

# 5 Coronavirus disease (COVID-19)

## Key information

Mode of transmission	Aerosolised droplets.
Incubation period	Most commonly 2–5 days (range 1–14 days).
Period of communicability	From 1–2 days before, and typically transmissibility peaks 5 days after symptom onset. Asymptomatic spread is documented.
Incidence and burden of disease	Global pandemic ongoing. The burden of disease predominantly lies with older adults, those with comorbidities and health care workers exposed to patients with high viral loads. Children generally experience milder disease.
Funded vaccines	mRNA-CV: Comirnaty (manufacturer Pfizer/BioNTech). ChAd-CV: COVID-19 vaccine AstraZeneca (manufacturer AstraZeneca) Adjuvanted rCV: Nuvaxovid (manufacturer Novavax).
Dose, presentation, route (see sections 5.4.4 and 5.4.5)	<b>mRNA CV: Comirnaty</b> <u>mRNA-CV (30 µg)</u> <ul style="list-style-type: none"><li>• purple cap</li><li>• 0.3 mL dose</li><li>• multi-dose vial, to be diluted before use</li><li>• intramuscular injection</li><li>• Storage once thawed:<ul style="list-style-type: none"><li>– undiluted, +2° to 8°C expiry 1 month (31 days)</li><li>– diluted (in vial or drawn up), +2° to 30°C expiry 6 hours</li></ul></li></ul> <u>mRNA-CV (10 µg)</u> <ul style="list-style-type: none"><li>• orange cap</li><li>• 0.2 mL dose</li><li>• Multi-dose vial, to be diluted before use</li><li>• Intramuscular injection</li><li>• Storage once thawed:<ul style="list-style-type: none"><li>– undiluted, +2° to 8°C expiry 10 weeks</li><li>– diluted, in vial +2° to 8°C expiry 12 hours or drawn up +2° to 30°C expiry 6 hours</li></ul></li></ul>

Dose, presentation, route (continued)	<p><b>ChAd-CV: COVID-19 Vaccine AstraZeneca</b></p> <ul style="list-style-type: none"> <li>• 0.5 mL dose</li> <li>• Red cap</li> <li>• multi-dose vial, no dilution required</li> <li>• intramuscular injection</li> <li>• storage: +2° to 8°C (up to 6 months) <ul style="list-style-type: none"> <li>– expiry after 48 hours once cap has been removed at +2° to 8°C use drawn up vaccine within 5 hours (and before expiry)</li> </ul> </li> </ul> <p><b>Adjuvanted rCV: Nuvaxovid</b></p> <ul style="list-style-type: none"> <li>• 0.5 mL dose</li> <li>• Blue cap</li> <li>• multi-dose vial, no dilution required</li> <li>• intramuscular injection</li> <li>• storage: +2° to 8°C (up to 6 months) <ul style="list-style-type: none"> <li>– Use opened vial within 6 hours of first use, store at +2° to 8°C</li> <li>– drawn up vaccine within 6 hours (and before expiry)</li> </ul> </li> </ul>
Funded vaccine indications and schedule (see section 5.4.5)	<p><u>mRNA-CV (30 µg)</u></p> <ul style="list-style-type: none"> <li>• Two doses, given at least 21 days apart</li> <li>• For use from age 12 years</li> <li>• A third primary dose given at least 8 weeks after first two doses for those with severe immunocompromise from age 12 years</li> <li>• A booster dose given at least 3 calendar months to those aged 18 years or at least 6 months to those aged 16–17 years after completion of primary course</li> </ul> <p><u>mRNA-CV (10 µg)</u></p> <ul style="list-style-type: none"> <li>• Two doses given at least 21 days apart, recommended at least 8 weeks apart</li> <li>• For use in children aged 5 to 11 years, inclusively</li> <li>• A third primary dose given at least 8 weeks after first two doses for those with severe immunocompromise from age 5 years</li> </ul>
Other funded vaccine indication and schedule	<p>Two doses of ChAd-CV, given from 4 to 12 weeks apart for use from age 18 years.</p> <p>Two doses of adjuvanted rCV, given at least 21 days apart for use from age 18 years</p> <p>These vaccines can be used for a two-dose primary course without prescription. If these vaccines are used as second dose or booster after mRNA-CV, a prescription is required.</p>
Contraindications (see section 5.6.1)	<p>mRNA-CV, ChAd-CV and rCV: A history of anaphylaxis to any component or previous dose.</p> <p>ChAd-CV: A history of capillary leak syndrome, thrombosis with thrombocytopenia to previous dose.</p>
Precautions (see section 5.6.2)	<p>mRNA-CV, ChAd-CV and rCV: A definite history of anaphylaxis to any other product is a precaution not contraindication.</p> <p>mRNA-CV: Defer further doses if individual develops myocarditis/pericarditis after first or second dose of mRNA-CV.</p> <p>ChAd-CV is not recommended for use during pregnancy. A history of thrombosis, certain prothrombotic autoimmune diseases, thrombocytopenia is a precaution.</p>

Potential responses to vaccine (see section 5.7.1)	mRNA and ChAd-CV: Generally mild or moderate: injection site pain, headache, fever, muscle aches, dizziness and nausea, a day or two after vaccination. For mRNA-CV, these responses are more commonly reported after second dose and in younger adults (<55 years). For ChAd-CV, responses are more commonly reported after first dose.
Vaccine effectiveness (see section 5.4.3)	<p>mRNA-CV (30 µg): Clinical trial data showed efficacy against confirmed symptomatic COVID-19 of 90–98% after two doses. Effectiveness is maintained against severe disease caused by SARS-CoV-2 Delta variant.</p> <p>mRNA-CV (10 µg): Clinical trial data showed efficacy against confirmed, symptomatic COVID-19 of 68–98% after two doses in children aged 5-11 years.</p> <p>ChAd-CV: Pooled data from four clinical trials gave overall efficacy against symptomatic COVID-19 of 41-75.7% after doses. Effectiveness of 61-72% against symptomatic disease and of 75-97% against hospitalisation with Delta variant.</p> <p>Effectiveness of both vaccines shows waning, particularly against mild disease and for elderly, from several weeks after the primary course.</p> <p>rCV: clinical trial data gave efficacy of 80–95% against symptomatic COVID-19.</p>
Public health measures	Ongoing rapid contact tracing and testing for all suspected cases and their close contacts. Quarantine and isolation of household contacts and cases. Control measures differ according to vaccination status.

## 5.1 Virology

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a member of the Coronaviridae family and the *Betacoronavirus* genus. This enveloped, positive-strand RNA virus encodes four major structural proteins – spike (S), membrane (M), envelope (E) and a helical nucleocapsid (N). To enter host cells, the spike protein, which forms the characteristic crown-like (Latin: *corona*) surface structures, binds to the angiotensin-converting enzyme-2 (ACE2) receptor most frequently found on human respiratory tract epithelium.<sup>1, 2</sup>

The precise origin of this virus is unknown. First identified in humans in Wuhan, China, this virus shares a strong genetic sequence similarity to bat coronaviruses found in China,<sup>3</sup> and is a suspected zoonosis from bats via an intermediary animal, such as a pangolin.<sup>4</sup> As with most RNA viruses, mutations occur and variant strains of SARS-CoV-2 have been identified.

## 5.2 Clinical features

Coronavirus disease 2019 (COVID-19) is caused by the SARS-CoV-2 virus, which infects the respiratory tract and is transmitted human to human primarily through respiratory droplets and aerosols. Documented transmission has also occurred through direct contact and rarely fomites (objects or materials that can carry infection).

The reproduction number ( $R_0$ ) (see section 1.2.1) was initially estimated to be around 2–3.<sup>5, 6</sup> Transmissibility varies by setting, and recently identified variant strains of SARS-CoV-2 have been well beyond the initial estimated  $R_0$  values.<sup>7, 8</sup> The formerly dominant Delta (B.1.617.2) variant was twice as transmissible as the ancestral strain ( $R_0$  5–6).<sup>9</sup> The rapidly spreading Omicron variant (B.1.1.529) has an even higher  $R_0$  value.<sup>10</sup>

The symptoms of COVID-19 range widely from asymptomatic or a mild respiratory tract infection to severe and pneumonia, which can lead to severe inflammatory disease and respiratory failure. The most common symptoms of COVID-19 are like those of other common respiratory illnesses and include a new or worsening dry cough, sneezing and rhinorrhoea or nasal congestion, fever, sore throat and shortness of breath. Unlike other respiratory viral infections, COVID-19 was frequently associated with a temporary loss of smell or altered sense of taste, and sometimes this is the only symptom; this symptom is less common with Omicron variant infections than reported with Delta.<sup>11</sup> Some cases have reported gastrointestinal symptoms including nausea, diarrhoea, vomiting and abdominal pain, headache, muscle aches, malaise, chest pain, joint pain, and confusion or irritability; these symptoms almost always occur with one or more of the common symptoms. For around 80 percent of cases, COVID-19 is a mild disease, but some develop more severe disease, particularly older adults, pregnant women and those with comorbidities, which can progress to multi-organ and respiratory failure. As for influenza and other respiratory viruses, many of those with laboratory-confirmed infection remain asymptomatic.

In the early stages, it is difficult to distinguish COVID-19 from other common viral infections and, as of early 2022, the most reliable diagnostic test has been detection of viral mRNA from a nasopharyngeal swab, using PCR assay. Further methods of testing (such as saliva sampling and rapid antigen/lateral flow tests) are being increasingly used. SARS-CoV-2 serology can help distinguish historic disease from mild current symptoms but is not in routine use.

The incubation period is typically around two to five days (up to 14 days). Individuals may be infectious from up to two days before becoming symptomatic, with infectiousness typically peaking within five days of symptom onset.<sup>12</sup> High viral loads are detected in the nose at time of symptom onset.<sup>13</sup> Viable virus is not usually detectable for more than ten days after symptom onset, although SARS-CoV-2 mRNA has been detected for up to 83 days in respiratory and stool samples.<sup>12, 14</sup> Unlike previous coronavirus outbreaks (SARS and MERS), transmission of SARS-CoV-2 can also occur before the onset of symptoms or from asymptomatic individuals.<sup>15</sup> Viral loads and infectiousness are highest immediately after symptom onset, and most transmission occurs in household settings.<sup>16, 17</sup>

It is currently unclear what protection previous infection with SARS-CoV-2 provides. A study in the UK in health care workers found protection against symptomatic COVID-19 to be similar to that reported for mRNA COVID-19 vaccine.<sup>18</sup> A previous history of SARS-CoV-2 infection was associated with an 83 percent lower risk of infection, with a median time to re-infection of over five months.<sup>19</sup> Only about one third of the reinfections in health care workers presented as typical COVID-19 symptoms, as compared with 78 percent of new infections.<sup>18</sup> Neutralising antibodies have been detected and remained relatively stable between eight to 11 months after primary infection, even without natural boosting as in New Zealand.<sup>20, 21</sup>

## 5.2.1 Children and young adults

Initially, the rate of SARS-CoV-2 symptomatic infection in children appeared to be lower than in adults,<sup>22, 23, 24</sup> but since adults are increasingly being vaccinated, the proportion of cases in children being detected has increased and severe outcomes are emerging.<sup>25</sup> Commonly, children have mild or no symptoms of COVID-19 with a short duration of illness; symptoms typically include headache, fever, cough, and may include sore throat, nasal congestion, sneezing, muscle aches and fatigue.<sup>26</sup> Around one in five children with symptomatic COVID-19 present with gastrointestinal symptoms, such as nausea, vomiting, abdominal pain and diarrhoea. A systematic review found that diarrhoea was significantly associated with a severe clinical course (odd ratio 3.97; 95% CI 1.80-8.73).<sup>26</sup>

The incidence of severe or fatal disease in children is significantly lower than in adults.<sup>27</sup> Children at risk of more severe disease include those living with pre-existing health conditions and socioeconomic barriers to accessing health care. These risk factors are prevalent in New Zealand children, particularly children of Māori and Pacific ethnicity.<sup>28, 29</sup> Pre-existing conditions associated with higher risk from COVID-19 in children include obesity, diabetes, asthma, cardiac and pulmonary diseases, immune disorders, metabolic disease, cancer, neurological, neurodevelopmental (in particular, Down syndrome [trisomy 21]) and neuromuscular conditions.<sup>30, 31</sup> A systematic review found children with comorbidities were 25 times more likely to have severe COVID-19 than those without (5.1 percent vs 0.2 percent) and have a 2.8 times higher relative risk of death.<sup>31</sup> Children who develop pulmonary complications (eg, pneumonia) have a similar progression of disease as seen in adults, requiring oxygenation in hospital and in some cases corticosteroids treatments.<sup>32</sup> In the US, as of 24 February 2022, over 12.6 million cases of COVID-19 have been reported in children aged under 18 years (19 percent of all reported cases), and among reporting states, 0.1–1.5 percent of cases in children resulted in hospitalisation and mortality was zero to 0.01 percent of all child cases.<sup>25</sup>

## 5.2.2 Transmission

The role children play in transmitting SARS-CoV-2 is still unclear and is changing as new variants evolve and older populations are increasingly vaccinated. Transmission within educational settings is limited and is influenced by broader transmission in the community.<sup>33, 34</sup> Although children are susceptible to infection, transmission is more likely to occur between adults and from adults to children; the risk of child to child or child to adult transmission is considerably less.<sup>33, 34, 35</sup> The risk of transmission within education settings is highest for children aged 10–19 years.<sup>36</sup> Non-pharmaceutical interventions (masks, ventilation, spatial and temporal distancing, 'stay at home' policies and hygiene) can help to protect children from infection in schools.<sup>27</sup>

