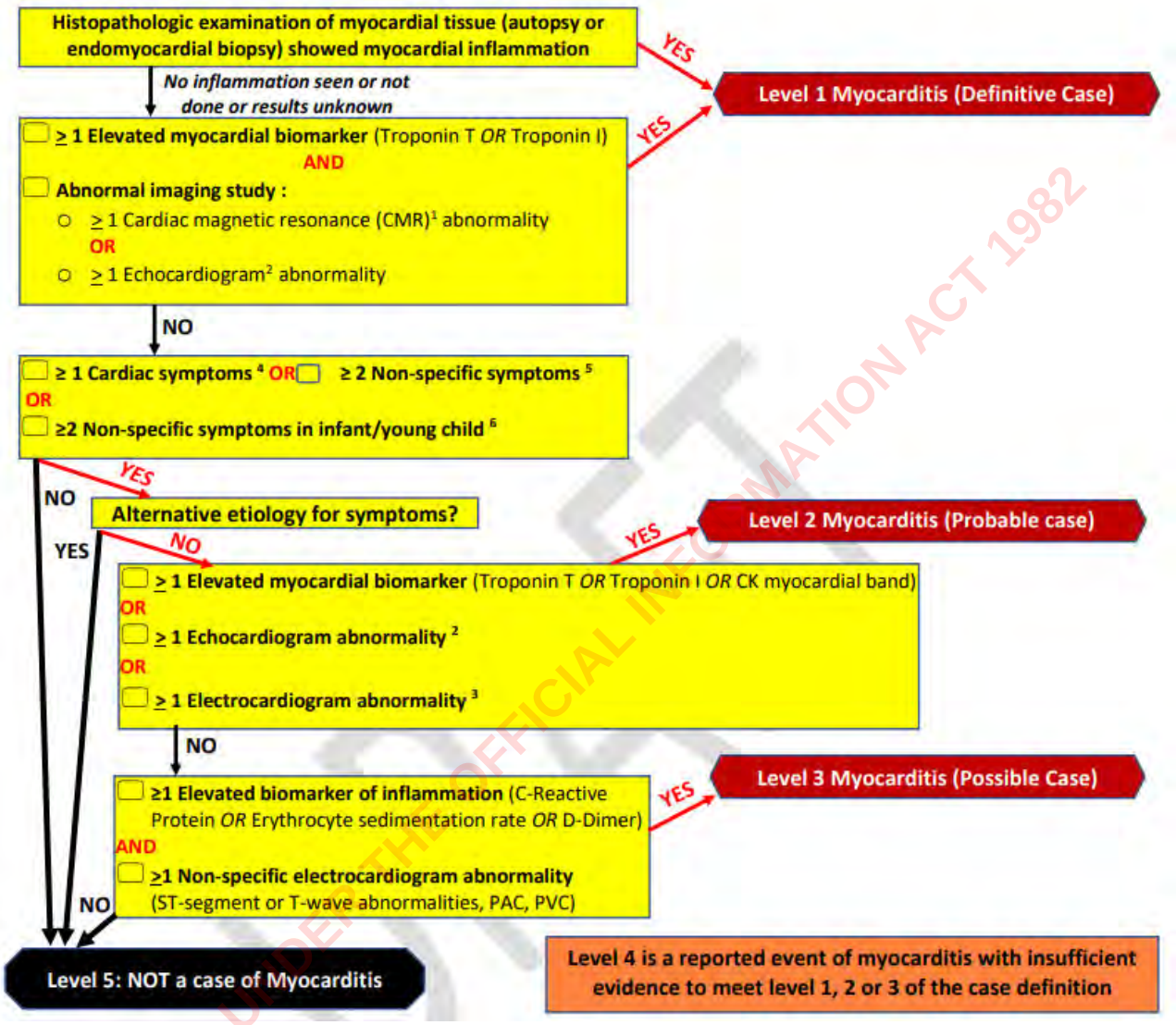

Figure 2 Brighton Collaboration draft case definition for myocarditis, as of 30 May 2021

- 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, which 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	

References

1. FDA, *FACT SHEET FOR HEALTHCARE PROVIDERS ADMINISTERING VACCINE (VACCINATION PROVIDERS)*, in *EMERGENCY USE AUTHORIZATION (EUA) OF THE PFIZER-BIONTECH COVID-19*

VACCINE TO PREVENT CORONAVIRUS DISEASE 2019 (COVID-19), FDA, Editor. 2021, United States Food and Drug Adminstration: fda.gov. p. 41.

2. Centers for Disease Control and Prevention (CDC). *Assessment June 23*. COVID-19 Vaccine Safety Technical Work Group 2021; Available from: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/04-COVID-Lee-508.pdf.
3. Centers for Disease Control and Prevention (CDC). *Update on COVID-19 vaccine safety, including myocarditis after mRNA*. ACIP Presentation Slides 23 June - Coronavirus Disease 2019 (COVID-19) Vaccines 2021; Available from: https://www.cdc.gov/vaccines/acip/meetings/slides-2021-06.html.
4. Belay, E.D., et al., *Trends in Geographic and Temporal Distribution of US Children With Multisystem Inflammatory Syndrome During the COVID-19 Pandemic.* JAMA Pediatrics, 2021.
5. Feldstein, L.R., et al., *Characteristics and Outcomes of US Children and Adolescents With Multisystem Inflammatory Syndrome in Children (MIS-C) Compared With Severe Acute COVID-19.* JAMA, 2021. **325**(11): p. 1074-1087.
6. Payne, R., Longet S, Austin JA, et al., *Sustained T cell immunity, protection and boosting using extended dosing intervals of BNT162b2 mRNA vaccine.* PITCH REGIMEN study preprint, 2021. **1**(1): p. 22.
7. Gubernot, D., et al., *U.S. Population-Based background incidence rates of medical conditions for use in safety assessment of COVID-19 vaccines.* Vaccine, 2021. **39**(28): p. 3666-3677.
8. Petousis-Harris, H., *Background rates of myocarditis in New Zealand DRAFT*. 2021. p. 1.
9. ACCESS, *vaCCine covid-19 monitoring readinESS (ACCESS): Background rates of Adverse Events of Special Interest for monitoring COVID-19 vaccines*, in *D3-Draft Final Report*. 2021. p. 94.
10. Arola, A., et al., *Occurrence and Features of Childhood Myocarditis: A Nationwide Study in Finland.* Journal of the American Heart Association. **6**(11): p. e005306.
11. Gargano JW, W.M., Hadler SC, et al., *Use of mRNA COVID-19 Vaccine After Reports of Myocarditis Among Vaccine Recipients: Update from the Advisory Committee on Immunization Practices — United States, June 2021.* MMWR Morb Mortal Wkly Rep, 2021. **70**(27): p. 977–982.
12. Shimabukuro, T., *COVID-19 Vaccine safety updates*, in *COVID-19 Vaccine safety updates*, V.S. Team, Editor. 2021, Advisory Committee on Immunization Practices (ACIP) CDC COVID-19 Vaccine Task Force: https://www.cdc.gov/vaccines/acip/meetings/slides-2021-06.html. p. 51.
13. Bozkurt, B., I. Kamat, and P.J. Hotez, *Myocarditis with COVID-19 mRNA Vaccines.* Circulation, 2021.
14. Israel, M.o.H. *Surveillance of Myocarditis (Inflammation of the Heart Muscle) Cases Between December 2020 and May 2021 (Including)*. Press release 2021 02 June 2021 [cited 2021 02 July 2021]; Available from: https://www.gov.il/en/departments/news/01062021-03.
15. PRAC. *Comirnaty and Spikevax: possible link to very rare cases of myocarditis and pericarditis*. News 2021 09 July 2021 [cited 2021 12 July 2021]; Available from: https://www.ema.europa.eu/en/news/comirnaty-spikevax-possible-link-very-rare-cases-myocarditis-pericarditis.
16. Administration, T.G. *COVID-19 vaccine weekly safety report - 08-07-2021*. COVID-19 vaccine safety monitoring and reporting [Website] 2021 08 July 2021 [cited 2021 12 July 2021]; COVID-19 vaccine weekly safety report - 08-07-2021]. Available from: https://www.tga.gov.au/periodic/covid-19-vaccine-weekly-safety-report-08-07-2021.
17. ATAGI. *ATAGI update following weekly COVID-19 meeting – 7 July 2021*. An update from the Australian Technical Advisory Group on Immunisation (ATAGI) following their weekly meeting on 7 July 2021. [Website] 2021 08 July 2021 [cited 2021 12 July 2021]; 1:[Available from: https://www.health.gov.au/news/atagi-update-following-weekly-covid-19-meeting-7-july-2021.
18. Canada, G.o. *Reported side effects following COVID-19 vaccination in Canada*. 2021 16 July 2021 [cited 2021 21 July 2021]; Available from: https://health-infobase.canada.ca/covid-19/vaccine-safety/#a3.
19. Canada, G.o. *COVID-19 vaccination in Canada*. Vaccines for COVID-19 2021 16 July 2021 [cited 2021 21 July 2021]; Available from: https://health-infobase.canada.ca/covid-19/vaccination-coverage/.

