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28 February 2022

s 9(2)(a)

By email: s 9(2)(a)
Ref: H202200106

Dear s 9(2)(a)

Response to your request for official information

Thank you for your request under the Official Information Act 1982 (the Act) to the Ministry of Health (the Ministry) on 10 January 2022 for information relating to vaccine safety. Please find a response to each part of your request below.

> *the statistical data the NZ Government is relying on to support the decision to vaccinate children over 5 years old from 17 January 2022?*

A copy of a study evaluating the COVID-19 vaccine in children 5-11 years of age is publicly available at the following link: www.nejm.org/doi/full/10.1056/NEJMoa2116298. In addition, the quality and clinical evaluation reports of COVID-19 vaccines applications received by Medsafe are publicly available on the Ministry's website: www.health.govt.nz/system/files/documents/information-release/h202117877_response.pdf.

On the basis of data reviewed by Medsafe to support Pfizer's application, the likely therapeutic value of the vaccine outweighed the risk of its use in this age group, as required by section 22(1)(a) of the Medicines Act.

One document has been identified within scope of you request and enclosed with this letter. Document One, entitled Request for Advice: COVID-19 and Vaccination in 5 – 11 year olds is being released to you in full.

> *Given there is no long term safety data as clinician trials end in 2023, what risk analysis has been adopted to ensure that harm from the vaccine does not outweigh the risk of death from contracting covid-19?*

Information on how Medsafe assess the safety and efficacy of the COVID-19 Vaccine is available at: www.medsafe.govt.nz/COVID-19/q-and-a-vaccine-approval.asp.

> *Can the MOH please confirm that the vaccine is 100% safe for children, as children should never be used to protect the elderly, therefore will the MOH guarantee that the rollout will not result in a single death of a NZ child?*

While the Act allows for information to be requested from Ministers and government agencies, there is no requirement for agencies to create new information, compile information they do not hold or provide or prove an opinion. Your questions and the statements that support them appear designed to engage in a debate about the Government's COVID-19 vaccination programme, rather than a

request for official information. The Act does not support requests where an opinion, comment, argument, or hypothetical statement is put to the Ministry for response, couched as a request for information. Therefore, this part of your request is refused under section 18(g) of the Act on the grounds that the information sought is not held by the Ministry.

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

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

Yours sincerely

Chris James
Group Manager
Medsafe

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

Request for Advice (RfA)

MINISTRY OF HEALTH | MANATŪ HAUORA

This form contains the details relevant to the questions posed to the Science and Technical Advisory (STA). STA will respond to the request using this form which will also be stored in STA content management system for future reference.

This form, or parts of it, may also be forwarded to other relevant parties as appropriate.

Title	COVID-19 and Vaccination in 5-11-year-olds		
Subject	Supporting evidence to inform discussions of the risks and benefits of vaccination in 5-11-year-olds		
Reference No.	330	Date Received	12/11/2021
Requestor	Ian Town	Date Due	22/12/2021
Advisor	Brooke Hollingshead and Sarah Mitchell	Date Completed	Click or tap to enter a date.
Peer reviewed by	Pippa Scott and Imogen Roth		
Advice issued to	CV TAG		
Approved by	Ian Town		
Deliverables	Completed summary of evidence of COVID-19, transmission risk, and vaccination in 5-11-year-olds		
Request Outline	**Background/Context** Pfizer will be applying for the use of vaccines in 5-11-year-olds to Medsafe, and advice is required from the COVID-19 Vaccine Technical Advisory Group on the risks and benefits of vaccinating this age group, alongside if and where there may be a need for prioritisation. **Questions** *COVID-19 and children* • How does COVID-19 present in children? • What do we know about Delta's impact on children? • What is the risk of infection/severe disease/ hospitalisation? • What is the risk of long COVID? • Who is more at risk of severe outcomes among 5-11-year-olds? What are the individual level risk factors? What are broader social risk factors? *Vulnerable populations in the context of Aotearoa New Zealand* • Within the Aotearoa New Zealand context, what risk factors are more common and who would be most at risk within this age group?		

	• What impact has the current Delta outbreak had on 5-11-year olds? How many cases have there been? What severity and how many hospitalisations? Who is more at risk? *Transmission* • What is known about the role of children in transmission? • What is known about transmission in education and household settings? *Non-pharmaceutical interventions for the prevention of COVID-19 in children* • What non-pharmaceutical interventions are available for children to prevent COVID-19? • What evidence is there on the effectiveness of masks, distancing, cohorting, school closures? *Vaccine* • What is the safety and reactogenicity profile of the Pfizer vaccine for 5-11-year-olds? • What is known about the risk of myocarditis in 5-11-year-olds? Is there a risk profile/factors other than being male and young? What is there info on and what is there not? • What is the efficacy of the vaccine in 5-11-year-olds against infection, severe disease and hospitalisation? • Which countries have approved the vaccine for 5-11-year-olds, who has rolled it out, and what data is available from the real-world rollout? • Do these countries have any specific guidance in relation to the dosing interval and co-administration? *Risks and Benefits of vaccinating 5 – 11-year-olds in Aotearoa New Zealand* • What are the relative risks and benefits of vaccinating 5–11-year-old in New Zealand? **Intended application of advice** To inform discussions at CV TAG and the Decision to Use. **Timeline** CV TAG to review this RfA on 30 November, 7 December, 14 December. Memo to be drafted by 7 December and finalised by 21 December.
What are the implications and considerations of this advice on Te Tiriti o Waitangi and equity?	Equity and Te Tiriti are relevant to assessing who is at risk of infection and severe disease, and who is at greater risk and more vulnerable. It is important to examine the increased burden for Māori and Pacific People within New Zealand, particularly in the Delta outbreak.

Equity issues are relevant in relation to uptake of public health measures and vaccines, and support options available to people with COVID-19. There may be disparities in who can access services.

Individual risk factors such as prevalence of pre-existing conditions or comorbidities increase the risk of severe COVID-19 disease and hospitalisation, and therefore it will be important to examine which conditions this is true for and where there may be increased vulnerability.

Equity is important to consider in relation to different physical and social environments, with Māori and Pacific People more likely to live in overcrowded housing, multigenerational housing, and more likely to face socioeconomic barriers with access to poor housing.[1] People living in rural communities (especially Māori) are more isolated and inaccessible to healthcare interventions including vaccination clinics. These broader social determinants of health will need to be explored to examine where they may be increased vulnerability to infection.

These risks also need to be balanced against the risks of prolonged school closure on wellbeing and education for young people, the need for access to education, and how this could impact on equity by further increasing current social and economic inequities.

The principles of Te Tiriti o Waitangi provide the framework to guide the health and disability system towards health equity for Māori, and principles of tino rangatiratanga, equity, active protection, options and partnership will be forefront in the research. Tino rangatiratanga and self-determination are important in applying public health measures, and therefore it is essential that autonomy and options are given to communities to protect themselves, and in communicating public health measures. Partnership with diverse Māori communities in developing and communicating risk and public health measures are essential to ensure clear understandings of risk and develop appropriate public health measures tailored to the communities' needs.

Response to Request for Advice

Contents

Key Points

- COVID-19 disease is rarely severe or fatal in previously well children between 5 and 11 years of age. However, COVID-19 is still a significant public health issue in this age group. The risk is not negligible, and incidence of the severe post-infection Multisystem Inflammatory Syndrome in Children (MIS-C) is highest in this age group. Current evidence is that children in this age group sometimes experience prolonged symptoms post recovery from SARS-CoV-2 infection (long COVID), but the frequency of this is not well established.
- Children living with pre-existing health conditions or comorbidities, disadvantage, low socioeconomic or minority ethnic status have a greater risk of severe disease from COVID-19.
- Māori and Pacific adults are at greater risk of COVID-19 hospitalisation and severe disease and more likely to live in multigenerational families housed in overcrowded conditions. Access to vaccines has been inequitable for Māori and Pacific adults and access issues for children aged 5-11 in these groups need close consideration.
- Children can transmit the virus, though they appear to play less of a role in transmission than teenagers and adults. Evidence to date has shown that transmission of SARS-CoV-2 in the school environment is more likely to occur between adults, followed by adult-to-child transmission, with lower risks of child-to-child or child-to-adult transmission.
- The phase 3 trial of the lower-dose formulation of the Pfizer vaccine in 5–11-year-olds showed local and systemic side effects generally in the same range as those observed with the full dose in 12-to-15-year-olds. Importantly, fever (7 vs 20%) and antipyretic use (20 vs 51%) after the second dose was less common. No cases of myocarditis were observed, but there was an excess of lymphadenopathy cases (10 (0.9%) vs 1 (0.1%) with the placebo).
- In the same phase 3 trial, vaccine efficacy against symptomatic COVID-19 7 days post-second dose was 90.7%, based on 3 cases in the vaccine group and 16 in the placebo group between 21 and 126 days. No cases were severe, but the number of participants was relatively small, with a total of 1,518 vaccine and 750 placebo participants.
- While there is some urgency for vaccination in order to protect New Zealand's population, the only available safety and efficacy data are from the phase 3 trial with 2268 participants. This trial had a very limited ability to study rare, but serious, side effects. More data on potential side effects from the vaccine roll-out in this age group in other countries would be beneficial in determining the risk-benefit ratio in New Zealand.
- The decision to vaccinate children requires careful weighing of the known and potential risks and benefits. The balance of risks and benefits of COVID-19 vaccination in children is more complex than in adults. In addition to direct potential effects (both positive and negative) from vaccination for this group, there are also potential indirect effects. Indirect benefits include, but are not limited to, the avoidance of school closures and other indirect harms of lockdowns for these children and for other population groups. Indirect potential harms include, but are not limited to, the risk that a COVID-19 vaccination roll out in this group may negatively impact the national immunisation schedule for children.
- If vaccination is offered to this age group, to mitigate against unintended consequences such as stigmatisation and exclusion, children aged 5-11 should not be subject to vaccine mandates and should not have to be vaccinated in order to participate in any of their usual activities, including education, childcare, and recreational activities.

Introduction

Vaccination of 5 to 11 year olds has begun internationally. Planning is underway for a New Zealand roll-out in this age group if it is approved by Medsafe and Cabinet decides to use it. The COVID-19 Vaccine Technical Advisory Group (CV TAG) also has an important role in the Decision to Use. Their advice is required on the risks and benefits of vaccinating this age group, alongside if and where there may be a need for prioritisation. This RfA collates a wide range of information related to children, COVID-19 and the Pfizer vaccine to inform discussions at CV TAG and the Decision to Use.

COVID-19 and Children

COVID-19 presentation and severity

Children and adolescents who have COVID-19 will commonly have no or only mild symptoms, similar to a cold. Those who are symptomatic generally have a short duration of illness and a low symptom burden. A systematic review of COVID-19 in children conducted early in the pandemic found typical symptoms included fever, cough, a sore throat, blocked or runny nose, sneezing, muscle aches, and fatigue. Changes in smell or taste, diarrhoea and vomiting were less common.[2]

COVID-19 disease in children is rarely severe and significantly less likely to cause death than in adults. However, it is important to bear in mind that COVID-19 in children is still a major public health problem,[3] and that the impact of COVID-19 on children should not be minimised by comparison to the impact experienced in adult populations. Even though the direct effects of infection are generally less severe in children, this does not diminish the significance for those who do experience worse outcomes. On 24 November 2021, the WHO published an interim statement on COVID-19 vaccination for children and adolescents,[4] where they note that overall, there are proportionally fewer symptomatic infections and cases with severe disease and deaths from COVID-19 in children and adolescents, compared with older age groups. Age-disaggregated cases reported to WHO from 30 December 2019 to 25 October 2021 show that older children and younger adolescents (5 to 14 years) account for 7% (7,058,748) of reported global cases and 0.1% (1,328) of reported global deaths. Milder symptoms and asymptomatic presentations may mean less testing in these groups, and cases may go unreported.[4] A systematic review and meta-analysis including over 350 studies from between January 2020 and April 2021 estimated that the percentage of cases that never developed clinical symptoms (i.e. truly asymptomatic, rather than pre-symptomatic), was 35.1% (95%CI: 30.7 to 39.9%). Asymptomatic infection was higher among children, at 46.7% (95%CI: 32.0 to 62.0%).[5] A study of 2,143 clinically diagnosed or laboratory confirmed cases among children found that more than 90% were asymptomatic or had mild or moderate disease.[6] The prevalence of severe and critical disease was 10.6% in children aged <1 at diagnosis, 7.3% in those aged 1-5 years, 4.2% in those aged 6-10 years, 4.1% in those aged 11-15 years, and 3% in those aged 16-17 years.[6] When severe COVID-19 occurs in children, it is usually characterised by pneumonia and respiratory distress, and may lead to admission to hospital or intensive care.[7]

Two longer term risks or consequences of SARS-CoV-2 infection might be more of a concern in this age: Multisystem inflammatory syndrome in children (MIS-C, also known as Paediatric Inflammatory Multisystem Syndrome temporally associated with SARS-CoV-2, or PIMS-TS) and long COVID (discussed below).