Transmission in households is common, particularly with the more infectious variants Delta and Omicron.<sup>10</sup> The potential for households to be a significant source of transmission likely reflects the self-isolation of confirmed or suspected COVID-19 cases at home.<sup>37, 38</sup> In England, children were at a lower risk of transmission or being the

index case within households,<sup>39, 40</sup> but unpublished data found that households with at least one child had higher prevalence of COVID-19 than those without children (3.0 percent vs 0.75 percent).<sup>41</sup>

### 5.2.3 Risk groups

Risk factors for severe disease include older age, male, smoking,<sup>42</sup> obesity and chronic medical conditions, including diabetes,<sup>43</sup> cancer, chronic respiratory disease, cardiovascular disease, chronic kidney disease, hypertension and being immunocompromised.<sup>44</sup> Increased incidence is well documented in some ethnic groups but seems primarily related to prevalence of the risk factors listed above. Increasing age is the most important risk factor for severe disease, due to declining immune function and high prevalence of comorbidities. The highest rates of mortality are in the oldest age groups, especially those aged over 80 years (at a rate 20-fold higher than for those aged 50–59 years in the United Kingdom).<sup>44</sup>

#### Health care workers

Patient-facing health care workers caring for patients with COVID-19 are likely to be exposed to higher viral loads, placing them and their household members at greater risk of developing COVID-19 than the general population.<sup>45</sup> In Scotland, one-sixth of the COVID-19 cases admitted to hospital were health care workers and their household members.<sup>45</sup> Health care workers have also been implicated in the spread of SARS-CoV-2 within health and long-term care facilities.<sup>45, 46, 47</sup> However, the use of personal protective equipment (PPE) and other measures aimed at reducing nosocomial viral transmission have been shown to be effective, such that, where COVID-19 is prevalent in the community, health care workers are more likely to catch COVID-19 from an infected household member.<sup>17</sup>

#### Pregnancy

Although pregnant women are not at increased risk of SARS-CoV-2 infection, they are at increased risk of severe disease and death compared with age-matched non-pregnant women.<sup>48, 49, 50, 51</sup> While the absolute risk of severe outcomes among pregnant women is low compared with absolute risk due to advanced age, the risk of hospital admissions is three times higher and the rate of ICU care for COVID-19 has been found to be five times higher (relative risk 5.04; 95% CI 3.13–8.10) for pregnant women than for non-pregnant women.<sup>50</sup> Obesity, hypertension, asthma, autoimmune disease, diabetes and older age are also associated with severe COVID-19 in pregnant women.<sup>52</sup>

Infants of mothers with COVID-19 are at increased risk of preterm birth, particularly due to early delivery, and neonatal ICU admission.<sup>49, 52</sup> Early studies do not suggest intrauterine transmission, but transmission during birth has been shown in around 3 percent of neonates.<sup>53</sup> Most neonatal infections are asymptomatic or mild, but around 12 percent experience severe disease with dyspnoea and fever as the most commonly reported signs.<sup>54</sup>

## 5.2.4 Post-infection complications

Post-acute COVID-19 sequelae or commonly called 'long COVID' is characterised by persistent symptoms lasting for more than three months and appears to affect around 10 percent of those infected, particularly those with at least five symptoms in the first week of illness.<sup>55, 56, 57</sup> Post-acute manifestations include cardiovascular, pulmonary and neurological effects, including chronic fatigue, dyspnoea, specific organ dysfunction and depression.<sup>58</sup>

Long COVID-19 is not well described in children but appears to be less common, particularly under the age of 12 years, than in adults.<sup>32, 59, 60, 61</sup> Similar symptoms are seen in children following other viral infections and some symptoms could be related to social restrictions during lockdowns.

## Paediatric multisystem inflammatory syndrome

Paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 (PIMS-TS or MIS-C) is a rare, delayed complication of COVID-19 following largely asymptomatic SARS-CoV-2 infection in children and adolescents.<sup>62, 63</sup> PIMS-TS can occur approximately one month after symptomatic or asymptomatic SARS-CoV-2 infection affecting different parts of the body and usually presents as a fever, rash and abdominal pain, although in more severe cases, myocarditis and low blood pressure can occur.<sup>64</sup> Early diagnosis and appropriate treatment improve outcomes. Data from the US has shown that the risk PIMS-TS is highest in marginalised and ethnic minority groups.<sup>65</sup>

## 5.2.5 SARS-CoV-2 variants

As with all viruses, new variants have evolved. Most recently, certain variants have been shown to bind the ACE2 receptor more readily, making the variants more transmissible. It is unclear whether these variants result in more cases of severe disease, but irrespectively, the greater numbers of people becoming infected is increasing the burden of the disease.<sup>7, 8</sup> There is evidence that recent variants, Delta and Omicron, are more infectious than the former strains.<sup>9, 66</sup> WHO has classified genetic variants in to three classes:<sup>67</sup>

- Variants of interest – genetic changes that are predicted or known to affect transmission, diagnostic, therapeutic or immune escape (for example, reduced antibody neutralisation) and identified to cause significant community transmission or COVID-19 clusters, in multiple countries with increasing prevalence or other epidemiological impacts, suggesting emerging risk to global public health
- Variants of concern – meet variant of interest definition with evidence of increased transmissibility or detrimental change in COVID-19 epidemiology, change in clinical disease or virulence, reduced vaccine or treatment efficacy or diagnostic detection failures.
- Variants under monitoring – genetic changes that are suspected to affect SARS-CoV-2 characteristics with indication of potential risk, but evidence of impact unclear.

## 5.3 Epidemiology

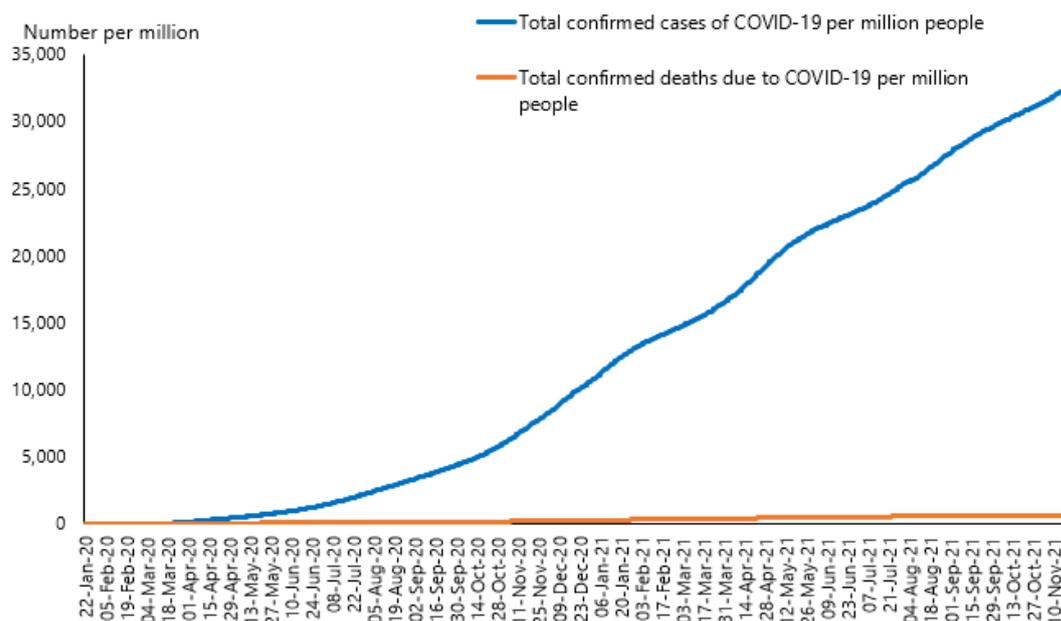
### 5.3.1 Global burden of disease

Clusters of distinctive pneumonia cases were observed in Wuhan, China during December 2019. The cause was identified in January 2020 as a novel coronavirus that had genetic and clinical similarity to the coronavirus causing the severe acute respiratory syndrome (SARS) epidemic from 2002 to 2004. Consequently, the novel coronavirus was named SARS-CoV-2 and the associated disease named Coronavirus Disease 2019 (COVID-19). Due to the rapid spread, a public health emergency of international concern (PHEIC) was announced in late January 2020. By the time the COVID-19 pandemic was declared by the World Health Organization (WHO) on 11 March 2020, there were 118,000 reported COVID-19 cases and 4,291 associated deaths in 114 countries. The global death toll surpassed one million by late September 2020.

As of 6 April 2022, over 6 million deaths and over 490 million confirmed cases were reported to the WHO, around 11 million new cases per week continue to be reported. Cases numbers increased rapidly from the end of December 2021 as the Omicron variant spread. The Americas and Europe have the highest numbers of recorded cases (205 million in Europe, 151 million in the Americas) with 57 million case reported in South-East Asia, 48 million cases in the Western Pacific region and case numbers are increasing in Africa (8.6 million). See the WHO Coronavirus Disease (COVID-19) Dashboard ([covid19.who.int](https://covid19.who.int)) for the latest official data. Actual rates are expected to be considerably higher than officially reported rates, especially since milder infections may not be reported.

The infection-fatality rate, while still high particularly in the older age groups, has reduced since the start of the pandemic, with vaccination, improved clinical recognition and management and the use of therapies of demonstrated value, such as dexamethasone (see Figure 5.1).<sup>68, 69</sup>

**Figure 5.1: Total confirmed COVID-19 deaths and cases per million people, World (as of 21 November 2021)**



Note: The confirmed counts shown here are lower than the total counts. The main reason for this is limited testing and challenges in the attribution of the cause of death.

Sources: Center for Systems Science and Engineering (CSSE) Johns Hopkins University of Medicine; Our World in Data

The use of vaccines is anticipated to reduce the global burden of COVID-19 significantly. The first phase I clinical trial for a COVID-19 vaccine commenced in March 2020. The first public vaccination dose was given as part of a mass campaign in the United Kingdom on 8 December 2020. As of 4 April 2022, around 11 billion doses had been administered with 4.5 billion people fully vaccinated, globally. Ten COVID-19 vaccines have been granted emergency use listing by the WHO.

See the WHO Coronavirus Disease (COVID-19) Dashboard ([covid19.who.int](https://covid19.who.int)) and the Our World in Data website ([ourworldindata.org/covid-vaccinations](https://ourworldindata.org/covid-vaccinations)) for the latest official data.

### 5.3.2 New Zealand epidemiology

Prior to the outbreak of the Delta variant in August 2021, during 2021 most of the reported cases were imported from overseas (over 95 percent from 1 January to 9 August 2021). From 16 August 2021, the number of cases in New Zealand began to increase sharply due initially to the highly infectious Delta variant. From January 2022, when the even more infectious Omicron variant entered the community, case numbers rose rapidly. By the end of March 2022, a total of 627,898 cases had been notified and 266 people had died with COVID-19. From August 2021 to end of February 2022, the highest proportions of hospitalised cases by prioritised ethnicity were Pacific Peoples (34 percent), European or Other (30 percent) and Māori (25 percent) followed by Asian (9 percent) and MELAA (2 percent). For current details on case demographics see [health.govt.nz/covid-19-novel-coronavirus/covid-19-data-and-statistics](https://health.govt.nz/covid-19-novel-coronavirus/covid-19-data-and-statistics)

## Strategy for prevention

The first case of COVID-19 was reported in New Zealand on 28 February 2020. During March, cases numbers increased, and clusters of transmission were identified. Border restrictions were implemented on 16 March 2020. On 25 March 2020, New Zealand entered a nationwide lockdown (alert level four). New Zealand implemented an elimination strategy with four defined levels of pandemic response to prevent the spread of SAR-CoV-2. A mobile phone app aided rapid contact tracing.

These strategies were effective in containing the spread of SARS-CoV-2 in New Zealand and restrictions were able to rapidly stop the spread of the virus within the country. Only 19 percent of the introductions of virus in 2020 resulted in ongoing transmission or more than one additional case.<sup>5</sup> Subsequently on 3 December 2021, once around 90 percent of the eligible population had been vaccinated in most regions, a revised COVID-19 protection framework using 'traffic lights' was introduced.

## 5.4 Vaccines

### 5.4.1 Introduction

Clinical trials for COVID-19 vaccine candidates began shortly after the pandemic was announced in March 2020. Between October to December 2020, the New Zealand Government signed advanced purchase agreements for four vaccine candidates, with purchase dependent on approval for use from the New Zealand Medicines and Medical Devices Safety Authority (Medsafe). This is an ongoing process and, therefore, the availability and eligibility for these different vaccines may change.

### 5.4.2 Available vaccines

Vaccines for COVID-19 continue to undergo phase III clinical trials, and the Medsafe review process is ongoing for each vaccine candidate examining clinical trial and post-marketing surveillance data. The first vaccine to receive approval for use in New Zealand was an mRNA-based COVID-19 vaccine (mRNA-CV, trade name Comirnaty) manufactured by Pfizer/BioNTech. Provisional consent approval was granted on 3 February 2021. Two adenoviral vector COVID-19 vaccines were granted provisional approval in July 2021: COVID-19 Vaccine AstraZeneca (available from late November 2021) and COVID-19 Vaccine Janssen (not available in New Zealand). On 4 February 2022, provisional approval was granted to an adjuvanted recombinant spike protein subunit COVID-19 vaccine (rCV; trade name Nuvaxovid) manufactured by Serum Institute of India on behalf of Novavax and sponsored in New Zealand by Biocelect (available from March 2022).

