Document 1

Memo

Third Primary Pfizer mRNA COVID-19 vaccine dose in the immunocompromised: COVID-19 Vaccine Technical Advisory Group (CV TAG) Updated recommendations

Date:	17 November 2021
To:	Joanne Gibbs, Director of National Operations, COVID Vaccine Immunisation Programme
From:	Dr Ian Town, Chief Science Advisor
For your:	Consideration

Purpose of report

1. To summarise the COVID-19 Vaccine Technical Advisory Group's (CV TAG) updated recommendations on the use of a third primary Pfizer mRNA COVID-19 vaccine dose in those who are severely immunocompromised.

Background and context

2. On 21 September 2021, CV TAG issued recommendations for a third primary Pfizer mRNA COVID-19 vaccine dose in the immunocompromised. CV TAG recommended that:
    a. Those with severe immunocompromise be offered an additional dose of the Pfizer vaccine. The list of eligible individuals is taken from the one developed by the UK's Joint Committee on Vaccination and Immunisation (JCVI).[1]
    b. The additional dose should be administered more than 8 weeks after the second dose, with special attention paid to current or planned immunosuppressive therapies. Where possible, the third primary dose should be delayed until 2 weeks after the period of immunosuppression, in addition to the time period for clearance of the therapeutic agent. If not possible, consideration should be given to vaccination during a treatment 'holiday' or at a nadir of immunosuppression between doses of treatment.
    c. The administration of an additional dose is covered by s25 of The Medicines Act 1981, and as such, should only be offered by an authorised prescriber with informed consent from the consumer.
    d. The standard two-dose course of vaccine should be offered to any eligible unvaccinated household contacts aged 12 and over, of immunocompromised individuals.
3. Since then, the Australian Technical Advisory Group on Immunisation (ATAGI) issued updated guidance on the use of a third primary dose of COVID-19 vaccine in individuals who are severely immunocompromised.[2]

4. The Ministry has also received requests for a revised list of individuals from rheumatologists, haematologists, and gastroenterologists.

5. Accordingly, CV TAG met on 9 November 2021 to update recommendations for the use of a third primary Pfizer COVID-19 vaccine dose in the immunocompromised, based on the recently released ATAGI guidance.

Recommendations

6. CV TAG recommend that:

   a. All individuals aged 12 years and over who are severely immunocompromised should be offered a third primary dose of the Pfizer vaccine.

      i. The updated guidance on individuals who should be offered a third primary dose of the Pfizer COVID-19 vaccine is provided in Appendix 1. The list is not exhaustive but provides guidance on scenarios where a consumer should receive a third primary dose. The list may expand or be modified over time as more evidence emerges. Advice for clinicians on the guidance is available through the Immunisation Advisory Centre, and this information will be updated periodically through the Immunisation Handbook.

      ii. Clinical judgement should be applied by the prescriber to determine whether a third primary dose is required for conditions or medicines that are not listed that are associated with severe immunocompromise.

   b. The third primary dose should be administered from 8 weeks after the second dose but can be administered from 4 weeks after the second dose after consideration of current or planned immunosuppressive therapies.

      i. For time limited immunosuppressive treatment, where possible the dose should be delayed until 2 weeks after the period of immunosuppression, in addition to the time period for clearance of the therapeutic agent.

      ii. For long term immunosuppressive treatment, consideration should be given to vaccination during a treatment 'holiday'.

   c. Pfizer is the preferred vaccine in New Zealand for the third primary dose. AstraZeneca can be used for the third dose if a significant adverse reaction has occurred after a previous mRNA vaccine dose which contraindicates further doses of mRNA vaccine (e.g. anaphylaxis, myocarditis).

   d. The administration of a third primary dose is covered by s25 of The Medicines Act 1981, and as such, should only be offered by an authorised prescriber with informed consent from the consumer.

   e. The third primary dose should be distinguished from the booster dose. Those aged over 18 who are immunocompromised and have received a third primary dose of a COVID-19 vaccine should only receive a booster dose 6 months after completion of their primary course (i.e., 6 months after their third dose). The booster dose can be spaced strategically to allow for optimal dosing in the immunocompromised.

   f. The standard two-dose course of vaccine should be offered to any eligible unvaccinated household contacts (aged 12 and over) of immunocompromised individuals.

7. CV TAG will continue to monitor all relevant information and will update their recommendations as further evidence becomes available.

Dr Ian Town

Chief Science Advisor and

Chair of the COVID-19 Vaccine Technical Advisory Group

Appendix 1

Updated guidance on individuals who should be offered a third primary dose of the Pfizer COVID-19 vaccine

Note: *This list has been updated based on the recent ATAGI guidance. It is not exhaustive but provides guidance on scenarios where a consumer should receive a third primary dose. Drug dose, disease activity, and co-morbidity can affect the severity of immunocompromise. The list may expand or be modified over time as more evidence emerges. Advice for clinicians on the guidance is available through the Immunisation Advisory Centre, and this information will be updated periodically through the Immunisation Handbook.*

- *Clinical judgement should be applied by the prescriber to determine whether a third primary dose is required for conditions or medicines that are not listed below that are associated with severe immunocompromise.*
- *Conversely, clinicians may decide that individual patients with conditions or medicines listed below are at low risk of being severely immunocompromised and do not require a third primary vaccine dose.*

1. Individuals with primary or acquired immunodeficiency states at the time of vaccination due to conditions including but not limited to (see note above):
    a. acute and chronic leukaemias, and clinically aggressive lymphomas (including Hodgkin's lymphoma) who were under treatment or within 12 months of achieving cure.
    b. individuals under follow up for chronic lymphoproliferative disorders including haematological malignancies such as indolent lymphoma, chronic lymphoid leukaemia, myeloma, Waldenstrom's macroglobulinemia and other plasma cell dyscrasias.
    c. immunosuppression due to HIV/AIDS with a current CD4 count of <200 cells/µl for adults or children 12 years of age and over.
    d. primary or acquired cellular and combined immune deficiencies – those with lymphopaenia ($<10^9$ lymphocytes/L) or with a functional lymphocyte disorder.
    e. those who had received an allogeneic (cells from a donor) or an autologous (using their own cells) stem cell transplant in the previous 24 months.
    f. those who had received a stem cell transplant more than 24 months ago but had ongoing immunosuppression or graft versus host disease (GVHD).
    g. persistent agammaglobulinaemia (IgG <3g/L) due to primary immunodeficiency (for example, common variable immunodeficiency) or secondary to disease/therapy.

2. Individuals on, or recently on, immunosuppressive therapy at the time of vaccination including but not limited to (see note above):
    a. receiving immunosuppressive therapy for a solid organ transplant.
    b. received within the previous 6 months rituximab or other B cell-depleting biologic therapy for autoimmune or autoinflammatory disease.
    c. received within the previous 3 months other biologics or targeted therapy for autoimmune or autoinflammatory disease. Examples are provided in **Table 1** and are

based on the ATAGI list. Clinicians may use their judgement for medicines which are not listed.

d. received within the previous 6 months cytotoxic chemotherapy or immunosuppressive radiotherapy for any indication.

3. Individuals with chronic immune-mediated inflammatory disease who were receiving or had received immunosuppressive therapy prior to vaccination including but not limited to (see note above):
    a. high dose or long-term moderate dose corticosteroids. Indicative dosage thresholds are provided in **Table 2**.
    b. immunosuppressants:
        i. including mycophenolate, methotrexate, leflunomide, thiopurines (e.g., azathioprine), 6-mercaptopurine, alkylating agents (e.g., cyclophosphamide, chlorambucil), and systemic calcineurin inhibitors (e.g., cyclosporin, tacrolimus). Clinical judgement should be applied by the prescriber to determine whether a third primary dose is required.
        ii. excluding hydroxychloroquine, sulfasalazine, or mesalazine, when used as monotherapy
    c. combinations of immunosuppressive therapy where the cumulative effect is considered to be severely immunosuppressive, as determined by clinical judgement.

4. Individuals receiving long term haemodialysis or peritoneal dialysis should be offered a third primary dose of the Pfizer COVID-19 vaccine.

Table 1: Examples for biologics

A third primary dose **is recommended** for people taking the following biologics	
Class	Examples
Anti CD 20 antibodies	rituximab, obinutuzumab, ocrelizumab
BTK inhibitors	ibrutinib,
JAK inhibitors	ruxolitinib
Sphingosine 1-phosphate receptor modulators	fingolimod
Anti-CD52 antibodies	alemtuzumab
Anti-complement antibodies	eculizumab
Anti-thymocyte globulin	anti-thymocyte globulin
A third primary dose **is not routinely recommended** for people taking the following biologics*	
Anti-integrins	natalizumab
Anti-TNF-α antibodies	infliximab, adalimumab, etanercept
Anti-IL1 antibodies	anakinra
Anti-IL6 antibodies	tocilizumab
Anti-IL17 antibodies	secukinumab
Anti-IL4 antibodies	dupilumab
Anti-IL23 antibodies	ustekinumab
Immune checkpoint inhibitors	nivolumab, pembrolizumab, ipilimumab, atezolizumab

*A third primary dose is recommended for people taking multiple immunosuppressants where the cumulative effect is considered to be severely immunosuppressive.

Table 2: Indicative dosage thresholds for corticosteroids

A third primary dose **is recommended** for:
a. Individuals with chronic immune-mediated inflammatory disease: i. on high dose corticosteroids (equivalent to ≥20mg prednisone per day for more than 10 days, in the previous month) ii. on long-term moderate dose corticosteroids (equivalent to ≥10mg prednisone per day for more than 4 weeks, in the previous 3 months) b. Individuals who had received high-dose steroids (equivalent to >40mg prednisone per day for more than a week) for any reason, in the previous month
A third primary dose **is not routinely recommended** for:
a. Individuals who had received brief immunosuppression (equivalent to ≤40 mg prednisone per day), for example, asthma / chronic obstructive pulmonary disease / COVID-19) b. Individuals receiving low dose locally acting steroids (inhaled or topical) c. Individuals on replacement corticosteroids for adrenal insufficiency

References

1. JCVI. *Updated JCVI guidance for vaccinating immunosuppressed individuals with a third primary dose*. 2021 02 September 2021 [cited 2021 12 September]; Available from: https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2021/09/C1399-Updated-JCVI-guidance-for-vaccinating-immunosuppressed-individuals-with-third-primary-dose.pdf.
2. Australian Government Department of Health. *ATAGI recommendations on the use of a third primary dose of COVID-19 vaccine in individuals who are severely immunocompromised*. 3 November 2021; Available from: https://www.health.gov.au/resources/publications/atagi-recommendations-on-the-use-of-a-third-primary-dose-of-covid-19-vaccine-in-individuals-who-are-severely-immunocompromised.

Document 2

Memo

COVID-19 Vaccine Technical Advisory Group (CV TAG) position statement: Vaccination mandates in those under 18 years of age

Date:	9 December 2021
To:	Dr Ashley Bloomfield, Director-General of Health
Cc:	Astrid Koorneef, Director of National Operations, COVID Vaccine Immunisation Programme Maree Roberts, DDG, System Strategy and Policy Dr Caroline McElnay, Director of Public Health
From:	Dr Ian Town, Chief Science Advisor
For your:	Consideration

Purpose of report

1. To state the COVID-19 Vaccine Technical Advisory Group's (CV TAG) position on requiring two doses of Pfizer COVID-19 vaccine to fulfil vaccine mandates in those aged under 18 years.