The Delta variant does not appear to cause more severe disease than previous variants, but because it spreads faster, the number of children who will develop severe disease and go to hospital will be greater.[7] In addition, in areas where an increasing percentage of adults are fully vaccinated but where children are not vaccinated, there are likely to be relatively more infections among children.[7, 8]

Initial reports through the media from South Africa indicate that the Omicron variant is resulting in a disproportionately large number of children being admitted to hospital with COVID-19, particularly in the under 5 age group, however evidence on this is still emerging. [9]

Multisystem Inflammatory Syndrome in children (MIS-C)

MIS-C is a very rare but serious condition that can occur approximately one month after COVID-19, causing inflammation in different parts of the body.[10] Children and adolescents with MIS-C usually have a fever, rash and abdominal pain. Severe MIS-C may cause inflammation of the heart muscle, and this may result in low blood pressure. Some MIS-C patients do not require treatment, but patients with more severe disease often need admission to an intensive care unit.

MIS-C has caused deaths among a small proportion of children overseas, mainly early in the pandemic. However, increased awareness of MIS-C has allowed for earlier diagnosis, more appropriate treatments and improved outcomes. MIS-C can occur even in those with no symptoms from initial COVID-19 infection. In 2021, almost all children with MIS-C have recovered fully, and the long-term outcomes appear good, with resolution of the inflammation of the heart.[7, 10] In the US, evidence has shown that MIS-C occurs more frequently among marginalised Black, non-Black Hispanic, Pacific and indigenous children compared to white children, and similar inequities may occur for Māori and Pacific children [11, 12]. As of 4 October 2021, the CDC had received reports of 5,217 cases of MIS-C; 44% of MIS-C cases were in children aged 5–11 years.[3]

Long COVID in children

For some people COVID-19 can lead to persistent illness, with ongoing and often debilitating symptoms.[13-15] Long COVID is a generic term used to describe signs and symptoms that continue or develop after acute COVID-19. Symptoms of long COVID are wide ranging, and the World Health Organization has recently developed a clinical case definition of post COVID-19 conditions by a Delphi consensus:[16]

Post COVID-19 condition occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms and that last for at least 2 months and cannot be explained by an alternative diagnosis. Common symptoms include fatigue, shortness of breath, cognitive dysfunction but also others and generally have an impact on everyday functioning. Symptoms may be new onset following initial recovery from an acute COVID-19 episode or persist from the initial illness. Symptoms may also fluctuate or relapse over time.

The WHO notes that a separate definition may be applicable for children.

Long COVID in children is not well described, and the studies to date have generally been of poor quality, with some major limitations (such as a lack of a clear case definition, arbitrary follow up time points, subjective assessment, lack of control groups, and low response rates).[7, 17] Evidence is predominantly limited to select populations without control groups.[18] Relatively few studies have focused on SARS-CoV-2 infection sequelae in children and adolescents, and large, harmonised longitudinal studies are

needed.[19] Persistent illness in children has been noted in some studies and in patient support groups, but its prevalence, characteristics and duration are unclear.[20, 21]

Estimates of the prevalence of long COVID in children vary widely.[17] The variability in prevalence estimates could be due to a range of factors, such as initial SARS-CoV-2 infection severity, different methodological approaches (clinical assessment vs self-report), definition of cases (diagnosed vs suspected), variable follow-up times, and prevalence of pre-existing clinical conditions.[18] In the U.S, a large long-term study of the impacts of COVID-19 on children has recently begun. It will track up to 1,000 children and young adults and evaluate the impacts on their physical and mental health over three years.[14] Some studies suggest that long COVID in children is less common and tends to be less protracted than in adults. [22]

Some of the studies of long COVID in children include:

- A review of studies of long COVID in children and adolescents identified 14 heterogeneous studies (4 cross-sectional, 9 prospective cohort, 1 prospective cohort) investigating long COVID symptoms in a total of 19,426 children and adolescents. The prevalence of long COVID symptoms varied from 4% to 66%, and there was also large variation in the reported frequency of different symptoms. Zimmerman et al (2021) note that all the studies in their review were likely to have been conducted before the delta variant became dominant, which may have a different risk of long COVID.[17]
- A recent pre-print describes a German study of 157,134 individuals (11,950 children/adolescents and 145,184 adults) with confirmed COVID-19.[23] The COVID-19 and control cohorts were well-balanced regarding covariates. For all adverse health outcomes combined, incidence rates (IRs) in the COVID-19 cohort were significantly higher than those in the control cohort in both children/adolescents. Incidence rate ratio (IRR) estimates were similar for the age groups 0-11 and 12-17. Incidence rates in children/adolescents were consistently lower than those in adults. Among the specific outcomes with the highest IRR and an incidence rate of at least 1/100 person-years in the COVID-19 cohort in children and adolescents were malaise/fatigue/exhaustion, cough, and throat/chest pain.
- The UK Office of National Statistics found that 9.8% of children aged 2–11 years and 13% aged 12–16 years reported at least one ongoing symptom five weeks after a positive diagnosis, whereas 25% of adults aged 35–69-year had symptoms five weeks after a positive diagnosis.[24, 25]
- A paper describing data from the UK COVID Symptom Study (a citizen science project with data collected via an app, which has some associated limitations) found that of 1,734 children aged 5-17 years who were symptomatic at the time of their positive test and reported symptoms regularly for at least 28 days, 4.4% had an illness duration of at least 28 days.[20] Ongoing symptoms for at least 28 days was less common in younger children aged 5-11 years (3.1%, p=0.046). Over 98% of 1,379 children had recovered by 56 days.[20] Using apps is likely to select participants from higher socio-economic background, who have a lower risk of poor outcomes.[17]
- One of the earliest studies on long COVID in children (a cross-sectional study of 129 children in Italy who were diagnosed with COVID-19 between March and November 2020) reported that 42.6% of children surveyed had 1 or more symptoms >60 days post infection.[26] This included children with mild or asymptomatic initial infection.
- A cohort study of 136 children (most of whom had mild or asymptomatic COVID-19) in Melbourne in 2020 observed that 8% of children had post-acute symptoms. They found that full recovery

occurred within weeks of acute symptom onset and reported symptoms were mild in severity, but noted this was a young cohort (median age three years).[22]

Long-term SARS-CoV-2 infection–associated symptoms can be difficult to distinguish from pandemic-associated symptoms.[7, 17] Some studies have found that children who tested negative for COVID-19 have had similar symptoms, which are common after other viral infections, and could also be due to the experience of lockdown and other social restrictions.[27, 28] Given that acute COVID-19 generally poses a low risk to children, an accurate determination of the risk of long COVID is important in the debate about the risks and benefits of vaccination in this age group.[17] Similar to adults, it is likely that long COVID in children may have a greater impact on those from socioeconomically disadvantaged areas and ethnic minortity groups.[19]

In summary, "the relative scarcity of studies of long COVID and the limitations of those reported to date mean the true incidence of this syndrome in children and adolescents remains uncertain. The impact of age, disease severity and duration, virus strain, and other factors on the risk of long COVID in this age group also remains to be determined."[17] However, even if the proportion of children experiencing post acute impacts is relatively low, if transmission is widespread then the impact of persisting symptoms will be considerable.

At-risk and vulnerable children

Children living with pre-existing health conditions or comorbidities, disadvantage, low socioeconomic or minority ethnic status have a greater risk of severe disease from COVID-19.[7] Paediatric studies have found comorbidities that increase the risk of severe COVID-19 include, but are not limited to: cancer, obesity, chronic respiratory disease, chronic kidney disease, cardiovascular disease, neurological disorders, immune disorders, metabolic disease and hematologic disorders.[29-31] A systematic review of children and adolescents analysing 42 studies that included 275,661 without comorbidities and 9,353 with comorbidities found that severe COVID-19 occurred in 5.1% of those with comorbidities, and in 0.2% without. There was also a higher risk of COVID-19 associated mortality in those with comorbidities (relative risk ratio 2.81, 95% CI 1.31 - 6.02; I^2 = 82%).[29]

One meta-analysis found comorbidities in children with the highest risk (in terms of relative risk) include obesity, asthma or chronic respiratory disease, cardiovascular disease, neurologic or neuromuscular disorders, immune disorders, or metabolic disease.[4, 32] Another systematic review identifying predictors of unfavourable prognosis of COVID-19 in children and adolescents found an association with congenital heart disease, chronic pulmonary disease, neurological diseases, obesity, MIS-C, shortness of breath, acute respiratory distress syndrome, acute kidney injury, gastrointestinal symptoms, elevated C-reactive protein and D-dimer.[32] Children with obesity had a relative risk ratio of 2.87 (95% CI 1.16 - 7.07; I2 = 36%).[29] A Scottish study of over 750,000 school-aged children found that 5–17 year olds with poorly controlled asthma (who have been hospitalised with asthma or prescribed two or more courses of oral steroids for asthma within the past two years) are between three to six times more likely to be hospitalised with COVID-19 compared to those without asthma.[33] A recent multinational cohort study (pre-print) of 403 COVID admissions found that in age-stratified adjusted analyses, neurological disorder was associated with disease severity in children under 12 years of age.[34] There is also a strong argument for vaccinating children and adolescents who live with immunosuppressed or other high-risk household members, not only for the protection of the latter but also to benefit the mental health of the former.[35]

The ECDC notes that the presence of an underlying condition among children aged 5-11 years is associated with about 12 times higher odds of hospitalisation and 19 times higher odds or of ICU admission.[36] However, the majority (78%) of hospitalised children of this age had no reported underlying medical condition.

Indirect impacts of COVID-19 on children

Given the knowledge of the often-mild nature of COVID-19 in children, the Murdoch Children's Research Institute has argued that the main risks to children and adolescents' health in this pandemic continues to be due to indirect effects on mental health, wellbeing and education, which are worsened by continued lockdowns and school closures.[7, 37] Negative impacts of the pandemic, including effects of school closures, have impacts on communities, families and children.

Studies are continuing to emerge that highlight the negative effects of the pandemic on the mental health of children and adolescents. The pandemic limits opportunities for social connection and physical activity while increasing loneliness, uncertainty, fear, and boredom.[19] The WHO has also identified that children have been disproportionately affected by COVID-19 control measures, particularly due to school closures.[4]

Closure of daycares and schools may not only have affected educational outcomes, but also had an effect on social and emotional wellbeing of children through physically being disconnected to schools, with these impacts even more severe for children living with disadvantage.[38, 39] A New Zealand study found that hospital avoidance and reduced access to primary and secondary care were associated with significant potential harm for children in New Zealand during the first lockdown.[40]

Adverse childhood experiences, including family violence, nonaccidental trauma and mental illness, are expected to increase during lockdowns and worsen during the anticipated economic recession. Employment and financial instability as a result of service closures or economic recession also has flow-on effects to children.[41, 42]

Aside from an educational setting, children are also impacted by COVID-19 if a parent or caregiver is hospitalised or dies due to COVID-19. These outcomes result in psychological and socioeconomic harms. It is estimated that more than 1.1 million children worldwide would have experienced the death of a primary parent or caregiver grandparent after the first year of the COVID-19 pandemic.[43] Importantly, indigenous and ethnic minority children are up to 4.5 times more likely to lose a parent or caregiver due to COVID-19 compared to white children.[44] In the United States, 140,000 children are estimated to have lost a parent or grandparent caregiver, with an estimated 1/753 white children, 1/412 Hispanic children, 1/310 Black children, and 1/168 indigenous children experiencing this loss.[44] These losses are likely to be similarly inequitable in Aotearoa New Zealand.