Provisional consent imposes conditions on these vaccines to restrict their use by health professionals according to the available data at time of approval. This approval status allows New Zealanders early access to medicines with significant unmet clinical need under the Medicines Act.

## Funded vaccines

The mRNA-CV, Comirnaty, consists of messenger ribonucleic acid (mRNA) encoding the full-length spike glycoprotein of the SARS-CoV-2 virus inside a lipid nanoparticle (named tozinameran). The spike protein has an adjuvant effect, so no additional adjuvant is included. It is designated BNT162b2 in clinical trials conducted by Pfizer and BioNTech. This mRNA vaccine delivers the instructions for human cells to build the viral antigen, SARS-CoV-2 spike protein. The mRNA is temporarily protected from degradation by the lipid nanoparticle that also facilitates fusion with the recipient's cell wall.<sup>70, 71</sup>

An adenoviral vector COVID-19 vaccine, COVID-19 vaccine AstraZeneca (also known as Vaxzevria), was provisionally approved for use in New Zealand on 29 July 2021. It is manufactured by AstraZeneca (clinical trial designation AZD122). This vaccine, abbreviated here to ChAd-CV, contains a recombinant non-replicating chimpanzee adenovirus, ChAdOx1-S, contain a transgene encoding the prefusion SARS-CoV-2 spike glycoprotein. The adenovirus delivers the instructions to make replicas of the SARS-CoV-2 viral protein. It has been modified to be unable to replicate and only the gene encoding the spike protein (the antigen) can be expressed. Once the protein instructions have been delivered virus is destroyed.

The adjuvanted recombinant COVID-19 vaccine (abbreviated here as rCV), Nuvaxovid, contains recombinant SARS-CoV-2 spike protein in a stabilised prefusion conformation. The spike protein is produced by an insect cell-line that has been infected with an insect baculovirus expressing SARS-CoV-2 spike protein genes. Together, the purified spike proteins and the adjuvant matrix are formed into immunogenic nanoparticles. The proprietary adjuvant (Matrix-M) contains two purified saponin fractions from *Quillaja saponaria* (soapbark tree) which enhances the innate immune response and activates the production of neutralising antibodies and T and B cell immunity. The vaccine was designated NVX-2373 in clinical trials conducted by Novavax and is sponsored in New Zealand by Biocelect.

### **mRNA-CV (Comirnaty, Pfizer/BioNtech)**

*mRNA-CV (30 µg) for ages from 12 years (Comirnaty, purple cap)*

Each 0.3 mL dose of mRNA-CV contains:

- 30 µg of tozinameran, a single-stranded 5'-capped mRNA encoding pre-fusion stabilised SARS-CoV-2 full-length spike glycoprotein embedded in a lipid nanoparticle. The mRNA is produced using cell-free in vitro transcription from DNA templates.
- The lipid nanoparticle contains ALC-0315 ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)), ALC-0159 (2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide), distearoylphosphatidylcholine (DSPC) and cholesterol.
- Also contains potassium chloride, monobasic potassium phosphate, sodium chloride, dibasic sodium phosphate dihydrate, sucrose and water for injection.

*mRNA-CV (10 µg) for children aged 5 to 11 years (orange cap)*

Each 0.2 mL dose contains:

- 10 µg of tozinameran, a single-stranded 5'-capped mRNA encoding pre-fusion stabilised SARS-CoV-2 full-length spike glycoprotein embedded in a lipid nanoparticle. The mRNA is produced using cell-free in vitro transcription from DNA templates.
- The lipid nanoparticle contains ALC-0315 ((4 hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)), ALC 0159 (2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide), distearoylphosphatidylcholine (DSPC) and cholesterol.
- Also contains Tris/sucrose buffer: tromethamine (also known as Tris), tromethamine hydrochloride, sucrose and water for injection

The 10 µg paediatric formulation of mRNA-CV (with orange cap) uses a Tris/sucrose buffer to improve the stability at +2° to 8°C.

### **ChAd-CV (COVID-19 Vaccine AstraZeneca or Vaxzevria)**

Each 0.5 mL dose of ChAd-CV contains:

- $5 \times 10^{10}$  viral particles of ChAdOx1-S (recombinant, replication deficient chimpanzee adenovirus encoding the SARS-CoV-2 spike glycoprotein)
- Also contains approximately 2 mg ethanol, L-histidine, L-histidine hydrochloride monohydrate, magnesium chloride hexahydrate, polysorbate 80, sucrose, sodium chloride, disodium edetate dihydrate (EDTA) and water for injection.

### **Adjuvanted recombinant COVID-19 vaccine (Nuvaxovid)**

Each 0.5 mL dose of adjuvanted rCV contains:

- 5 µg of recombinant SARS-CoV-2 spike protein (produced in insect cell line, Sf9)
- 50 µg adjuvant Matrix M - fraction A and fraction C saponins from *Quillaja saponaria* formed into lipid nanoparticles containing cholesterol, phosphatidyl choline, monobasic potassium phosphate and potassium chloride
- Also contains: dibasic sodium phosphate heptahydrate, monobasic sodium phosphate monohydrate, sodium chloride, polysorbate 80, sodium hydroxide (for adjustment of pH), hydrochloric acid (for adjustment of pH) and water for injections

## **Other vaccines**

Another adenoviral vector COVID-19 vaccine (Ad26.COV2.S, brand name COVID-19 Vaccine Janssen) was approved for use in New Zealand on 7 July 2021. Using a similar platform to ChAd-CV, this vaccine (abbreviated here to Ad26-CV) contains a modified non-replicating human adenovirus, Ad26, that carries a transgene coding for the COVID-19 pre-fusion SARS-CoV-2 spike protein. This vaccine is not currently available in New Zealand.

## 5.4.3 Efficacy and effectiveness

### mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

#### Immunogenicity

Assessing immunogenicity was a key component of the early-phase clinical trials of COVID-19 vaccines before the phase III efficacy studies were conducted. Virus neutralising antibody responses measured the killing of live SARS-CoV-2 and/or pseudo-virus in cell culture. Since no correlates of protection have yet been established, humoral responses were compared with human convalescent sera collected from patients who had recovered from COVID-19.

Two vaccine candidates were evaluated (BNT162b1 and BNT162b2) in the initial phase I and II clinical trials. Both demonstrated similar dose-dependent neutralising antibody titres, which were similar or higher to the titres in convalescent sera.<sup>72</sup> Anti-receptor binding domain (anti-RBD) IgG antibodies also increased with dose.<sup>73</sup> As seen for other vaccines, the antibody response was lower in older people (aged 55–85 years) than in younger people (aged 18–55 years), but both groups had higher average neutralising antibody levels than those with prior SARS-CoV-2 infection.

The immunogenicity of mRNA-CV in adolescents aged 12–15 years was non-inferior to those aged 16–25 years in a phase III clinical trial. The neutralising antibody response in 190 adolescents was higher than in 170 young adults (geometric mean ratio 1.76; 95% CI 1.47–2.10).<sup>74</sup>

#### *Immunogenicity in children aged 5–11 years*

A phase II/III clinical trial involving 2,268 children aged 5–11 years found that the immunogenicity of mRNA-CV vaccine in children (10 µg dose) was similar to that seen in 1,147 young adults aged 16–25 years (30 µg dose).<sup>75</sup> At one month after two doses (given 21 days apart), the neutralising antibody geometric mean ratio was 1.04 (0.93–1.18) between the 264 children and young adults.

#### Efficacy – clinical trial data

Efficacy of 30 µg mRNA-CV (BNT162b2) was assessed in the phase III component of a large clinical trial in which 43,448 participants aged 16–85 years in Argentina, Brazil, Germany, Turkey, South Africa and the United States were randomised to receive vaccine or saline placebo.<sup>76</sup> Two doses were given 21 days apart. According to interim data, vaccine efficacy (VE) against symptomatic PCR-confirmed COVID-19 was 94.8 percent (95% CI: 89.8–97.6 percent); eight cases in the vaccinated group and 162 cases in control group developed COVID-19 at least seven days after dose two. Evidence of previous SARS-CoV-2 infection did not alter this efficacy (VE 95.0 percent without and 94.6 percent including those with previous infection). Similar efficacy (90–100 percent) was observed across all subgroups as defined by age, sex, race, ethnicity, baseline body-mass index (35 percent of participants were obese, BMI ≥ 30) and the presence of at least one co-existing medical conditions (in 21 percent). Moderate early protection against COVID-19 was observed before the second dose.<sup>76</sup> This clinical trial is ongoing, and further data is anticipated as predefined endpoints are reached. The trial is due to be completed in January 2023.

The observed vaccine efficacy for mRNA-CV (30 µg) in adolescents aged 12–15 years during a phase III clinical trial was 100 percent (95% CI 75.3–100) against symptomatic COVID-19. A total of 2,220 randomised participants received two doses of vaccine or saline placebo given 21 days (19–42 days) apart. No cases of severe COVID-19 were observed in this age group.<sup>74</sup>

#### *Efficacy in children aged 5–11 years*

Vaccine efficacy of 90.7 percent (95% CI 67.7–98.3) against symptomatic COVID-19 was seen from seven days after dose two in 1,305 children (without evidence of previous infection) aged 5–11 years who received mRNA-CV (10 µg) compared with 663 who received placebo in the phase II/III clinical trial.<sup>75</sup>

#### *Effectiveness – real-world experience*

Early data from Israel at the start of its national COVID-19 immunisation programme, which included around 1.2 million vaccinated and unvaccinated individuals aged from 16 years, demonstrated that mRNA-CV was highly effective at preventing COVID-19 and severe disease, and these data were in line with those observed during clinical trials.<sup>77</sup>

In the UK, a single dose of mRNA-CV was associated with a significant reduction in symptomatic COVID-19 cases in older adults (aged from 70 years) for at least six weeks. Vaccine effectiveness was observed from 10–13 days after vaccinations, by days 28–34 vaccine effectiveness reached 70 percent (95% CI 59–78 percent), then plateauing to 61 percent (51–59 percent). Additionally, those that had been vaccinated were 43 percent (33–52 percent) less likely to require emergency hospitalisation and at 51 percent (37–62 percent) lower risk of death. A second dose (given 12 weeks after dose one) provided further protection against symptomatic disease (at day 14, vaccine effectiveness reached 89 percent (85–93 percent)).<sup>78</sup>

#### *Effectiveness against transmission*

Effectiveness of mRNA-CV against transmission of SARS-CoV-2 is unclear and likely to depend on a range of factors, including rate of viral growth once infected. It is expected that with fewer symptomatic people producing virus for a shorter time, the spread of the virus will decrease. Evidence from the UK has shown that vaccination against COVID-19 reduces the risk of infection with the Delta variant and accelerates the viral clearance.<sup>79</sup> Although peak viral loads were similar between infected vaccinated and unvaccinated individuals, which can efficiently transmit virus within households, the secondary attack rate between household contacts was 25 percent (95% CI 18–33 percent) in for fully vaccinated individuals compared with 38 percent (24–53 percent) in unvaccinated individuals.<sup>79</sup> Evidence (non-peer reviewed) from the UK has also demonstrated that transmission within a household was reduced by approximately half when the index case was vaccinated with mRNA-CV.<sup>80</sup> Transmission to non-immune individuals in households in Sweden was shown to be significantly reduced and correlated with the proportion of family members vaccinated.<sup>81</sup>

### *Effectiveness against SARS-CoV-2 variants*

Effectiveness of mRNA-CV against symptomatic COVID-19 caused by the Delta variant is reduced in comparison with previous variants (ranging from around 78–93 percent).<sup>78</sup> According to preprint literature, from 7–14 days after two doses, the vaccine remains highly effective against hospitalisation (73–94 percent), severe disease and death (80–97 percent) in a range of groups.<sup>82</sup> The risk of infection with Delta is lower in fully vaccinated compared with unvaccinated individuals (hazard ratio 0.35; 95% CI 0.32–0.39), but some vaccinated individuals may spread infection.<sup>83</sup>

### *Effectiveness in adolescents*

Interim effectiveness against Delta variant SARS-CoV-2 infection, irrespective of symptoms, was estimated to be 92 percent (95% CI 79–97) in adolescents aged 12–17 years in Arizona.<sup>84</sup> A test-negative case-control study in the US showed vaccination with mRNA-CV (30 µg) to be protective against PIMS-TS in adolescents aged 12–18 in the US with an estimated effectiveness of 91 percent (95% CI 78–97 percent), a median of 84 days (range 52–122) after vaccine dose two.<sup>85</sup>

## Adenovirus vector COVID-19 vaccine – COVID-19 Vaccine AstraZeneca

### *Efficacy*

The initial data, pooled from four phase III clinical trials conducted in Brazil, South Africa and the UK, showed two doses of ChAd-CV given four weeks apart had vaccine efficacy against symptomatic COVID-19 of 62.1 percent (95% CI 41.0–75.7 percent) from 14 days after the second dose.<sup>86</sup> Another phase III clinical trial in US, Peru and Chile reported an estimated overall vaccine efficacy of 74.0 per cent (95% CI 65.3–80.5) in those aged under 65 years and 83.5 percent (95% CI 54.2–94.1) in those aged 65 years or older from 15 days after two doses given four weeks apart. Among 17,662 participants, no cases of severe or critical COVID-19 were seen in the fully vaccinated group compared with eight cases out of 8,550 participants who received placebo (vaccine efficacy of 100 percent [72.2–100]).<sup>87</sup>

### *Effectiveness*

Early data (pre-Delta variant) after the first dose from study conducted in Scotland gave a vaccine effectiveness of 88 percent (95% CI 75–94) against hospital admission 28–34 days post vaccination with the first dose for older adults (median age 65 years).<sup>88</sup> A significantly protective effect was seen against hospitalisation and death due to COVID-19 from 14 days after the first dose of ChAd-CV or mRNA-CV.<sup>89</sup> Data is limited about effectiveness against transmission.