Context

2. In November 2021, CV TAG advice was sought to determine the definition of fully vaccinated within New Zealand.
3. That advice set out which vaccination schedules would allow an individual to be considered fully vaccinated and was signed by you on 11 November 2021.
4. This definition of fully vaccinated has been used to immediate effect as part of mandatory vaccination orders and the issuing of vaccination certificates.
5. As part of its recommendations, CV TAG noted in this memo that 'younger age groups are more at risk than older age groups of myocarditis after the second dose of Pfizer vaccine, while a robust antibody response and early limited clinical effectiveness data indicate some protection from COVID-19 after a ***single dose*** of Pfizer vaccine in these younger age groups'.
6. Consequently, CV TAG expressed concern about vaccine mandates requiring younger age groups (e.g. <18 years) to be vaccinated with 2 doses of the Pfizer vaccine and stated: ***'consideration should be given to permitting younger people who have had one dose to be permitted to work or undertake other activities covered by the mandate'.***
7. This particular detail has not been carried through to the implementation of this advice.
8. CV TAG met on 23 and 30 November 2021 and discussed the requirement for two doses of the Pfizer vaccine in those aged <18 years, noting a wish to reiterate their previous position.

9. **CV TAG noted that:**

   a. The individual risk to young people of severe disease is very low. For them to make an informed decision not to get a second dose of the vaccine eg, due to potential myocarditis risk is justified.

   b. Risks associated with the transmission of COVID-19 throughout Aoteraoa New Zealand among those aged <18 years are insufficient to justify mandating a 2 dose schedule of the Pfizer vaccine prior to working in any environment.

   c. The 2 dose schedule, particularly when administered in the shortest possible clinical timeframe, may add unnecessary risk to increasing the likelihood of myocarditis as an outcome in this population.

   d. Requiring vaccination certificates for children could produce unintended consequences such as exclusion from educational activities

   e. 2 doses of Pfizer vaccine represent a full primary course of vaccination, but in the young (aged <18 years), there should not be pressure to receive these doses at the shortest possible interval as indicated by the current approach to vaccination certificates and mandates.

   f. Aside from the mandatory vaccination settings, informal exclusions are facilitated by issuing vaccination certificates for those under the age of 18 years, disproportionately disadvantaging children against a minimal reduction in public health risk.

10. **CV TAG recommends that consideration be given to:**

   a. Those aged <18 years only being required to have received 1 dose of Pfizer vaccine to meet the vaccine requirements for employment.

11. CV TAG will continue to monitor all relevant information and will update their recommendations as further evidence becomes available.

Dr Ian Town

Chief Science Advisor and

Chair of the COVID-19 Vaccine Technical Advisory Group

Document 3

MINISTRY OF HEALTH
MANATŪ HAUORA

Memo

Decision to use the Pfizer mRNA COVID-19 vaccine for children aged 5-11 years: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations

Date:	15 December 2021
To:	Dr Ashley Bloomfield, Director-General of Health
Copy to:	Astrid Koornneef, Director of National Operations, COVID Vaccine Immunisation Programme Allison Bennett, Manager, System Enablers, System Strategy and Policy Dr Caroline McElnay, Director of Public Health
From:	Dr Ian Town, Chief Science Advisor and Chair of CV TAG
For your:	Information

Purpose of report

1. To summarise the CV TAG recommendations on the decision to use the paediatric formulation of the Pfizer mRNA COVID-19 vaccine ('the Pfizer vaccine') for children who are 5 to 11 years of age.

Background and context

2. In February 2021, CV TAG advice was sought for use of the Pfizer COVID-19 vaccine in people who were 16 years and over, following Medsafe approval. Cabinet agreed that the COVID-19 Immunisation Programme proceed with the roll out of the Pfizer vaccine, and this has been underway since February.
3. In August 2021, CV TAG confirmed support to extend the age of people who can receive the Pfizer vaccine to 12- to 15-year-olds, noting that this would likely lead to a reduction in school closures and disruption to education, and contribute to equitable vaccination coverage in Māori and Pacific peoples.
4. Medsafe is assessing an application submitted by Pfizer for the use of a paediatric formulation of the vaccine in 5- to 11-year-olds within New Zealand. The CV TAG recommendations presented here are subject to Medsafe approval and any listed clinical conditions.
5. The Ministry's Policy team has sought clinical and scientific advice from CV TAG on the use of the Pfizer vaccine for children who are 5- to 11-years of age. This advice will be considered as

part of the Decision to Use Framework, and alongside policy considerations for the sequencing of the COVID-19 Immunisation Programme.

The COVID-19 vaccine in 5- to 11-year-olds

Phase 2/3 trial findings

6. One phase 2/3 randomised control trial was conducted to assess the safety, immunogenicity, and efficacy of two doses of the Pfizer vaccine administered 21 days apart in children aged 6 months to 11 years, with findings published for 5- to 11-year-olds to date [1].

7. In the phase 2/3 trial, participants were randomly assigned in a 2:1 ratio to receive two doses of either the Pfizer vaccine at 10 µg (a lower dose than the 30 µg used in older age groups), or a placebo. A total of 2268 children were assigned to receive the Pfizer vaccine (1517 children) or placebo (751 children) [1].

8. The trial was run across 81 sites in the US, Spain, Finland and Poland. Overall, 52% were male, 79% were White, 6% were Black, 6% were Asian, and 21% were Hispanic or Latinx. The mean age was 8.2 years; 20% of children had coexisting conditions (including 12% with obesity and approximately 8% with asthma), and 9% were SARS-CoV-2–positive at baseline. Demographic characteristics were similar between the 5- to 11-year-old and 16- to 25-year-old Pfizer recipients who were included in the immuno-bridging subset, apart from younger age and the percentage of Black and Hispanic or Latinx in the 5- to 11-year-old group (6% and 18%, respectively) being lower than in the 16- to 25-year-old group (12% and 36%, respectively) [1].

Safety and reactogenicity

9. In the 5- to 11-year-olds, as in other age groups, the Pfizer vaccine had a favourable safety profile, with side effects generally comparable to those observed in 16- to 25-year-olds who received the standard 30 µg doses [1].

10. Safety evaluations included assessment of reactogenicity events reported by a parent or guardian using an electronic diary for 7 days after each dose. Data on unsolicited adverse events, including confirmed diagnoses of myocarditis or pericarditis, were collected from the first dose through 1 month after the second dose. Data on serious adverse events will be collected from the first dose through 6 months after the second dose [1]. At data cut-off, the median follow-up was 2.3 months [1].

11. Most local reactions were mild to moderate, lasting 1-2 days. Injection-site pain was the most common local reaction, occurring in 71-74% of Pfizer recipients. Fatigue and headache were the most frequently reported systemic events. In general, systemic events were reported more frequently after the second dose than first dose. As compared with adults and adolescents in the pivotal trial, 5- to 11-year-olds reported a higher incidence of injection-site redness (15 to 19%, vs. 5 to 7%) and swelling (10 to 15%, vs. 5 to 8%), but a generally lower incidence of systemic events, including fever (3 to 7%, vs. 1 to 20%) and chills (5 to 10%, vs. 6 to 42%) [1-3].

12. From the first dose through to one month after the second dose, adverse events were reported by 10.9% of Pfizer recipients and 9.2% of placebo recipients. Slightly more Pfizer recipients (3.0%) than placebo recipients (2.1%) reported adverse events that were considered by the investigators to be related to the vaccine or placebo [1].

13. No vaccine-related serious adverse events were noted in the clinical trial; however, the trial was too small to detect rare side effects such as myocarditis. Three serious adverse events were reported from two participants (postinjury abdominal pain and pancreatitis in a placebo recipient and arm fracture in a Pfizer recipient). None of these were considered to be related to the vaccine or placebo. No deaths or adverse events leading to withdrawal were reported [1]. No cases of severe COVID-19 or Multisystem Inflammatory Syndrome in Children (MIS-C) were reported—a condition associated with COVID-19 where body parts can become inflamed [1, 4]. Lymphadenopathy was reported in 10 Pfizer recipients (0.9%) and 1 placebo recipient (0.1%). No myocarditis, pericarditis, hypersensitivity, or anaphylaxis in Pfizer recipients was reported. Four rashes in Pfizer recipients (observed on the arm, torso, face, or body, with no consistent pattern) were considered to be related to vaccination; the rashes were mild and self-limiting, and onset was typically 7 days or more after vaccination [1].

14. No safety data are yet available from the large-scale roll out of the Pfizer vaccine to 5- to 11-year-olds in the USA, though will likely be available by late December 2021 or early January 2022.

Immunogenicity and efficacy

15. Immune responses in the single clinical trial conducted were assessed one month after the second dose of the Pfizer vaccine were equivalent to those in 16- to 25-year-olds. Children aged 5-11 receiving two 10 µg doses had a similar, statistically non-inferior, neutralising antibody responses with a geometric mean titre (GMT) of 1,197.6 (95% CI: 1,106.1, 1,296.6) vs 1,146.5 (95% CI: 1,045.5, 1,257.2) for ages 16-25 [1].

16. Vaccine efficacy against symptomatic NAAT-confirmed COVID-19 at 7 days or more after the second dose (to a median follow up of 2.3 months at data cut-off) was assessed. Among participants without evidence of previous SARS-CoV-2 infection, symptomatic COVID-19 was reported in three recipients of the Pfizer vaccine and in 16 placebo recipients, producing a vaccine efficacy of 90.7% (95% CI, 67.7 to 98.3) [1].

CV TAG Recommendations

17. CV TAG discussed the use of the Pfizer COVID-19 vaccine in children aged 5-11 years at meetings between October and December 2021 and consulted with Māori paediatricians and Māori general practitioners at two meetings in December 2021.[1]

18. CV TAG noted:

    a. **The direct and indirect impacts on children.** Children who have COVID-19 will commonly have few or only mild respiratory symptoms. COVID-19 in this age group is rarely severe or fatal [5, 6], and the rate of severe COVID-19 disease in this age group is the lowest of any age group. However, there is a very small but real risk of MIS-C (described above) at this age which has occurred more frequently among ethnic minorities in the US [4, 7]. A very small proportion of children also experience

[1] CV TAG discussed use of the Pfizer vaccine in the 5-11 age group on: 19 October, 2 November, 9 November, 23 November, 30 November, 7 December, and 14 December.

persistent illness and ongoing symptoms, though evidence about its incidence is limited.

b. In the current Delta outbreak in New Zealand (data to 19 November 2021), children aged 5-11 made up 14.9% of cases (1,003/6,714). Eight of these children were hospitalised but none were admitted to ICU. Of those who were hospitalised, all but one had a pre-existing condition and three were in hospital for less than six hours. As a comparison, between 16 June and 13 November 2021 in Sydney, 14,154 cases (19.4%) were aged 0-11 years and not eligible for vaccination. Of these cases, 632 were hospitalised, 9 were in ICU, and 0 patients died. It was not mentioned whether any of these cases had pre-existing conditions or comorbidities. The Sydney data further demonstrates that COVID-19 is relatively mild in most young children as despite accounting for 19.4% of cases in Sydney since 16 June, they account for only 5.9% of hospitalisations, 0.6% of ICU admissions, and no deaths [8].

c. Children living with pre-existing conditions or comorbidities, from disadvantaged backgrounds, or those living within a lower socioeconomic status have a greater risk of severe disease from COVID-19 [7, 9-11].

d. Even though the direct effects of infection are generally less severe in children, this should not diminish the significance for those who have experienced worse outcomes [6]. Alongside the direct risks and impacts to health and individuals, COVID-19 also has indirect impacts for children on mental health, wellbeing, education and social development, and these are worsened by lockdowns and school closures [7, 12-14].

e. **Children do play a role in transmission however it is significantly smaller than for adults**. Transmission within education settings has occurred but is limited and is more likely to occur between adults [15-17]. Transmission in households is much more common [18, 19]. The benefit of vaccination on onward transmission in households could be lower than in other settings due to the ongoing and close nature of exposure [20, 21], but this is not confirmed. The effect of vaccination of children on household transmission is unknown.

f. **There are a number of equity considerations which are important to consider**:

   i. Māori and Pacific children have been disproportionately affected in the current outbreak. To 19 November 2021, Māori made up 52% of cases in 5- to 11-year-olds, and Pacific children have made up 30% of cases among 5- to 11-year-olds.

