

Memo

Myocarditis following vaccination: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations on the use of the Pfizer vaccine

Date:	21 July 2021
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From:	Dr Ian Town, Chief Science Advisor
For your:	Information

Purpose of report

1. To summarise the COVID-19 Vaccine Technical Advisory Group's (CV TAG) recommendations on the use of Pfizer mRNA COVID-19 vaccine in the context of the risk of myocarditis and/or pericarditis following vaccination.

Context

2. Myocarditis is an inflammation of the heart muscle; pericarditis is an inflammation of the thin tissue surrounding the heart (pericardium). Hereafter the risk will be referred to as myocarditis and/or pericarditis.
3. Emerging data from countries such as the United States of America (USA) and Israel, indicate that there is a risk of myocarditis and/or pericarditis following Pfizer and Moderna mRNA COVID-19 vaccination. The risk appears to be higher following the second dose, in males and in younger age groups.
4. Background rates for myocarditis and/or pericarditis in younger populations tend to be age-dependent; based on international data, the estimated incidence rate ranges from 8.4-20 per million person-years for 0-19 year-olds (which corresponds to a risk of approximately 1 in 50,000 to 1 in 119,000 people over the course of a year). However, the background risk for children and young adults (i.e. how often myocarditis and/or pericarditis occurs each year from general observation) is highest for male children and adolescents aged over 12 years (see Table 1).

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[1]
	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[2]
UK	0-19 years	20.0	1 in 50,000	ACCESS (based on CPRD GP database)[3]
Italy	0-19 years	8.4	1 in 119,000	ACCESS (based on PediaNET, Italian GP database)[3]
Finland	0-15 years	19.5	1 in 513,000	Arola et al, 2017[4]
	Males, 0-11 years	Approximately 0-20	1 in 50,000 to NE*	
	Males, 12-15 years	Approximately 50-135	1 in 7,400 to 1 in 20,000	
	Females, 0-11 years	Approximately 0-10	1 in 100,000 to NE*	
	Females, 12-15 years	Approximately 10-35	1 in 29,000 to 1 in 100,000	

*NE=Not estimable

5. COVID-19 itself is associated with a range of cardiac complications, the most common of which are heart failure, myocardial injury and arrhythmias.[5] The magnitude of the risk of myocarditis after COVID-19 is uncertain. A USA study published in JAMA Cardiology of 1,597 young college athletes with a history of COVID-19 reported that between 0.3-2.3% had myocarditis, depending on the diagnostic criteria.[6]
6. 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.[1]

7. Based on data presented on 23 June 2021 to the United States Centre for Disease Control and Prevention (CDC) Advisory Committee on Immunisation Practices (ACIP) and follow-up data published 06 July 2021, the risk of myocarditis and/or pericarditis over the 7 days after the second dose of the mRNA COVID-19 vaccines was estimated to be approximately 1 in 25,000 for males 12-29 years, and 1 in 240,000 for females 12-29 years (see Table 2). For individuals 30 years and over, the corresponding risks were 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.[7, 8] In addition, lower rates of myocarditis could in part be due to under-diagnosis in women.[9]

Table 2. 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[7] based on confirmed and unconfirmed cases after administration of an mRNA COVID-19 vaccine (Pfizer or Moderna), reported to VAERS.
	Males, 30 years and over, within 7 days post dose 2 of mRNA vaccine	2.4	1 in 417,000	
	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[8]
	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[8]
	Females, 12-39 years, within 21 days post dose 2 of Pfizer COVID-19 vaccine	NE*	NE	

*NE=not estimable

8. 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.**
9. On 25 June 2021, the United States Food and Drug Administration (FDA) added a warning for myocarditis and pericarditis to the Pfizer and Moderna COVID-19 vaccine fact sheets after

observing cases following vaccination.[10] Although evidence is still emerging, data presented to the US CDC's ACIP support a causal link to mRNA vaccines.