20. (GACVS), W.G.A.C.o.V.S. *COVID-19 subcommittee of the WHO Global Advisory Committee on Vaccine Safety (GACVS): updated guidance regarding myocarditis and pericarditis reported with COVID-19 mRNA vaccines*. COVID-19 subcommittee of the WHO Global Advisory Committee on Vaccine Safety (GACVS): updated guidance regarding myocarditis and pericarditis reported with COVID-19 mRNA vaccines 2021 09 July 2021 [cited 2021 12 July 2021]; Available from: https://www.who.int/news/item/09-07-2021-gacvs-guidance-myocarditis-pericarditis-covid-19-mrna-vaccines.
21. Kunutsor, S.K. and J.A. Laukkanen, *Cardiovascular complications in COVID-19: A systematic review and meta-analysis.* Journal of Infection, 2020. **81**(2): p. e139-e141.
22. F. Annie, H.A., A. Nanjundappa, A. Elashery, *Association Between Myocarditis and Mortality in SARS-CoV-2 Patients in a Large Registry.* The Lancet, 2021.
23. Hurwitz, B. and O. Issa, *Management and Treatment of Myocarditis in Athletes.* Current Treatment Options in Cardiovascular Medicine, 2020. **22**(12): p. 65.
24. Daniels, C.J., et al., *Prevalence of Clinical and Subclinical Myocarditis in Competitive Athletes With Recent SARS-CoV-2 Infection: Results From the Big Ten COVID-19 Cardiac Registry.* JAMA Cardiology, 2021.
25. Knowlton, K.U., *Pathogenesis of SARS-CoV-2 induced cardiac injury from the perspective of the virus.* Journal of molecular and cellular cardiology, 2020. **147**: p. 12-17.
26. Spain, D.M., V.A. Bradess, and V. Parsonnet, *Myocarditis in poliomyelitis.* Am Heart J, 1950. **40**(3): p. 336-44.
27. Bengtsson, E. and G. ÖRndahl, *Complications of Mumps with Special Reference to the Incidence of Myocarditis.* Acta Medica Scandinavica, 2009. **149**: p. 381-388.
28. Lucke, B., *Postmortem findings in measles-bronchopneumonia and other acute infections.* Journal of the American Medical Association, 1918. **70**(26): p. 2006-2011.
29. Dalldorf, G., *The Coxsackie Viruses.* Annual Review of Microbiology, 1955. **9**(1): p. 277-296.
30. Howlett, J.G., et al., *Canadian Cardiovascular Society Consensus Conference guidelines on heart failure, update 2009: diagnosis and management of right-sided heart failure, myocarditis, device therapy and recent important clinical trials.* Can J Cardiol, 2009. **25**(2): p. 85-105.
31. Ferreira, V.M., et al., *Cardiovascular Magnetic Resonance in Nonischemic Myocardial Inflammation: Expert Recommendations.* J Am Coll Cardiol, 2018. **72**(24): p. 3158-3176.
32. Waitangi Tribunal, *Hauora : Report on Stage One of the Health Services and Outcomes Kaupapa Inquiry* 2019, Legislation Direct: Lower Hutt, New Zealand.
33. Curtis, E., et al., *Why cultural safety rather than cultural competency is required to achieve health equity: a literature review and recommended definition.* International Journal for Equity in Health, 2019. **18**(1): p. 174.
34. Rhiannon Walker, *Understanding how immunisation health services can achieve equity for Māori whānau in Aotearoa*. 2019, Auckland University: Auckland, New Zealand.
35. Liu, X., et al., *Safety and Immunogenicity Report from the Com-COV Study – a Single-Blind Randomised Non-Inferiority Trial Comparing Heterologous And Homologous Prime-Boost Schedules with An Adenoviral Vectored and mRNA COVID-19 Vaccine.* SSRN, 2021.
36. Borobia, A.M., et al., *Reactogenicity and Immunogenicity of BNT162b2 in Subjects Having Received a First Dose of ChAdOx1s: Initial Results of a Randomised, Adaptive, Phase 2 Trial (CombiVacS). .* SSRN, 2021.
37. Schmidt, T., et al., *Immunogenicity and reactogenicity of a heterologous COVID-19 prime-boost vaccination compared with homologous vaccine regimens.* medRxiv, 2021: p. 2021.06.13.21258859.
38. Hillus, D., et al., *Safety, reactogenicity, and immunogenicity of homologous and heterologous prime-boost immunisation with ChAdOx1-nCoV19 and BNT162b2: a prospective cohort study.* medRxiv, 2021: p. 2021.05.19.21257334.
39. Ministry of Health. *Enrolment in a primary health organisation*. 2021 12 February 2021 16 February 2021]; Available from: https://www.health.govt.nz/our-work/primary-health-care/about-primary-health-organisations/enrolment-primary-health-organisation.

40. Irurzun-Lopez, M., M. Jeffreys, and J. Cumming, *The enrolment gap: who is not enrolling with primary health organizations in Aotearoa New Zealand and what are the implications? An exploration of 2015-2019 administrative data*. 2020.
41. Wehipeihana, N., et al., *More than just a jab: Evaluation of the Māori influenza vaccination programme as part of the COVID-19 Māori health response.* 2020, Ministry of Health: Wellington.
42. Ministry of Health. *National and DHB immunisation data*. 2021 27 January 2021; Available from: https://www.health.govt.nz/our-work/preventative-health-wellness/immunisation/immunisation-coverage/national-and-dhb-immunisation-data.
43. Allen & Clark, *Improving New Zealand's childhood immunisation rates: Evidence review.* 2019: Wellington.
44. Cram, F., *Mahi aroha: Māori work in times of trouble and disaster as an expression of a love for the people.* Kōtuitui: New Zealand Journal of Social Sciences Online, 2021: p. 1-15.
45. McMeeking, S., H. Leahy, and C. Savage, *An Indigenous self-determination social movement response to COVID-19.* AlterNative: An International Journal of Indigenous Peoples, 2020. **16**(4): p. 395-398.
46. Pihama, L. and M. Lipsham, *Noho Haumaru: Reflecting on Māori approaches to staying safe during Covid-19 in Aotearoa (New Zealand).* Journal of Indigenous Social Development, 2020. **9**(3): p. 92-101.
47. Charania, N.A., et al., *Exploring immunisation inequities among migrant and refugee children in New Zealand.* Human Vaccines & Immunotherapeutics, 2018. **14**(12): p. 3026-3033.

Document 7

MINUTES: COVID-19 Vaccine Technical Advisory Group

Date:	Tuesday 27 July 2021
Time:	11:00am to 12:00pm
Location:	Teams: s 9(2)(k) [redacted]
Chair:	Ian Town
Members:	Elizabeth Wilson, James Ussher, Nikki Moreland, Nikki Turner, Peter McIntyre, Sue Crengle, Tony Walls
Ministry of Health Attendees:	s 9(2)(g)(ii) [redacted]
Guests:	
Apologies:	

2.0	**Myocarditis Recommendations Update** The final memo on Myocarditis after Pfizer mRNA vaccination was shared with CV TAG and discussed. • The final memo included input and advice from Medsafe. • The Director-General has received the recommendations, and an implementation plan is currently being prepared within the Ministry, once the recommendations have been agreed by Ministers • CV TAG discussed the data supporting longer dosing intervals for Pfizer; Data showed higher immunogenicity was associated with an extended dosing interval (median 10 weeks) compared to the usual 3-4 weeks. • CV TAG discussed the recommended dosing interval for people under 30 years. CV TAG discussed the while an 8-week interval is recommended for this age group, administering the second dose between 6 and 12 weeks is acceptable, and that the exact timing is a programming decision. • It was agreed that all changes must communicated in a way to provide clarity.

Document 8

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	Update on Myocarditis following COVID-19 Vaccination		
Subject			
Reference No.	334	Date Received	12/10/2021
Requestor	CV TAG	Date Due	Click or tap to enter a date.
Advisor	s 9(2)(g)(ii) [redacted]	Date Completed	19/10/2021
Peer reviewed by			
Advice issued to	CV TAG		
Approved by			
Deliverables	Rapid review of recent literature		
Request Outline	**Background/Context** The Chair of CV TAG has requested a review of recent literature on myocarditis following COVID-19 vaccination. **Questions** What are the recently published international data for myocarditis? What international vaccine rollout changes have occurred due to a risk of myocarditis? **Intended application of advice** For CV TAG information **Timeline** Draft due on 18 October 21 for CV TAG review 19 October 2021 - No further changes to RfA		
What are the implications and considerations of this advice on Te Tiriti o Waitangi and equity?	Equity and Te Tiriti implications must be considered to assess who is most at risk from severe outcomes of COVID-19 vaccination side effects. To date, New Zealand safety reports have not indicated any ethnic disparities with respect to adverse events following immunisation, however, reporting rates are not consistent among different ethnic groups.		

Response to Request for Advice

Executive Summary

- This document provides a preliminary rapid review of recent literature on international myocarditis rates that was undertaken at pace.
- Data presented at the latest US Advisory Committee on Immunization Practices (ACIP) meeting on 30 August 2021 indicate that myocarditis reporting rates following mRNA COVID-19 vaccination continue to be high after the second dose, particularly in younger males aged 12-29.[1] Rates were largely similar for Pfizer and Moderna, except in the 16-17 age group, where Pfizer rates after the second dose were almost twice as high.
- Data from Israel has also shown that young males aged 16-29 are at high risk of developing myocarditis following Pfizer vaccination, particularly after the second dose.[2]
- Ontario data shows that the crude reporting rate of myocarditis/pericarditis among 18-24 year-old males following the second dose was significantly higher for Moderna than Pfizer (263.2 vs 37.4 per million doses).[3] Based on these data, Ontario is recommending only the Pfizer vaccine be used in this age group.[4]
- Sweden, Denmark, Norway, and Finland have also announced recently that they are either pausing or discouraging the use of Moderna in younger age groups due to possible increased risk of myocarditis and pericarditis.[5] Safety data from these countries is yet to be published but media reports state that the data has been submitted to the EMA for assessment.
- This RfA does not include New Zealand data, however, Medsafe has been monitoring the rate of myocarditis through data provided by CARM and international regulators. Medsafe has briefed the Independent Safety Monitoring Board (ISMB) frequently with updates on safety data, including myocarditis. A Medsafe communication published on 21 July 2021 states that myocarditis is a rare side effect of vaccination with Pfizer and that the benefits of vaccination continue to outweigh the risk of experiencing a side effect for people of all ages in the approved indication.[6] The information about myocarditis has been added to the Pfizer data sheet.

Recent international data on myocarditis

Advisory Committee on Immunization Practices (ACIP) meeting - 30 August 2021

- Centers for Disease Control and Prevention (CDC) reported that as of 18 August 2021, there were a total of 1,903 preliminary reports of myopericarditis submitted to Vaccine Adverse Event Reporting System (VAERS), see Table 1.[1]

Table 1: Preliminary myopericarditis reports to VAERS following COVID-19 vaccination by dose number (data through to 18 August 2021)[1]

Manufacturer	Reports after dose 1	Reports after dose 2	Reports after unknown dose
Pfizer-BioNTech (n=1,282)	169	922	191
Moderna (n=557)	133	339	85
Janssen (n=49)	33	1	15
Not reported (n=15)	2	9	4
Total (N=1,903)	**337**	**1,271**	**295**

* Includes total preliminary reports identified through VAERS database searches for reports with myopericarditis MedDRA* codes and pre-screened VAERS reports with signs and symptoms consistent with myopericarditis; **excludes reports of solely pericarditis**

* Follow-up, medical record review, application of CDC working case definition, and adjudication is ongoing or pending

* Medical Dictionary for Regulatory Activities https://www.meddra.org/

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- The median time to symptom onset was 3 days post first dose and 2 days post second dose of mRNA vaccines. Majority of the cases were in males (72% for first dose and 82% for second dose).[1]
- Observed reports are higher than expected, particularly after the second dose for males. For Pfizer, the highest number or reports were in males aged 12-29, and for Moderna in males aged 16-29, see Table 2.[1]
- Of the 1,339 preliminary reports in those aged ≤29 years, 742 met the case definition and 95% (701) were hospitalised. At the time of the report, 77% had recovered, while five cases were in ICU.[1]

Table 2: Reporting rates of myopericarditis (per million doses administered), by manufacturer, sex, and dose number, 7-day risk period*[1]

	Pfizer		Moderna		Janssen	Pfizer		Moderna		Janssen	Pfizer		Moderna		Janssen
	(All)		(All)		(All)	(Males)		(Males)		(Males)	(Females)		(Females)		(Females)
Ages† (yrs)	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1
12–15	2.6	20.9	0.0	not calc.	0.0	4.8	42.6	0.0	not calc.	0.0	0.5	4.3	0.0	0.0	0.0
16–17	2.5	34.0	0.0	14.6	0.0	5.2	71.5	0.0	31.2	0.0	0.0	8.1	0.0	0.0	0.0
18–24	1.1	18.5	2.7	20.2	2.7	2.4	37.1	5.1	37.7	3.0	0.0	2.6	0.7	5.3	1.6
25–29	1.0	7.2	1.7	10.3	1.9	1.8	11.1	3.2	14.9	2.0	0.3	1.3	0.4	6.3	0.0
30–39	0.8	3.4	1.0	4.2	0.4	1.1	6.8	1.6	8.0	0.0	0.6	1.0	0.4	0.7	1.0
40–49	0.4	2.8	0.5	3.2	1.2	0.7	4.4	0.6	4.6	2.2	0.1	1.8	0.4	2.1	0.0
50–64	0.2	0.5	0.6	0.8	0.2	0.2	0.5	0.4	1.0	0.0	0.3	0.8	0.8	0.7	0.5
65+	0.2	0.3	0.2	0.3	1.0	0.2	0.4	0.4	0.4	1.0	0.2	0.4	0.1	0.2	0.9

* Reports with time to symptom onset within 7 days of vaccination

† Reports among persons 12–29 years of age were verified by provider interview of medical record review

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Data from international sources

- The table below summarises selected data for myocarditis from international sources. Additional studies not included here can be found in the next section.

