MINISTRY OF HEALTH
MANATŪ HAUORA

New Zealand Government

(MOH, 2021s)

Immunisation Handbook 2020

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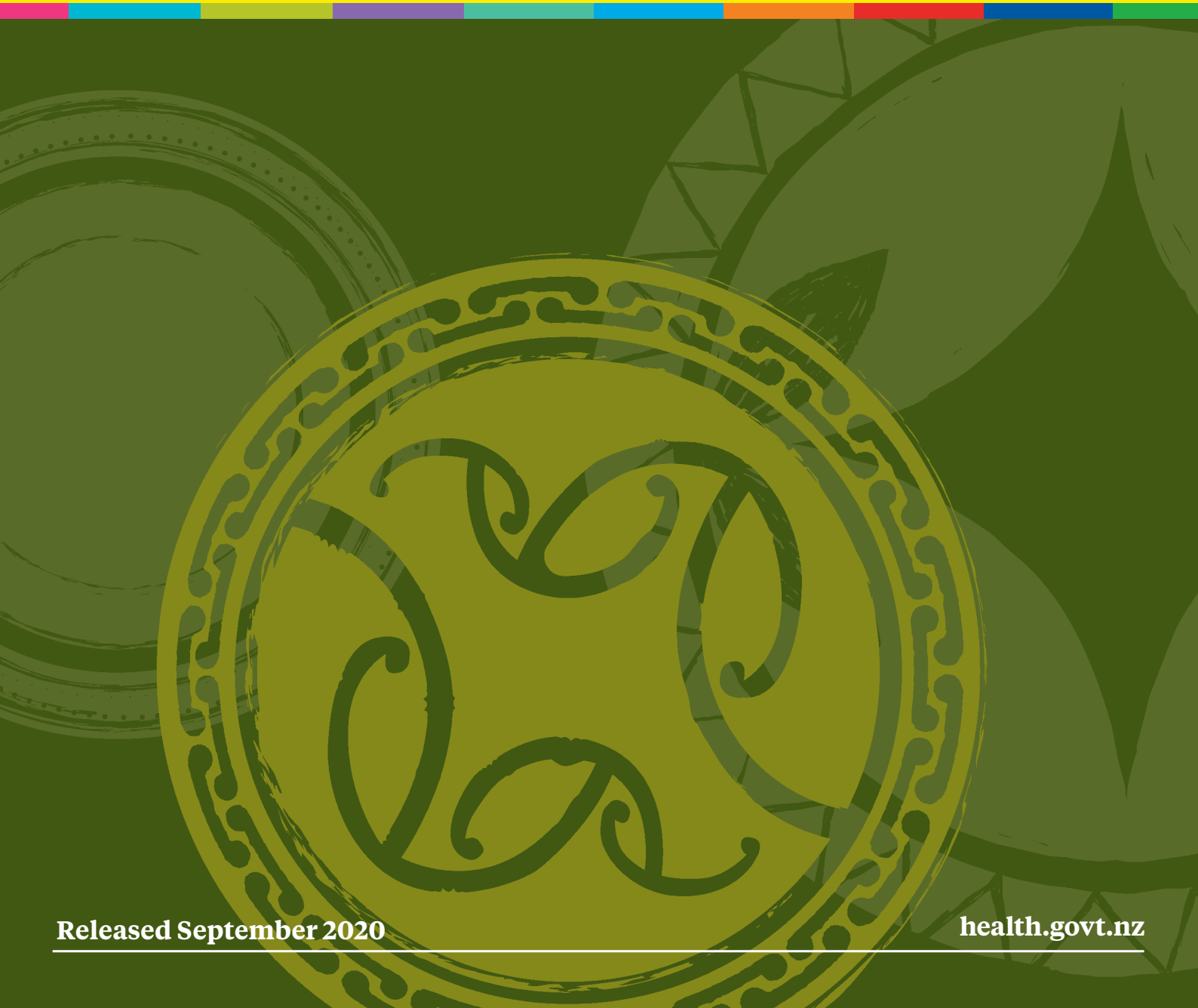