Aotearoa New Zealand context

COVID-19 infections, hospitalisations and deaths in children aged 5-11 years in New Zealand Delta outbreak

To 19 November 2021, children under 12 made up 22.9% of cases in the current Delta outbreak (1,538/6,714), and there had been 1,003 5–11-year-old children who tested positive for SARS-CoV-2 (14.9% of cases, 1,003/6,714). Data about these cases are shown in Table 1.

Currently, the Ministry of Health's Public Intelligence team cannot specify why the COVID-19 positive cases among 5-11-year-olds were hospitalised, and it is possible that some were in hospital for a reason other than COVID-19. As an estimate of the severity of the hospitalisation event, it is possible to look at length of stay, if they were ever admitted to ICU, and to look at the list of symptoms and comorbidities for each case. All but one case had pre-existing conditions, which included a respiratory disorder (asthma). However, this and the other cases were never admitted to ICU. Four cases had unknown lengths of stay, while three stayed in hospital between 4 and 6 hours. Of note, one case is recorded staying in hospital for 14 days -- but once again this cannot be attributed to COVID-19. No cases showed symptoms at the time of diagnosis apart from one, and none showed serious respiratory symptoms such as dyspnoea (shortness of breath). If needed, any further medical and hospitalisation details should be obtained from local DHB and PHU authorities

Table 1: SARS-CoV-2 infection in children aged 5-11 years in New Zealand (Delta outbreak, data from August 17th - November 19th 2021)

Characteristic	Number of cases (N =1,003)	% of total
Number of Symptoms[1]		
0 symptoms	832	83
1 symptoms	62	6
2 symptoms	59	6
3 symptoms	31	3
4 symptoms	14	1.4
5 symptoms	5	0.5
Hospitalised[2]		
yes	8	1
no	995	99
Number of co-morbidities[3]		
0 comorbidities	982	98
1 comorbidities	18	2
2 comorbidities	2	0.2
3 comorbidities	1	0.1
Ethnicity[4]		
Maori	521	52
Pacific Peoples	304	30
European or Other	130	13
Asian	33	3
Unknown	15	1
Socioeconomic deprivation		
1 (least deprived)	26	3
2	22	2

3	26	3
4	35	3
5	39	4
6	54	5
7	81	8
8	102	10
9	238	24
10 (most deprived)	367	37
Unknown	13	1

[1] Includes cardiovascular disease, chronic lung disease, diabetes, immunodeficiency, malignancy, liver disease and renal failure
[2] Symptoms at time of diagnosis
[3] Includes hospitalisation of any duration (hours to days)
[4] This is prioritised ethnicity (prioritised order Māori, Pacific, Asian and European/Other)

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 prexisting conditions or comorbidities. The Sydney data further demonstrates that COVID-19 is relatively mild in most young children as despite children aged 0-11 years 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.[45]

This data shows that the burden of COVID-19 has disproportionately affected Māori and Pacific Peoples aged 5-11, which intersects with socioeconomic deprivation reported for these cases. This mirrors the wider shift in the ethnic groups affected by COVID-19 in Aotearoa, with the outbreak now dominated by those of Māori descent, with 43% of cases identifying as Māori, and 32% of hospitalised cases identifying as Māori.

At-risk groups and vulnerable children in Aotearoa New Zealand

There is limited data on the prevalence of serious health conditions in children in Aotearoa New Zealand. In the 2020 New Zealand Health Survey, 2.1% of under 14-year-olds (estimated 20,000 children) were rated as having poor or fair health by their parents. The percentage rating varied considerably between regions and socioeconomic area. Northland (3%), Tairāwhiti (3.1%), Lakes (3.4%), Hawkes Bay (4.9%) Hutt Valley (4.2%), and the West Coast (5.2%) had the highest rates of children and young people experiencing poor health.[46] There is considerable overlap between areas with poor child health and areas with low vaccination rates. Nationally, as of 19th November 2021, 82% of eligible people are fully vaccinated while 73% are fully vaccinated in Northland, 72% in Tairāwhiti, 75% in Lakes, and 75% in the West Coast.

In adults, risk factors for poor outcomes associated with COVID-19 include respiratory disease and obesity. According to data from the 2020/2021 New Zealand Health Survey, New Zealand has a high prevalence of childhood asthma, with 11.9% (101,000) of children aged 2–14 years reporting taking current asthma medication (though this number is lower than previous years which ranged from 13-15%, and recruitment for the study was impacted by COVID-19 lockdowns).[47] OECD statistics indicate New Zealand has one of the highest hospital admission rates for asthma of OECD countries, and these rates are higher among

Māori, Pacific, and in more deprived areas.[48] New Zealand also has a high prevalence of obesity, with 12.7% (107,000) children aged 2–14 years classified as obese in the 2020/2021 New Zealand Health Survey (with a BMI equivalent to an adult BMI of 30 or greater).[47] Prevalence of obesity also increases in the most deprived living areas with quintile five prevalence at 18.7%. Pacific children are nearly three times as likely to be obese (28.8%).[46]

The other high-risk factor for poor outcomes in the adult population is being disabled, particularly for learning or intellectual disabilities. Ministry of Education enrolment data indicates that at 1 July 2020, there were 10,160 students receiving Ongoing Resourcing Support (ORS) for high or very high educational support needs, with the regions of Auckland (3,359), Waikato (1,019) Wellington (1,050), and Canterbury (1,091) providing education for the bulk of these students.[49] Māori and Pacific students were significantly over represented in these enrolments.[49] Higher Māori enrolment rates are possibly due to a notable increase in tamariki Māori starting school with serious disability in the last 10 years.[50] Child poverty statistics show that 1 in 5 disabled children live in material hardship, two and a half times more often than children who are not disabled.[51]

Māori and Pacific adults are also at greater risk of hospitalisation due to COVID-19 and severe COVID-19, with an 80-year-old patient with COVID-19 who is NZ European/Other without reported comorbidities having the same predicted risk of hospitalisation as a 59.3-year-old (95%CI, 46.9–73.7) patient who is Māori without reported comorbidities.[52] Similar differences are seen across all ages and for cases with at least one reported comorbidity, and therefore it is likely to also be represented in children. Steyn et al. found that Māori have 2.5 times higher odds of being hospitalised (95%CI, 1.39-4.51) than non-Māori and are likely to spend around 4.9 days longer in hospital than other ethnicities, even after controlling for age and pre-existing conditions, while Pacific People have three times greater odds (95%CI, 1.75-5.33).[52] There are an estimated 115,562 tamariki Māori aged 5 to 11 years in Aotearoa, and an estimated 49,398 Pacific children.[53] This amounts to over 160,000 children that are likely at higher risk by virtue of their ethnicity.

In New Zealand, factors which increase the risk of transmission include social deprivation, quality of housing, fuel and heating, poverty and household crowding, and each of these are also more likely to affect Māori and Pacific People.[1] One in five Māori live in overcrowded housing compared to one in 25 New Zealand European.[54]

If and when vaccination does roll out, risk will be higher among areas with low uptake among 5-11-year-olds and examining the uptake of other childhood vaccinations may indicate where there is greater risk of this occurring. Over the last decade there has been increasing concern about falling rates of immunisation for many infectious diseases, and the widening inequities and gaps in immunisation coverage rates in Aotearoa New Zealand.[55] In a 10 year immunisation coverage analysis, Marek et al. showed that although the least deprived regions have the highest immunisation coverage, there was a declining trend in coverage rates over 2006-2017 in high decile regions. Immunisation coverage was lowest in the most deprived areas with the northern part of the South Island, the central-southern part of the North Island, around Auckland, and Northland most negatively impacted by this. Additionally Māori tamariki were more likely to not be fully immunised.[55] The younger age demographic of the Māori population also means that a relatively larger proportion of Māori compared to the wider population are children who are unable to be vaccinated at present and remain susceptible to infection, with a risk of onwards spread to their whānau and communities. Not only does the Māori population have a younger age structure, but Māori whānau often have more tamariki and live in intergenerational households, alongside experiencing disproportionate levels of socioeconomic inequality.[1, 54] 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% [56].

Transmission

During the early pandemic, children were rarely identified as index cases of household transmission clusters,[57] though this was likely influenced by the closure of schools and lockdowns. Meta-analyses from 2020 gave some support to the hypothesis that children are less susceptible to SARS-CoV-2 infection, though their infectivity and overall role in transmission was less clear.[57, 58] However, with schools reopening and extracurricular activities resuming, outbreaks have demonstrated that children do play a role in transmission, though likely less of a role than adults. ATAGI notes that available evidence suggests that the transmissibility of infection in younger children is lower than in older age groups.[56]

Children and young people have become more prevalent in positive case numbers in many countries as the pandemic has progressed,[59] and this population group is also being recognised as a growing community 'reservoir' for the virus.[60] Since the Delta variant emerged, the USA has recorded cumulative increases of childhood cases in most states each week - a trend that is just abating in October after three months.[61] In July 2021 the ECDC updated its assessment of the susceptibility of children to SARS-CoV-2 infection, now noting that children appear to be equally susceptible to SARS-CoV-2 infection compared to other age groups (low confidence), although severe disease is much less common in children than in adults [8]. They note that while multiple studies have suggested that children may be less susceptible to SARS-CoV-2 infection than adults, potential reporting biases due to lower-case ascertainment in children may contribute to this interpretation, particularly for studies published during 2020. Recent prevalence and seroprevalence studies have tended to conclude that there are no significant differences across age groups. However, they note that cases of SARS-CoV-2 in younger children appear to lead to onward transmission less frequently than cases in older children and adults.

Transmission in education settings

Within education settings, transmission of SARS-CoV-2 occurs but appears to belimited. Transmission of SARS-CoV-2 in schools appears to be affected by how widespread the virus is in the broader community.[62-64] The CDC notes that although outbreaks in schools can occur, multiple studies have shown that transmission in school settings is typically lower than – or at least similar to – levels of community transmission, when prevention strategies are in place in schools. [65]

Overall, in the school environment, transmission is more likely to occur between adults, followed by adult-to-child transmission, with the risks of child-to-child or child-to-adult transmission being considerably less.

- An investigation of SARS-CoV-2 transmission in a Georgia school district during December 1, 2020–January 22, 2021, identified nine clusters of COVID-19 cases involving 13 educators and 32 students at six elementary schools. Two clusters involved probable educator-to-educator transmission that was followed by educator-to-student transmission in classrooms and resulted in approximately one half (15 of 31) of school-associated cases. The paper concluded that educators might play a central role in in-school transmission networks.[63]
- Data from a prospective, cross-sectional analysis from the UK's national surveillance also found the majority of cases were in staff. Following the reopening of educational settings during the summer mini-term from 01 June-21 July 2020, staff were found to have an increased risk of infection. Staff

had higher incidence than students (27 cases [95%CI, 23–32] per 100,000 per day among staff compared with 18 cases [14–24] in early years students, 6.0 cases [4.3–8.2] in primary school students, and 6.8 cases [2.7–14] in secondary school students]), and most cases linked to outbreaks were in staff members (154 [73%] staff vs 56 [27%] children of 210 total cases). The probable transmission direction for the 55 confirmed outbreaks was: staff-to-staff (n=26), staff-to-student (n=8), student-to-staff (n=16) and student-to-student (n=5).[64, 66]

- Data from New South Wales shows that the largest risk to children in schools is from adults. There were 59 individuals (34 students [57.6%] and 25 staff members [42.3%]) from 51 educational settings (19 schools and 32 ECEC services) confirmed as primary COVID-19 cases who had an opportunity to transmit SARS-CoV-2 to others in their school or early childhood centres. 2,347 individuals (1,830 students [77.9%] and 517 staff members [22.0%]) were identified as close contacts of these 59 primary cases. 106 secondary cases (69 students and 37 staff members) occurred in 19 of the 51 educational settings resulting in a secondary attack rate (SAR) of 4.7%. The highest transmission rate occurred between staff members (16.9%). The rate was low in primary schools (1.7%), however this would have been affected by many primary schools being closed. Early childhood education centres remained fully open during the report period, and there was an overall SAR of 6.4%. When transmission did occur to children, the household tertiary attack rates following exposure to a secondary case from a school was 70.7%.[67] Figure 1 provides a breakdown of transmission routes and the associated risks.