Country/Region, type of data	Demographic, vaccine type (follow up time)	First dose	Second dose	Source
Canada (Ontario only), Crude reporting rate for myocarditis/pericarditis	Males, 12-17 years, Pfizer vaccine (not specified)	30.4 per million doses	62.1 per million doses	Public Health Ontario report [3] (data during December 2020 to August 2021) based on reports that met the Brighton Collaboration definition.
	Males, 18-24 years, Pfizer vaccine (not specified)	24.5 per million doses	37.4 per million doses	
	Males, 25-39 years, Pfizer vaccine (not specified)	10.6 per million doses	9.5 per million doses	
	Males, all ages (12+), Pfizer vaccine (not specified)	10.3 per million doses	14.6 per million doses	
	Males, 12-17 years, Moderna vaccine (not specified)	0 per million doses	0 per million doses	
	Males, 18-24 years, Moderna vaccine (not specified)	7.8 per million doses	263.2 per million doses	
	Males, 25-39 years, Moderna vaccine (not specified)	10.2 per million doses	59.4 per million doses	
	Males, all ages (12+), Moderna vaccine (not specified)	7.1 per million doses	49.6 per million doses	
Israel, Approximate risk for myocarditis	Males, 16-19 years, Pfizer vaccine (within 21 days)	1.34 per 100,000 persons	15.07 per 100,000 persons	Mevorach et al. [2] based on cardiologist assessment of cases using the Brighton Collaboration definition.
	Males, 20-24 years, Pfizer vaccine (within 21 days)	1.91 per 100,000 persons	10.86 per 100,000 persons	
	Males, 25-29 years, Pfizer vaccine (within 21 days)	1.22 per 100,000 persons	6.99 per 100,000 persons	
	Males, all ages (16+), Pfizer vaccine (within 21 days)	0.64 per 100,000 persons	3.83 per 100,000 persons	

	Females, 16-19 years, Pfizer vaccine (within 21 days)	0 per 100,000 persons	1 per 100,000 persons	
	Females, 20-24 years, Pfizer vaccine (within 21 days)	0 per 100,000 persons	2.16 per 100,000 persons	
	Females, 25-29 years, Pfizer vaccine (within 21 days)	0 per 100,000 persons	0 per 100,000 persons	
	Females, all ages (16+), Pfizer vaccine (within 21 days)	0.07 per 100,000 persons	0.46 per 100,000 persons	
	Males, 16-29 years, Pfizer vaccine (within 42 days)	10.69 per 100,000 persons	No data	Witberg et al. [7] based on cardiologist assessment of cases using the CDC definition.
	Males, ≥30 years, Pfizer vaccine (within 42 days)	2.11 per 100,000 persons	No data	
	Females, 16-29 years, Pfizer vaccine (within 42 days)	0.34 per 100,000 persons	No data	
	Females, ≥30 years, Pfizer vaccine (within 42 days)	0.20 per 100,000 persons	No data	
US, Incidence rates	Adults aged 18+, mRNA vaccines (within 10 days)	0.8 per million doses	5.8 per million doses	Simone et al. [8] based on clinical reports and hospital discharge diagnosis of myocarditis. Cases were independently adjudicated by at least 2 cardiologists.
UK, Crude reporting rate for myocarditis	Adults (age and sex not specified), Pfizer vaccine (not specified)	7.93 per million vaccinated, who had received at least one dose		Lane et al. [9] (pre-print 14 September 2021) based on events labelled "Myocarditis" Yellow card scheme reports.
	Adults (age and sex not specified), Moderna vaccine (not specified)	2.07 per million vaccinated, who had received at least one dose		
European Economic Area, Crude reporting rate for myocarditis	Adults (age and sex not specified), Pfizer vaccine (not specified)	4.23 per million vaccinated, who had received at least one dose		Lane et al. [9] (pre-print 14 September 2021) based on events labelled "Myocarditis" in the EudraVigilance database.
	Adults (age and sex not specified), Moderna vaccine (not specified)	6.15 per million vaccinated, who had received at least one dose		

Other US studies

- A US military study found that among 2.8 million doses of mRNA COVID-19 vaccines administered, 23 male patients developed clinical myocarditis within 4 days, with 20 of these cases occurring after the second dose. A total of 9 received the Pfizer vaccine and 16 received the Moderna vaccine.[10]
- An analysis of records from forty hospitals in the US reported that among 2 million individuals receiving at least 1 dose of a COVID-19 vaccine, 11 people developed myocarditis after the Moderna vaccine and 9 after Pfizer.[11] Four cases developed symptoms after the first vaccination and 16 after the second. Of the total cases, 75% were in males aged 26-48 years.
- In an MMWR report published on 6 August 2021, CDC reported that 9,246 reports were filed in VAERS after Pfizer vaccination in approximately 8.9 million adolescents aged 12–17 years.[12] Of these, 9.3% were for serious adverse events, including myocarditis (4.3%). The most commonly reported conditions and diagnostic findings among reports of serious events were chest pain (56.4%), increased troponin levels (41.7%), myocarditis (40.3%), increased c-reactive protein (30.6%), and negative SARS-CoV-2 test results (29.4%). These findings are consistent with a diagnosis of myocarditis. However, it should be noted that passive surveillance is subject to underreporting and reporting biases, and this analysis was not designed to identify all the cases of myocarditis.
- In an MMWR report published on 13 August 2021, CDC reported that as of 30 June 2021, 497 reports of myocarditis were filed in VAERS after approximately 141 million second mRNA COVID-19 vaccine doses had been administered to persons aged ≥18 years.[13] The overall reporting rate for myocarditis among adults was 3.5 cases per million second doses of mRNA COVID-19 vaccine, with the highest being among males aged 18–29 years (24.3 cases per million mRNA COVID-19 vaccine second doses administered). Reports of cases in persons aged 18–29 years were individually reviewed and confirmed to meet case definitions, whereas reports of cases in persons aged ≥30 years were received and processed but not individually reviewed. There were no confirmed myocarditis-associated deaths.
- An interim analysis of safety surveillance data between December 2020 through June 2021 from the US Vaccine Safety Datalink database reported a total of 34 cases of confirmed myocarditis/pericarditis after more than 11.8 million doses of mRNA COVID-19 vaccines had been administered.[14] These cases were in individuals aged 12–39 years and occurred within 21 days following vaccination. 85% of the cases were in males and 53% were aged 12–24 years and. The overall adjusted rate ratio (RR) was 9.83 (95% CI: 3.35-35.77) within 7 days after vaccination (vaccinated comparators), corresponding to 6.3 additional cases per million mRNA doses. Both Moderna and Pfizer had higher RR estimates after dose 2 compared with dose 1.

Note

- To note, Hoeg et al. conducted an analysis of VAERS reports filed between 1 January 2021 and 18 June 2021 among adolescents ages 12-17 that received mRNA COVID-19 vaccination and reported a rate for myocarditis that was much higher than that reported by others.[15] However, this study is not included in the review above as the methodology had several major limitations and does not

provide reliable estimates of myocarditis risk post-vaccination. Limitations included: cases were not adjudicated by a cardiologist; cases with COVID-19 infection were not excluded (making it unable to distinguish between myocarditis associated with disease or potentially due to vaccination); severity of myocarditis was not reported, which is important for characterising the overall risk, as events of myocarditis post-vaccination appear to be less severe than myocarditis due to other causes (based on other literature).

International rollout changes due to risk of myocarditis

- **Canada**: Based on the higher rates of myocarditis following the Moderna vaccine, Ontario is recommending only the Pfizer vaccine be used in 18-24 year-olds.[4] NACI continues to recommend that the second dose in the mRNA COVID-19 vaccination series should be deferred in individuals who experience myocarditis or pericarditis following the first dose of an mRNA COVID-19 vaccine until more information is available.[16]
- Since 6 October 2021, several Nordic countries (Sweden, Denmark, Norway, Finland) have announced that they are either pausing or discouraging the use of Moderna's Spikevax COVID-19 vaccine in some age groups due to possible increased risk of myocaridits and pericarditis.[5] Sweden is not offering Spikevax to anyone under 30, while Denmark does the same for anyone under 18. Finland is suspending the use of Spikevax in men under 30. Norway is discouraging anyone under 30 from receiving Spikevax. Safety data from these countries is yet to be published but media reports state that the data has been submitted to the EMA for assessment.
- There have been no substantial changes to international recommendations for the Pfizer COVID-19 vaccine with regards to myocarditis.