### *Effectiveness against variants*

A modest reduction in effectiveness after two doses of ChAd-CV against symptomatic disease caused by Delta (67 percent; 95% CI 61–72) compared with Alpha variant (74.5 percent; 68–89) has been reported.<sup>78</sup> UK Health Security Agency (formerly Public Health England) found the effectiveness against hospitalisation with Delta was 71 percent (51–83) after one dose and 92 percent (75–97) after two doses of ChAd-CV; similar to the vaccine effectiveness against Alpha. The non-peer-reviewed study linked

symptomatic COVID-19 cases with hospital admission and vaccine status.<sup>82</sup> Vaccine effectiveness against Omicron variant was reduced, starting at 45 to 50 percent at two weeks after second dose and has almost no effect against symptomatic disease by 20 weeks. Protection against hospitalisation drops to around 35 percent after 25 weeks.<sup>90, 91</sup>

## Adjuvanted recombinant COVID-19 vaccine – Nuvaxovid (Novavax)

### Immunogenicity

Two doses of adjuvanted rCV were immunogenic in adults aged 18–59 years and 60–84 years. At 14 days after two doses given 21 days apart, neutralising antibody levels in both groups were higher than those in a panel of convalescent sera and all participants who received rCV seroconverted. A total of 1,283 participants were randomised 1:1:1:1 to receive one or two doses of vaccine (5 µg spike protein), a higher dose (25 µg) or placebo, and were stratified by age in the US and Australia. Both age groups had robust immune responses, although the older participants had lower antibody titres of anti-spike protein IgG or wild-type neutralising antibody than the younger group.<sup>92</sup>

Coadministration with influenza vaccine was investigated in a small phase I/II sub-study in UK hospitals. Around 400 participants were randomised to receive rCV and inactivated quadrivalent influenza vaccine for those aged 18–64 years or adjuvanted trivalent influenza vaccine for those aged 65 years or over, or rCV alone. Immunogenicity showed no change in the response to influenza vaccine but a reduction in antibody response to SARS-CoV-2. There was no difference in the seroconversion rates. Although the anti-spike protein IgG response were 0.6-fold lower in the groups that received both vaccines, when post-hoc analysis of efficacy was considered, this reduction was not suggested to be clinically meaningful and in the younger age group, the anti-spike antibody levels were three-fold greater than found in convalescent serum.<sup>93</sup>

### Efficacy – clinical trial

Data from two phase III clinical trials gave overall vaccine efficacy of 90 percent (95% CI 82.9–94.6 in PREVENT-19 study in US/Mexico and 80.2–94.6 percent in UK trial) against symptomatic COVID-19 from at least 7 days after dose two of adjuvanted rCV.<sup>94, 95</sup> By age group, in approximately 10,000 vaccinated and placebo participants in the UK (randomised 1:1), vaccine efficacy against COVID-19 in those aged 18–64 years was 89.8 percent (79.7–95.5) versus 88.9 percent (20.2–99.7) in approximately 4,000 participants aged 65–84 years.<sup>95</sup> In a subgroup of approximately 6,000 participants with coexisting illness, vaccine efficacy was 90.9 (70.4–97.2).<sup>95</sup> These clinical trials were conducted during early 2021, against predominantly Alpha not Delta or Omicron variants.

### Effectiveness – real-world

This vaccine has only been recently approved for use and real-world effectiveness is beginning to be evaluated. There is no published data to date.

## Duration of immunity

### mRNA COVID-19 vaccine

There has been insufficient time since the commencement of clinical trials and vaccination campaigns to assess fully how long immunity lasts following immunisation or natural infection, especially with the emergence of more infectious variants. Prior to widespread Delta variant, a gradual decline in vaccine efficacy was observed to 6 months after vaccination to 91.3 percent (95% CI 89–93.2 percent), but protection against severe disease was maintained (vaccine efficacy of 96.7 percent; 80.3–99.9).<sup>96</sup> Waning in neutralising antibody levels has been correlated with predominantly mild or asymptomatic breakthrough infections in health care workers.<sup>97</sup> The greatest waning was observed in those aged over 65 years and those aged 40–64 years with underlying medical conditions compared with healthy adults.<sup>98</sup> Early data indicate that vaccine effectiveness with the primary course against symptomatic infection caused by Omicron variant declines more rapidly than was seen against Delta.<sup>90</sup> Although neutralising antibody levels wane and become less effective against the emerging variants, such as Omicron, T cell responses and memory are maintained in vaccine recipients (mRNA-CVs, rCV and Ad26-CV).<sup>99, 100</sup>

### Adenovirus COVID-19 vaccine AstraZeneca

Limited waning was observed the UK over nine months from when the COVID-19 vaccines were first introduced. Vaccine effectiveness was shown to peak in the early weeks after the second dose but for ChAd-CV effectiveness across all age groups fell to 47.4 percent (95% CI 45–49.6) after 20 weeks against symptomatic disease caused by the Delta variant. Effectiveness against hospitalisation was maintained at 77.0 percent (70.3–82.3) and 78.7 percent (52.7–90.4) against death. The greatest waning was observed in those aged over 65 years and those aged 40–64 years with underlying medical conditions compared with healthy adults.<sup>98</sup> Further UK data (non-peer-reviewed) found that ChAd-CV primary course was no longer effective against symptomatic infection with the Omicron variant after 15 weeks, before a booster dose with mRNA-CV was given.<sup>90</sup>

### Adjuvanted recombinant COVID-19 vaccine

There is limited data on duration of immunity for rCV. In a phase II study, IgG antibody titres and neutralising antibody activity waning was seen from day 35 (14 days after dose 2) to day 189 prior to booster.<sup>101</sup>

## Effectiveness of booster doses

To prolong protection many countries, including New Zealand, have introduced a booster dose given from three months after the primary course. Booster doses, given from five months after the primary course, were shown to reduce the rates of COVID-19 by a factor of 11.3 (95% CI 10.4–12.3) and severe illness by a factor of 5.4 (4.8–6.1) in older adults aged from 60 years in Israel.<sup>102</sup> Booster dose programmes were accelerated following the emergence of the Omicron variant from late 2021.

## mRNA COVID-19 vaccine

The UK Health Security Agency reported that vaccine effectiveness against symptomatic infection was significantly lower against Omicron than Delta variant, such that by 15 weeks vaccine effectiveness had declined to between 34–37 percent after a two doses of mRNA-CV and was unprotective after two doses of ChAd-CV. Against hospitalisations due to Omicron variant, at more than 25 weeks after two primary doses, mRNA-CV and ChAd-CV were found to have a vaccine effectiveness of 25–35 percent. Protection against hospitalisation was boosted to over 90 percent by mRNA-CV then declined to 75 percent after 10–14 weeks.<sup>91</sup> From two weeks after a booster dose of mRNA-CV (30µg) given from 25 weeks after the primary course, effectiveness against mild infection was increased to 70–75 percent: 71 percent (95% CI 42–86) in those ChAd-CV primed; 75.5 percent (56–86) in those mRNA-CV primed.<sup>90</sup>

These findings were supported by data from Canada, which showed vaccine effectiveness waned more rapidly after the primary series against symptomatic infection with Omicron compared with Delta variant. Vaccine effectiveness was significantly improved against symptomatic infection with Delta, from 80 percent (74–84 percent) to 97 percent (96–98 percent), and Omicron variants, from <1% (-8 to 10 percent) to 61 percent (56–65 percent), by a booster dose of an mRNA COVID-19 vaccine given from 240 days the second dose of primary course (with at least 1 dose of an mRNA vaccine). The booster dose was highly effective against severe outcomes of Delta or Omicron (98–99 percent and 87–98 percent, respectively).<sup>103</sup>

## Adjuvanted recombinant COVID-19 vaccine

Antibody levels induced by the booster doses of rCV in healthy adults were higher than levels associated with efficacy in the primary response phase III trials.<sup>101</sup> This phase II clinical trial assessed immunogenicity of a booster dose given approximately six months after two-dose primary course of rCV to 105 healthy adults aged 18 to 84 years. Immune responses at 28 days post booster (day 217) were compared with those at 14 days post dose two (day 35). Serum IgG GMTs increased 4.7-fold from day 35 to day 217 against ancestral SARS-CoV-2, and 4.1-fold in the neutralisation assay. Increases in functional ACE2 receptor binding inhibition were also observed from day 189 to day 217 (pre and post booster) against various variants, including by 24-fold against Delta and 20-fold against Omicron. Anti-spike IgG activity also showed improved titres against a range of variants, including 92.5-fold increase against Delta and 73.5-fold increase against Omicron.<sup>101</sup>

## Mixed COVID-19 vaccine schedules

### Heterologous priming

Much of the data available around mixed (heterologous) COVID-19 vaccine schedules have investigated ChAd-CV (AstraZeneca) followed by mRNA-CV (Comirnaty) as the second dose (heterologous prime-boost schedules).<sup>104, 105</sup> The humoral immune response was shown to be stronger with a ChAd/mRNA primary schedule than ChAd/ChAd schedule against different SARS-CoV-2 variants including Delta.<sup>104, 106</sup> The T cell response was found to be higher following heterologous dosing.<sup>107</sup> The ComCOV study in the UK found that when ChAd-CV was given 4 weeks after mRNA-CV, the anti-S protein IgG antibody response was lower than homologous mRNA-CV dosing

(geometric mean ratio [GMR] 0.51; 95% CI 0.43–∞), but higher than ChAd/ChAd. Giving mRNA-CV after ChAd-CV first dose, produced a higher response than ChAd/ChAd dosing (GMR 9.2; 7.5–∞). Taking age, comorbidity and different immunological outcomes into consideration, the overall humoral response of mRNA/mRNA was favoured over mRNA/ChAd dosing and ChAd/mRNA was favoured over ChAd/ChAd.<sup>108</sup>

A phase 2 study investigated safety and immunogenicity of mixed priming schedules in the UK. Between April and May 2021, 1,072 participants aged 50–78 years received a second dose of one of three COVID-19 vaccines a median of 9.4 weeks after receipt of a single dose of ChAd-CV or mRNA-CV.<sup>109</sup> Although, the antibody response after a dose of rCV was inferior to a second dose of mRNA-CV (GMR 0.5; 95% CI 0.4 to 0.7), rCV induced an 18-fold rise in anti-spike antibody concentration 28 days after vaccination, and both were higher compared two doses of ChAd-CV. For those who received a first dose of ChAd-CV, a second dose with rCV antibody concentration was non-inferior to a second dose of ChAd-CV (GMR 2.8; 2.2 to 3.4).<sup>109</sup>

### Heterologous boosting

As part of the UK COV-BOOST study, all vaccines used as third-dose boosters demonstrated superior immunogenicity compared with MenACWY control (except an inactivated virus COVID-19 vaccine in mRNA-CV primed group) as measured by anti-spike IgG and neutralising assays.<sup>110</sup> Participants aged 30 years or over with no history of laboratory-confirmed SARS-CoV-2 infection were given booster doses at least 84 days post two doses of mRNA-CV (Comirnaty) or at least 70 days post two doses of ChAd-CV. Participants received one of six vaccine doses: either rCV, half dose rCV, ChAd-CV or menACWY; mRNA-CV (Comirnaty), whole inactivated SARS-CoV-2 vaccine (Valneva) or Ad26-CV; mRNA-CV (Spikevax) or Curevac (withdrawn). Cellular responses in ChAd-CV primed individuals were better boosted by rCV than in those primed with mRNA-CV. Optimal timing of the dosing intervals remains unclear.<sup>110</sup>

## 5.4.4 Transport, storage and handling

### mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

#### mRNA-CV (30 µg) for ages 12 years and over

To preserve the integrity of the mRNA in this vaccine, storage at ultra-low temperature freezer (between -90°C and -60°C) is required. At these ultra-low temperatures, the shelf-life is nine months. Trays of unopened vials may be stored and transported at -25°C to -15°C for a total of two weeks on one occasion only. Once an individual vial has been removed from the vial tray, it should be thawed for use.

The vaccine will be thawed in batches, packed into cartons and distributed from the central warehouse. Each carton will have a label with an updated batch number and expiry date and time. Expiry reduces from 6 months to 31 days once thawed. Thawed vaccines will be shipped to vaccination sites as per the standard cold chain distribution process.