   ii. Māori and Pacific adults are at greater risk of COVID-19 hospitalisation and severe disease. Māori and Pacific adults have respectively 2.5-fold and 3-fold higher odds of being hospitalised compared to non-Māori, and Māori are likely to spend 4.9 days longer in hospital [22, 23].

   iii. Māori and Pacific children are more likely to live in multigenerational families housed in overcrowded conditions, increasing the risk of transmission. The younger age structure of the Māori population also means that a larger proportion are currently unable to be vaccinated and remain susceptible to infection and transmission, with a risk of onwards transmission to whānau and communities [24, 25], though the risk of transmission from children is lower than from adults.

iv. The vaccine rollout in adults resulted in inequities for Māori and Pacific adults, and the rollout for Māori and Pacific children aged 5-11 will need close consideration and more tailored implementation. This emphasises the need for culturally appropriate messaging and Māori-led initiatives. Whānau-based approaches to the 5-11 rollout may also improve uptake among Māori adults.

v. According to a Horizon Research survey, 72% of those who care for 5- to 11-year-olds would allow their child to receive the COVID-19 vaccine, however this was lower among Māori caregivers at 51% [26]. However, we note that the Māori adult rate of uptake and the Māori childhood immunisation rates are much higher than 51%. Given this we believe with a correctly tailored programme, high rates of immunisation in tamariki Māori are achievable.

g. **The paediatric formulation of the vaccine has been approved for emergency use and rolled out in the USA, Canada, and Israel**. The Advisory Committee on Immunization Practices (ACIP) made an interim recommendation for the emergency use of the Pfizer vaccine in children aged 5-11 years in the United States for prevention of COVID-19 [6, 27]. This was unanimously supported by the Committee. In making this recommendation, ACIP considered the importance of COVID-19 as a public health problem, as well as benefits and harms, parents' values and preferences, acceptability, feasibility, resource use, and equity for use of the vaccine among children [6, 27]. ACIP additionally stated: "children from racial and ethnic minority groups have experienced a disproportionately high incidence of COVID-19 as well as secondary impacts of the COVID-19 pandemic such as reduced in-person learning"[6]. These comments have high relevance for New Zealand given the similar effects of the pandemic on Māori and Pacific peoples as described above.

h. **In Australia, the Therapeutic Goods Administration (TGA)** provisionally approved the Pfizer vaccine as safe and effective for use among this age group on 5 December [28]. ATAGI recommends all 5–11-year-olds be vaccinated with an 8-week interval between doses, and that those at risk of severe disease, Aboriginal and Torres Strait Islanders, and children in crowded conditions or outbreak areas be prioritised [29].

i. **Data are still accumulating from the real-world rollout of vaccines in 5- to 11-year-olds, and there is currently limited safety data available post-second dose**. Some adverse events in other age groups (e.g. myocarditis) have only become apparent following widespread rollout, and as noted above the trials in young children are too small to be able to detect rare side effects. Further data on potential side effects from the vaccine rollout in this age group in other countries will become progressively available.

j. **On coadministration and other vaccines,** there is limited evidence on the safety and immunogenicity of coadministration of the Pfizer vaccine with other vaccines in all populations, however based on first principles of vaccinology it is likely to be safe and effective, particularly in younger age groups.

k. **The wider National Immunisation Schedule** has been facing challenges for some time with declining vaccination rates since before COVID-19, and are particularly marked for Māori and Pacific infants and children. Catch-up campaigns for the MMR, HPV and Tdap vaccines were further delayed by COVID-19 and lockdowns. There is a risk that rolling out the Pfizer vaccine in this age group could further adversely impact the wider immunisation programme through diverting public health resources. This

could increase the risk of outbreaks of other infectious diseases. The risk of a significant measles outbreak is of particular concern once the international borders re-open. Vaccination rates are lowest among Māori, and therefore there are equity concerns that there will be greater risk in this population. However, there is also the opportunity to increase coverage with other vaccines with a thoughtfully implemented COVID-19 vaccination programme in this age group.

l. **On dosing intervals,** there are no data available about extending the interval between doses of the paediatric formulation of the Pfizer vaccine, however, emerging data in adults suggests that the immune response is likely improved by extending the dosing interval [30, 31]. This is consistent with basic principles of vaccinology and immunology which suggests that immune responses are generally better with longer intervals. There may also be a connection between shorter intervals and increased reactogenicity or adverse events, and one pre-print paper on individuals aged 12 and over has shown a statistically significant increase in myocarditis if the second dose was given at a shorter interval of less than 30 days [32]. Australia and Canada have recommended an 8-week interval between doses for 5-11-year-olds, noting this may improve immunogenicity and reduce side effects. Having a longer interval would also allow greater time to monitor international safety data.

m. **On vaccine requirements,** there is a significant risk that use of vaccination mandates or certificates in this age group will result in exclusion and an inability to fully participate in schooling and extracurricular activities. This is likely to inequitably impact communities who are already experiencing disadvantage and where current vaccine coverage is poor. Concerns regarding possible stigmatisation and exclusions could be addressed in ways that do not necessarily influence the decision to use. For example, there could be a policy decision that children cannot be denied access to locations/events on the basis of vaccination status, which could be operationalised by not issuing vaccine certificates for this age group.

19. **CV TAG recommended:**

a. **Two doses of the paediatric Pfizer vaccine be offered to all 5-11-year-olds in Aotearoa New Zealand, with an 8-week interval between doses.**

b. Māori and Pacific children, children with high-risk pre-existing conditions, and children living with vulnerable people should be prioritised for vaccination and tailored programmes developed.

c. On the schedule between doses:

i. The interval between doses can be shortened in limited circumstances to a minimum of 3 weeks, such as prior to the initiation of significant immunosuppression or international travel.

ii. Children who turn 12 after their first dose should follow the authorised schedule which uses the paediatric primary formulation (10 µg). They should not be offered the adolescent/adult formulation (30 µg) of the Pfizer COVID-19 vaccine.

iii. Children in this age group who experience a clinically significant adverse event after their first dose should be carefully reviewed by a specialist clinician. An individual risk:benefit assessment should be made on whether to administer the

second dose. Children in this age group are not obliged to receive a second dose if not clinically appropriate.

d. The paediatric Pfizer vaccine can be administered before, after, or at the same time as other vaccines in this age group.

e. The adolescent/adult Pfizer vaccine formulation (30 µg) should not be used in children aged 5-11 years.

f. Mandates, vaccine certificates or vaccine targets **must not** be used or required for this age group, and children in this age group should not be denied access to locations or events based on their vaccination status. There should be no unintended consequences in terms of participation if children in this age group are not vaccinated, and any use of mandates, certificates or targets that may formally or informally encourage inappropriate exclusion from activities. Exemptions from vaccination should therefore also not be required for this age group. We recommend specific public education campaigns about why children should not be excluded from activities, in order to reduce the risk of informal exclusions.

g. Specific consideration must be given to promoting and improving vaccine access to groups that have experienced disproportionate COVID-19 morbidity and mortality, as well as those with barriers to routine health care, especially for Māori and Pacific peoples. This could be achieved through using the broad geographic accessibility of pharmacies and expanding school-focused strategies. Whānau centred approaches should be considered within these environments to improve primary vaccination and booster rates in the adult population.

h. Emphasis must be given to using the rollout of the COVID-19 vaccine as an opportunity to improve delivery and uptake of the wider National Immunisation Schedule, and large-scale events with whānau-based approaches should be organised to aid catch-up campaigns for other vaccines. The coverage of the childhood National Immunisation Schedule should be closely monitored to ensure that the COVID-19 vaccination rollout for this age group does not adversely impact on the uptake of other important childhood vaccines.

i. In making vaccination available, it should not be solely relied upon and other public health measures in schools and other educational settings should be strengthened, including ensuring good ventilation and filtration of air indoors, use of masks, physical distancing, and promotion of children staying at home if sick.

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

a. New Zealand and international safety data will be carefully monitored, and the recommendations here will be reassessed by CV TAG in February 2022 prior to second doses being given to any 5–11-year-olds in Aotearoa New Zealand.

b. Advice for severely immunocompromised children who may need a third primary dose will be reconsidered once further evidence emerges on the need, safety, and efficacy.

Document 3

Recommendations

It is recommended that you:

2.	Note this advice has been received.	Yes/No

Ian G Town

Dr Ian Town
Chief Science Advisor and
Chair of the COVID-19 Vaccine Technical Advisory Group

Signature _____ Date: 16/12/21

Dr Ashley Bloomfield
Director-General of Health

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Memo

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

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

Purpose of report

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

Background and context

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

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

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

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

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

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

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

Evidence and international guidance

Timing of a third (booster) dose in pregnant people

Evidence

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

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

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

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

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

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

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

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

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

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

Advice from other jurisdictions

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

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

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

A fourth dose (first booster) in the immunocompromised

Evidence

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

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

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

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

International guidance

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

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

Recommendations

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

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

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

Dr Ian Town

Chief Science Advisor and

Chair of the COVID-19 Vaccine Technical Advisory Group

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

Memo

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

Purpose

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

Context

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Recommendations

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

40. **CV TAG noted that:**

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

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

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

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

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

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

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

41. **CV TAG recommends that:**

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

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

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

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

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

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

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

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

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

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

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

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

Ian G Town

Dr Ian Town

Chief Science Advisor

Chair, CV TAG

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

Memo

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

Purpose

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

Context

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

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

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

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

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

    c) Booster doses for pregnant people.

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

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

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

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

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

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

51. Potential reasons to consider early booster doses include:

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

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

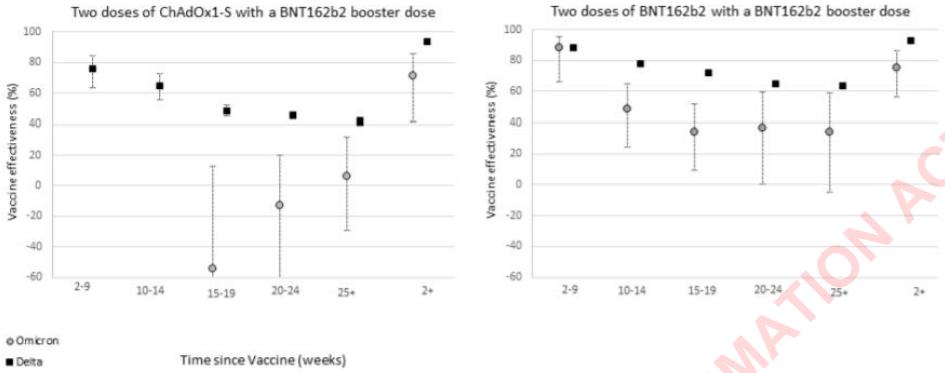
52. It is not yet clear if Omicron can evade vaccine-induced immunity. The laboratory data on Omicron from antibody neutralisation studies to date is very limited and preliminary [50-52], and cannot be used to infer an impact on vaccine protection in real world settings at this stage. Additional information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

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

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

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

Supplementary data are not available for this figure.



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

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

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

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

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

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

    c) in outreach vaccination programs where access is limited.

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

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

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

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

59. In those under 18 years of age, severe COVID-19 is uncommon, and the primary course of COVID-19 vaccines generates a strong immune response. Therefore, the benefit from additional doses of vaccine is thought to be to be small. In addition, there are currently only very limited data on the safety of repeated mRNA vaccine doses in this age group.
60. On 9th December 2021, the U.S. Food and Drug Administration (FDA) amended the emergency use authorization for the Pfizer vaccine, allowing the use of a booster in individuals 16 and 17 years of age at least six months after completion of primary vaccination with Pfizer vaccine.
61. ATAGI does not currently recommended boosters for those aged <18 years.