Primary case type	Close contact type	n positive NAT/N tested	Attack rate (%)
Overall			
Any	All	106/2253	4.7%
Adult	All	88/1027	8.6%
Adult	Adult	33/294	11.2%
Adult	Child	51/733	7.0%
Child	All	21/1316	1.6%
Child	Adult	4/274	1.5%
Child	Child	17/1042	1.6%
High schools			
Any	All	0/202	0.0%
Primary schools			
Any	All	9/526	1.7%
Adult	All	3/162	1.9%
Adult	Adult	0/60	0.0%
Adult	Child	3/102	2.9%
Child	All	9/454	2.0%
Child	Adult	2/86	2.3%
Child	Child	7/368	1.9%
ECEC services			
Any	All	97/1515	6.4%
Adult	All	85/823	10.3%
Adult	Adult	33/195	16.9%
Adult	Child	51/628	8.1%
Child	All	12/692	1.7%
Child	Adult	2/151	1.3%
Child	Child	10/541	1.8%

Note: For one primary school where both a staff member and student were co-primary cases, the close contacts have been counted in attack rate calculations for both categories of primary cases.

Figure 1: Secondary attack rates in NSW educational settings, by primary and secondary case type and educational setting type, between 16 June and 31 July 2021 [67]

Transmission in household settings

Transmission within households is common. This is where the greatest risk of transmission is due to the ongoing and close nature of exposure. Pre-Delta, the risk of transmission to a household contact was approximately 30%, however the risk ranged in studies between 10% and 60%.[68-71] This will be higher with the Delta variant, with transmission to households occurring with most cases in the current Delta outbreak. Pre-Delta, children under the age of 10 appeared to be about half as susceptible to infection,[72-75] though in a household cohort study, Li et al. found the secondary attack rate was even lower for children, at 4% compared with 17.1% for adults.[76]

Children were also at a lower risk of transmission or being the index case in households.[74, 77] However, one study suggests that children and adolescents are more likely to infect others.[78] Another study reported that household transmission was more common from children aged 0–3 years than from children aged 14–17 years.[79]

New data from the Imperial-led REACT coronavirus monitoring programme found the highest prevalence was found in children aged 5-12 years at 5.85% (1 in 17), followed by secondary school-aged children aged 13-17 years at 5.75%. Prevalence was also more than four times higher in households with one or more children at 3.09%, compared to those without children (0.75%).[80]

Modelling impact of vaccination of 5-11 year olds on case numbers in New Zealand

The Ministry is undertaking ongoing internal modelling studies. The model considers vaccination of 5 to 11-year-olds in a subset of the scenarios. Assuming roughly 50% uptake in this group and the same vaccine effectiveness as in older age groups, preliminary analysis suggests that vaccination of 5-11 year-olds could substantially decrease transmission, resulting in half as many cases, hospitalisations and deaths.

Non-pharmaceutical interventions for the prevention of COVID-19 in children

Given that aerosol transmission is a key mechanism for spread of SARS-CoV-2, there is increasing focus on the need for strategies such as optimising ventilation, air quality and mask wearing. OzSAGE (a multidisciplinary group of experts in Australia) recommends the following strategies to help protect children from SARS-CoV-2 infection:[81]

- Vaccinating eligible children, their parents and teachers as soon as possible
- Ensuring access to safe indoor air through ventilation and filtration
- Using high quality masks for children and teachers in schools
- Providing families flexible learning options so they can make their own decisions about their children attending school in-person.

The ECDC [62] recommends the following measures to prevent the spread of infection in schools (adapted to levels of community SARS-CoV-2 transmission as well as to the education setting and age group):

- Physical distancing (by cohorting, ensuring physical distance in the classroom, reducing class sizes, staggering arrival and break times, and holding classes outdoors)
- Improved ventilation
- Promotion of ‘stay-at-home’ when sick policies
- Promotion of respiratory etiquette
- Regular hand-washing
- Use of masks when feasible.

In addition, testing strategies for educational settings aiming at timely testing of symptomatic cases are recommended to ensure isolation of cases and tracing and quarantine of their contacts.[8] The ECDC notes that the decision to close schools to control the COVID-19 pandemic should be used as a last resort, given the negative physical, mental and educational impacts on children and the economic impact on society more broadly[6]: "While a measure of last resort, school closures can contribute to a reduction in SARS-CoV-2 transmission, but are by themselves insufficient to prevent community transmission of COVID-19 in the absence of other non-pharmaceutical interventions and the expansion of vaccination coverage. The effectiveness of school closures appears to have declined in the second wave as compared to the first wave of the COVID-19 pandemic, possibly in part due to better hygiene measures in school settings."

Evidence from the United States shows wearing masks in classrooms may reduce the chance of transmission. After adjusting for potential described confounders, the odds of a school-associated COVID-19 outbreak in schools without a mask requirement were 3.5 times higher than those in schools with an early mask requirement (OR = 3.5; 95% CI = 1.8–6.9).[82] Another MMWR analysis indicated that increases in paediatric COVID-19 case rates during the start of the 2021–22 school year were smaller in U.S. counties with school mask requirements than in those without school mask requirements.[83]

A recent systematic review has investigated the effectiveness of public health measures in reducing the incidence of COVID-19, SARS-CoV-2 transmission, and COVID-19 mortality, focussing only on empirical studies.[84] They noted two studies [85, 86] that assessed the effectiveness of school closures on incidence of COVID-19 or COVID-19 mortality. Both were rated at moderate risk of bias.[84] One of these studies was a US population-based time series analysis conducted in 2020, and it found that school closure was temporally associated with decreased COVID-19 incidence (adjusted relative change per week, −62%) and mortality (adjusted relative change per week, −58%).[86] States that closed schools earlier, when the cumulative incidence of COVID-19 was low, had the largest relative reduction in incidence and mortality. However, some of the reduction could have been related to other concurrent pharmaceutical interventions.[87] On the other hand, time series analyses to evaluate the effectiveness of school closure in Japan found no effect on the incidence of COVID-19.[85]

The systematic review identified three studies investigating the impact of school closures on transmission, all rated at moderate risk of bias.[84] The review notes that two natural experiments from the US reported a reduction in transmission (i.e., reproductive number); One study reported a reduction of 13% (relative risk 0.87, 95% CI 0.86 - 0.89) and another reported a 10% reduction(0.90, 0.86 to 0.93). It also cites a Swedish study that reported an association between school closures and a small increase in confirmed SARS-CoV-2 infections in parents (odds ratio 1.17, 95% CI 1.03 to 1.32), but observed that teachers in lower secondary schools were twice as likely to become infected than teachers in upper secondary schools (odds ratio 2.01, 95% CI 1.52 to 2.67).

Another study experimentally evaluated the impact of ventilation on aerosol dynamics and distribution, along with the effective filtration efficiency (EFE) of four different mask types, with and without mask fitters, in a classroom setting.[88] They reported that infection probability estimates indicate that ventilation alone is not able to achieve probabilities <0.01 (1%). The use of moderate to high EFE masks reduces infection probability, by >5× in some cases. Reductions provided by ventilation and masks are synergistic and multiplicative.

A retrospective cohort study from the US investigated the effectiveness of 3 versus 6 ft of physical distancing for controlling spread among primary and secondary students and staff.[89] Student case rates

were similar in the 242 districts with ≥3 versus ≥6 ft of physical distancing between students (IRR, 0.891; 95% confidence interval, .594-1.335); results were similar after adjustment for community incidence (adjusted IRR, 0.904; .616-1.325). Cases among school staff in districts with ≥3 versus ≥6 ft of physical distancing were also similar (IRR, 1.015, 95% confidence interval, .754-1.365).

A recent study used epidemiological models to simulate the spread of SARS-CoV-2 among students, teachers, and staff in both primary and secondary schools and applied these to better understand the risks of reopening schools and to explore the effectiveness of different mitigation strategies.[90] They reported that the risk of school outbreaks increases as community prevalence increases, and that secondary schools pose greater control challenges than primary schools. The models indicate that a number of measures can help substantially: dividing students into multiple cohorts who attend school on an alternating basis, frequently testing teachers and students, and vaccinating teachers and staff. The authors emphasise that basic transmission control strategies such as mask use, social distancing, and ventilation remain essential.[90]

Prior to COVID-19 vaccines being available for children, UNICEF and WHO developed guidance on how to minimise transmission in schools and keep schools open.[4] These recommendations are still applicable, even with vaccines now being available. The CDC recommends layering multiple prevention strategies, including: promoting vaccination; consistent and correct use of masks; physical distancing; screening for prompt identification of cases; improved ventilation; handwashing and respiratory etiquette; staying home when sick and getting tested; contact tracing in combination with isolation and quarantine; and routine cleaning with disinfection under certain conditions.[65] Studies of SARS-CoV-2 transmission in schools that consistently implemented layered prevention strategies have shown success in limiting transmission in schools, even when testing of close contacts has been incomplete. [65] In June 2020 the Harvard School of Public Health published “Healthy Schools Risk Reduction Strategies for Reopening Schools” which outlined a range of mitigation strategies under the themes of healthy classrooms, healthy buildings, healthy policies, healthy schedules and healthy activities.[91]

The Pfizer COVID-19 vaccine for 5-11 year olds

A phase 3 randomised control trial was conducted to assess the safety, immunogenicity and efficacy of two doses of the Pfizer Comirnaty (BNT162b2) vaccine (‘the Pfizer vaccine’) administered 21 days apart in children aged 6 months to 11 years, with findings thus far published for 5-11-year-olds.[92]

During the phase 1 study from 24 March through 14 April 2021, a total of 48 children 5-to-11 years of age received 10 µg, 20 µg, or 30 µg of the Pfizer vaccine (16 children at each dose level). For the phase 1 trial, a total of 50 children 5 to 11 years of age were screened for inclusion at four US sites, and 48 received escalating doses of the Pfizer vaccine. Half the children were male, 79% were White, 6% were Black, 10% were Asian, and 8% were Hispanic or Latinx. The mean age was 7.9 years. Based on reactogenicity and immunogenicity, a dose level of 10 µg was selected for further study.[92]

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 10ug or placebo. A total of 2268 children were randomly assigned to receive the Pfizer vaccine (1517 children) or placebo (751 children). At data cut-off, the median follow-up was 2.3 months.[92] 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. Apart from younger age and a lower percentage of Black and Hispanic or Latinx 5-to-11-year-olds (6% and 18%, respectively) than 16-to-25-year-olds (12% and 36%, respectively), demographic characteristics were similar among the 5-to-11-year-old and 16-to-25-year-old Pfizer recipients who were included in the immunobridging subset.[92]

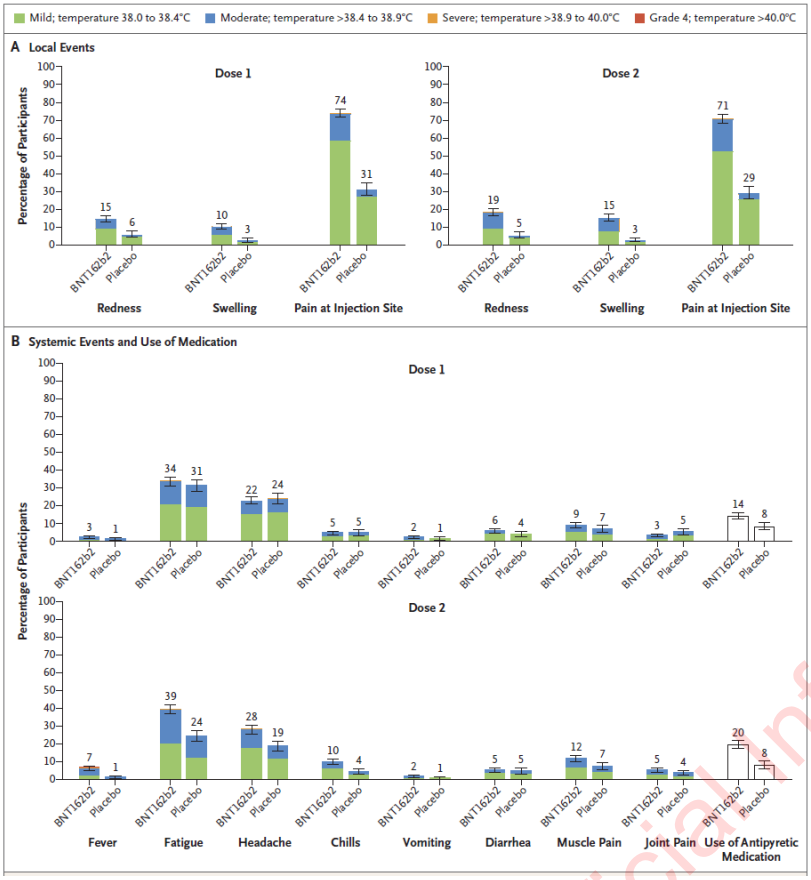
Children with no or stable pre-existing conditions were eligible to participate, except those with an immunocompromising or immunodeficiency disorder, those with a history of MIS-C, or those receiving immunosuppressive therapy (including cytotoxic agents and systemic glucocorticoids). In addition, in the phase 1 study, children with a previous clinical or virologic COVID-19 diagnosis were excluded.[92]