Store undiluted vials (with purple cap) at +2°C to +8°C for up to 31 days (including up to 12 hours for transportation) including up to two hours at room temperature (up to

+30°C). After dilution, store vials between +2°C and +30°C and use within six hours. Any remaining vaccine in the vial must be discarded after six hours. Do not refreeze. See 2021 Addendum to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at [health.govt.nz/publication/2021-addendum-national-standards-vaccine-storage-and-transportation-providers-2017-2nd-edition](https://health.govt.nz/publication/2021-addendum-national-standards-vaccine-storage-and-transportation-providers-2017-2nd-edition)). See also 'Guidance supporting the administration of mRNA-CV vaccine' factsheet available from [covid.immune.org.nz](https://covid.immune.org.nz).

### mRNA-CV (10 µg) for ages 5–11 years

This vaccine requires storage at ultra-low temperatures (-90°C to -60°C) and at this temperature has a shelf-life of 12 months. Store unopened, undiluted vials (with orange cap) at +2°C to 8°C for up to 10 weeks. Do not freeze. Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* [health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017](https://health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017)

Store diluted vaccine in vials at +2°C to 8°C for a maximum of 12 hours, or store vaccine drawn-up in syringe for a maximum of six hours at +2°C to 30°C. Prior to use, once an undiluted vial is taken out of the refrigerator, allow time (up to 2 hours) for the vaccine to reach room temperature and to be diluted. Discard any vaccine exceeding these times, accordingly. See also the IMAC COVID-19 Education factsheet 'Paediatric Pfizer/BioNTech mRNA-CV 10µg Vaccine Preparation' available from [covid.immune.org.nz](https://covid.immune.org.nz).

### Adenovirus vector COVID-19 vaccine (ChAd-CV) – COVID-19 Vaccine AstraZeneca

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* [health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017](https://health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017)

Store at +2°C to +8°C. Do not freeze. Protect vials from light. Unopened vials (with red cap) have a shelf-life of up to six months. Once cap has been removed from vial, store in fridge and use within 48 hours. Vaccines should ideally be used within an hour of preparation, however, any doses that are drawn up into syringes must be used within five hours (stored at +2°C to 30°C) or before vial 48-hour expiry is reached, whichever is soonest. To ensure optimum use, in New Zealand, the vaccine is recommended to be always stored in the fridge.

### Adjuvanted recombinant COVID-19 vaccine – Nuvaxovid (Novavax)

Transport and store according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* [health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017](https://health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017)

Store at +2°C to +8°C. Do not freeze. Protect vials from light. Unopened vials (with blue cap) have a shelf-life of up to six months. Opened vials should be used within six hours of first use. Vaccines should ideally be used within an hour of being drawn up. The maximum time the vaccine can be stored in a syringe is six hours when stored at +2°C to 25°C, and before the vial six-hour expiry is reached, whichever is soonest. To ensure optimum use, in New Zealand, the vaccine is recommended to be always stored in the fridge and, where practical, doses are drawn up as required.

## 5.4.5 Dosage and administration

### mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

#### mRNA-CV (30 µg) for ages from 12 years

Each dose of mRNA-CV is 0.3 mL (30 µg) to be administered intramuscularly. Two doses are given at least 21 days apart for individuals aged 12 years or older.

Each multi-dose vial (with purple cap) contains 0.45 mL of vaccine and should be diluted with 1.8 mL of 0.9% NaCl. Once diluted, each reconstituted vaccine will supply six (up to seven) doses of 0.3 mL. If the amount of vaccine remaining in the vial cannot provide a full 0.3 mL dose, discard the vial and any excess volume. Do not pool excess vaccine from multiple vials.

An observation period following vaccination of at least 15 minutes is recommended (see section 5.6.2). This is to ensure that any anaphylactic-type reactions can receive prompt treatment.

This vaccine is latex-free. The vial stopper is made with synthetic rubber (bromobutyl), not natural rubber latex.

#### mRNA-CV (10 µg) for ages 5 to 11 years

Each 0.2 mL dose (10 µg) is to be administered intramuscularly. Two doses are given at least 21 days apart for individuals aged 5 to <12 years. An interval of at least 8 weeks is recommended between doses for this age group partly because it is expected give an optimal immune response.

Each multidose vial (with an orange cap) contains 1.3 mL and should be diluted with 1.3 mL 0.9% NaCl. Once reconstituted, each reconstituted vial will supply ten doses of 0.2 mL. If the amount of vaccine remaining in the vial cannot provide a full 0.2 mL dose, discard the vial and any excess volume. Do not pool excess vaccine from multiple vials.

An observation period following vaccination of at least 15 minutes is recommended (see section 5.6.2). This is to ensure that any anaphylactic-type reactions can receive prompt treatment.

This vaccine is latex-free. The vial stopper is made with synthetic rubber (bromobutyl), not natural rubber latex.

## Preparing mRNA-CV multi-dose vial

Note that the process for drawing up mRNA-CV differs from the recommendations for other multi-dose vial vaccines as described in section A7.2 in Appendix 7. To follow international guidance around the use of low dead space needles, the needle used to draw up mRNA-CV is also used to administer the injection. Unless you plan to administer the vaccine dose immediately, carefully replace the needle guard and place syringe onto a ridged tray for storage, for example, if all six doses are prepared at one go in a mass vaccination setting.

For detailed instructions for mRNA-CV multi-dose vial preparation and administration see the most current IMAC COVID-19 education factsheets '*Instructions for multi-dose vial Pfizer/BioNTech vaccine: preparation and administration*' and '*Paediatric Pfizer/BioNTech mRNA-CV 10µg Vaccine Preparation*' available from [covid.immune.org.nz](https://covid.immune.org.nz).

## Adenovirus vector COVID-19 vaccine (ChAd-CV) – COVID-19 Vaccine AstraZeneca

Each dose of ChAd-CV is 0.5 mL to be administered intramuscularly. Two doses are given from 4 to 12 weeks apart for individuals aged 18 years or older.

Each multidose vial contains ten doses (total 5 mL; with red cap). The vials do not require dilution or reconstitution. For detailed instructions for ChAd-CV multidose vial administration see the most current IMAC COVID-19 education factsheet, '*Guidance for AstraZeneca COVID-19 vaccine preparation*' available from [covid.immune.org.nz](https://covid.immune.org.nz).

An observation period following vaccination of at least 15 minutes is recommended (see section 5.6.2). This is to ensure that any anaphylactic-type reactions can receive prompt treatment.

This vaccine is latex-free. The vial stopper is made with synthetic rubber (an elastomeric with an aluminium overseal), not natural rubber latex.

## Adjuvanted recombinant COVID-19 vaccine – Nuvaxovid (Novavax)

A primary course of two 0.5 ml doses of adjuvanted rCV are given intramuscularly at least 21 days apart.

The ready-to-use multidose vials (with blue cap) contain ten doses. The vials do not require dilution or reconstitution. Do not pool excess from multiple vials. For detailed instructions for adjuvanted rCV multidose vial administration see the most current IMAC COVID-19 education factsheet, '*Guidance for Novavax COVID-19 vaccine preparation*' available from [covid.immune.org.nz](https://covid.immune.org.nz).

This vaccine is latex-free. The vial stopper is made with bromobutyl or chlorobutyl rubber, not natural rubber latex.

The safety and efficacy of rCV has not yet been established for children and adolescent aged under 18 years. Limited clinical trial data are available for those aged 12-17 years.<sup>111</sup>

## Coadministration with other vaccines

There are no anticipated safety concerns regarding coadministration any of the currently available COVID-19 vaccines (mRNA-CV (10 µg or 30 µg), ChAd-CV or rCV) with other vaccines. These vaccines can be administered at any time before, after or simultaneously (in separate syringes, at separate sites) with other Schedule vaccines including MMR, varicella, influenza, HPV, Tdap and meningococcal vaccines. Note: the only exceptions are the live herpes zoster vaccine (ZV; Zostavax), for which, spacing of at least seven days is recommended before or after a COVID-19 vaccine (mRNA-CV, ChAd-CV or rCV). Due to limited experience at this time, it is also recommended to allow spacing of at least three days between rCV and rZV (Shingrix) and adjuvanted influenza vaccine (Fluad Quad).

TST/Mantoux testing for tuberculosis can also be conducted at any time before, after or simultaneously with mRNA-CV, ChAd-CV or rCV.

## 5.5 Recommended immunisation schedule

The COVID-19 vaccines were initially only available according to a prioritisation schedule for defined groups, however, since January 2022, all individuals in New Zealand aged from 5 years are eligible to be vaccinated.

For the legal definition of who is considered up to date with vaccination against COVID-19 within the New Zealand border see '*Fully vaccinated against COVID-19 within Aotearoa New Zealand policy statement*' available from the Ministry of Health website, as below. See section 5.8.2 for examples of approved vaccination schedules.

Temporary medical exemptions from vaccine mandates for the first or second dose of COVID-19 vaccination, where a suitable appropriate and approved COVID-19 vaccine is not available, may be granted by the Director General of Health, as defined by the Ministry of Health (available from [health.govt.nz/covid-19-novel-coronavirus/covid-19-response-planning/covid-19-mandatory-vaccinations/covid-19-exemptions-mandatory-vaccination](https://www.health.govt.nz/covid-19-novel-coronavirus/covid-19-response-planning/covid-19-mandatory-vaccinations/covid-19-exemptions-mandatory-vaccination)). See also section 5.8.3.

For further details around vaccine policy statements and clinical guidance for the COVID-19 Vaccine Immunisation Programme refer to [health.govt.nz/covid-19-novel-coronavirus/covid-19-vaccines/covid-19-vaccine-information-health-professionals/covid-19-vaccine-policy-statements-and-clinical-guidance](https://www.health.govt.nz/covid-19-novel-coronavirus/covid-19-vaccines/covid-19-vaccine-information-health-professionals/covid-19-vaccine-policy-statements-and-clinical-guidance).

## 5.5.1 mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

### mRNA-CV (30 µg) for ages from 12 years (purple cap)

All individuals from the age of 12 years are recommended to receive two doses of mRNA-CV, given at least 21 days after the first dose. Individuals are considered fully vaccinated after completing the full primary course, full immunity develops from around seven days after the second dose. For booster doses, see section 5.5.11.

### mRNA-CV (10 µg) for ages 5 to 11 years (orange cap)

Two doses mRNA-CV (10 µg) given at least 8 weeks apart to children aged from 5 years up to 11 years. In situations where the longer interval is not possible (eg, prior to planned immunosuppression), give the second dose a minimum of 21 days after first.

For children who turn 12 years after their first dose, it is recommended to give the same vaccine for the second dose as was given for the first dose, ie for both doses give paediatric mRNA-CV (10 µg), not the 30 µg formulation. It is not considered an error when mRNA-CV 30 µg is given instead.

To date, mRNA-CV has not been approved for use in children aged younger than 5 years in New Zealand. Clinical trials are ongoing in younger age groups.

## 5.5.2 Adenovirus vector COVID-19 vaccine (ChAd-CV) – COVID-19 Vaccine AstraZeneca

The preferred vaccine for the Schedule is mRNA-CV, however, ChAd-CV can be offered (if not contraindicated, see section 5.6), where available, to individuals who are contraindicated mRNA-CV or have experienced an adverse reaction to the first dose of mRNA-CV. It can also be offered to individuals who have declined mRNA-CV and would prefer an alternative vaccine. Individuals opting for this vaccine are recommended to discuss the benefit and potential risks of receiving this vaccine with a health professional. Written consent is recommended for all ChAd-CV doses.

Where two primary doses of ChAd-CV are given, no prescription is required. In cases where another COVID-19 vaccine was given previously, ChAd-CV given as the second primary or booster dose (see section 5.5.11) are off-label uses and will require prescription from an authorised provider (under regulation s25 of the Medicines Act 1981).

### 5.5.3 Adjuvanted recombinant COVID-19 vaccine – Nuvaxovid (Novavax)

The preferred vaccine for the Schedule is mRNA-CV, however, adjuvanted rCV can be offered (if not contraindicated, see section 5.6), where available, to individuals who are contraindicated mRNA-CV or have experienced an adverse reaction to the first dose of mRNA-CV. It can also be offered to individuals who have declined mRNA-CV and would prefer an alternative vaccine. Individuals opting for this vaccine are recommended to discuss the benefit and potential risks of receiving this vaccine with a health professional.

Where two primary doses of rCV are given, no prescription is required. In cases where another COVID-19 vaccine was given previously, rCV given as the second primary or as a booster dose (if considered appropriate by a clinician, see section 5.5.11) are off-label uses and will require prescription from an authorised provider (under regulation s25 of the Medicines Act 1981). Written consent is recommended when a prescription for any rCV doses is required.

### 5.5.4 Breastfeeding

As with all schedule vaccines, there are no safety concerns about giving mRNA-CV to lactating women. There is limited data to date around the use of ChAd-CV or adjuvanted rCV in lactating women.

### 5.5.5 Pregnancy

Anyone who is pregnant or planning pregnancy is encouraged to be routinely vaccinated with mRNA-CV at any stage of pregnancy. The risk of an adverse outcomes from COVID-19 infection during pregnancy is significantly higher compared to non-pregnant adults (see section 5.2.3).<sup>52</sup> Internationally, many women have been given this vaccine while pregnant and safety surveillance data of large numbers of pregnant women indicate that there are no safety concerns with administering mRNA-CV in any stage of pregnancy.<sup>112, 113, 114</sup> There is also evidence of antibody transfer in cord blood and breast milk which can offer protection to infants through passive immunity.<sup>115, 116,</sup>  
<sup>117</sup> Infants born to mothers vaccinated in pregnancy have some protection from COVID-19-associated hospitalisation for up six months.<sup>118</sup>

Pregnant women with questions or concerns are encouraged to discuss them with their health professional. People who are trying to become pregnant do not need to avoid pregnancy after receiving mRNA-CV.