Booster doses for pregnant people

62. CV TAG recommendations from 10th November (Appendix 1) excluded pregnant people who received a primary course earlier in pregnancy from priority groups, but there was no specific recommendation given about booster vaccination in pregnancy outside of a prioritisation framework. Specifically, there is concern that messaging that those vaccinated in early pregnancy should not receive a booster dose while still pregnant is raising unintended concerns about the safety of vaccination with COVID-19 vaccines while pregnant (both primary and booster doses).
63. The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) states that "a booster dose can be considered if you are 18 years or older and had your initial COVID-19 vaccine course (called the primary course) ≥ 6 months ago. Pfizer is the preferred brand for booster doses for all people, including in pregnancy, regardless of the brand used initially". RANZCOG argue "mRNA vaccines are safe and effective for those trying to conceive, pregnant and breastfeeding women. Booster doses have not yet been studied in those who are pregnant but have been shown to be safe and effective in non-pregnant adults. We do know that COVID-19 infection in pregnancy poses a significant risk for mothers and their babies, and RANZCOG recommends that pregnant women receive booster vaccinations in line with the recommendations for the non-pregnant adult population".[15]

Recommendations

64. CV TAG met on 14 December 2021 to consider recommendations regarding COVID-19 booster vaccinations in specific situations.
65. **CV TAG noted that:**
    a) Data are still accumulating about whether early booster doses offer any advantages in protection against the Omicron variant.
    b) There are no long term data available about the safety of early booster doses but short term side effects appear to be modest.
    c) There is insufficient data on the safety profile for booster doses in pregnant people.
    d) Medsafe has authorised boosters only from six months after completion of the primary dose.
66. **CV TAG recommends that:**

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

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

   i. those aged 65 years and over

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

   iii. Māori and Pacific peoples

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

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

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

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

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

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Chair, CV TAG

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MINISTRY OF HEALTH
MANATŪ HAUORA

Memo

Decision to use a primary course of the Novavax COVID-19 vaccine: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations

Date:	10 February 2022
To:	Dr Ashley Bloomfield, Director-General of Health
Cc:	Astrid Koornneef, Director, National Immunisation Programme Allison Bennett, Manager, System Enablers, System Strategy and Policy Dr Caroline McElnay, Director of Public Health
From:	Dr Ian Town, Chief Science Advisor
For your:	Information

Purpose of report

1. To summarise the COVID-19 Vaccine Technical Advisory Group's (CV TAG) recommendations on the decision to use a primary course (two doses) of the Nuvaxovid COVID-19 Vaccine with Matrix-M Adjuvant ('the Novavax vaccine').

Background and Context

2. In February 2021, CV TAG advice was sought about the use of the Pfizer COVID-19 vaccine for people who were 16 years and over, following Medsafe provisional approval. Cabinet agreed that the COVID-19 Vaccine Immunisation Programme proceed with the rollout of the Pfizer vaccine. It was noted that further advice would be provided to Cabinet on each of New Zealand's four vaccine candidates as they became available for use (following Medsafe approval), without knowing if a future vaccine was going to be more suitable or effective. In order to make decisions given the uncertainty, a Decision to Use framework was developed.

3. In July 2021, CV TAG advice was sought about the use of the Janssen COVID-19 vaccine for people aged 18 years and over, following Medsafe provisional approval. CV TAG advised that there was no current indication for wide use of the Janssen vaccine, however, it could be considered at an individual level where the Pfizer vaccine was not suitable e.g., anaphylaxis or other rare side effects following the first dose of the Pfizer vaccine.

4. In October 2021, CV TAG advice was sought about the use of the AstraZeneca COVID-19 vaccine for people aged 18 years and over. CV TAG advised that the AstraZeneca vaccine should be used as a second-line vaccine, with Pfizer remaining the first-line and preferred vaccine. It was recommended that the AstraZeneca vaccine be restricted to people who have a contraindication to the Pfizer vaccine, or people who would prefer to get the AstraZeneca vaccine. For example, those currently under a Vaccination Order, people who are unvaccinated or have only received one dose, and people who are hesitant about getting the Pfizer vaccine.

5. The Novavax vaccine was granted provisional approval by Medsafe for use in people aged 18 and over in New Zealand on 4 February 2022, under section 23(1) of the Medicines Act 1981, with conditions. It is a two-dose recombinant spike protein nanoparticle vaccine containing the Matrix-M adjuvant, with the second dose approved to be administered at least 3 weeks after the first dose [1].

6. The Ministry's Policy team sought clinical and scientific advice from CV TAG on the use of the Novavax vaccine in New Zealand.

Data on a primary course of the Novavax vaccine

7. The overall efficacy and safety of the Novavax vaccine is based on analysis of data from clinical trials conducted in the UK, South Africa, the US and Mexico (PREVENT-19 trial).

8. *UK phase III trial*[2]*:* Per protocol efficacy against symptomatic, laboratory-confirmed COVID-19 (in an Alpha-variant-dominant setting) ≥7 days post-second dose was 89.7% [95% CI: 80.2-94.6]. Solicited local adverse events were reported more frequently in the vaccine group than in the placebo group after both the first dose (57.6% vs. 17.9%) and the second dose (79.6% vs. 16.4%). Solicited systemic adverse events were also reported more frequently in the vaccine group than in the placebo group after both the first dose (45.7% vs. 36.3%) and the second dose (64.0% vs. 30.0%). Overall, reactogenicity was generally mild to moderate and transient. The frequency of unsolicited adverse events was higher among vaccine recipients than among placebo recipients (25.3% vs. 20.5%), with similar frequencies of severe adverse events (1.0% vs. 0.8%) and serious adverse events (0.5% vs. 0.5%) between the two groups. There was one case of myocarditis that occurred three days after the second dose, which was considered possibly immune related, however, it was adjudicated to most likely be viral myocarditis.

9. *US and Mexico phase III trial (PREVENT-19)*[3]: Per protocol efficacy against PCR-confirmed, symptomatic COVID-19 (in an Alpha-variant-dominant setting) ≥7 days post-second dose was 90.4% (95% CI: 82.9-94.6) and against moderate or severe disease was 100% (95% CI: 87-100). Similar to the results from the UK phase III trial, reactogenicity was mostly mild to moderate and transient but was more frequent among Novavax recipients compared to placebo recipients and was more frequent after the second dose (local adverse events: 58.0% vaccine vs. 21.1% placebo after dose 1, and 78.9% vaccine and 21.7% placebo after dose 2; systemic adverse events: 47.7% vaccine and 40.0% placebo after dose 1, and 69.5% vaccine and 35.9% placebo after dose 2). Serious adverse events were balanced between the vaccine and placebo groups (0.9% vs. 1.0%). No episodes of the Guillain–Barré syndrome and there were no differences reported in myocarditis, pericarditis or in vaccine-induced immune thrombosis with thrombocytopenia observed between groups in the two-month follow-up period.

10. *South Africa phase IIa–b trial*[4]: Per protocol efficacy against symptomatic, laboratory-confirmed COVID-19 (in a Beta-variant-dominant setting) among HIV-negative participants was 60.1% (95% CI: 19.9-80.1) but was lower when HIV-positive participants were included (49.4% [95% CI: 6.1-72.8]). Solicited local and systemic adverse events, which were predominantly mild to moderate and transient, were more common in the vaccine group than in the placebo group. Serious adverse events were rare in both groups.

11. *Heterologous schedules:* Data are still emerging on the efficacy and safety of heterologous ("mixed dose") vaccine schedules incorporating approved vaccines in New Zealand. Results from the UK Com-CoV2 trial found that immunogenicity following a Novavax dose in

participants primed with Pfizer was inferior to those who received a homologous schedule of Pfizer. However, immunogenicity following a Novavax dose in those who were primed with AstraZeneca was superior to immunogenicity in those who received a homologous AstraZeneca course. Novavax did not increase reactogenicity when administered following a first dose of either Pfizer or AstraZeneca [5].

12. *Efficacy against variants of concern:* In the UK phase III trial, a post hoc analysis showed an efficacy of 86.3% (95% CI: 71.3-93.5) against the Alpha variant [2]. In the PREVENT-19 trial, efficacy against all variants of concern or interest circulating at that time of the trial was 92.6% (95% CI: 83.6 to 96.7) [3]. This included the Alpha, Beta, Gamma, Epsilon, and Iota variants that were predominant in the US and Mexico during the trial. In the South Africa phase IIa–b trial, post hoc efficacy against Beta was 51.0% (95% CI: -0.6-76.2) among the HIV-negative participants [4]. There are no efficacy data available for the Delta and Omicron variants.

13. *Co-administration with influenza vaccine[6]:* The UK phase III trial had a sub-study investigating co-administration of a licensed influenza vaccine (Flucelvax Quadrivalent for those aged 18-64 years and adjuvanted trivalent influenza vaccine Fluad for those ≥65 years) in 431 participants, given on the opposite deltoid to that of the first dose. The point estimate for efficacy against symptomatic PCR-confirmed COVID-19 was similar between the co-administration group at 87.5% (95% CI: -0.2-98.4) and the main study (Novavax only) at 89.8% (95% CI: 79.7-95.5). However, this observation was based on only nine cases in the co-administration sub-study.

Approval of the Novavax vaccine by other jurisdictions

14. The UK Medicines and Healthcare products Regulatory Agency (MHRA) approved the Novavax vaccine for use in over 18-year-olds on 3 February 2022 [9].

15. The European Medicines Agency approved the use of the Novavax vaccine on 20 December 2021 [7].

16. At the beginning of February 2022 Novavax filed for emergency use authorisation of its COVID-19 vaccine in the United States, however approval is yet to be granted.

17. The Novavax vaccine is provisionally approved by the Australian Therapeutics Goods Administration for use in a primary course of vaccination [11]. The Australian Technical Advisory Group on Immunisation (ATAGI) has recommended the Novavax vaccine be given in two doses, at least three weeks apart.

Recommendations

14. CV TAG met on 1 February 2022 and 8 February 2022 to discuss use of a primary course of the Novavax COVID-19 vaccine, noting the information provided in the vaccine Data Sheet.

15. CV TAG noted that:

15.1 The contraindications for the Novavax vaccine are anaphylaxis to a previous dose of Novavax COVID-19 vaccine or to a component of the vaccine, as outlined in the vaccine Data Sheet.

15.2 In general, the Novavax vaccine offers a high level of protection against symptomatic COVID-19 and severe disease. However, it is not known how effective the primary course is against variants of concern that have emerged recently, such as Delta and Omicron.

15.3 The Novavax vaccine is reactogenic, particularly after the second dose. Side effects are generally mild to moderate and transient, and the overall safety profile does not raise any significant concerns. Continued safety monitoring is essential to understand the long-term safety profile of this platform.

15.4 Data on efficacy and safety of the Novavax vaccine in people aged less than 18 years, in pregnant people, and in people who become pregnant after receiving the vaccine are limited.

15.5 Novavax has been trialled in heterologous primary schedules. It produced a stronger immune response in those primed with AstraZeneca as a first dose, and a slightly inferior immune response in those primed with Pfizer as a first dose. There was no increase in reactogenicity in the heterologous schedules.

15.6 There is a potential for Novavax to be used as a booster dose in the context of Omicron, however, at this stage data are limited and this item will be considered separately.

16. CV TAG recommends that:

16.1 The COVID-19 Vaccine Immunisation Programme use the Novavax vaccine as a second-line vaccine, with Pfizer remaining the first-line and preferred vaccine for a primary course.

16.2 Use of the Novavax vaccine should be restricted to people who:

a) have a contraindication to the Pfizer vaccine,

b) would prefer to get the Novavax vaccine and are currently under a Vaccination Order,

c) are unvaccinated or have only received one dose and are hesitant about getting the Pfizer vaccine, or

d) experienced anaphylaxis or other rare side effects following the first dose of the Pfizer vaccine.