Next Steps	CV TAG to review
In the development of this work, the following parties have been consulted with:	

Resources used:		
Ministry of Health Policies and Procedures	☐ Yes ☐ No	

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

Request for Advice (RfA)

MINISTRY OF HEALTH | MANATŪ HAUORA

External Health Scientific organisations	☐ Yes ☐ No	
Existing database of RFAs	☒ Yes ☐ No	245 Myocarditis Update for CV TAG
Internal Ministry of Health Advice	☐ Yes ☐ No	
External Expert Advice	☐ Yes ☐ No	
Literature Review	☐ Yes ☐ No	

References

1. Su, J.R. *Myopericarditis following COVID-19 vaccination: Updates from the Vaccine Adverse Event Reporting System (VAERS)*. August 30, 2021; Available from: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-08-30/03-COVID-Su-508.pdf.
2. Mevorach, D., et al., *Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel.* New England Journal of Medicine, 2021.
3. Public Health Ontario. *Myocarditis and Pericarditis Following Vaccination with COVID-19 mRNA Vaccines in Ontario: December 13, 2020 to August 7, 2021*. Available from: https://www.publichealthontario.ca/-/media/documents/ncov/epi/covid-19-myocarditis-pericarditis-vaccines-epi.pdf?sc_lang=en.
4. City News Toronto. *Ontario recommending Pfizer over Moderna vaccine for young adults*. September 29, 2021; Available from: https://toronto.citynews.ca/2021/09/29/ontario-moderna-vaccine-side-effect/.
5. CNBC. *Nordic countries are restricting the use of Moderna's Covid vaccine. Here's why*. October 8, 2021; Available from: https://www.cnbc.com/2021/10/08/nordic-countries-are-restricting-the-use-of-modernas-covid-vaccine.html.
6. Medsafe. *Myocarditis and pericarditis – rare adverse reactions to Comirnaty (Pfizer COVID-19 vaccine)*. 21 July 2021; Available from: https://www.medsafe.govt.nz/safety/Alerts/comirnaty-myocarditis-alert.htm.
7. Witberg, G., et al., *Myocarditis after Covid-19 Vaccination in a Large Health Care Organization.* New England Journal of Medicine, 2021.
8. Simone, A., et al., *Acute Myocarditis Following COVID-19 mRNA Vaccination in Adults Aged 18 Years or Older.* JAMA Internal Medicine, 2021.
9. Lane, S. and S. Shakir, *Reports of myocarditis and pericarditis following mRNA COVID-19 vaccines: A review of spontaneously reported data from the UK, Europe, and the US.* medRxiv, 2021: p. 2021.09.09.21263342.
10. Montgomery, J., et al., *Myocarditis Following Immunization With mRNA COVID-19 Vaccines in Members of the US Military.* JAMA Cardiology, 2021. **6**(10): p. 1202-1206.
11. Diaz, G.A., et al., *Myocarditis and Pericarditis After Vaccination for COVID-19.* JAMA, 2021. **326**(12): p. 1210-1212.
12. Hause, A.M., et al., *COVID-19 Vaccine Safety in Adolescents Aged 12–17 Years — United States, December 14, 2020–July 16, 2021.* MMWR. Morbidity and Mortality Weekly Report, 2021. **70**(31): p. 1053-1058.
13. Rosenblum, H.G., et al., *Use of COVID-19 Vaccines After Reports of Adverse Events Among Adult Recipients of Janssen (Johnson & Johnson) and mRNA COVID-19 Vaccines (Pfizer-BioNTech and Moderna): Update from the Advisory Committee on Immunization Practices — United States, July 2021.* MMWR. Morbidity and Mortality Weekly Report, 2021. **70**(32): p. 1094-1099.
14. Klein, N.P., et al., *Surveillance for Adverse Events After COVID-19 mRNA Vaccination.* JAMA, 2021. **326**(14): p. 1390-1399.
15. Høeg, T.B., et al., *SARS-CoV-2 mRNA Vaccination-Associated Myocarditis in Children Ages 12-17: A Stratified National Database Analysis.* medRxiv, 2021: p. 2021.08.30.21262866.
16. Government of Canada. *Recommendation on the use of mRNA COVID-19 vaccines in adolescents 12 to 17 years of age*. August 27, 2021; Available from: https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines/mrna-adolescents.html.

Document 9

MINUTES: COVID-19 Vaccine Technical Advisory Group

Date:	Tuesday 19 October 2021
Time:	11:00am to 12:00pm
Location:	Teams: s 9(2)(k) [redacted]
Chair:	Ian Town
Members:	David Murdoch, Elizabeth Wilson, Helen Petousis-Harris, James Ussher, Nikki Moreland, Peter McIntyre, Sean Hanna,
Ministry of Health Attendees:	s 9(2)(g)(ii) [redacted]
Guests:	
Apologies:	

5.0 Myocarditis Update

- An update was provided from STA on the risk of myocarditis according to international evidence. Data presented at the latest US ACIP meeting on 30 August 2021 and data from Israel indicate that myocarditis reporting rates following mRNA COVID-19 vaccination continue to be rare overall, but highest risk tends to occur after the second dose, particularly in younger males.
- Medsafe also shared the latest data on cases. The safety profile differs to the US in that New Zealand is seeing more cases after dose 1 than dose 2, however this could reflect the vaccine rollout with more young people being vaccinated later. Onset tends to be reported in the first five days for both dose. Data on dosing intervals has not been analysed, however it has been noted that cases have still occurred at an interval of 6-8 weeks. Overall, the rate is approximately 7 per million doses after dose 1, and 10 per million doses after dose 2. Peopled aged 30-39 are the most affected age group in New Zealand overall, and after dose 1, and people aged 20-29 are most affected after dose 2. Long-term follow-up data is expected by end of November.
- ISMB shared that levels of reporting seem to correlate with the numbers of reports being received, looking at the number of hospitalisations in vaccinated individuals. Every case reported to CARM is reviewed by a medical assessor, and when there is insufficient data, further information is requested. If there is a risk of death, biopsies and post-mortems of myocardiums are requested. No long-term outcome data is currently available.
- Information on symptoms to watch out for have been provided to all vaccinators, however it is possible that some centres are still using older booklets from before the advice was given.
- Milder cases may benefit from further clinical investigation, and greater standardisation in management of care may be needed with ECGs and provision of troponins. Accessiblity of the guidance for general practice and primary care will be reviewed.
- As previously noted, people who have myocarditis after their first dose should not be offered a second dose of an mRNA vaccine, and an alternative vaccine or no further doses should be considered for those people.
- No further evidence had emerged that decreasing the dose interval had impacted myocarditis.
- A clinical research project is one option to consider looking at myocarditis in greater detail.

Document 10

MINUTES: COVID-19 Vaccine Technical Advisory Group

Date:	Thursday 20 January 2022
Time:	11:00am to 12:30pm
Location:	Teams: s 9(2)(k) [redacted]
Chair:	Ian Town
Members:	Danny de Lore, David Murdoch, Elizabeth Wilson, Helen Petousis-Harris, James Ussher, Nikki Moreland, Nikki Turner, Owen Sinclair, Peter McIntyre
Ministry of Health Attendees:	s 9(2)(g)(ii) [redacted]
Guests:	
Apologies:	

2.3 Myocarditis post-vaccine

Discussion point: Should individuals who had myocarditis after their first Pfizer dose be recommended an exemption or AstraZeneca?

- Guidance should be balanced to ensure people are not unfairly assigned to social restrictions.
- It was noted that there is some evidence of a risk of myocarditis with the AstraZeneca dose too.
- The risk of myocarditis from infection may be greater for most.
- Evidence collation is required on the safety of AstraZeneca and Janssen given as a second dose. STA to collate an RfA at pace on the latest evidence.

5.0	**Myocarditis Research Project Update** • This research will be following up with people who have had myocarditis or pericarditis after their vaccination, and their healthcare providers. There are estimated to be 200-300 people eligible. CBG Health have been contracted to run the survey. Ethics application are being submitted this week, and the study will be starting mid-late-February. • This research will be put in touch with the research underway at the University of Auckland.

Document 11

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 risk with boosters		
Subject	Options for booster vaccines		
Reference No.	0443	Date Received	28/02/2022
Requestor	Immunisation Advisory Centre	Date Due	8/03/2022
Advisor	s 9(2)(g)(ii)	Date Completed	Click or tap to enter a date.
Peer reviewed by	s 9(2)(g)(ii)		
Advice issued to	The COVID-19 Vaccine Technical Advisory Group (CV TAG)		
Approved by	Dr Ian Town, Chief Science Advisor and CV TAG Chair		
Deliverables	Evidence brief to inform discussions		
Request Outline	**Background/Context** The Government currently requires certain sectors and professions to have received COVID-19 booster doses as part of their employment requirements as directed by the COVID-19 Public Health Response (Vaccinations) Order 2021. There is an exemption process to this order which enables individuals without a booster to continue in employment. The Immunisation Advisory Centre wrote to the COVID-19 Vaccine Temporary Exemption Committee on 3 February 2022 raising a potential anomaly in the handling of mandated boosters for some worker categories with respect to previously documented myocarditis. Previously, IMAC has been approached for advice primarily where myocarditis was proven or suspected after the first dose of Pfizer vaccine, and they have been advising that once all symptoms had resolved, the risk: benefit balance was in favour of going ahead with a second dose of Pfizer vaccine. IMAC is now being asked for clinical advice in the context of people who developed myocarditis following the second dose of Pfizer vaccine (more common than after the first dose) for workers mandated to receive a booster dose. IMAC have expressed concern about the use of the AstraZeneca vaccine as a booster for the reasons outlined below.		

	• They note AstraZeneca carries a risk of Thrombosis with Thrombocytopaenia Syndrome (TTS), which occurs at a greater rate among peopled aged under 50 than over 50 years. They also note some reports of myocarditis occurring after a primary course of AstraZeneca. • In the context of Omicron, the vaccine is less effective at reducing transmission than for previous variants, making the incremental benefit of the booster dose to reduce work-related transmission more difficult to justify in the case of a person who has had documented myocarditis following the second dose of Pfizer vaccine. **Questions** What is the risk of myocarditis with a primary course of Pfizer vaccine and after a booster dose? What is the risk myocarditis after a third (booster) dose if myocarditis was experienced after the first or second dose? What is the risk of myocarditis after a primary course of the AstraZeneca vaccine, and after a booster? What data is available regarding myocarditis after COVID-19 vaccination in New Zealand? What is the benefit provided by booster doses for reducing infection, transmission, and severe disease? What do international peak bodies advise in relation to boosters, if myocarditis has been experienced after the second dose of a primary course? **Intended application of advice** To inform discussions and recommendations at CV TAG of whether exemptions to mandatory booster vaccination should be available for individuals who have experienced myo-pericarditis, or whether alternative COVID-19 vaccinations should be made available for booster vaccines. **Timeline** Draft RfA due to CV TAG on 8 March 2022
What are the implications and considerations of this advice on Te Tiriti o Waitangi and equity?	Equity considerations are relevant to who is at higher risk of vaccine-induced myocarditis with the COVID-19 vaccine, and to background rates of myocarditis. This is particularly important given the Delta and Omicron outbreaks have largely been in Māori and Pacific peoples. Given that these groups are more likely to have severe outcomes as a consequence of SARS-CoV-2 infection, it is important they are prioritised for all vaccination. Importantly, the primary consideration of the vaccine programme should remain focussed on administering first and second doses. 87.3% of eligible Māori have

received a vaccine (link), and first and second doses should be priorities for those who have not yet been reached prior to rolling out a booster programme, with acknowledgement that there are disparities in relation to accessing vaccines, and who is able to access services.