There are no known safety concerns, but due to limited experience, ChAd-CV and rCV are not currently recommended for use in pregnancy – see Precautions (section 5.6.2).

For information about booster doses, see section 5.5.11.

## 5.5.6 Frail elderly individuals

In general, it is recommended that all eligible adults, including the frail and elderly with comorbidities are offered vaccination against COVID-19, if there are no contraindications to its administration (see section 5.6.1), to provide protection for the individual as well as their community.

## 5.5.7 Individuals receiving cardiology care

It is recommended that all individuals from age 12 years receive two doses of mRNA-CV (30 µg) given at least 21 days apart. Children aged 5–11 years are recommended two doses of paediatric mRNA-CV (10 µg) given at least 8 weeks apart. Pre-existing cardiac conditions, in general, **are not** regarded as precautions or contraindications to vaccination. This includes pre-existing rheumatic heart disease. Note that many cardiac conditions increase the risk from COVID-19 disease. Those with a history of pericarditis or myocarditis, unrelated to mRNA-CV, can have the vaccination if the condition is completely resolved, (ie, no symptoms and no evidence of ongoing cardiac inflammation). See section 5.6.2 for those who have myocarditis associated with mRNA-CV.

For those with a history of myocarditis and pericarditis related to mRNA-CV, seek specialist immunisation advice on a case-by-case basis to consider an appropriate alternative vaccine (eg ChAd-CV, only from age 50 years, or rCV from age 18 years) or no further vaccination, and about timing for further primary or booster doses.

## 5.5.8 Vaccination following SARS-CoV-2 infection

Vaccination should be offered regardless of an individual's history of symptomatic or asymptomatic SARS-CoV-2 infection. As the duration of protection post infection is currently unknown, vaccination is recommended. Although, there are no specific safety concerns around giving mRNA-CV to individuals with a history of SARS-CoV-2 infection or symptomatic COVID-19, those who have had recent infection can experience more systemic reactogenicity after the first dose of mRNA-CV (see section 5.7.1).<sup>119</sup> Viral or serological testing is not required before vaccination.

A person aged from 5 years who has had prior SARS-CoV-2 infection is recommended to complete the full vaccination course of mRNA-CV (or another COVID-19 vaccine, see section 5.8.2). In these individuals, vaccination is recommended to be continued from three calendar months after recovery from acute illness, or three months from the first confirmed positive test if asymptomatic. This applies to any dose of the primary course or booster doses, as age-appropriate. Based upon clinical discretion, where the individual is at high risk of severe disease from reinfection and has not completed the full course, vaccination can be delivered sooner than three months after SARS-CoV-2 infection and completed with the recommended spacing between doses.

For all other vaccines, vaccination can commence as soon as the individual is no longer acutely unwell and when cleared to leave isolation.

## 5.5.9 Individual with immunodeficiencies or receiving immunosuppressive agents

There are no safety concerns around administering mRNA-CV, ChAd-CV or rCV to individuals who are immunocompromised and/or receiving immunosuppressive agents. As with other non-live vaccines, the antibody response to these vaccines may be reduced and protection may be suboptimal but, it is likely to be adequate to protect against severe disease. It is recommended to discuss the optimal timing for vaccination with a specialist before the vaccine appointment for those who are severely immunocompromised. Ideally, vaccination should be conducted prior to any planned immunosuppression (see section 4.3.7).

It is important that all close contacts of immunocompromised individuals aged from 5 years are up to date with immunisations. Close contacts aged from 18 years should also receive a booster dose at least three calendar months after their primary course and those aged 16-17 years should receive a booster dose at least six months after their primary course. For booster doses, see section 5.5.11.

### Individuals who are severely immunocompromised

A third primary dose of mRNA-CV (10 µg or 30 µg, as age-appropriate) is indicated for certain individuals aged from 5 years who are severely immunocompromised who are likely to have not responded adequately to the first two doses. Serology is not recommended. This third primary dose is distinct from the booster dose (for booster doses see section 5.5.11).

Preferably, this third dose should be administered at least eight weeks after the second dose. However, the timing also needs to consider current or planned immunosuppressive therapies. If the period of least immunosuppression is less than eight weeks, the vaccination can be given any time from four weeks after dose two. Where possible, delay the third dose until two weeks after the period of immunosuppression (in addition to the clearance time-period of therapeutic). If this is not possible, consider vaccination during a treatment 'holiday' or at a nadir of immunosuppression between doses of treatment.

These additional doses are currently considered off label and can only be offered by an authorised prescriber with informed, preferably written, consent (under regulation s25 of the Medicines Act 1981). This is under review with Medsafe. For further guidance see [health.govt.nz/covid-19-novel-coronavirus/covid-19-vaccines/covid-19-vaccine-information-health-professionals/covid-19-vaccine-policy-statements-and-clinical-guidance](https://www.health.govt.nz/covid-19-novel-coronavirus/covid-19-vaccines/covid-19-vaccine-information-health-professionals/covid-19-vaccine-policy-statements-and-clinical-guidance).

If a significant adverse reaction to mRNA-CV has occurred that contraindicates further mRNA-CV doses, then ChAd-CV or rCV may be considered for those aged from 18 years (if not contraindicated). This also requires prescription and written consent is recommended. It is recommended to seek advice from IMAC.

Table 5.1 provides guidance on types of immunocompromise for which a third primary dose is recommended. For further information on corticosteroid indicative dosages

and examples of non-corticosteroid agents considered immunosuppressive, see section below and Table 5.2.

**Table 5.1: Individuals (aged 5 and older) with severe immunocompromise recommended to receive a third primary dose of mRNA-CV (10 µg or 30 µg, as age-appropriate)**

Note: This list is not exhaustive but provides guidance on scenarios where a third primary dose is recommended. There is variation between individuals in response to immunosuppressive or immunomodulating therapy. **Clinicians may use their judgement** for conditions or medications that are not listed here that are associated with severe immunocompromise.

Eligible group / indication	Treatments or health status
<b>Individuals with primary or acquired immunodeficiency states at the time of vaccination</b>	
Acute and chronic leukaemia and clinically aggressive lymphomas (including Hodgkin's lymphoma)	under treatment, or within 12 months of achieving cure or remission
Chronic lymphoproliferative disorders, including haematological malignancies <sup>a</sup> and plasma cells dyscrasias	under specialist follow up
Active HIV infection / AIDS	current CD4 count <200 cells/µl
Primary or acquired cellular and combined immune deficiencies	lymphopenia (<1,000 lymphocytes/µl) or functional lymphocyte disorder.
Allogenic or autologous haematopoietic stem cell transplant	received in previous 24 months or received >24 months ago but had ongoing immunosuppression or graft-versus-host disease.
Persistent agammaglobulinaemia due to primary immunodeficiency and secondary to disease/therapy	IgG <3 g/L
<b>Individuals on, or recently on, immunosuppressive therapy at the time of vaccination</b>	
Following a solid organ transplant	receiving therapy
B cell depleting biologic therapy, including rituximab	receiving or received therapy in the previous 6 months
Biologics or targeted therapy <sup>b</sup> for autoimmune or autoinflammatory disease	received within the previous 3 months
Immunosuppressive cytotoxic chemotherapy or immunosuppressive radiotherapy for any indication	received within the previous 6 months

*Continued overleaf*

Eligible group / indication	Treatments or health status
<b>Individuals with chronic immune-mediated inflammatory disease who were receiving or had received immunosuppressive therapy prior to vaccination</b>	
High-dose or long-term moderate dose corticosteroids (for indicative dosages, see below)	for more than a week in the month before vaccination
For select immunosuppressant drugs <sup>b,c</sup>	in previous 3 months
Certain combination therapies at where cumulative effect is severely immunosuppressive, as determined by clinical judgment	in previous 3 months
<b>Individuals receiving long term haemodialysis or peritoneal dialysis</b>	

- Such as indolent lymphoma, chronic lymphoid leukaemia, myeloma, Waldenstrom's macroglobulinemia and other plasma cell dyscrasias. **Note** this list is not exhaustive but provides an indication of conditions where an individual is recommended to receive a third primary dose.
- For examples, see Table 5.2
- Excluding hydroxychloroquine, sulfasalazine, or mesalazine, when used as monotherapy.

## Individuals receiving corticosteroids

A third primary dose of mRNA-CV is recommended for individuals with chronic immune-mediated inflammatory disease who are receiving or have received high dose or long-term moderate doses of corticosteroids prior to vaccination, for example:

- high dose – equivalent to at least 20 mg prednisolone per day for more than ten days, in previous month
- moderate dose – equivalent to at least 10 mg prednisolone per day for more than four weeks, in previous three months
- also includes for those who received high dose corticosteroids for any reason – equivalent to at least 40 mg per day for more than a week, in the previous month.

Individuals for whom third primary dose **is not** routinely recommended include those who require:

- brief corticosteroid therapy, for example for asthma, chronic obstructive pulmonary disease or COVID-19 – equivalent to 40mg or less prednisolone per day
- low locally acting corticosteroids, inhaled or topical
- replacement corticosteroid treatment for adrenal insufficiency.

Clinical judgement is required to determine the level of immunosuppression and these dosages are only indicative examples. In some cases, combinations of therapies can have a cumulative effect that is severely immunosuppressive.

## Individuals receiving non-corticosteroid immunomodulatory agents

A third primary dose of mRNA-CV is recommended for individuals with chronic immune-mediated inflammatory diseases who were receiving or had received immunosuppressive therapy prior to primary COVID-19 vaccination. Indicative examples are given in Table 5.2. Clinical judgement is required to determine the level of immunosuppression. In some cases, combinations of therapies can have a cumulative effect that is severely immunosuppressive.

**Table 5.2: Examples of non-corticosteroid immunosuppressant therapies for which a third primary dose of mRNA-CV is recommended or not routinely recommended**

**Clinicians may use their judgement** for conditions or medications that are not listed here that are associated with severe immunocompromise and in some cases based on dosages or combinations of therapies

### Examples of non-corticosteroid agents for which a third dose is recommended

Agent	Example
Mycophenolate, methotrexate, leflunomide, 6-mercaptopurine	
Thiopurines	azathioprine
Alkylating agents	cyclophosphamide
Systemic calcineurin inhibitors	cyclosporin, tacrolimus
BTK inhibitors	ibrutinib
JAK inhibitors	ruxolitinib
Anti CD20 antibodies	rituximab, obinutuzumab, ocrelizumab
Sphingosine 1-phosphate receptor modulators	fingolimod
Anti-CD52 antibodies	alemtuzumab
Anti-complement antibodies	eculizumab
Anti-thymocyte globulin	

### Examples of non-corticosteroid agents<sup>a</sup> for which third primary dose is not routine recommended

Agent	Example
Anti-integrins	natalizumab
Anti-TNF- $\alpha$ antibodies	infliximab, adalimumab, etanercept
Anti-IL-1 antibodies	anakinra
Anti-IL-6 antibodies	tocilizumab
Anti-IL-17 antibodies	secukinumab
Anti-IL-4 antibodies	dupilumab
Anti-IL-23 antibodies	ustekinumab

a. For immune checkpoint inhibitors see section 4.3.2

## 5.5.10 Revaccination

COVID-19 vaccines (preferably with age-appropriate mRNA-CV) are available for revaccination of all eligible individuals from age 5 years who have undergone immunosuppressive treatment since their first course.

- Revaccination with a full (two or three dose) primary course, plus booster if age appropriate:
  - post-haematopoietic stem cell transplantation
- A single further dose of a COVID-19 vaccine is recommended (at least 3 months after last dose):
  - post chemotherapy
  - post-solid organ transplantation
  - post immunosuppressive therapy for longer than 28 days

## 5.5.11 Booster doses

All individuals aged 16 years and over are recommended to receive a booster dose. For those aged 18 years and above, a single dose of mRNA-CV (30 µg) is recommended to be given at least three calendar months after completion of the two-dose primary course. In cases where confirmed SARS-CoV-2 infection occurs between dose two of the primary course and booster dose, give a single dose of mRNA-CV from three calendar months after recovery from COVID-19, or at least three calendar months from the first confirmed positive PCR test if asymptomatic (see section 5.5.8).

For those aged 16-17 years, a single dose of mRNA-CV (30 µg) is recommended to be given at least six months after completion of the primary course. If SARS-CoV-2 infection occurs later than three months after primary course, give a booster dose at least three calendar months after recovery from acute illness or positive test in asymptomatic (see section 5.5.8) to provide the longest gap.

A booster dose is particularly recommended for individuals most at risk of exposure to SARS-CoV-2 or most at risk of serious COVID-19, as outlined below.