16.3 There are currently insufficient data on the use of the Novavax vaccine to recommend it during pregnancy. Use in pregnancy should be based on an assessment of benefits and risks by the consumer and their healthcare professional.

16.4 With regard to timing:

a) two doses of the Novavax vaccine, given at least 3 weeks apart, are required for a primary vaccination course.

b) Novavax can be administered as part of a heterologous primary schedule to people who have received another COVID-19 vaccine as their first dose, and this should occur at least 28 days after the first dose of the other COVID-19 vaccine, to account for recommended intervals for other vaccine brands.

c) there should be no upper limit on time since the first dose.

d) the Novavax vaccine may be administered before, after, or at the same time as the influenza, MMR, HPV, diphtheria/tetanus/pertussis combination vaccine (Boostrix), and other vaccines. The only exception to this advice is for the live-attenuated shingles vaccine (Zostavax) where a 7-day interval, before or after administering the Novavax vaccine is advised.

17. Guidance on the use of a booster dose of the Novavax vaccine will be considered separately, pending any future Medsafe approval.

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

Dr Ian Town

Chief Science Advisor and

Chair of the COVID-19 Vaccine Technical Advisory Group

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Document 6

Memo

Use of the paediatric Pfizer COVID-19 vaccine in 5-11 year-olds – second dose and dosing interval: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations

Date:	16 February 2022
To:	Dr Ashley Bloomfield, Director-General of Health
Copy to:	Astrid Koornneef, Director, National Immunisation Programme Allison Bennett, Manager, System Enablers, System Strategy and Policy Dr Caroline McElnay, Director of Public Health
From:	Dr Ian Town, Chief Science Advisor
For your:	Consideration

Purpose of report

1. To outline the COVID-19 Vaccine Technical Advisory Group's (CV TAG) advice about the administration of a second dose of the paediatric Pfizer vaccine and the interval between the first and second doses of the COVID-19 vaccine for 5–11 year-olds.
2. This report also provides an update on international and local safety data.

Background and context

3. Vaccination of 5–11-year-olds in New Zealand is now underway. The approved COVID-19 paediatric Pfizer vaccine being used has a lower dose (10 µg) and a smaller volume (0.2 mL) than the adult vaccine and is administered using a smaller needle. As at 13 February 2022, 214,857 (45%) of 5–11-year-olds had received their first dose in New Zealand. [1] Only 26% of Māori 5-11 year-olds and 36% of Pacific 5-11 year-olds have received their first dose. To be fully immunised against COVID-19, a child needs to receive two doses of the paediatric vaccine.
4. In December 2021, CV TAG recommended that two doses of the paediatric Pfizer vaccine be offered to all 5-11 year-olds in Aotearoa New Zealand, with an 8-week interval between doses (Appendix 1, *Decision to Use the Pfizer mRNA COVID-19 vaccine for children aged 5-11 years: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations*). It was also indicated that in February 2022, CV TAG would assess the latest data and provide updated recommendations prior to any second doses being given to this age group in New Zealand.

Safety data for the Pfizer vaccine in 5–11-year-olds

5. A randomised clinical trial to assess the safety, immunogenicity, and efficacy of the Pfizer vaccine in 5-11 year-olds of two doses administered three weeks apart reported more local reactions and systemic events than placebo recipients. [2] The reactions and events reported were generally mild to moderate, lasting 1 to 2 days. Injection-site pain was the most common local reaction, occurring in 71 to 74% of Pfizer recipients. Severe injection-site pain after the first or second dose was reported in 0.6% of Pfizer recipients and in no placebo recipients.

6. In the clinical trial, fatigue and headache were the most frequently reported systemic events (0.9%), headache (0.3%), chills (0.1%), and muscle pain (0.1%) were also reported after the first or second dose of Pfizer. [2] Frequencies of fatigue, headache, and chills were similar among Pfizer and placebo recipients after the first dose and were more frequent among Pfizer recipients than among placebo recipients after the second dose.

7. No vaccine-related serious adverse events were noted in the clinical trial; however, the trial was too small to detect rare side effects such as myocarditis. [2] Three serious adverse events were reported from two participants (postinjury abdominal pain and pancreatitis in a placebo recipient and arm fracture in a Pfizer recipient), however, none of these were related to the vaccine or placebo. No deaths or adverse events leading to withdrawal were reported. There were no cases of severe COVID-19 or Multisystem Inflammatory Syndrome in Children (MIS-C)—a condition associated with COVID-19 where body parts can become inflamed. Lymphadenopathy was reported in ten Pfizer recipients (0.9%) and one placebo recipient (0.1%). No myocarditis, pericarditis, hypersensitivity, or anaphylaxis in Pfizer recipients was reported. Rashes in four Pfizer recipients (observed on the arm, torso, face, or body, with no consistent pattern) were related to vaccination; the rashes were mild and self-limiting, and onset was typically 7 days or more after vaccination.

8. Real-world safety data has been collected from over 8 million doses of the Pfizer vaccine administered to children aged 5–11 years in the United States. These data have been collected in the Vaccine Adverse Event Reporting System (VAERS), a national passive vaccine safety surveillance system, and through V-safe, a voluntary smartphone-based safety surveillance system for adverse events after COVID-19 vaccination. [3] From November 3 to December 19, 2021, VAERS received and processed 4,249 reports of adverse events for children aged 5–11 years who received Pfizer COVID-19 vaccine. Overall, among VAERS reports for children aged 5–11 years who received the Pfizer vaccine, approximately 97% were non-serious. The most commonly reported conditions among the 100 reports of serious events were fever (29.0%), vomiting (21.0%), and increased troponin (15.0%). Among 12 serious reports of seizure, five children experienced new-onset seizures. Among 15 preliminary reports of myocarditis identified during the analytic period, 11 met the case definition for myocarditis. VAERS received two reports of death both of whom had complicated medical histories and were in fragile health before vaccination. None of the data suggested a causal association between death and vaccination. In V-safe, fever was found to be more frequently reported in 5-11 year-olds after dose 2 (4,001: 13.4%) than dose 1 (3,350; 7.9%) among 42,504 recipients of dose 1 and 29,899 recipients of dose 2. Overall, systemic reactions after dose 2 among registrants aged 5-11 years were less frequent than among children aged 12-15 years. Fourteen registrants aged 5–11 years received hospital care after vaccination. Information regarding reason for hospitalisation was available for five children

and included appendicitis (two), vomiting and dehydration (one), respiratory infection (one), and retropharyngeal cellulitis (one).

Reporting of Adverse Events following Vaccination in New Zealand

9. In New Zealand, preliminary unpublished data from Medsafe indicates that there have been 352 adverse events following immunisation (AEFIs) reported from 17 January to 30 January 2022 in children aged 5-11 who received the approved COVID-19 paediatric Pfizer vaccine. Of these, 96.9% (341) reports were classified as non-serious. A small number of individuals (10) reported that an AEFI required emergency care and one AEFI case was admitted to hospital for observation (no evidence of myocarditis despite reporting chest discomfort). Of these 11 cases, six were reported as recovered or recovering, one was ongoing, and four had an unknown outcome. Chest discomfort was the most frequently reported reaction (6), followed by vasovagal reaction (4), and there was one case of anaphylaxis (Brighton criteria level 4).

10. Medsafe is in regular contact with other regulators and have noted that to date nothing of concern has been drawn to their attention regarding the safety profile of the paediatric Pfizer vaccine.

Rationale for an 8-week interval

11. The manufacturer's recommended schedule for the paediatric Pfizer vaccine is 2 doses, 3 weeks apart.

12. Research conducted in adults into extending the dosing interval (e.g., to 8 weeks or longer) has shown that longer intervals between the first and second Pfizer dose can lead to higher humoral and cellular immune responses, improved vaccine effectiveness, and potentially a longer duration of protection compared with the standard interval. [4-7] In addition, data from adults show that an extended dosing interval may also reduce the risk of myocarditis and pericarditis after vaccination. [8]

13. Extended dosing intervals has not yet been studied in children, but it is expected that similar effects would be observed to those after extended dosing intervals in adults, such as improved immunogenicity and the potential for a lower risk of serious side effects. The recommendation for an 8-week interval between doses is consistent with other international advisory groups, such as in the UK, Canada, and Australia. [9-11] In addition, a longer interval between doses would allow more time to continue monitoring international safety data as it emerges.

Priority groups for children aged 5-11 years

14. Māori and Pacific children have been disproportionately affected in this pandemic. For community-acquired cases up to 11 February 2022, Māori made up 45.7% of total cases in 5- to 11-year-olds, and Pacific children have made up 28.7% of cases among 5- to 11-year-olds. Of these cases, a total of ten have been hospitalised, with Māori and Pacific children combined making up 90% of these cases. As noted above, in the vaccine rollout for 5–11-year-olds, fewer Māori and Pacific children have been vaccinated than other ethnicities. Prioritisation of Māori and Pacific children remains important, and the emphasis should be to get the first dose administered to as many as children as possible.

15. Children living with pre-existing conditions or comorbidities, from disadvantaged backgrounds, or those living within a lower socioeconomic status have a greater risk of severe disease from COVID-19. [12-16]

16. Starship Child Health has listed risk factors for COVID-19 disease [17] that may be used as guidance for prioritising children with high-risk pre-existing conditions. The current list of risk factors includes children with:
    - Chronic lung disease including bronchiectasis, cystic fibrosis, BiPAP for OSA
    - Non-repaired congenital heart disease, acquired heart disease or congestive heart failure
    - Poorly controlled asthma (regular symptoms occurring in a usual week that affect the patient's quality of life and includes anyone with an admission in the last 2 years or anyone with 2 or more courses of steroids in the last two years)
    - Obesity (BMI ≥95th centile for age)
    - Diabetes (insulin-dependent)
    - Chronic kidney disease (GFR <15 ml/min/1.73m^2)
    - Severe cerebral palsy (or neurodevelopmental disorder)
    - Complex genetic, metabolic disease or multiple congenital anomalies.

17. Children in other recognised clinical risk groups who are at higher risk of severe COVID-19 should also include those who are a household contact of someone who is immunosuppressed (defined as those who expect to share living accommodation on most days (and therefore for whom continuing close contact is unavoidable) with individuals of any age who are immunosuppressed).

Recommendations

18. CV TAG met on 1, 8, and 15 February 2022 to consider guidance on administering a second dose of the vaccine and the interval between doses for 5–11-year-olds.