Safety and reactogenicity

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.[92]

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 - 25-year-olds who received standard 30 µg doses.[93] 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 after the second dose than first dose (see Figure 2). 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%).[92, 94, 95]

Figure 2: Local Reactions and Systemic Events Reported in the Phase 2–3 Trial (5-11 year olds) within 7 Days of Injection of Pfizer or Placebo.[92]



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 or thrombosis with thrombocytopaenia. The trial was therefore not powered to detect any rare unanticipated adverse events in this age group.[96] From the first dose through 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. Severe adverse events were reported in 0.1% of Pfizer recipients and 0.1% of placebo recipients. Three serious adverse events in two participants were reported by the cut-off date; all three (postinjury abdominal pain and pancreatitis in a placebo recipient and arm fracture in a Pfizer recipient) were considered to be unrelated to the vaccine or placebo. No deaths or adverse events leading to withdrawal were reported. 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.[92]

Immunogenicity and Efficacy

For all participants in the phase 1 and for a subset of participants in phase 2/3, blood samples were collected for immunogenicity assessments, which included determination of SARS-CoV-2 neutralisation titres. Serum samples collected from 5-to-11-year-olds and 16-to-25-year-olds were assayed in parallel to ensure comparability of titres.[92]

Immune responses one month after the second dose of the Pfizer vaccine were immunologically bridged to those in 16-to-25-year-olds from the pivotal trial of two 30 µg doses of Pfizer. 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.[93] One month after the second dose, the geometric mean ratio (GMR) of SARS-CoV-2 neutralising titres in 5-to-11-year-olds to those in 16-to-25-year-olds was 1.04 (95% CI, 0.93 to 1.18), a ratio meeting the prespecified immunogenicity success criterion (lower bound of two-sided 95% CI,>0.67; GMR point estimate, ≥0.8).[92, 93] One month after the second dose, the GMR of SARS-CoV-2 neutralising titres in 5-to-11-year-olds to those in 16-to-25-year-olds was 1.04 (95% CI, 0.93 to 1.18), a ratio meeting the prespecified immunogenicity success criterion (lower bound of two-sided 95% CI,>0.67; GMR point estimate, ≥0.8).[92]

Vaccine efficacy against symptomatic NAAT-confirmed COVID-19 at 7 days or more after the second dose was assessed. COVID-19 with onset 7 days or more after the second dose was reported in three recipients of the Pfizer vaccine and in 16 placebo recipients, producing a vaccine efficacy or 90.7% (95% CI, 67.7 to 98.3).[92] No cases of severe COVID-19 or MIS-C were reported.

Data are not yet available on the real world effectiveness of the vaccine to protect against hospitalisation or infection in this age group, but are expected in coming months.[96]

Real-world rollout

In October 2021, the Global Advisory Committee on Vaccine Safety (GACVS) concluded that in all age groups the benefits of mRNA COVID-19 vaccines in reducing hospitalisations and deaths due to COVID-19 outweigh the risks.[4] The Advisory Committee on Immunization Practices (ACIP) made an interim recommendation for use of the Pfizer vaccine in children aged 5-11 years in the United States for prevention of COVID-19.[3, 97] 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.[3, 97]

ACIP conducted a systematic review of published and unpublished evidence for benefits and harms. Key conclusions from ACIP included:

> *"ACIP determined that use of the Pfizer-BioNTech COVID-19 vaccine among children is a reasonable and efficient allocation of resources. To expand COVID-19 vaccine access, additional considerations should be given to demographic groups that have experienced disproportionate COVID-19 morbidity and mortality, as well as those with barriers to routine health care (e.g., members of certain racial/ethnic groups and those living in a rural or frontier area, experiencing homelessness, with a disability, or lacking health insurance). Children from racial and ethnic minority groups have experienced a disproportionally high incidence of COVID-19 as well as secondary impacts of the COVID-19 pandemic such as reduced in-person learning (12). Providing rapid and equitable access to COVID-19 vaccines for children will necessitate increasing the enrollment of pediatric health care providers into the COVID-19 vaccination program, using the broad geographic accessibility of pharmacies, and expanding school-focused strategies to ensure vaccination opportunities for a diverse population, as well as engagement with community leaders, pediatric health care providers, and parents or guardians."*[3]

These equity related comments have high relevance for New Zealand.

The US FDA approved a modified formulation of the Pfizer vaccine (10 µg each dose, administered 3 weeks apart) for children aged 5-11 on 29 October 2021.[98] On 2 November, CDC recommended the use of the vaccine in this age group.[99] The White House announced on 18 November that 2.6 million children received the vaccine.[100] From December 14, children aged 5-11 will need to show proof of at least one dose of COVID-19 vaccine to participate in indoor activities in New York City. As of 12 December, almost 5.4 million children aged 5-11 in the US had received at least one dose and almost 2.5 million children had received their second dose. [101] Other countries including Canada, Israel, UAE, Costa Rica, Singapore, Malaysia, Bahrain, Slovakia, Saudi Arabia, Australia and Kuwait have authorised use of the Pfizer vaccine in children aged 5-11 years. Data are yet to be reported from any of these countries.

On 25 November, the European Medicines Agency recommended granting approval for children aged 5 to 11. On 1 December 2021 the European Centre for Disease Prevention and Control published interim public health considerations for COVID-19 vaccination of children aged 5-11 years.[36]

In Australia, on 5 December the Therapeutic Goods Administration (TGA) provisionally approved the Pfizer vaccine as safe and effective for use among this age group.[102] On 10 December 2021, the Australian Technical Advisory Group on Immunisation (ATAGI) recommended use of this vaccine in 5-11 year-olds.[96] The Australian Government will start rolling out the Pfizer vaccine to 5 to 11-year-olds from early January 2022.

Regulators in the UK and New Zealand are reviewing the data for 5-11 year-olds and are yet to approve the vaccine for this age group.

Dosing intervals

The US has recommended a 3 week interval between doses as in the clinical trials. There are no data available about extending the interval of the paediatric formulation of the Pfizer vaccine, however Canada is recommending a minimum 8 week interval. [103] Similarly, in Australia, the schedule recommended by ATAGI for this age group is 2 doses, 8 weeks apart. In special cicrumstances the interval may be shortened to a minimum of 3 weeks. [96] Data from older age groups has showed that an extended dosing interval may improve immunogenicity and the effectiveness after the second vaccine, and may also reduce the risk of myocarditis and pericarditis after vaccination. [96]

Data are also very limited on extended dosing intervals for the Pfizer vaccine in adults and the impact on vaccine efficacy and safety. However, emerging data suggests that the immune response is likely improved somewhat by extending the dosing interval. This is consistent with basic principles of vaccinology and immunology, that suggests that immune responses are generally better with longer intervals.

Several countries have been using extended intervals, ranging from approximately 6-16 weeks for the Pfizer vaccine for their general populations, including England, Canada, and several countries in Europe. A study of 750 participants aged 50-89 years in the UK found higher protection following extended schedules. GMTs at 14-34 days were 6703 (95%CI, 5887-7633), higher than those receiving Pfizer 19-29 days apart (694; 540 - 893). Higher two-dose vaccine efficacy was also observed with >6 week intervals between Pfizer doses compared to the authorised 3-week schedule, including ≥80 year-olds.[104] Another study from Canada found efficacy was significantly higher against both infection and hospitalisation with longer 7-8-week vs. manufacturer-specified 3-4-week interval between doses.[105] With both studies however it's

unclear whether this results in more durable protection, as waning protection, at least against infection, seems to be similar across different interval periods used. The studies have also had small sample sizes.

There may also be a connection between shorter intervals and increased reactogenicity or adverse events. One study found reactogenicity after a late second dose (given at 44-45 weeks post-first dose) or a third dose was lower than reactogenicity after a first dose.[106] Considering the increased risk of serious adverse events such as myocarditis in younger age groups, there could be an argument for an extended dosing interval. However, is without direct evidence that an extended dosing interval reduces the risk of myocarditis. Relevant to operational considerations, a pre-print paper has shown a statistically significant increase in myocarditis occurrence following the second dose of the Pfizer vaccine if the second dose was given at a shorter interval of less than 30 days between doses.[107] However, the study was limited to those aged 12 and over.

Coadministration

There is yet to be specific recommendations in the New Zealand setting for the coadministration of COVID-19 vaccines in children, or the possibility of the COVID-19 vaccine being combined in a formulation with other vaccines.

There are limited clinical trial, observational, or laboratory data on the safety and immunogenicity associated with the coadministration of the Pfizer COVID-19 vaccine and other vaccines in all populations. Based on first principles, there is the potential for a reduced immune response when two different types of vaccine are administered together or within several days of each other. However, there are no additional safety concerns associated with coadministration, over and above each vaccine's individual safety profile. Given that the catch-up campaigns for MMR, HPV, and Boostrix are largely among younger age groups, and that these individuals are likely to have a robust immune response, younger age groups are less likely to be adversely impacted by coadministration of vaccines. Younger age groups have lower vaccination rates compared to others. Any obstacles to accessing and completing vaccinations should be removed and steps should be taken to encourage completion of the recommended vaccine schedules. In general, the risk of reduced immune protection from coadministration of the Pfizer COVID-19 vaccine and other vaccines is low in younger age groups, while the public health benefit gained from higher vaccine coverage is substantial.

In New Zealand adults, CV TAG earlier recommended either dose of the Pfizer vaccine can be administered at any time before, after or simultaneously with other Schedule vaccines (in separate syringes, at separate sites), including MMR, influenza, HPV, Tdap and meningococcal vaccines, and this has been included within the Immunisation Handbook. The only exception is the live herpes zoster vaccine for which, spacing of at least 7 days is recommended before or after the Pfizer vaccine.[108]

The CDC has stated that COVID-19 vaccines 'may be administered without regard to timing of other vaccines, which includes simultaneous administration of COVID-19 vaccine and other vaccines on the same day'.[109] The American Medical Association states it is considered best practice to administer all the vaccines someone is eligible for in the same visit as it helps ensure that people are up to date with their vaccinations, though there are some exceptions, such as children with asplenia, complement component deficiency or HIV infection.[110] They also state that for those children who need two doses of the influenza vaccine, they should receive their first dose early as the second dose cannot be given until four weeks later but the circulation of influenza can fluctuate at different times.

In Australia, ATAGI has said that the paediatric Pfizer COVID-19 vaccine can be co-administered with other vaccines, though parents and guardians should be aware that this may be associated with an increase in mild-moderate adverse events.[96] Health Canada recommends that if possible, children shouldn't receive the Pfizer vaccine within 14 days of other vaccines, such as the flu vaccine. This is a precaution to monitor any side effects from the COVID-19 vaccine or another vaccine.[103]

Number needed to treat

The number needed to treat (NNT) for a vaccine is interpreted as the average number of people who need to be vaccinated to prevent one additional adverse outcome from the disease. It is calculated as 1/(incidence in unvaccinated – incidence in vaccinated).