Response to Request for Advice

Key points

- Myocarditis is listed as a rare adverse event on the Pfizer data sheet. However, it is not listed as being a rare adverse event or contraindication for the AstraZeneca vaccine or Novavax vaccine.
- Data from the real-world rollout of boosters in the US and Israel shows rates of myocarditis after a Pfizer booster are lower than rates reported after second doses of Pfizer.
- Currently only the Pfizer and AstraZeneca vaccines are approved for use as a booster. However, an application from Novavax is expected to be submitted to Medsafe in the near future.
- There have been reports of myocarditis after AstraZeneca vaccine through adverse event monitoring systems. However, ATAGI reports that in Australia, myocarditis after AstraZeneca vaccination does not occur more frequently than the background rate. The risk of thrombosis with thrombocytopaenia syndrome (TTS) has been shown to be linked to the AstraZeneca vaccine in post-marketing roll-out.
- International guidance from peak bodies states that after confirmed myocarditis, further doses should be deferred. The need and choice of further doses is informed by age and sex after discussing the risks and benefits with their healthcare provider, with AstraZeneca given in Australia on a case-by-case basis for people aged over 18. NACI recommends further mRNA doses can be given at least 90 days after vaccination.
- In the context of Omicron, the vaccine is less effective at reducing transmission than for previous variants. Therefore, the balance of the benefits of a reduction in the risk of transmission within the workplace compared to the risk of a recurrence of in a person who has had documented myocarditis following the second dose of Pfizer vaccine, will be different to those for the delta variant and primary vaccination.
- Booster vaccination will result in a significant reduction of severe disease. Decreasing the requirement for prolonged absence from employment for critical workers could assist in the preservation of life-saving services within the community.
- While both deferment of booster vaccination and the use of an alternative vaccine are associated with a low risk of severe outcomes and improve personal protection, the safety threshold and clinical benefit for mandating booster vaccination requires clarification.

- Of cases of myocarditis and/or pericarditis after COVID-19 vaccination in New Zealand (with a clinical diagnosis), 72% are European , 12% Asian, 11% Māori, 2% Pacific Peoples and 4% other/unknown ethnicity. The ethnicity distribution is very similar for all reported cases (including verified and unverified cases).

Risk of myocarditis/ pericarditis/ myopericarditis

Risk from a primary course of Pfizer

Myocarditis is a recognised but rare complication of mRNA vaccines. The incidence is greater after a second compared to first dose and reduced for a booster dose compareds to a second dose. There are strong epidemiological links to male sex and age in the late second and third decade (15 – 30 years).

- Evidence of adverse events followed vaccination have been reported by different systems: USA-VAERS, New Zealand's MedSafe, EEA-EudraVigilance and UK-MHRA, as well as in clinical trials.
- There is an established link between the Pfizer vaccine and the risk of myocarditis, with the greatest risk within 7 days of administration of the second dose. The age group at greatest risk are adolescent and younger males. Most individuals recover with conservative management. The risk of myocarditis has been added to the product sheet for the Pfizer vaccine in many countries including by the FDA, and within New Zealand.
- A report from Israel indicates that t**he overall risk difference between the first and second doses was 1.76 per 100,000 persons (95%CI, 1.33-2.19), with the largest difference among male recipients between the ages of 16 and 19 years (difference, 13.73 per 100,000 persons; 95%CI, 8.11-19.46).**
- As compared with the expected incidence based on historical data, **the standardised incidence ratio was 5.34 (95%CI, 4.48-6.40) and was highest after the second dose in male recipients between the ages of 16 and 19 years (13.60; 95% CI, 9.30 to 19.20).** The rate ratio 30 days after the second vaccine dose in fully vaccinated recipients, as compared with unvaccinated persons, was 2.35 (95% CI, 1.10 to 5.02); the rate ratio was again highest in male recipients between the ages of 16 and 19 years (8.96; 95% CI, 4.50 to 17.83), with a ratio of 1 in 6637.[1]
- A study of US military personnel found that among 2.8 million doses of mRNA COVID-19 vaccines administered (Pfizer and Moderna), 23 male patients developed clinical myocarditis within 4 days, with 20 of these cases occurring after the second dose. A total of 9 received the Pfizer vaccine and 16 received the Moderna vaccine.[2]
- An analysis of records from 40 hospitals in the US reported that among 2 million individuals receiving at least 1 dose of a COVID-19 vaccine, 11 people developed myocarditis after the Moderna vaccine and 9 after Pfizer.[3] Four cases developed symptoms after the first vaccination and 16 after the second. Of the total cases, 75% were in males aged 26-48 years.
- In an MMWR report published on 25 January 2022, CDC reported that between December 2020 and August 2021, 1626 cases of myocarditis were reported to VAERS within 7 days of vaccination among 192,405,448 persons receiving mRNA-based COVID-19 vaccines. The rates of myocarditis cases were highest after the second vaccination dose in adolescent males aged 12 to 15 years (70.7

per million doses of the Pfizer vaccine), in adolescent males aged 16 to 17 years (105.9 per million doses of the Pfizer vaccine), and in young men aged 18 to 24 years (52.4 and 56.3 per million doses of the Pfizer vaccine and the mRNA-1273 vaccine, respectively). Approximately 96% of persons (784/813) were hospitalized and 87% (577/661) of these had resolution of presenting symptoms by hospital discharge. The most common treatment was nonsteroidal anti-inflammatory drugs (589/676; 87%).[4]

New Zealand data on adverse events of myocarditis

- Up to 23 February, 649 adverse events following immunisation (AEFI) reports of myocarditis and/or pericarditis have been received for the Pfizer vaccine. All of these reports are evaluated and assessed by a medical assessor at the Centre for Adverse Reactions Monitoring (CARM) and staff at Medsafe.
- Of these reported cases, 262 have received a clinical diagnosis (e.g., diagnosed by a doctor or relevant healthcare professional). Other cases are still currently under follow-up or a clinical diagnosis was unable to be verified (e.g., reports where a self-diagnosis was made). A number of the reports which could not be verified have since gone on to receive a further dose of the Pfizer vaccine.
- From the information reported to CARM, there have been 21 people who had a clinical diagnosis of myocarditis or pericarditis (mostly pericarditis) after dose 1 who have had dose 2 (no further report received).
- There have also been 10 people who had a clinical diagnosis of myocarditis or pericarditis after dose 2 who have had dose 3 (no further report received), however it should be noted that less time has passed for people to have boosters and this number is likely to increase.
- Ethnicity information on affected cases was not provided.

The risk of recurrent myocarditis

It is not possible to quantify the risk of recurrent myocarditis. Case reports exist of individuals who have experienced documented or probable myocaridits after sequential COVID-19 vaccinations [5] or after a previous episode of myocarditis unrelated to vaccination [6]. As the majority of acases occur after the second dose of a primary course, there will be a considerable delay before a further, booster dose, is required.

Further information regarding the risk of recurrent myocarditis associated with vaccination may become available.

Document 11

Risk from a booster dose of Pfizer or Moderna

The risk of myocarditis reported to VAERS for mRNA vaccines is reported below (Table 1.)

Table1. Cases and rates of myocarditis reported to the Vaccine Adverse Event Reporting System following receipt of an mRNA COVID-19 booster dose among adults aged ≥18 years (N = 37), by age, sex, and vaccine product received

	No. of cases (rates)*,§			
	Pfizer-BioNTech (n = 18)		Moderna (n = 18)	
Age group, yrs	Men (n = 16)	Women (n<5)	Men (n = 10)	Women (n = 8)
18–24	5 (4.1)	<5 (<1.0)	6 (8.7)	<5 (1.1)
25–29	<5 (1.1)	0 (—)	<5 (3.2)	<5 (1.2)
30–39	<5 (1.7)	<5 (<1.0)	<5 (<1.0)	<5 (1.5)
40–49	0 (—)	0 (—)	0 (—)	<5 (<1.0)
50–64	<5 (<1.0)	0 (—)	0 (—)	<5 (<1.0)
≥65¶	5 (<1.0)	0 (—)	<5 (<1.0)	0 (—)

- The CDC also investigated if heterologous boosting was associated with altered odds for side effects. They found Moderna booster to be associated with increased odds for side effects irrespective of primary vaccination, a finding consistent with earlier data. During the same time period, 37 reports of myocarditis were made via VAERS and one death was reported. The rate was highest among men aged 18-24 following Moderna booster (8.7 per million doses), but was lower than after the second dose (56.3 per million doses).[7] These data further support the current recommendation for persons aged ≥18 to receive a booster, however data was not collected for 12-17-year-olds.[7]
- Israel published second dose and booster dose safety data for Pfizer vaccination on 15 December 2021. Local and systemic reactions in the 30 days following Pfizer booster were less frequent than after the second dose across all age groups. Myocarditis rates following Pfizer booster were also lower than after the second dose across all age groups(Figure 1). While the trend of fewer side effects following the booster dose relative to the second dose is congruous with the CDC data, the raw frequency of events differs greatly, likely due to the use of different data collection methods (phone app-based reporting vs. reporting to Israel Ministry of Health) and varying surveillance times (7 days vs. 30 days). From a safety standpoint, these data support the continued use of boosters in these age groups.[8]

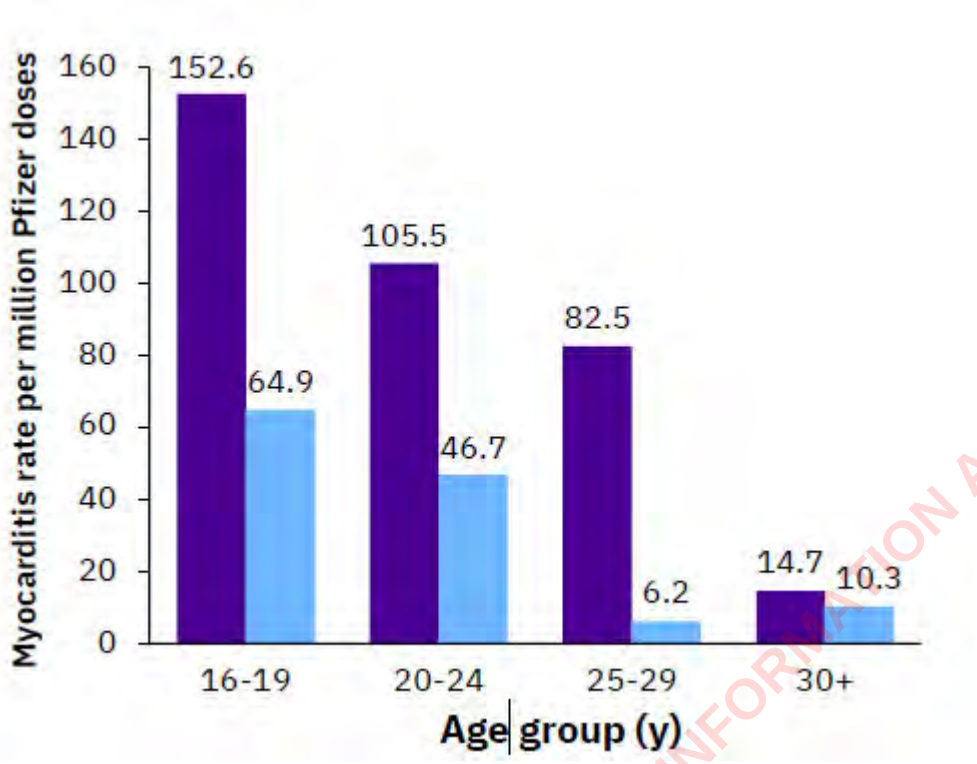

Figure 1 Israel's myocarditis rates following second and booster dose of Pfizer in males. Source: Airfinity

Pfizer and Moderna are the preferred vaccines in the UK booster programme, and the rates reported by the MRHA for suspected myocarditis and pericarditis following booster or third doses of these vaccines are lower than those estimated for the first and second doses. There is extremely limited usage of AstraZeneca as a booster. Due to this limited usage and very small numbers of reports of suspected myocarditis and pericarditis after booster doses, it is not possible to calculate a reliable reporting rate for these conditions for AstraZeneca when used as a booster.[9]

Risk from a primary course of the AstraZeneca vaccine

- Evidence of adverse events followed vaccination have been reported by different systems: USA-VAERS, New Zealand's MedSafe, EEA-EudraVigilance and UK-MHRA, as well as in clinical trials.
- Myocarditis/ pericarditis/ myopericarditis is not currently listed as having an established, potential, or theoretical risk with the AstraZeneca vaccine. AstraZeneca is linked to Thrombosis with thrombocytopenia syndrome (TTS), anaphylaxis, angioedema, and Guillan-Barre syndrome (GBS) and potential links to capillary leak syndrome and transverse myelitis.
- While there has been a consistent pattern of higher reporting of myocarditis after mRNA vaccines (Pfizer and Moderna), the association between myocarditis and vaccination with AstraZeneca is less clear[9]. In particular, the pattern of reported myocarditis after AstraZeneca vaccination does not display the age or sex characteristics seen with the mRNA vaccines (Tables 2 and 3).