19. CV TAG noted:

    a. **The direct and indirect impacts on children.** Children who have COVID-19 will commonly have few or only mild respiratory symptoms. COVID-19 in this age group is rarely severe or fatal, [18, 19] and the rate of severe COVID-19 disease in this age group is the lowest of any age group. However, there is a very small but real risk of MIS-C (described above) at this age which has occurred more frequently among ethnic minorities in the US. [12, 20] A very small proportion of children also experience persistent illness and ongoing symptoms, though evidence about its incidence is limited.

    b. Children living with pre-existing conditions or comorbidities, from disadvantaged backgrounds, or those living within a lower socioeconomic status have a greater risk of severe disease from COVID-19. [12-15]

    c. Even though the direct effects of infection are generally less severe in children, this should not diminish the significance for those who have experienced worse outcomes. [19] Alongside the direct risks and impacts to health and individuals, COVID-19 also has indirect impacts for children on mental health, wellbeing, education and social development, and these are worsened by lockdowns and school closures. [12, 21-23]

    d. **Children do play a role in transmission however it is significantly smaller than for adults**. Transmission within education settings has occurred but is limited and is more

likely to occur between adults. [24-26] Transmission in households is much more common. [27, 28] The benefit of vaccination on onward transmission in households could be lower than in other settings due to the ongoing and close nature of exposure. [29, 30] but this is not confirmed. The effect of vaccination of children on household transmission is unknown.

e. **There are a number of equity considerations which are important to consider**:

   i. Māori and Pacific children have been disproportionately affected in the current outbreak. To 11 February 2022, Māori made up 45.7% of cases in 5-11 year-olds, and Pacific children have made up 28.7% of cases among 5-11 year-olds.

   ii. Māori and Pacific adults are at greater risk of COVID-19 hospitalisation and severe disease. Māori and Pacific adults have respectively 2.5-fold and 3-fold higher odds of being hospitalised compared to non-Māori, and Māori are likely to spend 4.9 days longer in hospital. [31, 32]

   iii. Māori and Pacific children are more likely to live in multigenerational families housed in overcrowded conditions, increasing the risk of transmission. The younger age structure of the Māori population also means that a larger proportion are currently unable to be vaccinated and remain susceptible to infection and transmission, with a risk of onwards transmission to whānau and communities, [33, 34] though the risk of transmission from children is lower than from adults.

f. **The paediatric formulation of the vaccine has been approved for emergency use and rolled out in the USA, Canada, and Israel**. The Advisory Committee on Immunization Practices (ACIP) made an interim recommendation for the emergency use of the Pfizer vaccine in children aged 5-11 years in the United States for prevention of COVID-19. [19, 35] This was unanimously supported by the Committee. In making this recommendation, ACIP considered the importance of COVID-19 as a public health problem, as well as benefits and harms, parents' values and preferences, acceptability, feasibility, resource use, and equity for use of the vaccine among children. [19, 35] ACIP additionally stated: "children from racial and ethnic minority groups have experienced a disproportionately high incidence of COVID-19 as well as secondary impacts of the COVID-19 pandemic such as reduced in-person learning". [19] These comments have high relevance for New Zealand given the similar effects of the pandemic on Māori and Pacific Peoples as described above.

g. **In Australia, the Therapeutic Goods Administration (TGA)** provisionally approved the Pfizer vaccine as safe and effective for use among this age group on 5 December 2021. [36] ATAGI recommends all 5–11-year-olds be vaccinated with an 8-week interval between doses, and that those at risk of severe disease, Aboriginal and Torres Strait Islanders, and children in crowded conditions or outbreak areas be prioritised. [37]

h. **On dosing intervals,** there are no data available about extending the interval between doses of the paediatric formulation of the Pfizer vaccine, however, emerging data in adults suggests that the immune response is likely improved by extending the dosing interval. [4-7] This is consistent with basic principles of vaccinology and immunology which suggests that immune responses are generally better with longer intervals. There may also be a connection between shorter intervals and increased reactogenicity or adverse events, and one pre-print paper on individuals aged 12 and over has shown

a statistically significant increase in myocarditis if the second dose was given at a shorter interval of less than 30 days. [8] Australia, Canada, and the UK have recommended an 8-week interval between doses for 5-11 year-olds, noting this may improve immunogenicity and reduce side effects. Having a longer interval would also allow more time to monitor international safety data.

i. **On vaccine requirements,** there is a significant risk that use of vaccination mandates or certificates in this age group will result in exclusion and an inability to fully participate in schooling and extracurricular activities. This is likely to inequitably impact communities who are already experiencing disadvantage and where current vaccine coverage is poor. Concerns regarding possible stigmatisation and exclusions could be addressed in ways that do not necessarily influence the decision to use. For example, there could be a policy decision that children cannot be denied access to locations/events on the basis of vaccination status, which could be operationalised by not issuing vaccine certificates for this age group.

j. **On safety of the paediatric vaccine,** real-world data on the rollout of the vaccine to 5–11-year-olds have reported nothing of concern to date.

20. **CV TAG recommended that:**

    a. A second dose of the paediatric Pfizer vaccine be offered to all 5–11 year-olds in Aotearoa New Zealand, with a minimum 8-week interval between doses.

    b. Māori and Pacific children, children with high-risk pre-existing conditions, and children living with vulnerable people should continue to be prioritised for vaccination.

21. CV TAG will continue to monitor all relevant information (including safety data) and will update their recommendations as information becomes available.

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Appendix 1 – Decision to Use the Pfizer mRNA COVID-19 vaccine for children aged 5-11 years: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations

Memo

Decision to use the Pfizer mRNA COVID-19 vaccine for children aged 5-11 years: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations

Date:	15 December 2021
To:	Dr Ashley Bloomfield, Director-General of Health
Copy to:	Astrid Koornneef, Director of National Operations, COVID Vaccine Immunisation Programme Allison Bennett, Manager, System Enablers, System Strategy and Policy Dr Caroline McElnay, Director of Public Health
From:	Dr Ian Town, Chief Science Advisor and Chair of CV TAG
For your:	Information

Purpose of report

1. To summarise the CV TAG recommendations on the decision to use the paediatric formulation of the Pfizer mRNA COVID-19 vaccine ('the Pfizer vaccine') for children who are 5 to 11 years of age.

Background and context

2. In February 2021, CV TAG advice was sought for use of the Pfizer COVID-19 vaccine in people who were 16 years and over, following Medsafe approval. Cabinet agreed that the COVID-19 Immunisation Programme proceed with the roll out of the Pfizer vaccine, and this has been underway since February.

3. In August 2021, CV TAG confirmed support to extend the age of people who can receive the Pfizer vaccine to 12- to 15-year-olds, noting that this would likely lead to a reduction in school closures and disruption to education, and contribute to equitable vaccination coverage in Māori and Pacific peoples.

4. Medsafe is assessing an application submitted by Pfizer for the use of a paediatric formulation of the vaccine in 5- to 11-year-olds within New Zealand. The CV TAG recommendations presented here are subject to Medsafe approval and any listed clinical conditions.

5. The Ministry's Policy team has sought clinical and scientific advice from CV TAG on the use of the Pfizer vaccine for children who are 5- to 11-years of age. This advice will be considered as part of the Decision to Use Framework, and alongside policy considerations for the sequencing of the COVID-19 Immunisation Programme.

The COVID-19 vaccine in 5- to 11-year-olds

Phase 2/3 trial findings

6. One phase 2/3 randomised control trial was conducted to assess the safety, immunogenicity, and efficacy of two doses of the Pfizer vaccine administered 21 days apart in children aged 6 months to 11 years, with findings published for 5- to 11-year-olds to date [2].

7. In the phase 2/3 trial, participants were randomly assigned in a 2:1 ratio to receive two doses of either the Pfizer vaccine at 10 µg (a lower dose than the 30 µg used in older age groups), or a placebo. A total of 2268 children were assigned to receive the Pfizer vaccine (1517 children) or placebo (751 children) [2].

8. The trial was run across 81 sites in the US, Spain, Finland and Poland. Overall, 52% were male, 79% were White, 6% were Black, 6% were Asian, and 21% were Hispanic or Latinx. The mean age was 8.2 years; 20% of children had coexisting conditions (including 12% with obesity and approximately 8% with asthma), and 9% were SARS-CoV-2–positive at baseline. Demographic characteristics were similar between the 5- to 11-year-old and 16- to 25-year-old Pfizer recipients who were included in the immuno-bridging subset, apart from younger age and the percentage of Black and Hispanic or Latinx in the 5- to 11-year-old group (6% and 18%, respectively) being lower than in the 16- to 25-year-old group (12% and 36%, respectively) [2].

Safety and reactogenicity

9. In the 5- to 11-year-olds, as in other age groups, the Pfizer vaccine had a favourable safety profile, with side effects generally comparable to those observed in 16- to 25-year-olds who received the standard 30 µg doses [2].

10. Safety evaluations included assessment of reactogenicity events reported by a parent or guardian using an electronic diary for 7 days after each dose. Data on unsolicited adverse events, including confirmed diagnoses of myocarditis or pericarditis, were collected from the first dose through 1 month after the second dose. Data on serious adverse events will be collected from the first dose through 6 months after the second dose [2]. At data cut-off, the median follow-up was 2.3 months [2].

11. Most local reactions were mild to moderate, lasting 1-2 days. Injection-site pain was the most common local reaction, occurring in 71-74% of Pfizer recipients. Fatigue and headache were the most frequently reported systemic events. In general, systemic events were reported more frequently after the second dose than first dose. As compared with adults and adolescents in the pivotal trial, 5- to 11-year-olds reported a higher incidence of injection-site redness (15 to 19%, vs. 5 to 7%) and swelling (10 to 15%, vs. 5 to 8%), but a generally lower incidence of systemic events, including fever (3 to 7%, vs. 1 to 20%) and chills (5 to 10%, vs. 6 to 42%) [2, 38, 39].

12. From the first dose through to one month after the second dose, adverse events were reported by 10.9% of Pfizer recipients and 9.2% of placebo recipients. Slightly more Pfizer recipients (3.0%) than placebo recipients (2.1%) reported adverse events that were considered by the investigators to be related to the vaccine or placebo [2].

13. No vaccine-related serious adverse events were noted in the clinical trial; however, the trial was too small to detect rare side effects such as myocarditis. Three serious adverse events were reported from two participants (postinjury abdominal pain and pancreatitis in a placebo recipient and arm fracture in a Pfizer recipient). None of these were considered to be related to the vaccine or placebo. No deaths or adverse events leading to withdrawal were reported [2]. No cases of severe COVID-19 or Multisystem Inflammatory Syndrome in Children (MIS-C) were reported—a condition associated with COVID-19 where body parts can become inflamed [2, 20]. Lymphadenopathy was reported in 10 Pfizer recipients (0.9%) and 1 placebo recipient (0.1%). No myocarditis, pericarditis, hypersensitivity, or anaphylaxis in Pfizer recipients was reported. Four rashes in Pfizer recipients (observed on the arm, torso, face, or body, with no consistent pattern) were considered to be related to vaccination; the rashes were mild and self-limiting, and onset was typically 7 days or more after vaccination [2].

14. No safety data are yet available from the large-scale roll out of the Pfizer vaccine to 5- to 11-year-olds in the USA, though will likely be available by late December 2021 or early January 2022.

Immunogenicity and efficacy

15. Immune responses in the single clinical trial conducted were assessed one month after the second dose of the Pfizer vaccine were equivalent to those in 16- to 25-year-olds. Children aged 5-11 receiving two 10 µg doses had a similar, statistically non-inferior, neutralising antibody responses with a geometric mean titre (GMT) of 1,197.6 (95% CI: 1,106.1, 1,296.6) vs 1,146.5 (95% CI: 1,045.5, 1,257.2) for ages 16-25 [2].

16. Vaccine efficacy against symptomatic NAAT-confirmed COVID-19 at 7 days or more after the second dose (to a median follow up of 2.3 months at data cut-off) was assessed. Among participants without evidence of previous SARS-CoV-2 infection, symptomatic COVID-19 was reported in three recipients of the Pfizer vaccine and in 16 placebo recipients, producing a vaccine efficacy of 90.7% (95% CI, 67.7 to 98.3) [2].