- Frontline health care workers, particularly those most likely to be exposed to COVID-19 in the community or in regions where further risk of spread of SARS-CoV-2 is high.
- All individuals who are aged 65 years or over.
- Māori and Pacific People due to a greater risk of severe disease, especially if aged from 50 years or over.
- Anyone aged 16 years or over at increased risk of severe COVID-19:
  - eligible for funded influenza vaccine, including pregnancy (See Booster doses in pregnancy)
  - disabled or caring for a person with a disability
  - severely obese (BMI  $\geq 40$ )
  - hypertension, requiring two or more medications to control
  - in a custodial setting

- have been diagnosed with a severe mental illness (including schizophrenia, major depressive disorder, bipolar disorder or schizoaffective disorder, and adults currently accessing secondary and tertiary mental health and addiction services).

Individuals aged from 16 years who are severely immunocompromised who receive a third primary dose are recommended to also be given the booster dose at least three calendar months later, taking in consideration current or planned immunosuppressive therapies. A booster dose given prior to six months after primary course to those aged 16-17 years is considered off-label and requires a prescription.

A booster dose is not currently approved by Medsafe for individuals aged under 16 years. A booster dose can be considered for those aged 12-15 years who are at higher risk of severe COVID-19, to be given from three to six months after completing the primary course. This is an off-label use requiring a prescription and written consent is recommended. For underlying health conditions that increase risk for severe COVID-19 in children see <https://starship.org.nz/guidelines/covid-19-disease-in-children/>. This list is not exhaustive and clinicians may use their judgement for conditions that are not listed.

Although mRNA-CV is the preferred vaccine, ChAd-CV can also be used as a booster dose, if not contraindicated for those aged from 18 years. If using ChAd-CV as a booster dose, a prescription from an authorised prescriber is required as it is an off-label use (under regulation s25 of the Medicines Act 1981).

## Booster doses in pregnancy

Pregnant women aged from 16 years can receive a booster dose of mRNA-CV at any stage of pregnancy (from three calendar months after a primary course if aged 18 years or over, or from six months if aged 16-17 years). Although the use of booster doses in pregnancy is limited to date, as with the primary course, it is expected to be safe and effective. If the full primary course has been given in pregnancy, a booster can be given as time-appropriate before or after delivery, and at least three calendar months after completion of their primary course. Pregnant women are encouraged to discuss timing of a booster dose with their health professional. A booster dose given earlier than six months after the primary course to those aged 16-17 years, is considered off-label and requires a prescription and written consent is recommended.

Individuals who are severely immunosuppressed are recommended to receive three primary doses with the third dose given at least eight weeks after dose two (see section 5.5.9; this is not the same as booster doses).

## 5.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

## 5.6.1 Contraindications

### mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

A history of anaphylaxis to any component or previous dose of mRNA-CV is a contraindication.

### Adenovirus vector COVID-19 vaccine (ChAd-CV) – COVID-19 Vaccine AstraZeneca

A history anaphylaxis to any components or previous dose of ChAd-CV is a contraindication.

A history of major venous and/or arterial thrombosis in combination with thrombocytopenia following vaccination with any COVID-19 vaccine is a contraindication for ChAd-CV.

Individuals with a history of capillary leak syndrome should not receive ChAd-CV.

### Adjuvanted recombinant COVID-19 vaccine – Nuvaxovid (Novavax)

A history anaphylaxis to any components or previous dose of adjuvanted rCV is a contraindication.

## 5.6.2 Precautions

A definite history of immediate allergic reaction to any other product is considered as a precaution but not a contraindication to vaccination with COVID-19 vaccines (mRNA-CV, ChAd-CV or rCV). A slightly increased risk of a severe allergic response in individuals who have had a previous anaphylaxis-type reaction needs to be balanced against the risk of SARS-CoV-2 exposure and severe COVID-19. These individuals can still receive a COVID-19 vaccines, if not contraindicated, and observation extended to 30 minutes after vaccination in health care settings, where anaphylaxis can be immediately treated with adrenaline.

When vaccinating an elderly person who has an intercurrent or comorbid condition, ensure they are stabilised or as well as possible before they have the vaccine. Following vaccination ensure good hydration and careful management of potential systemic adverse events, such as fever. It is advisable for them to be with someone else for 24 hours after receipt of the vaccine to help manage potential adverse events.

## mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

If myocarditis, myopericarditis or pericarditis occurs after dose one or two of mRNA-CV, defer further doses of mRNA-CV. Seek specialist immunisation advice, on a case-by-case basis, to consider an appropriate alternative vaccine (eg ChAd-CV, only from age 50 years or rCV from age 18 years) or no further vaccination, and about timing for further primary or booster doses. Vaccination is not recommended for anyone with current active cardiac inflammation.

## Adenovirus vector COVID-19 vaccine (ChAd-CV) – COVID-19 Vaccine AstraZeneca

A rare but increased risk of thrombosis with thrombocytopenia syndrome (TTS) has been identified with adenoviral vector vaccines including ChAd-CV, typically occurring within 3 weeks of vaccination and more prevalent in younger adults (<50 years). Vaccinated individuals should seek immediate medical attention if they develop symptoms such as a severe or persistent headache, blurred vision, confusion, seizures, shortness of breath, chest pain, leg swelling, leg pain, persistent abdominal pain or unusual skin bruising and or petechiae after vaccination.

Individuals with diagnosed thrombosis within 21 days of vaccination with ChAd-CV should be investigated for thrombocytopenia. Similarly, those diagnosed with thrombocytopenia within 21 days of vaccination should be actively investigated for signs of thrombosis; if thrombosis is excluded, consider a diagnosis of vaccine-induced immune thrombocytopenia (ITP).

It is recommended that individuals with a history of thromboses, certain procoagulant autoimmune disorders or thrombocytopenia discuss the benefits and risks of vaccination with a health professional or specialist as they remain at risk of recurrent thromboses due to COVID-19.

The specific risks for TTS have not been identified. Individuals with a history of the following rare causes of thrombosis are not advised to receive ChAd-CV:

- cerebral venous sinus thrombosis (CVST)
- idiopathic thrombosis in the abdomen such as in splanchnic circulation, including mesenteric, portal or splenic veins
- heparin-induced thrombocytopenia
- antiphospholipid syndrome with thrombosis.

## Pregnancy

There is insufficient safety data to recommend ChAd-CV and rCV for use during pregnancy, pregnant women are advised to discuss the benefit and potential risks of receiving this vaccine in pregnancy with their health professional. There are no safety concerns should it be given inadvertently in pregnancy.

## 5.7 Potential responses and AEFIs

### 5.7.1 Potential responses

#### mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

Commonly reported responses to mRNA-CV (30 µg) during clinical trials and post-licensure surveillance are injection-site pain, headache, dizziness and fatigue; other responses included muscle aches, feeling generally unwell, chills, fever, chest discomfort, joint pain, nausea and axillar lymph node swelling. These occurred most often after dose two and in younger adults (aged 18–55 years), and within one or two days of vaccination. Most are mild or moderate in severity and are self-limiting.<sup>76, 120</sup> Analgesia, such as paracetamol or ibuprofen (as appropriate), can be taken for pain and discomfort following vaccination. It is advisable to limit vigorous exercise if feeling unwell.

During clinical trials, the responses in children aged 5–11 years given paediatric formulation mRNA-CV (10 µg) are similar to those seen for the adult formulation mRNA-CV (30 µg) in those age 16–25 years. Generally, reactions were mild to moderate and short-lived. Pain at injection site was commonly reported (by over 70 percent) after dose one and two. Overall fewer children reported systemic reactions than seen after the 30 µg dose in adults, with fever, fatigue, headache, chills and muscle ache as the most common and more frequent after the second dose.<sup>75</sup> These responses were mirrored in reports to VAERS and V-safe after 8.7 million doses given routinely to children in the US.<sup>121</sup>

See chapter 2 (section 2.3.3) for immunisation-stress related responses (ISRR).

#### Adenovirus vector COVID-19 vaccine (ChAd-CV): COVID-19 Vaccine AstraZeneca

Commonly reported responses to ChAd-CV (during clinical trials and post-licensure) are similar to mRNA-CV, including injection-site pain, headache and fatigue; other responses included muscle aches, feeling generally unwell, chills, fever, joint pain and nausea. These occurred most often after dose one and in younger adults (aged 18–55 years), and within one or two days of vaccination.<sup>86, 122</sup> Most are mild or moderate in severity and are self-limiting. Adverse reactions were generally milder and reported less frequently after dose two or a third dose.<sup>123</sup>

#### Adjuvanted recombinant COVID-19 vaccine – Nuvaxovid (Novavax)

The most reported responses to rCV in clinical trials were injection-site tenderness and pain, headache, fatigue, myalgia, malaise, arthralgia, nausea and vomiting. These reactions were more common after dose two, lasting for one to three days, and occurred at higher incidence in younger age groups (less than 65 years).<sup>95</sup>

## Breast screening and CT scans

Transient unilateral axillary adenopathy, a known response to vaccination, was particularly noted following vaccination with mRNA-CV due to the scale of the roll-out and age groups being immunised. Early estimates suggest that 12–16 percent of vaccine recipients experience axillary adenopathy after vaccination with mRNA-CV, starting one or two days after vaccination and which can persist for several weeks.<sup>124</sup>  
<sup>125</sup> Lymphadenopathy has also been commonly reported after booster doses of mRNA-CV.<sup>126</sup>

When attending breast screening and mammography appointments, it is recommended that individuals advise the radiographer or doctor that they have received a COVID-19 vaccine recently. It is advised to monitor any lymph node changes that persist for longer than six weeks after vaccination.<sup>124</sup>

Likewise, individuals undergoing FDG PET/CT scans for cancer screening are advised to inform the radiologist or their oncologist that they have been recently vaccinated, or, if possible, to have COVID-19 vaccination at least two weeks before a scheduled scan or as soon as possible afterwards. Treatment should not be delayed.

## 5.7.2 AEFIs

Adverse events following immunisation (AEFIs) with the COVID-19 vaccines are being closely monitored during clinical trials and by post marketing surveillance. A dedicated COVID-19 vaccine AEFI reporting tool is available online from CARM (see section 1.6.3). Medsafe reports weekly on the AEFI reported to CARM after COVID-19 vaccinations (see [medsafe.govt.nz/COVID-19/vaccine-report-overview.asp](https://medsafe.govt.nz/COVID-19/vaccine-report-overview.asp)).

A list of adverse events of special interest (AESIs), including those previously associated with immunisation in general and with the particular vaccine platforms, was created by Safety Platform for Emergency Vaccines (SPEAC) in collaboration with the Coalition for Epidemic Preparedness Innovations (CEPI) and based on existing and new Brighton Collaboration case definitions. For further information, see [brightoncollaboration.us/covid-19](https://brightoncollaboration.us/covid-19). Global pharmacovigilance and active safety monitoring systems continue to watch for both AESI and unexpected AEFI.

## mRNA COVID-19 vaccine – Comirnaty (Pfizer/BioNTech)

Overall, no AESI signals were detected by the Vaccine Safety Datalink in the US up to 21 days after vaccination, following the administration of over 13 million doses of mRNA-CV (Comirnaty), however, subgroup analyses did find mRNA-CV to be associated with a slight increase in myocarditis and pericarditis in younger people (aged under 30 years).<sup>127, 128</sup>

Preliminary phase II/III clinical trial safety data reported lymphadenopathy in 64 (0.3%) vaccine recipients and six (<0.1%) placebo recipients (follow-up of up to 14 weeks after second dose of a subset of 18,860 participants who received at least one dose of mRNA-CV). Four vaccine-related adverse events were recorded (namely, shoulder

injury related to vaccine administration, lymphadenopathy local to injection site, paroxysmal ventricular arrhythmia and right leg paraesthesia). No deaths were related to either the vaccine or the placebo.<sup>76</sup> During clinical trial follow-up to 1 February 2021, acute peripheral facial paralysis (Bell's palsy) was reported by four vaccinated participants and none in the placebo group.<sup>129</sup> No safety signal has been detected for this condition as an AESI,<sup>130</sup> and safety monitoring is ongoing.

No vaccine-related severe adverse events were seen during the phase II/III clinical trial of mRNA-CV (10 µg) in 1,518 children aged 5–11 years. Lymphadenopathy was reported in ten (0.9 percent) of mRNA-CV (10 µg) recipients. Rashes, with no consistent pattern, considered related to the vaccination were observed in four participants; these were mild and self-limiting with typical onset seven or more days after vaccination. No differences were apparent in vaccine safety between the children who had baseline evidence of previous SARS-CoV-2 infection.<sup>75</sup> As of 19 December 2021 following administration of approximately 8.7 million doses of mRNA-CV (10 µg) in children aged 5–11 years in the US, the majority of reports to VAERS (97.6 percent) were non-serious and 2.4 percent were serious. The most common non-serious reports were due to vaccine administration errors. Of the serious reports, 11 verified cases of myocarditis were reported to VAERS but no chart-confirmed myocarditis cases were reported through the Vaccine Safety Datalink in this age group.<sup>121</sup> Post-licensure surveillance is ongoing internationally.