Table 2: Number of UK ADR reports associated with suspected myocarditis, pericarditis and other related terms received for the COVID-19 Vaccine AstraZeneca, COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine Moderna by patient age up to and including 23 February 2022.

Age range (years)	COVID-19 Pfizer/BioNTech Vaccine	COVID-19 Vaccine Moderna	COVID-19 Vaccine AstraZeneca
Under 18	65	0	0
18-29	360	113	31
30-39	285	87	47
40-49	132	47	115
50-59	88	21	100
60+	140	15	100
Unknown	142	35	44
Total	1212	318	437

Table 3: Number of UK ADR reports associated with suspected myocarditis, pericarditis and other related terms received for the COVID-19 Vaccine AstraZeneca, COVID-19 Pfizer/BioNTech Vaccine and COVID-19 Vaccine Moderna by patient sex up to and including 23 February 2022

Sex	COVID-19 Vaccine Pfizer/BioNTech	COVID-19 Vaccine Moderna	COVID-19 Vaccine AstraZeneca
Female	477	105	198
Male	698	202	229
Unknown	37	11	10
Total	1212	318	437

- The below table reports the rate of myocarditis/pericarditis after AstraZeneca per million in the US, New Zealand, Europe, and UK. While these are significantly lower than for Pfizer, the UK rates are higher than New Zealand's myocarditis rate after Pfizer.

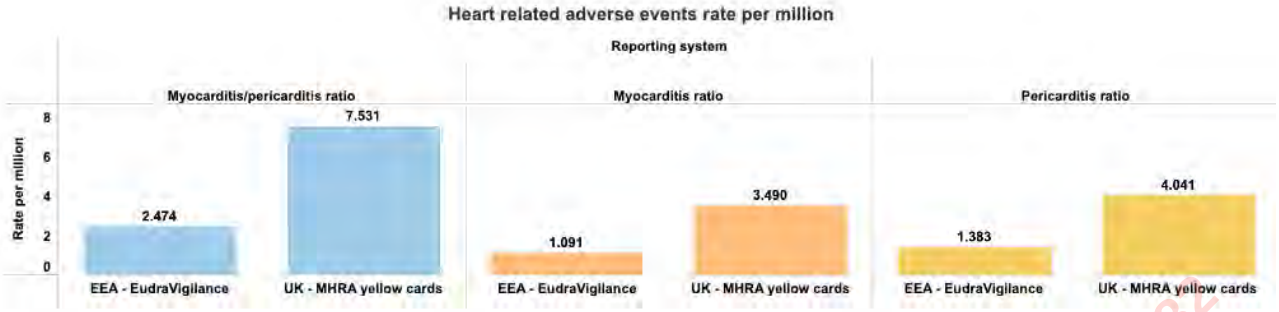

Figure 1: Rate of myocarditis/pericarditis after AstraZeneca per million. Source: Airfinity

New Zealand data on adverse events

- Up to 28 February, 262 AEFI reports have been received for the AstraZeneca COVID-19 vaccine, of which 17 have currently been classified as serious.
- The majority of serious reports have been allergic type reactions. There has been one reported case of a pulmonary embolism occurring in a consumer approximately two weeks after their first dose of the AZ vaccine. No cases of thrombosis with thrombocytopenia syndrome have been reported.
- There are currently two cases of reported pericarditis after the AstraZeneca vaccine under investigation:
    - A consumer who reported to have also developed pericarditis after their first dose of the Pfizer vaccine and it is unclear whether the report relates to this or a new onset of symptoms.
    - A report of pericarditis in a consumer with a previous history of pericarditis after their AstraZeneca booster. The person received the Pfizer vaccine for their primary course and no AEFI reports were received associated with those doses.
- The COVID-19 Vaccine Independent Safety Monitoring Board, reviewed the available safety data for the AstraZeneca vaccine at their meeting on 26th January, with no concerns noted and the Board supported the recommendation for Medsafe to continue to monitor the safety of the AstraZeneca vaccine through routine pharmacovigilance.
- At data cut-off for presentation to the Board (12 January), there were five anaphylaxis like reactions reported; four of these also had reactions to the Pfizer vaccine.
- No information was provided on the ethnicity of cases.

Risk from a booster dose of the AstraZeneca vaccine

- In general, no additional safety concerns have been identified when AstraZeneca has been administered as a booster dose.
- In the UK, due to this limited usage and very small numbers of reports of suspected myocarditis and pericarditis after booster doses, the MHRA report states it is not possible to calculate a reliable reporting rate for AstraZeneca when used as a booster; no association has been established between myocarditis or pericarditis and AstraZeneca.[9]
- A small study suggests that AstraZeneca, when used as a booster following a full primary course of Pfizer or Moderna, augments humoral and T cell immune responses, and is well tolerated.[10]

Risk from a primary course of the Novavax vaccine

- In the UK phase III trial, there was one case of myocarditis that occurred three days after the second dose, and this was considered possibly immune related; however, it was adjudicated to most likely be viral myocarditis.[11]
- This vaccine has not been widely rolled-out and therefore does not have the breadth of safety data that is available for other vaccines in the portfolio. However, recombinant protein vaccines have previously been widely used against viruses and bacteria, therefore the long-term safety profile of this platform is generally well established. Continued safety monitoring is essential. The following safety issues have been noted or are being investigated.

Risk from a booster dose of the Novavax vaccine

- A phase II randomised controlled trial investigated a booster dose of Novavax administered 6 months after a primary series of Novavax in healthy adults aged 18-84 years, compared with placebo (n=383 total participants). The likelihood of short-term adverse reactions increased with each subsequent dose of this vaccine. Local and systemic adverse events were reported more frequently after the booster dose compared with after the second primary dose (local: 82.5% vs. 70.0%; systemic: 76.5% vs. 52.8%).[12]
- Another phase II randomised controlled trial in adults aged 30 years or older (N=2,878) investigated a booster dose of Novavax administered approximately 2.5 months after a two dose primary series of AstraZeneca, or approximately 3 months after a two dose primary series of Pfizer in a heterologous vaccine schedule. Local and systemic adverse events following a Novavax booster dose were not frequently reported compared to the other booster vaccines investigated. However, they were more common in participants who had received an AstraZeneca primary series compared with those who received a Pfizer primary series. Overall, reactogenicity was greater in people aged 30 to 69 years compared to those aged 70 years and older.[13]

Regulatory approvals and contraindications

Currently only the Pfizer and AstraZeneca vaccines are approved for use as boosters within Aotearoa New Zealand, however there is a clinical pathway for an off-label prescription of other approved vaccines e.g., the Novavax vaccine. An application is expected to Medsafe on use of the Novavax vaccine as a booster shortly.

Pfizer vaccine

The Pfizer vaccine has been approved by Medsafe for use in a primary course and as a booster dose for the active immunisation to prevent COVID-19 caused by SARS-CoV2, in individuals 12 years of age and older. A lower dose 10 µg/0.2 mL has also been approved for the active immunisation to prevent COVID-19 caused by SARS-CoV2 as part of a primary course, in individuals 5 to 11 years of age. [14]

Current contraindications listed in the data sheet for the full dose formulation include ‘Hypersensitivity to the active substance or to any of the excipients listed in Section 6.1 [15].

Current contraindications listed in the data sheet for the lower dose formulation include 'Hypersensitivity to the active substance or to any of the excipients listed in Section 6.1 [16]

Both data sheets note:

- Very rare cases of myocarditis and pericarditis have been observed following vaccination with COMIRNATY. These cases have primarily occurred within 14 days following vaccination, more often after the second vaccination, and more often in younger men. Available data suggest that the course of myocarditis and pericarditis following vaccination is not different from myocarditis or pericarditis in general.
- Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination. Healthcare professionals should consult guidance and/or specialists to diagnose and treat this condition.

AstraZeneca

The AstraZeneca vaccine has been approved for use in a primary course and booster for the active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 18 years of age and older. [14]

Current contraindications to the AstraZeneca vaccine include:[17]

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Patients who have experienced major venous and/or arterial thrombosis in combination with thrombocytopenia following vaccination with any COVID-19 vaccine.
- Individuals who have previously experienced episodes of capillary leak syndrome

Novavax

The Novavax vaccine has been approved for use in a primary course for the active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 18 years of age and older [1]. It has not been approved for use as a booster, however an application to Medsafe is expected shortly.