CV TAG Recommendations

17. CV TAG discussed the use of the Pfizer COVID-19 vaccine in children aged 5-11 years at meetings between October and December 2021 and consulted with Māori paediatricians and Māori general practitioners at two meetings in December 2021.[1]

18. CV TAG noted:

[1] CV TAG discussed use of the Pfizer vaccine in the 5-11 age group on: 19 October, 2 November, 9 November, 23 November, 30 November, 7 December, and 14 December.

a. **The direct and indirect impacts on children.** Children who have COVID-19 will commonly have few or only mild respiratory symptoms. COVID-19 in this age group is rarely severe or fatal [18, 19], and the rate of severe COVID-19 disease in this age group is the lowest of any age group. However, there is a very small but real risk of MIS-C (described above) at this age which has occurred more frequently among ethnic minorities in the US [12, 20]. A very small proportion of children also experience persistent illness and ongoing symptoms, though evidence about its incidence is limited.

b. In the current Delta outbreak in New Zealand (data to 19 November 2021), children aged 5-11 made up 14.9% of cases (1,003/6,714). Eight of these children were hospitalised but none were admitted to ICU. Of those who were hospitalised, all but one had a pre-existing condition and three were in hospital for less than six hours. As a comparison, between 16 June and 13 November 2021 in Sydney, 14,154 cases (19.4%) were aged 0-11 years and not eligible for vaccination. Of these cases, 632 were hospitalised, 9 were in ICU, and 0 patients died. It was not mentioned whether any of these cases had pre-existing conditions or comorbidities. The Sydney data further demonstrates that COVID-19 is relatively mild in most young children as despite accounting for 19.4% of cases in Sydney since 16 June, they account for only 5.9% of hospitalisations, 0.6% of ICU admissions, and no deaths [40].

c. Children living with pre-existing conditions or comorbidities, from disadvantaged backgrounds, or those living within a lower socioeconomic status have a greater risk of severe disease from COVID-19 [12-15].

d. Even though the direct effects of infection are generally less severe in children, this should not diminish the significance for those who have experienced worse outcomes [19]. Alongside the direct risks and impacts to health and individuals, COVID-19 also has indirect impacts for children on mental health, wellbeing, education and social development, and these are worsened by lockdowns and school closures [12, 21-23].

e. **Children do play a role in transmission however it is significantly smaller than for adults**. Transmission within education settings has occurred but is limited and is more likely to occur between adults [24-26]. Transmission in households is much more common [27, 28]. The benefit of vaccination on onward transmission in households could be lower than in other settings due to the ongoing and close nature of exposure [29, 30], but this is not confirmed. The effect of vaccination of children on household transmission is unknown.

f. **There are a number of equity considerations which are important to consider**:

    i. Māori and Pacific children have been disproportionately affected in the current outbreak. To 19 November 2021, Māori made up 52% of cases in 5- to 11-year-olds, and Pacific children have made up 30% of cases among 5- to 11-year-olds.

    ii. Māori and Pacific adults are at greater risk of COVID-19 hospitalisation and severe disease. Māori and Pacific adults have respectively 2.5-fold and 3-fold higher odds of being hospitalised compared to non-Māori, and Māori are likely to spend 4.9 days longer in hospital [31, 32].

iii. Māori and Pacific children are more likely to live in multigenerational families housed in overcrowded conditions, increasing the risk of transmission. The younger age structure of the Māori population also means that a larger proportion are currently unable to be vaccinated and remain susceptible to infection and transmission, with a risk of onwards transmission to whānau and communities [33, 34], though the risk of transmission from children is lower than from adults.

iv. The vaccine rollout in adults resulted in inequities for Māori and Pacific adults, and the rollout for Māori and Pacific children aged 5-11 will need close consideration and more tailored implementation. This emphasises the need for culturally appropriate messaging and Māori-led initiatives. Whānau-based approaches to the 5-11 rollout may also improve uptake among Māori adults.

v. According to a Horizon Research survey, 72% of those who care for 5- to 11-year-olds would allow their child to receive the COVID-19 vaccine, however this was lower among Māori caregivers at 51% [41]. However, we note that the Māori adult rate of uptake and the Māori childhood immunisation rates are much higher than 51%. Given this we believe with a correctly tailored programme, high rates of immunisation in tamariki Māori are achievable.

g. **The paediatric formulation of the vaccine has been approved for emergency use and rolled out in the USA, Canada, and Israel**. The Advisory Committee on Immunization Practices (ACIP) made an interim recommendation for the emergency use of the Pfizer vaccine in children aged 5-11 years in the United States for prevention of COVID-19 [19, 35]. This was unanimously supported by the Committee. In making this recommendation, ACIP considered the importance of COVID-19 as a public health problem, as well as benefits and harms, parents' values and preferences, acceptability, feasibility, resource use, and equity for use of the vaccine among children [19, 35]. ACIP additionally stated: "children from racial and ethnic minority groups have experienced a disproportionately high incidence of COVID-19 as well as secondary impacts of the COVID-19 pandemic such as reduced in-person learning"[19]. These comments have high relevance for New Zealand given the similar effects of the pandemic on Māori and Pacific peoples as described above.

h. **In Australia, the Therapeutic Goods Administration (TGA)** provisionally approved the Pfizer vaccine as safe and effective for use among this age group on 5 December [36]. ATAGI recommends all 5–11-year-olds be vaccinated with an 8-week interval between doses, and that those at risk of severe disease, Aboriginal and Torres Strait Islanders, and children in crowded conditions or outbreak areas be prioritised [37].

i. **Data are still accumulating from the real-world rollout of vaccines in 5- to 11-year-olds, and there is currently limited safety data available post-second dose**. Some adverse events in other age groups (e.g. myocarditis) have only become apparent following widespread rollout, and as noted above the trials in young children are too small to be able to detect rare side effects. Further data on potential side effects from the vaccine rollout in this age group in other countries will become progressively available.

j. **On coadministration and other vaccines,** there is limited evidence on the safety and immunogenicity of coadministration of the Pfizer vaccine with other vaccines in all populations, however based on first principles of vaccinology it is likely to be safe and effective, particularly in younger age groups.

k. **The wider National Immunisation Schedule** has been facing challenges for some time with declining vaccination rates since before COVID-19, and are particularly marked for Māori and Pacific infants and children. Catch-up campaigns for the MMR, HPV and Tdap vaccines were further delayed by COVID-19 and lockdowns. There is a risk that rolling out the Pfizer vaccine in this age group could further adversely impact the wider immunisation programme through diverting public health resources. This could increase the risk of outbreaks of other infectious diseases. The risk of a significant measles outbreak is of particular concern once the international borders re-open. Vaccination rates are lowest among Māori, and therefore there are equity concerns that there will be greater risk in this population. However, there is also the opportunity to increase coverage with other vaccines with a thoughtfully implemented COVID-19 vaccination programme in this age group.

l. **On dosing intervals,** there are no data available about extending the interval between doses of the paediatric formulation of the Pfizer vaccine, however, emerging data in adults suggests that the immune response is likely improved by extending the dosing interval [42, 43]. This is consistent with basic principles of vaccinology and immunology which suggests that immune responses are generally better with longer intervals. There may also be a connection between shorter intervals and increased reactogenicity or adverse events, and one pre-print paper on individuals aged 12 and over has shown a statistically significant increase in myocarditis if the second dose was given at a shorter interval of less than 30 days [44]. Australia and Canada have recommended an 8-week interval between doses for 5-11-year-olds, noting this may improve immunogenicity and reduce side effects. Having a longer interval would also allow greater time to monitor international safety data.

m. **On vaccine requirements,** there is a significant risk that use of vaccination mandates or certificates in this age group will result in exclusion and an inability to fully participate in schooling and extracurricular activities. This is likely to inequitably impact communities who are already experiencing disadvantage and where current vaccine coverage is poor. Concerns regarding possible stigmatisation and exclusions could be addressed in ways that do not necessarily influence the decision to use. For example, there could be a policy decision that children cannot be denied access to locations/events on the basis of vaccination status, which could be operationalised by not issuing vaccine certificates for this age group.

19. **CV TAG recommended:**

a. **Two doses of the paediatric Pfizer vaccine be offered to all 5-11-year-olds in Aotearoa New Zealand, with an 8-week interval between doses.**

b. Māori and Pacific children, children with high-risk pre-existing conditions, and children living with vulnerable people should be prioritised for vaccination and tailored programmes developed.

c. On the schedule between doses:

   i. The interval between doses can be shortened in limited circumstances to a minimum of 3 weeks, such as prior to the initiation of significant immunosuppression or international travel.

   ii. Children who turn 12 after their first dose should follow the authorised schedule which uses the paediatric primary formulation (10 µg). They should not be offered the adolescent/adult formulation (30 µg) of the Pfizer COVID-19 vaccine.

   iii. Children in this age group who experience a clinically significant adverse event after their first dose should be carefully reviewed by a specialist clinician. An individual risk:benefit assessment should be made on whether to administer the second dose. Children in this age group are not obliged to receive a second dose if not clinically appropriate.

d. The paediatric Pfizer vaccine can be administered before, after, or at the same time as other vaccines in this age group.

e. The adolescent/adult Pfizer vaccine formulation (30 µg) should not be used in children aged 5-11 years.

f. Mandates, vaccine certificates or vaccine targets **must not** be used or required for this age group, and children in this age group should not be denied access to locations or events based on their vaccination status. There should be no unintended consequences in terms of participation if children in this age group are not vaccinated, and any use of mandates, certificates or targets that may formally or informally encourage inappropriate exclusion from activities. Exemptions from vaccination should therefore also not be required for this age group. We recommend specific public education campaigns about why children should not be excluded from activities, in order to reduce the risk of informal exclusions.

g. Specific consideration must be given to promoting and improving vaccine access to groups that have experienced disproportionate COVID-19 morbidity and mortality, as well as those with barriers to routine health care, especially for Māori and Pacific peoples. This could be achieved through using the broad geographic accessibility of pharmacies and expanding school-focused strategies. Whānau centred approaches should be considered within these environments to improve primary vaccination and booster rates in the adult population.

h. Emphasis must be given to using the rollout of the COVID-19 vaccine as an opportunity to improve delivery and uptake of the wider National Immunisation Schedule, and large-scale events with whānau-based approaches should be organised to aid catch-up campaigns for other vaccines. The coverage of the childhood National Immunisation Schedule should be closely monitored to ensure that the COVID-19 vaccination rollout for this age group does not adversely impact on the uptake of other important childhood vaccines.

i. In making vaccination available, it should not be solely relied upon and other public health measures in schools and other educational settings should be strengthened, including ensuring good ventilation and filtration of air indoors, use of masks, physical distancing, and promotion of children staying at home if sick.

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

    a. New Zealand and international safety data will be carefully monitored, and the recommendations here will be reassessed by CV TAG in February 2022 prior to second doses being given to any 5–11-year-olds in Aotearoa New Zealand.

    b. Advice for severely immunocompromised children who may need a third primary dose will be reconsidered once further evidence emerges on the need, safety, and efficacy.

Recommendations

It is recommended that you:

2.	Note this advice has been received.	Yes/No

Dr Ian Town
Chief Science Advisor and
Chair of the COVID-19 Vaccine Technical Advisory Group

Signature _____ Date:
Dr Ashley Bloomfield
Director-General of Health

Memo

The use of booster vaccinations in 12–17-year-olds: COVID-19 Vaccine Technical Advisory Group (CV TAG) recommendations

Date:	21 February 2022
To:	Dr Ashley Bloomfield, Director-General of Health
Copy to:	Astrid Koornneef, Director, National Immunisation Programme Allison Bennett, Manager, System Enablers, System Strategy and Policy Dr Caroline McElnay, Director of Public Health
From:	Dr Ian Town, Chief Science Advisor
For your:	Consideration

Purpose of report

1. To summarise the COVID-19 Vaccine Technical Advisory Group's (CV TAG) recommendations on the use of COVID-19 booster vaccinations in 12–17-year-olds.

Background and context

2. The adult formulation (30 µg) of the Pfizer COVID-19 vaccine (Comirnaty) has been granted provisional approval for a primary course schedule from Medsafe (New Zealand) for use in those aged 12 years and older, given as 2 doses at least 3 weeks apart.[1]

3. On 28 October 2021, Medsafe updated the provisional approval for the Pfizer vaccine to state: "*a booster dose of Comirnaty may be administered intramuscularly at least 6 months after completion of the primary course in individuals aged 18 years of age and older.*"[1]

4. In November 2021, CV TAG recommended the use of boosters in those aged over 18 years, providing a list of priority groups. The most recent recommendation about booster doses was provided by CV TAG on 1 February 2022, stating "*a booster dose of the COVID-19 vaccine should be given from 3 months after the primary course to all eligible people aged 18 years and over, including immunocompromised individuals and pregnant persons.*" A list of priority groups was again provided with this recommendation.