It is important to note that the NNT is not a fixed value for any one vaccine, outcome or population. It will vary with baseline risk (incidence in unvaccinated), which for infectious diseases can fluctuate with factors such as control measures in place (e.g. border controls, lockdowns, masks) and season. Although the simplest calculations of NNT can be performed using trial data, it should be noted that trial data are likely to overestimate the NNT. This is because trials are often "completed" relatively early which may appear to reduce the background risk (and increase the NNT). The NNTs for Pfizer vaccine trials are shown in Table 2.

Table 2: Numbers Needed to Treat, Pfizer COVID-19 vaccine trials

Trial	NNT confirmed COVID-19	NNT severe disease/ hospitalisation	NNT death	Notes
Pfizer phase 3 COVID-19 vaccine trial, adults (16 years and over)	141 Vacc: 8/21,720 Plac: 162/21,728	2716 Vacc: 1/21,720 Plac: 9/21,728	Not calculable (no cases in either group)	To October 9th 2020 [94]
	30 Vacc: 77/23,153* Plac: 850/23,153*	723 Vacc: 0/23,153* Plac: 32/23,153*	N/A (not reported)	To March 13th 2021[111]
Pfizer phase 3 COVID-19 vaccine trial, adolescents (12-15 years)	71 Vacc: 0/1131 Plac: 16/1129	N/A (not reported)	Not calculable (no cases in either group)	58% had at least 2 months of follow-up after their second vaccine dose[95]
Pfizer phase 3 COVID-19 vaccine trial, children (5-11 years)	51 Vacc: 3/1517 Plac: 16/751	Not calculable (no cases in either group)	Not calculable (no cases in either group)	Median 2.3 months follow up. All recruited early to mid June 2021[92]

* Denominators per group not reported but groups previously very closely balanced

It is challenging to present a fair comparisonof NNTs across childhood vaccines. This is because baseline incidence of these infectious disease can vary substantially over time period, and the length of time that the population is observed for. Table 3 presents NNTs for a range of scenarios, with worked examples for measles vaccine and COVID-19 in children. To make these comparisons as fair as possible, it is assumed that in a hypothetical, completely unvaccinated population of children, each virus is allowed to circulate freely

until the herd immunity threshold is reached. Because of this, the baseline risk for COVID-19 outcomes is substantially higher than in the Phase 3 trials reported in Table 2, and the NNTs therefore lower. Additionally, for the calculations around NNTs for COVID-19 in children, there are many uncertainties around numbers used to calculate these estimates, including R0 in children, and the proportion of infected children who go on to die. However, in these examples, the NNTs for COVID-19 vaccine for each outcome are generally around 5 times that for measles vaccine.

Table 3: Number needed to treat with different percentage of population with outcome with no vaccination, and vaccines of different efficacy

	Number Needed to Treat to Prevent One Occurrence of the Outcome									
	Percentage of population with outcome of interest in absence of vaccine									
	100%	75%	50%	10%	5%	1%	.75%	.5%	.1%	.01%
95% effective vaccine	1.1	1.4	2.1	11	21	105	140	211	1053	10526
80% effective vaccine	1.3	1.7	2.5	13	25	125	167	250	1250	12500
50% effective vaccine	2	2.7	4	20	40	200	267	400	2000	20000

Worked examples:

Measles in children: With no vaccination, around 92-94% of the population will become infected (usually in childhood), based on R0 of 12-15. With vaccine efficacy of 95%, NNT would be **just over 1 to prevent 1 case of measles.** The NNT to **prevent 1 hospitalisation would be just over 4** (based on around 1 in 4 cases needing hospitalisation), and just over **1000 to prevent one measles death** (based on around 1 per thousand).

Covid-19 in children: It should be noted there are many uncertainties around these estimates. With no vaccination, and assuming R0 of 6, around 83% of the population would become infected at some point (possibly fewer if R0 lower in children resulting in higher NNTs, possibly higher if natural infection doesn't prevent re-infection allowing on going circulation). With vaccine efficacy of 95%, NNT would be around **2.5 to prevent 1 symptomatic case** (based on around 50% of cases in children being symptomatic [5]). The NNT would be around **30 to prevent 1 hospitalisation** (based on 1 in 25 of cases in 6-11 year olds being severe [6]), and **5000 to prevent 1 death** (based on 1 in 4000 cases dying: 4% of cases being severe and 0.6% of severe cases dying.[112])

Risks and benefits of vaccinating 5-11 year olds in Aotearoa New Zealand

The decision to vaccinate children requires very careful weighing of the known and potential risks and benefits. The balance of risks and benefits of COVID-19 vaccination in children is more complex than in adults as the relative harms from vaccination and disease are less well established in this age group.[35]

The balance of direct benefits over potential vaccine risks (such as rare cases of myocarditis) is more limited in this age group compared to older individuals.[96]

Risks

Careful consideration must be given to the incidence of severe adverse events in this age group. The risk of myocarditis (or other rare, serious adverse events) in children has not yet been determined, nor has the long-term safety of the vaccine.[4] This is a new class of vaccine and it cannot be assumed that the responses of young children will be the same as older children or adults. Some adverse events in other age groups have only become apparent following widespread rollout, and the trials in young children (around 2,200 children) are too small to be able to detect rare side effects. Vaccination may have mild side effects in children, including fatigue resulting in absences from school. Given COVID-19 is generally mild and rarely severe, this risk of adverse events must be balanced. Within several months, millions of children in the US will have been vaccinated, which will provide much more information about safety as well as potential impact on community transmission. An option could be to wait for further real world data before making a final decision. The efficacy of vaccines against MIS-C and long COVID are still unknown, and therefore vaccines may not protect them against these conditions.

ATAGI states that the risk of myocarditis or pericarditis after mRNA COVID-19 vaccination in children aged 5-11 years is not yet known but appears to be rare based on preliminary data from US surveillance networks.[96] Paediatric cardiologists have noted that myocarditis after the vaccine is rarer and usually milder than the cardiac complications from COVID-19, including those from multisystem inflammatory syndrome (MIS-C).[113] In a US CDC report, myocarditis was reported up to 37 times more often in unvaccinated children less than 16 years old with COVID-19.[36]

Vaccination status and the potential for mandates also has inherent risk as it may be that this is a cause for exclusion (whether vaccinated or unvaccinated), and those who are unvaccinated may not be able to fully participate in some environments (even if not required by law). This is likely to inequitably impact communities who are already experiencing disadvantage and where current vaccine coverage is poor. Given parental consent is required for vaccination in this group, there may be some reluctance by some parents to vaccinate children who would like to be vaccinated. Importantly, the mode of delivery for vaccination in this age group will need to be equitable, noting that in-school models of vaccine delivery have been used in the past and been a success. This will not reach some children in this age group, and consideration will need to be given to those in isolated communities, undertaking distance learning, or home-schooled.

In terms of risks beyond individual level factors, the role of children in transmission still requires further evidence. It is possible that a national rollout in the 5-11 year old age group would not significantly reduce overall levels of infection. Most children who get COVID-19 do so from a household exposure, so high coverage in adults and older children is a good strategy for protecting children. Given that vaccinated and unvaccinated people can have similar peak viral loads during infection and transmission of the Delta variant in households occurs equally as often from vaccinated and unvaccinated individuals, [114] vaccination of this age group may have little impact on transmission in households in the context of high community transmission. However, there have been few studies that have specifically looked at the ability of children with breakthrough infections to transmit.

The WHO states that before considering implementing primary vaccination series in adolescents and children, it is important to attain high coverage of primary vaccination in highest risk subgroups, such as

older adults or peoeple with comorbidities (taking into account booster doses as needed based on evidence of waning and optimizing vaccination impact).[4] As a matter of global equity, as long as many parts of the world are facing extreme vaccine shortages, countries that have achieved high vaccine coverage in their high-risk populations should prioritise global sharing of COVID-19 vaccines through the COVAX facility before proceeding to vaccination of children and adolescents who are at low risk for severe disease.[4]

There is also the risk that rolling out the Pfizer vaccine in this age group will further negatively impact the national immunisation schedule for children, where vaccination rates for MMR, HPV and Boostrix are falling and campaigns have been impacted by COVID-19 and lockdowns. There is a danger that rolling out an additional vaccine will further derail catch-up campaigns that are currently underway through the diverting of public health resources, increasing the public health risk of outbreaks. Vaccination rates are lowest among Māori and Pacific, and therefore there are equity concerns that there will be greater risk in these populations. If unanticipated safety issues were to emerge with wider use of the Pfizer vaccine, this could also impact trust in the national immmunisation programme generally.

Benefits

The direct health benefit of vaccinating children and adolescents is lower compared with adults, due to the lower incidence of severe COVID-19 and deaths.[4] However, the risk of hospitalisation and death from COVID-19 is similar or even higher than that for other diseases for which vaccines are routinely given. In addition, if a high proportion of children are infected, even a very low rate of severe illness might translate to a high absolute number of cases.[35]

The benefits of vaccinating children in this age group are that it will help protect those who are immunocompromised, those who are very young or otherwise unable to be vaccinated, and provide protection for the vulnerable in multi-generational households. It will be very important for equity, as currently many of New Zealand's COVID-19 cases are in children and in disadvantaged communities. In high-income countries, children from deprived and ethnic minority groups are more frequently infected with SARS-CoV-2 which might be due to a greater likelihood of living with unvaccinated adults or in multigenerational and overcrowded households.[35] They may also have more severe outcomes associated with infection.[35]

While the role of children in transmission may be smaller, given the vaccine reduces the risk of infection, it will reduce the risk of children introducing COVID-19 into the home and exposing family members, who might then need to stand down from education and work.This is particularly important in households with several children. Having ongoing exposures and consecutive isolation periods may result in children having to isolate for a significant period of time.

Vaccination also brings wider benefits through the avoidance of isolation, quarantine, school closures and other indirect harms of lockdowns. School attendance is critical to the well-being and life prospects of children and to parental participation in the economy.[4] Vaccinating school-aged children may help minimise school disruptions by reducing the number of infections at school and the number of children required to miss school because of quarantine requirements.[4] In addition, some children are reliant on meals provided at schools, as food insecurity is increasingly common, particularly in low decile schools. Allowing schools to remain open will allow these programmes to continue.In an educational setting, vaccination may mean that other measures which have been challenging to implement can be reduced, such as social distancing and the wearing of masks. Vaccination will also help protect teaching staff and their whānau at home who may not be eligible to be vaccinated. From a wellbeing perspective, vaccination

will help maintain normality in the education system and keep learning in a structured classroom environment. This will help contribute to normal routines and a sense of stability for children after nearly two years of disruption, will mean a reduced need to subject children to testing which can be quite invasive, and will help make children feel more involved in the 'team of five million' messaging that has underpinned New Zealand's response to the pandemic.

Although severe or fatal COVID-19 is rare in the 5-11 age group, some children (e.g. those with certain co-morbidities) are substantially more vulnerable. These groups could be considered for accelerated access to the appropriately dosed Pfizer vaccine. In their case, the risk of harm from vaccination is estimated to be lower than the risk of harm from COVID-19. [35]

Another advantage of vaccinating children is the possibility of decreasing transmission and thus reducing severe cases in adults and the risk of new virus variants emerging.[35] If vaccinating 5- 11 year olds also reduces cases in other age groups, this might also lower the likelihood of increased restriction settings and lockdowns and minimise disruption to young people's lives.

However, it is possible that without introducing vaccines to this age group, there may be a series of rolling outbreaks in Māori and Pacific tamariki, resulting in significant impacts on their whānau and communities with isolations required for multiple children within families in succession, which could continue for an extended period of time. However, it is worth noting that isolation period length does not vary depending on vaccination status.

It is important to note the te ao Māori view of tamariki is not just as individual entities, as they have very strong links to whānau and communities and consider them inextricably interlinked. This has important implications if vaccination was to be offered to this age group. Older family members may be more likely to take up the opportunity to get vaccinated as a whānau, in settings familiar to them, such as those offered by Māori health providers or iwi/hapu-led vaccine initiatives. It is likely that the lower rates of vaccination in Māori are not due to hesitancy so much as inadequate access to the vaccine and culturally appropriate care and messaging.