Current contraindications to the Novavax vaccine include 'Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Efficacy of the booster vaccine

Infection and transmission

Vaccine mandates have largely been based on the impact of vaccines in reducing infection and transmission. Vaccine efficacy against infection is lower in the context of Omicron, however there is growing evidence that boosters restore protection against infection:

- A Danish cohort study has shown VE (Pfizer) against infection of 55.2% (95%CI, 23.5-73.7) in the month after primary vaccination. VE declines rapidly after the first month, however boosters increased VE back to 54.6% (95%CI, 30.4-70.4%). [18]
- VE analysis by the UKHSA of Pfizer, Moderna and AstraZeneca (combined data) found 2 dose VE against infection at 25+ weeks to be 9% (95%CI, 7–10) and 13% (95%CI, -26–40) respectively for

BA.1 and BA.2. After a booster dose, this increased to 63% (95%CI, 63–64) for BA.1 and 70% (95%CI, 58–79%) for BA.2. [19]

- A small longitudinal cohort study of elderly individuals (n = 37, median age 82 years), the proportion of individuals with detectable SARS-CoV-2-neutralising serum activity against Omicron increased from 0% at 5 months after a primary Pfizer course, to 89% 1 month after a booster dose of Pfizer. [20]
- Denmark:[21] Transmission data from 12,000 infected households (2,225 with Omicron), the household secondary attack rate was 31% for Omicron and 21% for Delta. However, there were differences when stratified by vaccination, and transmission was reduced for booster-vaccinated individuals:
    - Household SAR for unvaccinated: 29% for Omicron, 28% for Delta
    - Household SAR to fully vaccinated: 32% for Omicron, 19% for Delta
    - Household SAR for booster-vaccinated: 25% for Omicron, 11% for Delta
    - Comparing households infected with the Omicron to Delta, overall, they found a 1.17 (95%-CI: 0.99-1.38) times higher SAR for unvaccinated, 2.61 times (95%-CI: 2.34-2.90) higher for fully vaccinated and 3.66 (95%-CI: 2.65-5.05) times higher for booster-vaccinated individuals.
- UKHSA risk assessment on 9 February: The growth advantage seen with BA.2 relative to BA.1 is due to its increase in transmissibility and/or shorter serial interval, rather than an increase in immune evasion.[22]

Severe disease

- The reduction of severe disease and decreasing the requirement for prolonged absence from employment for critical workers could assist in the preservation of life-saving services within the community.
- Primary vaccination offers some protection against severe disease and hospitalisation however, VE is reduced compared to Delta. Rapid waning of VE occurs against Omicron but a booster dose restores protection. VE against hospitalisation appears to be 60-70% after a primary vaccine course but declines to ~45% from 25 weeks after second dose. VE against hospitalisation increases to ~90% after a booster dose (including in those over 65 years of age).
- Current data includes:
    - UKHSA COVID-19 Vaccine Surveillance Report from 27 January reported estimates from a test-negative case control study:
        - Protection against hospitalisation remained high, particularly after 3 doses. For a Pfizer booster (after either Pfizer or AstraZeneca primary 2 doses), VE against hospitalisation started at around 90% dropping to around 75% after 10 to 14 weeks. [23]
- South African data for VE against hospitalisation:
    - VE against hospitalisation for two doses of Pfizer was 70% (95%CI 62-76) during Omicron dominance (Delta dominance (93% [95%CI 90-94]) in South Africa.[24] Data were adjusted for age, sex, previous infection, surveillance week, geographic location, and CDC risk factors.
    - Results from another South African study show that VE against hospitalisation for the Janssen vaccine increased over time since the second (booster) dose. [25]

- UK data for VE against hospitalisation (all vaccines combined):
    - For adults 18+ years, VE was 64% (95% CI: 54-71) 2 to 24 weeks after dose 2, declining to 44% (95%CI: 30-54) at 25+ weeks. VE increased to 92% (95% CI: 89-94) 2+ weeks after a booster dose, declining to 83% (95% CI: 78-87) at 10+ weeks. [19]
    - For elderly aged 65+ years, booster VE was 94% (95% CI: 89-97) 2 to 9 weeks after a booster dose and 89% (95% CI: 80-95) at 10 weeks. VE after two doses was not reported in this analysis. [26]
- US data:
    - VE against Omicron-related hospitalisation for two doses of Pfizer was 68% (95% CI: 58−75), and VE for three doses of Pfizer was 89% (95% CI: 84−92). VE against omicron-related hospitalisation after two or three doses remained steady for several months. [27]
    - VE against Omicron-related ED admission for two doses of Pfizer was 60% (95% CI: 43−72) at <3 months and declined to 41% (95% CI: 32−50) at ≥6 months. [27]
    - VE against Omicron-related ED admission for three doses of Pfizer was 78% (95% CI: 73−82) at <3 months and declined to 48% (95% CI: 14−69) at ≥3 months. [27]
    - VE against Omicron-related hospitalisation for mRNA vaccines was 81% 14–179 days after dose 2, 57% ≥180 days after dose 2, and 90% ≥14 days after dose 3. [28]
    - VE against Omicron-related ED and UC encounters for mRNA vaccines was 52% 14–179 days after dose 2, 38% ≥180 days after dose 2, and 82% ≥14 days after dose 3. [28].

International guidance

JCVI, UK

- The UK's Joint Committee on Immunisation (JCVI) advised on 14 September 2021 that booster vaccines be offered to those more at risk from serious disease, and who were vaccinated during Phase 1 of the vaccine programme (priority groups 1 to 9) (link). This was seen as needed in order to maintain a high level of protection against hospitalisation or death from the virus through winter 2021/2 (while acknowledging that insufficient time has passed to know what levels of protection might be expected 6 to 12 months after the primary course). Those to be offered boosters in the UK include:
    - those living in residential care homes for older adult
    - all adults aged 50 years or over
    - frontline health and social care workers
    - all those aged 16 to 49 years with underlying health conditions that put them at higher risk of severe COVID-19, and adult carers
    - adult household contacts of immunosuppressed individuals
- The JCVI advised that the booster vaccine dose is offered no earlier than 6 months after completion of the primary vaccine course, in the same order as during Phase 1. They also indicated a preference for the Pfizer vaccine for the booster programme, regardless of which vaccine brand someone received for their primary doses.
- The JCVI has not issued specific guidance around further doses of vaccine if myocarditis has occurred after COVID-19 vaccination . However, the UK's "Green Book" (link, government-provided information for public health professionals on immunisation) currently provides advice:
    - An individual's second or subsequent doses should be deferred pending further investigation and careful consideration of the risks and benefits.
    - For those that experience myocarditis or pericarditis within two weeks of the first dose of an mRNA vaccine, testing for "N-antibody" may indicate prior exposure to COVID-19.

These individuals are likely to be well protected and therefore the benefit from a second or subsequent dose is likely to be more limited.

- Where N antibody is negative or in other circumstances where a further dose is considered necessary, for example in those higher risk of the complications of COVID-19 infection, a second or booster dose of Pfizer BioNTech vaccine should be considered once the patient has fully recovered. Emerging evidence suggests that an interval of at least 12 weeks should be observed from the previous dose. Pfizer BioNTech is preferred over Moderna due to a slightly higher rate of myocarditis reported after the latter vaccine; AstraZeneca should not be offered to those who have previously received an mRNA vaccine given the more serious nature of thrombosis and thrombocytopenia syndrome.

ATAGI, Australia

- On 1 March 2022, the Australia Technical Advisory Group on Immunisation (ATAGI) updated their recommendations on the use of a booster dose in COVID-19 vaccines (link).
    - Nuvaxovid (Novavax) can be used as a booster in an individual aged 18 years and above if no other COVID-19 vaccine is considered suitable for that individual.
    - Recommendations concerning the use of AstraZeneca COVID-19 vaccine as a booster dose have been updated. AstraZeneca is no longer recommended for use as the booster dose for people who received a primary vaccination course of the AstraZeneca COVID-19 vaccine, although it can still be used for this purpose if these individuals decline receiving an mRNA vaccine as a booster dose. AstraZeneca is now only recommended when there are medical contraindications to the mRNA vaccines.
    - Either of the available mRNA COVID-19 vaccines (Pfizer or Moderna) is preferred for this booster dose in those aged 18 years and above. For those aged 16 – 17 years, only Pfizer vaccine should be used.
    - Updated evidence of vaccine effectiveness of booster doses against the Omicron variant has been included.

- ATAGI updated guidance on myocarditis and pericarditis after mRNA vaccination on 2 December 2021 (link). They state there is a small increased risk after Pfizer and Moderna, however COVID-19 itself is associated with a substantially higher risk. Vaxzevria (AstraZeneca) is not associated with an increased risk of myocarditis and/or pericarditis. While cases have been reported after this vaccine, they have not been reported more frequently than what is expected in the absence of vaccination (the 'background rate'). People with a history of any of the following conditions can receive an mRNA vaccine but should consult a GP, immunisation specialist service or cardiologist about the best timing of vaccination and whether any additional precautions are recommended:
    - Recent (i.e., within the last 3 months) myocarditis or pericarditis
    - Acute rheumatic fever or acute rheumatic heart disease (i.e., with evidence of active inflammation)
    - Acute decompensated heart failure

- ATAGI also state that 'Further doses of an mRNA COVID-9 vaccine can be given to people who have been investigated for pericarditis but who had normal ECG, troponin and inflammatory markers, and who have been symptom-free for at least 6 weeks. This includes people with a clinical diagnosis of pericarditis despite normal investigations.
- For people with suspected or proven pericarditis and abnormal investigation results, the need and choice of further doses is informed by age and sex.
- People who have had confirmed myocarditis attributed to a dose of Comirnaty (Pfizer) or Spikevax (Moderna) should defer further doses of an mRNA COVID-19 vaccine and if they are > 18 years can consider Vaxzevria on a case-by-case basis, after they have recovered from their symptoms.

NACI, CANADA (link)

- On January 14, 2022, the Public Health Agency of Canada (PHAC) released updated guidance from the National Advisory Committee on Immunization (NACI) in the COVID-19 vaccine chapter of the Canadian Immunization Guide, on the topic vaccination following myocarditis and pericarditis. This chapter includes NACI's recommendations on the use of COVID-19 vaccines up to and including January 14, 2022.
- Rare cases of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the heart lining) following vaccination with COVID-19 mRNA vaccines have been reported in Canada and internationally. Most cases have occurred in males 12 to 29 years of age after a second dose of an mRNA vaccine. Most cases have been mild and resolved quickly.
- Following review of the latest evidence and consultation with Canadian cardiologists, NACI has issued updated guidance on re-vaccination with COVID-19 vaccines for those who experienced myocarditis and/or pericarditis after a previous dose of an mRNA COVID-19 vaccine.
- Since June 2021, NACI has recommended that people who experienced myocarditis and/or pericarditis after a first dose of an mRNA COVID-19 vaccine should wait to get their second dose until more information was available.
- NACI continues to recommend that:
    - In most circumstances, and as a precautionary measure until more information is available, further doses of mRNA COVID-19 vaccines should be deferred among people who experienced myocarditis (with or without pericarditis) within 6 weeks of receiving a previous dose of an mRNA COVID-19 vaccine. This includes any person who had an abnormal cardiac investigation including electrocardiogram (ECG), elevated troponins, echocardiogram, or cardiac MRI after a dose of an mRNA vaccine.
- NACI now recommends that:
    - Those with a history compatible with pericarditis and who either had no cardiac workup or had normal cardiac investigations, can receive the next dose once they are symptom free and at least 90 days has passed since vaccination

- Some people with confirmed myocarditis (with or without pericarditis) after a dose of an mRNA COVID-19 vaccine may choose to receive another dose of vaccine after discussing the risks and benefits with their healthcare provider. If another dose of vaccine is offered, they should be offered the Pfizer-BioNTech 30 mcg vaccine due to the lower reported rate of myocarditis and/or pericarditis following the Pfizer-BioNTech 30 mcg vaccine compared to the Moderna 100 mcg vaccine. Informed consent should include discussion about the unknown risk of recurrence of myocarditis and/or pericarditis following receipt of additional doses of Pfizer-BioNTech COVID-19 vaccine in individuals with a history of confirmed myocarditis and/or pericarditis after a previous dose of mRNA COVID-19 vaccine, as well as the need to seek immediate medical assessment and care should symptoms develop.