10. On 09 July 2021, the European Medicines Agency's (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) recommended adding myocarditis and/or pericarditis as a side effect for the Pfizer and Moderna vaccines, and added a warning for myocarditis to both vaccines. The PRAC reviewed 145 cases of myocarditis that were reported in the European Economic Area (EEA) among people who received Pfizer, and 19 cases among people who received Moderna. Separately, the PRAC also reviewed reports of 138 cases of pericarditis following the use of Pfizer and 19 cases following the use of Moderna. 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.
11. In Israel, the Ministry of Health reported in a press release that 121 cases of myocarditis had been reported within 30 days of a second dose of mRNA vaccine, out of approximately 5 million vaccinated individuals. This corresponds to an overall population risk after the second dose of approximately 1 in 42,000. Limited information was available in the press release, however, the Israeli Ministry of Health reported that events were mostly reported in young men aged 16-19 years, usually after the second dose. It was also reported that most cases were hospitalised but 95% of cases were considered to have mild illness with recovery over a few days.
12. 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.[13] Through 10 July 2021, approximately 7.8 million second doses of the Pfizer COVID-19 vaccine have been administered in Canada.[14] 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).
13. In Australia, to 04 July 2021, the Therapeutic Goods Administration (TGA) has received reports of 38 cases of suspected myocarditis and/or pericarditis following vaccination (note that the vaccine type was not specified in TGA's Weekly Safety Report for 08 July 2021). Approximately 3.2 million doses have been administered in Australia to the 08 July 2021, which corresponds to a risk of approximately 1 in 84,000 doses (this includes first and second doses). TGA stated that, of the 38 reports, "*...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. As of 08 July 2021, the TGA states that it plans to add a warning to the Product Information regarding myocarditis and/or pericarditis.
14. In Aotearoa New Zealand, as of 01 July 2021, 10 reports of myocarditis and/or pericarditis occurring in individuals following vaccination with the Pfizer COVID-19 vaccine have been received by Centre for Adverse Reactions Monitoring (CARM). Of the 10 cases, 4 were male, 2 were in individuals less than 30 years old (1 male, 1 female), and the ages of the individuals ranged from 24-63 years. Reported time from vaccination to onset was up to 18 days, with 2 cases occurring after the first dose and 8 after the second dose. All cases have been medically assessed by CARM and follow-up information sought.

15. 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 arrhythmias.*
16. 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.
17. 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.
18. 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.
19. In Aotearoa New Zealand, as of 14 July 2021, 64,298 individuals aged 15-29 years have received two doses of the Pfizer vaccine, including 5,922 Māori and 5,196 Pacific Peoples.
20. With regards to vaccine hesitancy, younger individuals (i.e., under the age of 30) tend to be more vaccine hesitant than older age groups. Vaccine hesitancy appears to not be differentially associated with ethnicity in Aotearoa New Zealand once age and educational differences are accounted for.

21. The Ministry's Policy team sought clinical and scientific advice from CV TAG on the potential risk of myocarditis following vaccination. This advice will be considered as part of the Decision to Use Framework and alongside policy considerations on the sequencing of the COVID-19 Vaccine and Immunisation Programme.

Recommendations

22. CV TAG met on 06 July 2021 and 20 July 2021, assisted by a paediatric cardiologist, to consider recommendations regarding the potential risk of myocarditis and/or pericarditis after Pfizer mRNA COVID-19 vaccination.
23. **CV TAG noted that:**
- Two doses of the Pfizer vaccine are recommended to achieve the maximum level of protection, as per the provisional Medsafe approval. This is true for people of all ages and is particularly important for those 30 years and over who are more at risk of severe disease from COVID-19.
 - Symptom onset for myocarditis and/or pericarditis following mRNA COVID-19 vaccination is usually within 7 days following the second dose, and can present with chest pain, breathlessness, and/or racing pulse.
 - There have been a small number of cases of myocarditis reported in Aotearoa New Zealand. There is limited information to fully characterise the risk of myocarditis after vaccination in Aotearoa New Zealand.
 - There are no pre-existing conditions or other factors known to be associated with increased risk of myocarditis in children or adults. Although the risks of myocarditis tend to be age and gender-dependent in the general population, there is not enough evidence to date to recommend a precaution for any pre-existing conditions.
 - There is no evidence, to date, to suggest that pre-existing rheumatic heart disease is a risk factor for myocarditis. In Aotearoa New Zealand, rheumatic heart disease is prevalent in several populations who may be particularly vulnerable to COVID-19, including in Māori and Pacific Peoples.
 - CARM and the COVID-19 Vaccine Independent Safety Monitoring Board (CV-ISMB) will continue to monitor closely and review any reports of myocarditis and/or pericarditis following COVID-19 vaccination in Aotearoa New Zealand.
24. **CV TAG recommends that:**
- People aged 16-29 years receive their second dose of the Pfizer COVID-19 vaccine at least 8 weeks after the first dose. A longer interval between doses may reduce the frequency of some side effects while conferring robust protection from COVID-19.
 - People aged 12-29 years who require regular clinical review by a cardiologist are advised to discuss the risks and benefits of the COVID-19 vaccine with their healthcare team in order to plan a vaccination schedule that best supports their needs.
 - People aged 30 years and over should still receive two doses of the vaccine, at least 21 days apart. Myocarditis and/or pericarditis after vaccination in this group is rare,

and the risks of severe disease and sequelae due to COVID-19 are substantially higher in older compared to younger age groups.

- d) 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 sources.
 - e) If, after discussion with their health care provider, the individual and/or their whānau decides that the benefits of receiving two doses and gaining robust protection against COVID-19 sooner, outweigh the potential risks, then the individual may receive the second dose as per the current indication.
25. The evidence on myocarditis and/or pericarditis following COVID-19 vaccination is still preliminary. CV TAG will continue to monitor all relevant information and will update their recommendations as further evidence becomes available.

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