### Myocarditis and pericarditis

A small increase in incidence of myocarditis, myopericarditis and pericarditis has been observed following the second dose of mRNA-CV vaccination (40.6 cases per million doses in young males and 4.2 cases per million in young females, aged 12–29 years, decreasing to 2.4 and 1.0 per million, respectively, in men and women aged over 30 years).<sup>131</sup> Most cases occur within 14 days of vaccination typically with full recovery after standard treatment and rest.<sup>132, 133</sup> A review of clinical records in the US observed the median time to onset for myocarditis was 3.5 days (interquartile range 3.0–10.8 days) after vaccination and a median of 20 days (range 6.0–41 days) for pericarditis.<sup>133</sup>

Myocarditis and pericarditis are uncommon conditions considered to be associated with viral infection, including COVID-19. Recently vaccinated individuals should seek immediate medical attention if they experience new onset of (acute and persisting) chest pain, shortness of breath or arrhythmia (palpitations). Diagnosis is based on elevated troponin, C-reactive protein and electrocardiogram and/or MRI findings. Report all suspected cases to CARM as Medsafe continues to monitor this AEFI closely. Defer further doses of mRNA-CV if myocarditis or pericarditis occurs after vaccination. Seek specialist immunisation advice, on a case-by-case basis, to consider an appropriate alternative vaccination option, and timing for further primary or booster doses (see section 5.6.2).

### Anaphylaxis

Following approval for use in the US, the VAERS detected 47 cases of anaphylaxis after administration of just under ten million doses (around five cases per million doses) mRNA-CV (Pfizer/BioNTech). The median interval to symptom onset was ten minutes (range <1–1140 minutes), almost 90 percent occurred within 30 minutes of

vaccination.<sup>134</sup> All were successfully treated with adrenaline. See section 5.6 for contraindications and precautions.

### Frail elderly

A follow-up, after approximately two million doses of mRNA-CV were delivered through long-term residential care facilities to elderly and frail residents in the US found no increase in deaths post vaccination.<sup>43</sup> Deaths were to be expected and consistent with the all-cause mortality rate and causes of death for these individuals, who have multiple comorbidities, declining health and require end-of-life care.<sup>43</sup> There are no added safety concerns about the use of this vaccine in the elderly.<sup>135</sup>

## Adenovirus vector COVID-19 vaccine (ChAd-CV): COVID-19 Vaccine AstraZeneca

### Thrombosis with thrombocytopenia syndrome

Adenoviral vector COVID-19 vaccines, including ChAd-CV (AstraZeneca), have been linked to a rare, newly identified condition called thrombosis with thrombocytopenia syndrome (TTS; also known as vaccine-induced immune thrombotic thrombocytopenia, VITT). This condition involves blood clotting in various sites, including the brain and abdomen, with thrombocytopenia (depletion of platelets in the blood). Onset occurs around 4 to 30 days after vaccination and is associated with younger age (under 60 years). The pathogenesis of this conditions resembles heparin-induced thrombocytopenia (HIT) and differs from the coagulation cascade activation seen during the immune response to SARS-CoV-2 infection.<sup>136, 137</sup>

As of 11 November 2021, in Australia, the overall incidence of TTS is estimated to be 2 per 100,000 vaccinated and higher for those aged under 60 years (two to three cases per 100,000) after the first dose of ChAd-CV and much lower after the second dose (0.4 per 100,000). Cases after the first dose in young age groups tend to be more serious with clots in unusual location such as brain and abdomen; whereas cases after second doses tend to be older with clots in common locations such as legs and lungs.<sup>138</sup> Similarly, in the UK as of 3 November 2021, the incidence of AEFI reports for TTS was after the first dose was 20.1 per million in those aged 18–49 years and 10.9 in those aged 50 and over. The incidence after the second dose was 1.9 cases per million doses and more frequent in older rather than younger age groups. There is no indication of an increased risk of these events after a second dose in any age group. Such that, second dose can be offered those who did not experience TTS after the first dose.<sup>139</sup>

### Immune thrombocytopenia

Cases of suspected immune thrombocytopenia (ITP, also known as idiopathic thrombocytopenic purpura) have been reported following vaccination with ChAd-CV. Fewer than one case per 100,000 vaccinations has been reported in Australia to date.<sup>138</sup> Many cases are mild but about 5 percent develop severe bleeding. Cases have extremely low platelet count and signs of thrombocytopenia, which may include unusual bruising, a nosebleed and/or blood blisters in the mouth, and no evidence of thrombosis.

## Capillary leak syndrome

Very rare cases of capillary leak syndrome have been reported following vaccination with viral vector vaccines, which appear more apparent in those who have had previous episodes of capillary leak syndrome. This is an extremely rare relapsing-remitting condition and triggers for relapses are not well understood.

## Guillain-Barré Syndrome

There is a possible, rare association with the ChAd-CV vaccine and Guillain-Barré syndrome (GBS). Like other infections, GBS has been reported as a potential complication of COVID-19.<sup>140, 141</sup> A causal link to the vaccine is still under investigation. Advise those receiving COVID-19 vaccination to seek medical attention if they experience symptoms that could suggest GBS early as medical care can reduce severity and improve outcomes. Symptoms include weakness and paralysis in the hands or feet that can progress to the chest and face over a few days or weeks.

## Adjuvanted recombinant COVID-19 vaccine – Nuvaxovid (Novavax)

Uncommon AEFI reported during clinical trials were lymphadenopathy, hypertension (observed in 1 percent of older adults for three days following vaccination), rash and injection site pruritus. One case of myocarditis was observed in a clinical trial occurring three days after second dose was deemed by the independent safety monitoring committee to most likely be viral myocarditis. No episodes of anaphylaxis were reported.<sup>95</sup> Three cases of myocarditis or myopericarditis and two cases of pericarditis were reported during two clinical trials (one case in placebo group) and in two cross-over studies. Although a causal relationship to the vaccine could not be confirmed, the European Medicines Agency listed heart inflammation as a potential risk.<sup>126</sup>

In a clinical trial, when rCV was given as a second dose after a first dose of mRNA-CV, similar systemic responses were observed to those given mRNA-CV as a second dose and local reactions were generally less frequent.<sup>109</sup>

# 5.8 Public health measures

There is an ongoing COVID-19 pandemic globally. New Zealand has implemented strict pandemic response control measures to limit the spread of SARS-CoV-2 in the community as described at [covid19.govt.nz](https://www.covid19.govt.nz).

All individuals with symptoms of COVID-19 are expected to self-isolate, seek medical advice and be tested for infection. Rapid contact tracing and nasopharyngeal testing continue to be fundamental components of the public health measures.

Immunisation using COVID-19 vaccines is part of the public health strategy aimed at reducing the risk of transmission of SARS-CoV-2 in the community to below an  $R_0$  of 1

and to reduce the severity of disease and minimise the burden on the health care system in the event of a community outbreak.

Further immunisation measures are likely to be implemented as other vaccines become available.

## 5.8.1 Post-exposure prophylaxis and outbreak control

Currently, there is no information on the use of COVID-19 vaccines for post-exposure prophylaxis or outbreak control.

## 5.8.2 Criteria for being considered fully vaccinated in New Zealand against COVID-19

Individuals who have had one dose of mRNA-CV should receive a second dose of the same mRNA-CV to complete the vaccination course (unless contraindicated). Since there is currently no maximum duration between doses one and two of mRNA-CV, it is not indicated to restart the course or to give a third dose (except in cases of severe immunocompromise for ages 12 years and over, see section 5.5.9).

Data is limited on the interchangeability between COVID-19 vaccines. It is preferable, where possible, to complete the course with the same vaccine. Generally, in cases where one dose of any two-dose COVID-19 vaccine has been given outside of New Zealand, one dose of mRNA-CV is recommended at least four weeks after the first vaccine dose.

Those who have a documented and appropriately completed course of a vaccine approved by Medsafe or World Health Organization Emergency Use Listing (WHO EUL) are considered fully vaccinated and require no further primary dose of mRNA-CV.

The '*Fully vaccinated against COVID-19 within Aotearoa New Zealand*' policy statement applies from the point of administration of the last dose for an accepted primary vaccination schedule as given in Table 5.3. There is no maximum time limit since the last dose. These definitions can differ for young people aged under 18 years. For mandates and issuing of vaccination certificates (domestic and internationally), check details with employer and Ministry of Health guidance. Individuals participating in registered COVID-19 vaccine clinical trials (as listed at [trialssearch.who.int](https://trialssearch.who.int)) can apply for temporary exemption (see section 5.8.3).

### **Table 5.3: Criteria for the definition of fully vaccinated for use within the New Zealand border and additional vaccination requirements**

Further changes to these criteria are likely, check the Ministry of Health COVID-19 website for the most up to date policies available from [www.health.govt.nz/covid-19-novel-coronavirus/covid-19-vaccines/covid-19-vaccine-information-health-professionals/covid-19-vaccine-policy-statements-and-clinical-guidance](https://www.health.govt.nz/covid-19-novel-coronavirus/covid-19-vaccines/covid-19-vaccine-information-health-professionals/covid-19-vaccine-policy-statements-and-clinical-guidance).

Vaccine	Vaccination received / required	Additional requirements
Medsafe or WHO EUL <sup>a</sup> approved vaccines	Approved number of doses or two doses of any combination (heterologous) schedule <sup>a</sup>	None
Any other vaccine authorised by at least 1 government or other authority <sup>b</sup>	Completed primary course	Plus one dose of a Medsafe approved vaccine <sup>c</sup> , given at least 28 days after previous vaccine dose
Any other vaccine authorised by at least 1 government or other authority <sup>b</sup>	Single dose	Plus one dose of a Medsafe approved vaccine <sup>c</sup> , given at least 28 days after previous vaccine dose

a. WHO Emergency Use Listing approved vaccines, including Sinopharm (BIBP), Coronovac (Sinovac), Covishield (AstraZeneca/Serum Institute of India), Covaxin (Bharat Biotech) and Covovax (Novavax/Serum Institute of India).

b. See [covid19.trackvaccines.org/vaccines/approved](https://covid19.trackvaccines.org/vaccines/approved)

c. Spikevax (Moderna) is also acceptable as an additional dose, where given outside of New Zealand.

For border workers, health and education sector worker (as per the COVID-19 Public Health Response [Vaccinations] Order 2021) who have been vaccinated previously with one dose of Ad26-CV (Janssen), the recommendation is that one dose of mRNA-CV should also be offered at least four weeks later.

Although not required to meet the definition of fully vaccinated, it is recommended to offer another dose of a vaccine approved by Medsafe to those who have had a single dose of Ad26-CV (Janssen) vaccine, particularly those at high risk of serious disease or occupational exposure, to increase protection against infection.

### 5.8.3 Temporary medical exemptions

Overall, the number of people in New Zealand estimated to be eligible for medical exemptions for COVID-19 vaccination is expected to be small. There are very few situations where a vaccine is contraindicated, and as such, a medical exemption is expected to be rarely required. In some cases, vaccinations may be temporarily deferred due to some acute major medical conditions (major surgery or hospital admission for serious illness).

A vaccination may reasonably be deferred for individuals with some acute major medical conditions, such as undergoing major surgery or hospital admission for a serious illness. Typically, these are time-limited conditions, and where a temporary exemption is considered appropriate, should be discussed with general practitioner, IMAC clinical advisory service or a relevant medical specialist.

- Exemptions are only to be given where a suitable alternative COVID-19 vaccine is not readily available for the individual.
- Exemptions should be for a specified time (up to a maximum of six months), for example, reflecting recovery from clinical conditions or pending the availability of alternative vaccines.

- It is likely that most people who are not medically exempt can be safely vaccinated, with some requiring extra care or precautions.

If the individual meets the strict clinical criteria for vaccination exemption, the doctor or nurse practitioner is required to apply to the Director-General of Health and temporary exemption to be decided by the 'temporary medical exemption panel'. For clinical guidance and further information on applying for temporary medical exemptions, see [health.govt.nz/covid-19-novel-coronavirus/covid-19-response-planning/covid-19-mandatory-vaccinations/covid-19-exemptions-mandatory-vaccination](https://www.health.govt.nz/covid-19-novel-coronavirus/covid-19-response-planning/covid-19-mandatory-vaccinations/covid-19-exemptions-mandatory-vaccination).

If a serious adverse event to a previous dose of a COVID-19 vaccine is used as a reason for the exemption, then this may require discussion with the individual's GP, IMAC clinical advisory service, or relevant medical specialist, if indicated. These reactions do not include common expected local or systemic reactions known to occur within the first few days after vaccination. Examples of serious AEFIs may include: a medically significant illness (eg, myocarditis), potentially life-threatening events (eg, anaphylaxis), severe myalgic encephalomyelitis/chronic fatigue syndrome (ME/CSF) or persistent or significant disability (eg, Guillain-Barré syndrome). See section 5.7.2 for further information on AEFIs.

Those who **are not** medically exempt from vaccination, include:

- people who had an otherwise negative experience with other vaccines in the past, that is not mentioned above
- disabled people once adequate resources are available to support safe delivery. People with disabilities are generally at higher risk from COVID-19, and therefore are a priority for vaccination
- pregnant women. Pregnancy is not a valid reason for exemption in the absence of any of the criteria listed in the above table. Pregnancy is associated with higher risk from COVID-19 compared to the general population and therefore this group are a priority for vaccination.

## 5.9 Variations from the vaccine data sheet

The maximum allowance for ChAd-CV storage at room temperature is reduced from 6 hours, as on the datasheet, to a maximum of 5 hours to take in account the time it takes to remove the vial from the fridge and vaccine drawn up. It is recommended that ChAd-CV always to be stored in the fridge (between +2 to +8°C).

Spacing of at least eight weeks between first and second dose is recommended for mRNA-CV (10 µg) in children aged 5 to 11 years. This differs from the data sheet which recommends an interval of at least 21 days.

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