In addition, whilst there may be some concerns about the effect of extending the vaccination programme to 5-11 year olds on other vaccination programmes, this operational consideration could be better seen as an opportunity to improve the system going forward, rather than a reason to recommend against vaccinating 5-11 year olds for SARS-CoV-2. There is potential for a COVID-19 vaccination roll-out in 5-11-year olds to be used to also catch children up on other childhood immunisations, assuming that coadministration of vaccines can occur.

Concerns regarding possible stigmatisation and exclusions could be addressed in other ways, and 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.

Next Steps	A memo based on this RfA and CV-TAG discussions will be written and shared with CV TAG for approval.

In the development of this work, the following parties have been consulted with:	Intelligence and Surveillance team, Science and Insights CV-TAG and invited guests, including Māori paediatricians

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

References

1. McLeod, M., et al., *COVID-19: we must not forget about Indigenous health and equity.* Australian and New Zealand Journal of Public Health, 2020. **44**(4): p. 253-256.
2. Ludvigsson, J.F., *Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults.* Acta Paediatr, 2020. **109**(6): p. 1088-1095.
3. Woodworth, K.R., et al., *The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Pfizer-BioNTech COVID-19 Vaccine in Children Aged 5–11 Years — United States, November 2021.* MMWR Morb Mortal Wkly Rep, 2021. **70**: p. 1579–1583.
4. World Health Organisation, *Interim statement on COVID-19 vaccination for children and adolescents*. 2021.
5. Sah, P., et al., *Asymptomatic SARS-CoV-2 infection: A systematic review and meta-analysis.* Proceedings of the National Academy of Sciences, 2021. **118**(34): p. e2109229118.
6. Eastin, C. and T. Eastin, *Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China: Dong Y, Mo X, Hu Y, et al. Pediatrics. 2020; doi: 10.1542/peds.2020-0702.* The Journal of Emergency Medicine, 2020. **58**(4): p. 712-713.

7. Murdoch Children's Research Institute (MCRI). *Research Brief: COVID-19 and Child and Adolescent Health*. Research Brief 2021 13 September 2021 [cited 2021 16 November]; Version 1:[Available from: https://www.mcri.edu.au/sites/default/files/media/documents/covid-19-and-child-and-adolescent-health-140921.pdf.
8. Stockholm: ECDC. *COVID-19 in children and the role of school settings in transmission - second update*. 2021 [cited 21 Oct 2021; Available from: https://www.ecdc.europa.eu/en/publications-data/children-and-school-settings-covid-19-transmission.
9. The Guardian. *Despite reports of milder symptoms Omicron should not be underestimated*. 30 November 2021; Available from: https://www.theguardian.com/world/2021/nov/30/despite-reports-of-milder-symptoms-omicron-should-not-be-understimated.
10. Centers for Disease Control and Prevention (CDC). *For Parents: Multisystem Inflammatory Syndrome in Children (MIS-C) associated with COVID-19*. Multisystem Inflammatory Syndrome 2021 20 September 2021 [cited 2021 16 November]; Available from: https://www.cdc.gov/mis/mis-c.html.
11. Godfred-Cato, S., et al., *COVID-19-Associated Multisystem Inflammatory Syndrome in Children - United States, March-July 2020.* MMWR Morb Mortal Wkly Rep, 2020. **69**(32): p. 1074-1080.
12. Payne, A.B., et al., *Incidence of Multisystem Inflammatory Syndrome in Children Among US Persons Infected With SARS-CoV-2.* JAMA Network Open, 2021. **4**(6): p. e2116420-e2116420.
13. National Institute for Health Research, *Living with COVID19*. 2020.
14. The Royal Society, *Long Covid: what is it, and what is needed?* 2020.
15. World Health Organization (WHO). *Policy Brief 39: In the wake of the pandemic - Preparing for Long COVID*. 2021; Available from: https://apps.who.int/iris/bitstream/handle/10665/339629/Policy-brief-39-1997-8073-eng.pdf.
16. WHO. *A clinical case definition of post COVID-19 condition by a Delphi consensus*. 2021 [cited 2021 16 November]; Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-Post_COVID-19_condition-Clinical_case_definition-2021.1.
17. Zimmermann, P., L.F. Pittet, and N. Curtis, *How Common is Long COVID in Children and Adolescents?* The Pediatric Infectious Disease Journal, 2021. **40**(12).
18. Radtke, T., et al., *Long-term Symptoms After SARS-CoV-2 Infection in Children and Adolescents.* JAMA, 2021. **326**(9): p. 869-871.
19. Munblit, D., L. Sigfrid, and J.O. Warner, *Setting Priorities to Address Research Gaps in Long-term COVID-19 Outcomes in Children.* JAMA Pediatrics, 2021. **175**(11): p. 1095-1096.
20. Molteni, E., et al., *Illness duration and symptom profile in symptomatic UK school-aged children tested for SARS-CoV-2.* The Lancet Child & Adolescent Health, 2021: p. 708-718.
21. Sigfrid, L., et al., *Long Covid in adults discharged from UK hospitals after Covid-19: A prospective, multicentre cohort study using the ISARIC WHO Clinical Characterisation Protocol.* medRxiv, 2021: p. 2021.03.18.21253888.
22. Say, D., et al., *Post-acute COVID-19 outcomes in children with mild and asymptomatic disease.* The Lancet Child & Adolescent Health, 2021. **5**(6): p. e22-e23.
23. Roessler, M., et al., *Post COVID-19 in children, adolescents, and adults: results of a matched cohort study including more than 150,000 individuals with COVID-19.* medRxiv, 2021: p. 2021.10.21.21265133.
24. Office for National Statistics UK, *Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK*. 2021.
25. Lewis, D. *Long COVID and kids: scientists race to find answers*. 2021.
26. Buonsenso, D., et al., *Preliminary evidence on long COVID in children.* Acta Paediatrica, 2021.
27. Jason, L.A., et al., *Predictors of Post-Infectious Chronic Fatigue Syndrome in Adolescents.* Health psychology and behavioral medicine, 2014. **2**(1): p. 41-51.
28. Katz, B.Z., et al., *Chronic fatigue syndrome after infectious mononucleosis in adolescents.* Pediatrics, 2009. **124**(1): p. 189-93.

29. Tsankov, B.K., et al., *Severe COVID-19 Infection and Pediatric Comorbidities: A Systematic Review and Meta-Analysis.* Int J Infect Dis, 2021. **103**: p. 246-256.
30. Ng, W.H., et al., *Comorbidities in SARS-CoV-2 Patients: a Systematic Review and Meta-Analysis.* mBio, 2021. **12**(1).
31. Mukkada, S., et al., *Global characteristics and outcomes of SARS-CoV-2 infection in children and adolescents with cancer (GRCCC): a cohort study.* Lancet Oncol, 2021. **22**(10): p. 1416-1426.
32. Shi, Q., et al., *Risk factors for poor prognosis in children and adolescents with COVID-19: A systematic review and meta-analysis.* EClinicalMedicine, 2021. **41**.
33. Shi, T., et al., *Risk of COVID-19 hospital admission among children aged 5–17 years with asthma in Scotland: a national incident cohort study.* The Lancet Respiratory Medicine, 2021.
34. Schober, T., et al., *Risk factors for severe PCR-positive SARS-CoV-2 infection in hospitalized children: a multicenter cohort study.* medRxiv, 2021: p. 2021.10.28.21265616.
35. Zimmermann, P., et al., *Should children be vaccinated against COVID-19?* Archives of Disease in Childhood, 2021: p. archdischild-2021-323040.
36. European Centre for Disease Prevention and Control, *Interim public health considerations for COVID-19 vaccination of children aged 5-11 years, 1 December 2021*. 2021, ECDC: Stockholm.
37. Health, A.I.o. and Welfare, *COVID-19 and the impact on young people*. 2021, AIHW: Canberra.
38. Brown, N., Te Riele, K., Shelley, B. & Woodroffe, J., *Learning at home during COVID-19: Effects on vulnerable young Australians. Independent Rapid Response Report.*, P.U.C.f.E. Attainment., Editor. 2020, University of Tasmania: Hobart.
39. Roubinov, D., N.R. Bush, and W.T. Boyce, *How a Pandemic Could Advance the Science of Early Adversity.* JAMA Pediatrics, 2020. **174**(12): p. 1131-1132.
40. Duncanson, M., et al., *Delayed access to care and late presentations in children during the COVID-19 pandemic New Zealand-wide lockdown: A New Zealand Paediatric Surveillance Unit study.* Journal of Paediatrics and Child Health, 2021. **57**(10): p. 1600-1604.
41. Chanchlani, N., F. Buchanan, and P.J. Gill, *Addressing the indirect effects of COVID-19 on the health of children and young people.* CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne, 2020. **192**(32): p. E921-E927.
42. Yoshikawa, H., et al., *Effects of the Global Coronavirus Disease-2019 Pandemic on Early Childhood Development: Short- and Long-Term Risks and Mitigating Program and Policy Actions.* The Journal of pediatrics, 2020. **223**: p. 188-193.
43. Hillis, S.D., et al., *Global minimum estimates of children affected by COVID-19-associated orphanhood and deaths of caregivers: a modelling study.* The Lancet, 2021. **398**(10298): p. 391-402.
44. Hillis, S.D., et al., *COVID-19-Associated Orphanhood and Caregiver Death in the United States.* Pediatrics, 2021.
45. NSW Health. *EPIDEMIOLOGICAL WEEK 45 ENDING 13 NOVEMBER 2021*. COVID-19 WEEKLY SURVEILLANCE IN NSW 2021 [cited 2021 2 December]; Available from: https://www.health.nsw.gov.au/Infectious/covid-19/Documents/covid-19-surveillance-report-20211113.pdf.
46. Ministry of Health. *New Zealand Health Survey Regional Results 2017-2020*. 2021; Available from: https://www.health.govt.nz/nz-health-statistics/national-collections-and-surveys/surveys/new-zealand-health-survey#published.
47. Ministry of Health. *New Zealand Health Survey 2020/2021*. New Zealand Health Survey 2021; Available from: https://minhealthnz.shinyapps.io/nz-health-survey-2020-21-annual-data-explorer/_w_7966b0d8/#!/home.
48. EHINZ. *Asthma hospitalisations (0-14 years)*. 2020; Available from: https://www.ehinz.ac.nz/assets/Factsheets/Released_2020/Asthma-hospitalisations-014-years-20012018-Published-May-2020-v6.pdf.
49. Education Counts. *School Rolls*. 2021; Available from: https://www.educationcounts.govt.nz/statistics/6028.