Next Steps	Share with CV TAG
In the development of this work, the following parties have been consulted with:	

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

1. Mevorach, D., et al., *Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel.* New England Journal of Medicine, 2021.
2. Montgomery, J., et al., *Myocarditis Following Immunization With mRNA COVID-19 Vaccines in Members of the US Military.* JAMA Cardiology, 2021. **6**(10): p. 1202-1206.
3. Diaz, G.A., et al., *Myocarditis and Pericarditis After Vaccination for COVID-19.* JAMA, 2021. **326**(12): p. 1210-1212.
4. Oster, M.E., et al., *Myocarditis Cases Reported After mRNA-Based COVID-19 Vaccination in the US From December 2020 to August 2021.* JAMA, 2022. **327**(4): p. 331-340.
5. Minocha, P.K., et al., *Recurrence of Acute Myocarditis Temporally Associated with Receipt of the mRNA Coronavirus Disease 2019 (COVID-19) Vaccine in a Male Adolescent.* The Journal of pediatrics, 2021. **238**: p. 321-323.
6. Giuseppe Di Tano, et al., *Recurrent Myocarditis after the First Dose of SARS-CoV-2 mRNA-1273 Vaccine.* Annals of Clinical Case Reports, 2021.
7. Hause, A., Baggs, J, Marquez, P, et al. , *Safety Monitoring of COVID-19 Vaccine Booster Doses Among Adults — United States, September 22, 2021–February 6, 2022.* . MMWR Morb Mortal Wkly Rep, 2022. **71**: p. 249–254.
8. Israel Ministry of Health. *Vaccine Safety Follow-Up*. 2021; Available from: https://www.gov.il/BlobFolder/reports/vacVaccine-efficacy-safety-follow-up-committee/en/files_publications_corona_vaccine-safty-15122021.pdf.
9. UK MHRA. *Coronavirus vaccine - weekly summary of Yellow Card reporting 24 February 2022*. 2022; Available from: https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting.
10. Self, W.H., et al., *Comparative Effectiveness of Moderna, Pfizer-BioNTech, and Janssen (Johnson & Johnson) Vaccines in Preventing COVID-19 Hospitalizations Among Adults Without Immunocompromising Conditions - United States, March-August 2021.* MMWR Morb Mortal Wkly Rep, 2021. **70**(38): p. 1337-1343.
11. Heath, P.T., et al., *Efficacy of the NVX-CoV2373 Covid-19 Vaccine Against the B.1.1.7 Variant*. 2021, Cold Spring Harbor Laboratory.
12. Mallory, R., et al. *Immunogenicity and Safety Following a Homologous Booster Dose of a SARS-CoV-2 recombinant spike protein vaccine (NVX-CoV2373): A Phase 2 Randomized Placebo-Controlled Trial*. medRxiv 2021; 2021.12.23.21267374]. Available from: http://medrxiv.org/content/early/2021/12/24/2021.12.23.21267374.abstract.
13. Munro, A.P.S., et al., *Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) following two doses of ChAdOx1 nCov-19 or BNT162b2 in the UK (COV-BOOST): a blinded, multicentre, randomised, controlled, phase 2 trial.* The Lancet, 2021. **398**(10318): p. 2258-2276.
14. Medsafe. *Approval status of COVID vaccines applications received by Medsafe*. 2021 25 August 2021 [cited 2021 18 October]; Available from: https://www.medsafe.govt.nz/COVID-19/status-of-applications.asp.
15. Medsafe - New Zealand Medicines and Medical Devices Safety Authority. *New Zealand Data Sheet, Comirnaty Covid-19 Vaccine*. 2021; Available from: https://www.medsafe.govt.nz/profs/Datasheet/c/comirnatyinj.pdf.
16. Medsafe - New Zealand Medicines and Medical Devices Safety Authority. *New Zealand Data Sheet, Comirnaty Covid-19 Vaccine 5 to 11 years of age (10 micrograms/0.2 mL dose)*. 2021; Available from: https://www.medsafe.govt.nz/profs/Datasheet/c/Comirnaty0.2mlOrangeCapinj.pdf.
17. Medsafe. *New Zealand Data Sheet: AstraZeneca*. 2022; Available from: https://www.medsafe.govt.nz/profs/Datasheet/c/Covid19VaccineAstraZenecainj.pdf.
18. Hansen, C.H., et al. *Vaccine effectiveness against SARS-CoV-2 infection with the Omicron or Delta variants following a two-dose or booster BNT162b2 or mRNA-1273 vaccination series: A Danish*

cohort study. 22 Dec 2021; Available from: https://www.medrxiv.org/content/10.1101/2021.12.20.21267966v2.full.pdf.

19. UK Health Security Agency. *SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 34*. 14 January 2022; Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1046853/technical-briefing-34-14-january-2022.pdf.
20. Vanshylla, K., et al. *Durability of Omicron-neutralizing serum activity following mRNA booster immunization in elderly individuals*. 2 Feb 2022; Available from: https://www.medrxiv.org/content/10.1101/2022.02.02.22270302v1.full.pdf.
21. Lyngse, F.P., et al. *SARS-CoV-2 Omicron VOC Transmission in Danish Households*. medRxiv 2021; 2021.12.27.21268278]. Available from: http://medrxiv.org/content/early/2021/12/27/2021.12.27.21268278.abstract.
22. UK Health Security Agency. *SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 35. 28 January 2022.*; Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1050999/Technical-Briefing-35-28January2022.pdf.
23. UK Health Security Agency. *COVID-19 Vaccine Surveillance Report. 27 January 2022.*; Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1050721/Vaccine-surveillance-report-week-4.pdf.
24. Collie, S., et al., *Effectiveness of BNT162b2 Vaccine against Omicron Variant in South Africa.* New England Journal of Medicine, 2021.
25. Gray, G.E., et al., *Vaccine effectiveness against hospital admission in South African health care workers who received a homologous booster of Ad26.COV2 during an Omicron COVID19 wave: Preliminary Results of the Sisonke 2 Study.* medRxiv, 2021: p. 2021.12.28.21268436.
26. UK Health Security Agency. *Effectiveness of 3 doses of COVID-19 vaccines against symptomatic COVID-19 and hospitalisation in adults aged 65 years and older*. 2022; Available from: https://khub.net/documents/135939561/338928724/Effectiveness+of+3+doses+of+COVID-19+vaccines+against+symptomatic+COVID-19+and+hospitalisation+in+adults+aged+65+years+and+older.pdf/ab8f3558-1e16-465c-4b92-56334b6a832a.
27. Tartof, S.Y., et al., *BNT162b2 (Pfizer–Biontech) mRNA COVID-19 Vaccine Against Omicron-Related Hospital and Emergency Department Admission in a Large US Health System: A Test-Negative Design.* SSRN Electronic Journal, 2022.
28. Thompson, M.G., et al., *Effectiveness of a Third Dose of mRNA Vaccines Against COVID-19–Associated Emergency Department and Urgent Care Encounters and Hospitalizations Among Adults During Periods of Delta and Omicron Variant Predominance — VISION Network, 10 States, August 2021–January 2022.* MMWR. Morbidity and Mortality Weekly Report, 2022. **71**(4).

Document 12

MINUTES: COVID-19 Vaccine Technical Advisory Group

Date:	Tuesday 08 March 2022
Time:	11:00am to 12:00pm
Location:	Teams: s 9(2)(k) [redacted]
Chair:	David Murdoch
Members:	Danny de Lore, Elizabeth Wilson, Helen Petousis-Harris, Ian Frazer, James Ussher, Nikki Moreland, Nikki Turner, Owen Sinclair, Sue Crengle, Tony Walls
Ministry of Health Attendees:	s 9(2)(g)(ii) [redacted]
Guests:	
Apologies:	

5.0	**Myocarditis and Booster Options** • The Ministry received a letter from IMAC in February requesting CV TAG's advice on boosters for mandated workers who had myocarditis after their second dose. Concern was expressed about the use of AstraZeneca in this population, due to some reports of myocarditis and the link to thrombosis with thrombocytopaenia (TTS) in age groups under 50. • An evidence review on the risk of myocarditis after Pfizer and AstraZeneca was presented to CV TAG. • Data from the roll-out of boosters in the US and Israel shows myocarditis rates were lower than from second doses. AstraZeneca rates were not higher than background rates, though the risk of TTS must be considered. • A member sort clarification from the RfA highlighting that IMAC was not currently recommending revaccination with Pfizer and have been recommending deferral until now, as is also the policy in the US. This will be updated. NACI in Canada suggest that further mRNA doses can be given at least 90 days post-myocarditis. Australia's advice is a case-by-case approach, noting the risks of AstraZeneca. • TAG members noted the risk of myocarditis for the vaccine against the risk from COVID-19, which still favour getting protection from a booster. • There was discussion among CV TAG members on the varying factors and risk associated with each vaccine booster with regards to previous symptoms, age, sex and infection. It was agreed that

if someone had presented with side effects such as myocarditis from Pfizer, they should not have to have a booster of Pfizer. Acknowledgments were made that there are other options for these individuals.

- It was agreed that advice must be nuanced and developed on a case-by-case basis, varying by individual to support individualised support plans, in order to account for specific risk factors relating to previous infection, age and sex.
- Discussions may be needed with the exemptions team to explore possibilities.
- Individuals should be considered for Novavax if approved as a booster.

ACTION: STA will draft a memo with CV TAG's recommendations and circulate.

Document 13

MINUTES: COVID-19 Vaccine Technical Advisory Group

Date:	Tuesday 13 September 2022
Time:	11:00am to 12:00pm
Location:	Teams: s 9(2)(k) [redacted]
Chair:	Ian Town
Members:	Danny de Lore, David Murdoch, Elizabeth Wilson, Helen Petousis-Harris, James Ussher, Nikki Moreland, Nikki Turner, Owen Sinclair, Peter McIntyre, Sue Crengle, Tony Walls
Ministry of Health Attendees:	s 9(2)(g)(ii) [redacted]
Guests:	
Apologies:	

8.0	**Update on Medsafe myocarditis Study** A Medsafe staff member gave a status update of the study which includes people aged 12+ years who experienced a case of myocarditis or pericarditis after receiving any dose of COVID-19 vaccine. Cases were identified through the Centre for Adverse Reactions Monitoring (CARM) and will be followed up for a minimum of three months after onset of illness. The recruitment phase has finished and results from the consumer survey (n=300, response rate of 68%) are expected by end of October; the health care professionals survey (n=143, response rate of 49%) is expected follow afterwards. An additional sub-analysis based on CDC criteria will be performed to make results internationally comparable. **Prescriber alert for Nuvaxovid issued by Medsafe**

Document 14

MINUTES: COVID-19 Vaccine Technical Advisory Group

Date:	Tuesday 6 December 2022
Time:	11:00am to 12:00pm
Location:	Teams: s 9(2)(k) [redacted]
Chair:	Ian Town
Members:	s 9(2)(g)(ii) [redacted]
Ministry of Health Attendees:	
Apologies:	

8.0	**Vaccine Safety Surveillance Studies** An overview and summary of the self-control case studies on Myocarditis and pericarditis following vaccination and infection with COVID-19 was presented to members.