5. The Ministry of Health sought clinical and scientific advice from CV TAG on the need for and use of the adult formulation of the Pfizer vaccine as a booster dose in those aged 12-17-years-old, including advice on timing after a primary course, and whether any subgroups require prioritisation.

Clinical trial evidence

6. Pfizer conducted a randomised blinded placebo-controlled trial of approximately 10,000 participants aged ≥16 years, including 78 people that were aged 16–17 years. The study included people who had completed a two-dose primary schedule of Pfizer vaccine at least 6 months prior. The relative vaccine efficacy against infection across all ages was 95.3% (95%CI: 89.5-98.3%) for boosted compared to non-boosted participants during a period of Delta variant circulation. Only two COVID cases occurred in the 16–17-year age cohort, both in the placebo non-boosted group.[2] Preliminary findings therefore suggest an increase of vaccine effectiveness against documented SARS-CoV-2 infection in adolescents in this age group who received a booster compared to adolescents who have recently completed the primary vaccination course. Data are still accumulating about waning of protective vaccination effects in periods of Omicron-dominance.

Advice from other jurisdictions

7. Recommendations have been made by several advisory bodies in other countries about booster vaccinations for 12–17-year-olds. Some countries have broken this age group down further into 12–15-year-olds and 16–17-year-olds and made differential recommendations. These recommendations are summarised here:

   a. ***Australian Technical Advisory Group on Immunisation (ATAGI)***

      i. *16–17-year-olds:* On 3 February 2022, ATAGI recommended a booster vaccination with Pfizer for all 16–17-year-olds who have previously received any Australian Therapeutic Goods Administration (TGA) approved or recognised vaccines for their primary vaccine schedule, from 3 months after receiving their last primary dose.[3] This includes those who were aged under 16 years when they received their last primary dose and are now aged 16 years.

         - Those who are severely immunocompromised and have received a third primary dose of COVID-19 vaccine should also receive a booster dose (4th dose) of the Pfizer vaccine when they become eligible from 3 months after receiving their third primary dose.
         - Those who have recently had a SARS-CoV-2 infection and are now eligible for a booster are still recommended to receive their booster dose. This booster dose can be administered immediately after recovery from acute illness or can be deferred for up to 4 months.
         - Those who have previously developed myocarditis or pericarditis after a primary dose should discuss the benefits and risks of a COVID-19 vaccine booster dose with their cardiologist/treating doctor.
         - People with previous anaphylaxis to an mRNA vaccine should not receive a Pfizer COVID-19 vaccine booster dose, and no other vaccines have yet been approved as boosters.

      ii. *12–15-year-olds:* No advice to date.

   b. ***Joint Committee on Vaccination and Immunisation (JCVI), United Kingdom***

      i. *16–17-year-olds:* JCVI advises that booster vaccinations with the adult formulation of the Pfizer vaccine should be offered to all persons aged 16–17 years, given at

least 3 months after completion of the primary course.[4] No advice has been given on timing after infection.

ii. *12–15-year-olds:* JCVI advises that booster vaccinations with the adult formulation of the Pfizer vaccine should be offered to 12–15-year-olds who are in a clinical risk group or who are a household contact of someone (of any age) who is immunosuppressed.[4] Booster vaccinations with the adult formulation of the Pfizer vaccine should also be offered to 12–15-year-olds who are severely immunocompromised and who have had a third primary dose.[4] No advice has been given about the timing after infection.

c. ***Advisory Committee on Immunization Practices (ACIP), USA.***[1]

i. *12–15-year-olds and 16–17-year-olds:* all 12–17-year-olds should receive a booster dose 5 months after their initial Pfizer vaccination series.[5] No advice has been given on timing after infection.

d. ***National Advisory Committee on Immunization (NACI), Canada***

i. *12–15-year-olds and 16–17-year-olds:* A booster dose of an mRNA COVID-19 vaccine (Pfizer adult formulation preferred) may be offered ≥6 months after completion of a primary COVID-19 vaccine series to adolescents 12–17 years of age:[6]

- with an underlying medical condition at high risk of severe illness (specific conditions listed [6]) due to COVID-19, including those who are immunocompromised and who received a three-dose primary series,
- who are residents of congregate living settings (e.g., shelters, group homes, quarters for migrant workers, correctional facilities),
- who belong to racialised and/or marginalised communities disproportionately affected by COVID-19.

ii. No recommendations for booster doses for the wider general adolescent population 12–17 years of age have been made to date.

iii. NACI recommends waiting 3 months after COVID-19 infection before administering a booster for all vaccinated people aged 12 and over, provided it is at least 6 months after completing a primary series.[7]

8. ATAGI and NACI cite substantial evidence supporting these decisions:[3, 6]

a. Epidemiology (e.g., a rise in the proportion of COVID-19 cases observed in younger age groups with Omicron compared to previous variants),

b. Disease severity (e.g., in indigenous 12–17-year-olds, and those with 2 or more chronic conditions),

c. Decreased effectiveness of the vaccine against Omicron,

d. Waning efficacy after a primary course in adolescents,[8]

e. Efficacy of booster in those aged 16–17 years old included in the Pfizer booster trial (no data available in 12–15-year-olds),[9]

[1] Note: official statement by ACIP not yet published, and statements here are based on Centers of Disease Control and Prevention (CDC) statements.

f. Potential reductions in transmission in 16–17-year-olds (based on results for Alpha and Delta variants after primary vaccination), and

g. Safety data (e.g., preliminary evidence from Israel, where rates of myocarditis after the booster dose in individuals aged 16–19 years was similar in females and lower in males than after a second primary dose).[8]

Recommendations

9. CV TAG met on Tuesday 8 February, Tuesday 15 February, and Friday 18 February 2022 to consider guidance on booster doses for 12–17-year-olds.

10. **CV TAG noted that:**

a. **Overall, there is very limited data on which to base any recommendations about boosters in this age group.**

b. The goal of offering booster doses in New Zealand is to prevent severe disease caused by SARS-CoV-2, and to reduce burden on hospitals and other healthcare providers.

c. Young New Zealanders are well protected against severe disease with a primary vaccination course. Healthy 12-17-year-olds who do not suffer from chronic or underlying conditions and who are not on immunosuppressant medication are unlikely to have significant additional health benefit from a third (booster) vaccination at this stage.

d. Māori and Pacific peoples are at an increased risk of severe disease and hospitalisation,[10] and therefore require prioritisation and targeted, community-led campaigns. Increasing the vaccination coverage of first and second doses, particularly for Māori and Pacific peoples over the age of 5 years, should remain the priority of the COVID-19 vaccination programme in New Zealand.

e. Some 16–17-year-olds have finished school and may be in the workforce, tertiary study, or communal accommodation settings, which places them at greater risk of exposure to SARS-CoV-2.

f. While the AstraZeneca vaccine has been used as a booster in the adult population, it is not currently indicated for use in those aged under 18 years of age. Other COVID-19 vaccines (e.g. Janssen, Novavax) also are not approved for use in this age group at this time.

g. Many peak bodies internationally (including ATAGI, JCVI and ACIP) have recommended all 16–17-year-olds receive a booster dose. NACI in Canada only recommend its use in those at-risk and at a ≥6 months interval. Advice for 12–15-year-olds varies from only recommending boosters for at-risk adolescents (Canada, UK), recommending all 12–15-year-olds receive a booster (US), and some have yet to provide advice (Australia).

h. Recommendations from the Australian, UK, USA and Canadian peak bodies about the interval between primary and booster doses for adolescents range from 3 to 6 months.

i. **Pfizer are yet to submit an application (and data) to Medsafe for the use of the booster in this age group. As a result, Medsafe have not assessed the use of the booster in this age group.** Data on the quality, safety, reactogenicity and efficacy of use of the Pfizer vaccine as a booster in 12–17-year-olds are likely to be submitted to Medsafe by Pfizer for consideration in late February or early March. The timeframe for a decision depends on the extent of the data and if expert advice is required from the Medicines Assessment Advisory Committee. Therefore, CV TAG recommendations would be for off-label use in the meantime.

11. **CV TAG recommends that:**

a. **For 16-17-year-olds:**

i. **A single Pfizer booster dose be made available to all 16–17-year-olds who wish to receive it.**

ii. Further to this, a Pfizer booster dose is **recommended** in 16–17-year-olds who are at higher risk of COVID-19 severe disease and hospitalisation. At-risk groups include:

- Adolescents with an underlying health condition or immunocompromise that increases the risk of severe disease (See Appendix 1), including those in 11.a.iii below
- Māori and Pacific adolescents, due to the greater risk of severe disease and hospitalisation
- Adolescents who are household contacts of persons (of any age) who are severely immunocompromised (as defined in the Ministry of Health Immunisation Handbook, these individuals are eligible for a three-dose primary course), noting that the main benefits from vaccination are related to the potential for indirect protection of their household contact who is immunocompromised.

iii. Those who have received a third primary dose of COVID-19 vaccine (because of severe immunocompromise) should also receive a booster dose (4th dose).

iv. 16–17-year-olds who have recently had a SARS-CoV-2 infection and are now eligible for a booster based on the recommendations above are recommended to defer their booster dose for 3 months after infection.

b. **For 12-15-year-olds:**

i. **Use of a booster dose in 12-15-year-olds is not currently recommended**.

ii. Clinicians may consider giving a booster dose to 12-15-year-olds who are clinically at-risk (as defined in Appendix 1), including those who received a three-dose primary course due to severe immunocompromise. Advice for clinicians is available from IMAC.

iii. Any wider recommendations will be deferred until after Medsafe has received and assessed an application from Pfizer in this age group.

c. **With regard to timing**, a booster dose in all eligible populations described here should be administered at least 3 months after the second dose, or in line with the timing for the general population.

d. **People with previous anaphylaxis** to an mRNA vaccine or other contraindications may not be advised to receive a Pfizer COVID-19 vaccine booster dose. Those who have previously developed myocarditis or pericarditis after a primary dose should discuss the benefits and risks of receiving a Pfizer booster dose with their cardiologist/treating doctor. Use of other vaccines as boosters in these groups can be considered on an individual basis. Support for clinicians on this decision-making is available from IMAC.

e. Consideration should be given to equity and whānau-based approaches and ensuring that other immunisation programmes are not compromised, e.g., measles and HPV vaccination.

12. **Ongoing concern was noted around formal and informal vaccine mandates requiring booster doses in this age group, and the associated implications for access to work, educational facilities, and recreational facilities.**

13. CV TAG will continue to monitor all relevant information and will update their recommendations on boosters in 12–17-year-olds as further evidence becomes available.

Dr Ian Town
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Chair of the COVID-19 Vaccine Technical Advisory Group

Appendix 1: Underlying health condition or conditions of immunocompromise [11]

Note: This list is not exhaustive, clinicians may use their judgement for conditions that are not listed here that are associated with severe outcomes from COVID-19 infection.

- Chronic lung disease including bronchiectasis, cystic fibrosis, BiPAP for OSA
- Non-repaired congenital heart disease, acquired heart disease or congestive heart failure
- Poorly controlled asthma (regular symptoms occurring in a usual week that affect the patient's quality of life and includes anyone with an admission in the last 2 years or anyone with 2 or more courses of steroids in the last two years)
- Obesity (BMI ≥95th centile for age)
- Diabetes (insulin-dependent)
- Chronic kidney disease (GFR <15 ml/min/1.73m2)
- Severe cerebral palsy (or neurodevelopmental disorder)
- Complex genetic, metabolic disease or multiple congenital anomalies
- Trisomy 21/Downs Syndrome
- Primary or acquired immunodeficiency
- Haematologic malignancy and post-transplant (solid organ or HSCT in last 24 months)
- On immunosuppressive treatment including chemotherapy, high-dose corticosteroids, biologics or DMARDS

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