50. Murray, S. *The state of wellbeing and equality for disabled people, their families, and whānau*. 2019.
51. Stats NZ Tatauranga Aotearoa. *Child poverty statistics: Year ended June 2020*. 2021; Available from: https://www.stats.govt.nz/information-releases/child-poverty-statistics-year-ended-june-2020.
52. Steyn, N., Binny, R. N., Hannah, K., Hendy, S. C., James, A., Lustig, A., Ridings, K., Plank, M. J., Sporle, A., *Māori and Pacific people in New Zealand have a higher risk of hospitalisation for COVID-19.* New Zealand Medical Journal, 2021. **134**(1538).
53. Stats NZ Tatauranga Aotearoa, *Infoshare: Connecting you to a wealth of information*. 2018: http://infoshare.stats.govt.nz/.
54. Johnson, A., P. Howden-Chapman, and S. Eaqub, *A stocktake of New Zealand's housing: February 2018*. 2018: Ministry of Business, Innovation and Employment (New Zealand).
55. Allen & Clark, *Improving New Zealand's childhood immunisation rates: Evidence review*. 2019: Wellington.
56. RNZ. *Concern over Covid-19 vaccine for children: 'Protective instinct kicks in'*. 2021 9 December 2021; Available from: https://www.rnz.co.nz/news/national/457592/concern-over-covid-19-vaccine-for-children-protective-instinct-kicks-in.
57. Zhu, Y., et al., *A meta-analysis on the role of children in SARS-CoV-2 in household transmission clusters*. 2020, medRxiv.
58. Viner, R.M., et al., *Susceptibility to SARS-CoV-2 Infection Among Children and Adolescents Compared With Adults: A Systematic Review and Meta-analysis.* JAMA Pediatrics, 2021. **175**(2): p. 143-156.
59. Malmgren, J., B. Guo, and H.G. Kaplan *Continued proportional age shift of confirmed positive COVID-19 incidence over time to children and young adults: Washington State March—August 2020*. Plos one, 2021. **16**, e0243042.
60. Carethers, J.M., *Insights into disparities observed with COVID-19.* Journal of Internal Medicine, 2021. **289**(4): p. 463-473.
61. American Academy of Pediatrics and the Children's Hospital Association, *Children and COVID-19: State Data Report 2/9/2021*. 2021.
62. European Centre for Disease Prevention and Control. *Questions and answers on COVID-19: Children aged 1 – 18 years and the role of school settings*. 2021 8 September 2021; Available from: https://www.ecdc.europa.eu/en/covid-19/questions-answers/questions-answers-school-transmission.
63. Falk A, B.A., Falk P, Steffen S, Wallace Z, Høeg TB. , *COVID-19 Cases and Transmission in 17 K–12 Schools — Wood County, Wisconsin, August 31–November 29, 2020.* MMWR Morb Mortal Wkly Rep, 2021. **70**: p. 136–140.
64. Ismail, S.A., et al., *SARS-CoV-2 infection and transmission in educational settings: a prospective, cross-sectional analysis of infection clusters and outbreaks in England.* The Lancet Infectious Diseases, 2021. **21**(3): p. 344-353.
65. Centres for Disease Control and Prevention, *Transmission of SARS-CoV-2 in K-12 schools*. 2021.
66. Ismail, S.A.a.S., Vanessa and Bernal, Jamie Lopez and Ramsay, Mary E. and Ladhani, Shamez,, *SARS-CoV-2 Infection and Transmission in Educational Settings: Cross-Sectional Analysis of Clusters and Outbreaks in England.* 2020.
67. National Centre for Immunisation Research and Surveillance. *COVID-19 in schools and early childhood education and care services – the experience in NSW: 16 June to 31 July 2021*. 2021 8 September 2021; Available from: https://ncirs.org.au/sites/default/files/2021-09/NCIRS%20NSW%20Schools%20COVID_Summary_8%20September%2021_Final.pdf.
68. Curmei, M., et al., *Estimating Household Transmission of SARS-CoV-2*. 2020, medRxiv.
69. Fung, H.F., et al., *The household secondary attack rate of SARS-CoV-2: A rapid review.* Clinical infectious diseases : an official publication of the Infectious Diseases Society of America, 2020.
70. Lei, H., et al., *Household transmission of COVID-19-a systematic review and meta-analysis.* The Journal of infection, 2020. **81**(6): p. 979-997.

71. Shah, K., N. Desai, and D. Mavalankar, *Secondary Attack Rate (SAR) in household contacts of expired primary cases of COVID-19: A study from Western India*. 2020, medRxiv.
72. Adamik, B., et al., *Estimation of the Severeness Rate, Death Rate, Household Attack Rate and the Total Number of COVID-19 Cases Based on 16115 Polish Surveillance Records*. 2020, SSRN.
73. Bi, Q., et al., *Household Transmission of SARS-CoV-2: Insights from a Population-based Serological Survey*. 2020, medRxiv.
74. Dattner, I., et al., *The role of children in the spread of COVID-19: Using household data from Bnei Brak, Israel, to estimate the relative susceptibility and infectivity of children.* PLOS Computational Biology, 2021. **17**(2): p. e1008559.
75. Goldstein, E., M. Lipsitch, and M. Cevik, *On the Effect of Age on the Transmission of SARS-CoV-2 in Households, Schools, and the Community.* The Journal of infectious diseases, 2021. **223**(3): p. 362-369.
76. Li, W., et al., *Characteristics of Household Transmission of COVID-19.* Clinical infectious diseases : an official publication of the Infectious Diseases Society of America, 2020. **71**(8): p. 1943-1946.
77. Ludvigsson, J.F., *Children are unlikely to be the main drivers of the COVID-19 pandemic - A systematic review.* Acta paediatrica (Oslo, Norway : 1992), 2020. **109**(8): p. 1525-1530.
78. Li, F., et al., *Household transmission of SARS-CoV-2 and risk factors for susceptibility and infectivity in Wuhan: a retrospective observational study.* The Lancet. Infectious diseases, 2021. **21**(5): p. 617-628.
79. Paul, L., et al., *Pediatric household transmission of SARS-CoV-2 infection*. 2021, medRxiv.
80. Chadeau-Hyam, M., et al., *REACT-1 round 15 interim report: High and rising prevalence of SARS-CoV-2 infection in England from end of September 2021 followed by a fall in late October 2021.* medRxiv, 2021: p. 2021.11.03.21265877.
81. OzSAGE. *Protecting children from COVID-19 and making schools and childcare safer*. 2021 [cited 2021 18 November]; Available from: https://ozsage.org/media_releases/protecting-children-from-covid-19-and-making-schools-and-childcare-safer/.
82. Jehn, M., et al., *Association Between K–12 School Mask Policies and School-Associated COVID-19 Outbreaks — Maricopa and Pima Counties, Arizona, July–August 2021.* AMMWR Morb Mortal Wkly Rep 2021, 2021. **70**: p. 1372–1373.
83. Budzyn SE, P.M., Parks SE, et al. , *Pediatric COVID-19 Cases in Counties With and Without School Mask Requirements — United States, July 1–September 4, 2021.* MMWR Morb Mortal Wkly Rep 2021, 2021. **70**: p. 1377–1378.
84. Talic, S., et al., *Effectiveness of public health measures in reducing the incidence of covid-19, SARS-CoV-2 transmission, and covid-19 mortality: systematic review and meta-analysis.* BMJ, 2021. **375**: p. e068302.
85. Iwata, K., A. Doi, and C. Miyakoshi, *Was school closure effective in mitigating coronavirus disease 2019 (COVID-19)? Time series analysis using Bayesian inference.* International Journal of Infectious Diseases, 2020. **99**: p. 57-61.
86. Auger, K.A., et al., *Association between statewide school closure and COVID-19 incidence and mortality in the US.* Jama, 2020. **324**(9): p. 859-870.
87. *COVID-19 Genomics UK Consortium (COG-UK)*. [cited 2021 31 March]; Available from: https://www.cogconsortium.uk/.
88. Rothamer, D.A., et al., *Strategies to minimize SARS-CoV-2 transmission in classroom settings: combined impacts of ventilation and mask effective filtration efficiency.* Science and Technology for the Built Environment, 2021. **27**(9): p. 1181-1203.
89. van den Berg, P., et al., *Effectiveness of 3 Versus 6 ft of Physical Distancing for Controlling Spread of Coronavirus Disease 2019 Among Primary and Secondary Students and Staff: A Retrospective, Statewide Cohort Study.* Clin Infect Dis, 2021. **73**(10): p. 1871-1878.
90. McGee, R.S., et al., *Model-driven mitigation measures for reopening schools during the COVID-19 pandemic.* Proceedings of the National Academy of Sciences, 2021. **118**(39): p. e2108909118.

91. Jones, E., et al., *Healthy Schools: Risk Reduction Strategies for Reopening Schools*. 2020, Harvard T.H. Chan School of Public Health.
92. Walter, E.B., et al., *Evaluation of the BNT162b2 Covid-19 Vaccine in Children 5 to 11 Years of Age.* New England Journal of Medicine, 2021.
93. *PFIZER AND BIONTECH ANNOUNCE POSITIVE TOPLINE RESULTS FROM PIVOTAL TRIAL OF COVID-19 VACCINE IN CHILDREN 5 TO 11 YEARS*. 20th September 2021; Available from: https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-announce-positive-topline-results.
94. Polack, F.P., et al., *Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine.* New England Journal of Medicine, 2020. **383**(27): p. 2603-2615.
95. Frenck, R.W., et al., *Safety, Immunogenicity, and Efficacy of the BNT162b2 Covid-19 Vaccine in Adolescents.* New England Journal of Medicine, 2021.
96. Australian Technical Advisory Group on Immunisation (ATAGI), *ATAGI recommendations on Pfizer COVID-19 vaccine use in children aged 5 to 11 years*. 2021.
97. Advisory Committee on Immunization Practices (ACIP), *ACIP Evidence to Recommendations for Use of Pfizer-BioNTech COVID-19 Vaccine under an Emergency Use Authorization*. 2021.
98. US Food and Drug Administration (FDA). *FDA Authorizes Pfizer-BioNTech COVID-19 Vaccine for Emergency Use in Children 5 through 11 Years of Age*. 2021; Available from: https://www.fda.gov/news-events/press-announcements/fda-authorizes-pfizer-biontech-covid-19-vaccine-emergency-use-children-5-through-11-years-age.
99. Centers for Disease Control and Prevention (CDC). *CDC Recommends Pediatric COVID-19 Vaccine for Children 5 to 11 Years*. 2021; Available from: https://www.cdc.gov/media/releases/2021/s1102-PediatricCOVID-19Vaccine.html.
100. Washington Post. *2.6 million children under 12 have received their first vaccine dose, White House says*. 2021; Available from: https://www.washingtonpost.com/nation/2021/11/18/covid-delta-variant-live-updates/.
101. Centres for Disease Control and Prevention. *COVID-19 Vaccination Demographics in the United States, National, 12 December 2021*. 2021 12 December 2021 [cited 2021 12 December]; Available from: https://data.cdc.gov/Vaccinations/COVID-19-Vaccination-Demographics-in-the-United-St/km4m-vcsb.
102. Department of Health. *TGA provisionally approves Pfizer COVID-19 vaccine for 5 to 11-year-olds*. 2021 5 December 2021; Available from: https://www.health.gov.au/ministers/the-hon-greg-hunt-mp/media/tga-provisionally-approves-pfizer-covid-19-vaccine-for-5-to-11-year-olds.
103. Government of Canada. *Vaccines for children: COVID-19*. 2021 3 December 2021 [cited 2021 12 December]; Available from: https://www.canada.ca/en/public-health/services/vaccination-children/covid-19.html.
104. Amirthalingam, G., et al., *Higher serological responses and increased vaccine effectiveness demonstrate the value of extended vaccine schedules in combatting COVID-19 in England.* medRxiv, 2021: p. 2021.07.26.21261140.
105. Skowronski, D.M., et al., *Two-dose SARS-CoV-2 vaccine effectiveness with mixed schedules and extended dosing intervals: test-negative design studies from British Columbia and Quebec, Canada.* medRxiv, 2021: p. 2021.10.26.21265397.
106. Flaxman, A., et al., *Tolerability and Immunogenicity After a Late Second Dose or a Third Dose of ChAdOx1 nCoV-19 (AZD1222).* SSRN Electronic Journal, 2021.
107. Buchan, S., et al., *Epidemiology of myocarditis and pericarditis following mRNA vaccines in Ontario, Canada: by vaccine product, schedule and interval*. 2021, medRxiv.
108. The Immunisation Advisory Centre (IMAC). *Immunisation Handbook 2020: 4. Immunisation of special groups*. 2020 [cited 2021 8 September]; Available from: https://www.health.govt.nz/our-work/immunisation-handbook-2020/4-immunisation-special-groups.
109. Centers for Disease Control and Prevention (CDC). *Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Authorized in the United States: Coadministration with other vaccines*. 16 July

2021 [cited 2021 27 July]; Available from: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#Coadministration.

110. American Medical Association. *What to know about coadministration of flu and COVID-19 vaccines*. 2021; Available from: https://www.ama-assn.org/delivering-care/public-health/what-know-about-coadministration-flu-and-covid-19-vaccines.
111. Pfizer. *Pfizer and BioNTech confirm high efficacy and no serious safety concerns through up to six months following second dose in updated topline analysis of landmark COVID-19 vaccine study*. 2021; Available from: https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-confirm-high-efficacy-and-no-serious.
112. Jones, J. *Epidemiology of COVID-19 in Children Aged 5 – 11 years, ACIP Meeting, November 2, 2021*. 2021; Available from: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-11-2-3/03-COVID-Jefferson-508.pdf.
113. Haelle, T. *The real risk of heart inflammation to kids is from COVID-19—not the vaccine*. 2021.
114. Singanayagam, A., et al., *Community Transmission and Viral Load Kinetics of SARS-CoV-2 Delta (B.1.617.2)Variant in Vaccinated and Unvaccinated Individuals.* SSRN Electronic Journal, 2021.