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5 Coronavirus disease (COVID-19)

Key information

Mode of transmission	Aerosolised droplets plus limited fomite transmission.
Incubation period	Most commonly 3–5 days (range 1–14 days).
Period of communicability	From 1–3 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 mild disease.
Funded vaccines	mRNA CV: Comirnaty (manufacturer: Pfizer/BioNTech).
Dose, presentation, route	• 0.3 mL dose • multi-dose vial, to be diluted before use • intramuscular injection. Storage once thawed: • undiluted, +2° to 8°C expiry five days (120 hours) • diluted, +2° to 30°C expiry six hours.
Funded vaccine indications and schedule	Two doses of mRNA-CV, given at least 21 days apart: • for use from age 16 years • given according to prioritised schedule to defined groups at high risk of exposure to SARS-CoV-2 and their close contacts.
Recommended, unfunded	Not available.
Contraindications	A history of anaphylaxis to any component or previous dose of mRNA-CV is a contraindication.
Precautions	A definite history of anaphylaxis to any other product is a precaution not contraindication.
Potential responses to vaccine	Generally mild or moderate: injection site pain, headache, fever, muscle aches a day or two after vaccination.
Vaccine effectiveness	Data from a phase III clinical trial showed efficacy against confirmed COVID-19 to be 95% after two doses.
Public health measures	Ongoing rapid contact tracing and testing for all suspected cases and their close contacts. Quarantine and isolation of close contacts and cases until negative PCR result, if a close contact or a case is deemed recovered.

5.1 Virology

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is 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.[1, 2]

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,[3] and is a suspected zoonosis from bats via an intermediary animal, such as a pangolin.[4] 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. Documented transmission has also occurred through aerosols, direct contact and fomites (objects or materials that can carry infection) – though the latter is rare.

The reproduction number (R_0) (see section 1.2.1) is estimated to be around 2–3.[5, 6] Transmissibility varies by setting, and recently identified variant strains of SARS-CoV-2 have been at the higher range of the estimated R_0 values.[7, 8]

The symptoms of COVID-19 range widely from asymptomatic or a mild respiratory tract infection to severe and unusual 'ground glass' pneumonia, which can lead to severe inflammatory disease and respiratory failure. Classically, COVID-19 presents as respiratory symptoms with new or worsening dry cough, nasal congestion and fever. Unlike other respiratory viral infections, COVID-19 is frequently associated with a loss of taste and smell, and sometimes this is the only symptom. Some cases have reported gastrointestinal symptoms (diarrhoea), muscle aches, headache, 'chills', breathlessness and confusion. For around 80 percent of cases, COVID-19 is a mild disease, but some develop more severe disease, particularly older adults 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 2021, 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) are under investigation. 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 four to five days (range 48 hours–14 days). Individuals may be infectious up to three days before becoming symptomatic, with infectiousness typically peaking within five days of symptom onset.[9] High viral loads are detected in the nose at time of symptom onset.[10] Viable virus is not usually detectable for more than 10 days after symptom onset, although SARS-CoV-2 mRNA has been detected for up to 83 days in respiratory and stool samples.[9, 11] Unlike previous coronavirus outbreaks (SARS and MERS), transmission of SARS-CoV-2 can also occur before the onset of symptoms or from asymptomatic individuals.[12] Viral loads and infectiousness are highest immediately after symptom onset, and most transmission occurs in household settings.[13, 14]

It is currently unclear what protection previous infection with SARS-CoV-2 provides, but neutralising antibodies have been detected for at least eight months after primary infection, even without natural boosting as in New Zealand.[15] 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.[16]

5.2.1 Children and young adults

In younger people, particularly infants and children under 10 years old, infection is often asymptomatic or mildly symptomatic. Those aged under 20 years appear to have a lower susceptibility than adults and are much less likely to develop severe infection requiring hospitalisation.[17] Current evidence suggests that preschool and young school-age children are much less significant in transmitting the disease than has been documented for influenza. In contrast, asymptomatic older school-age children, adolescents and young adults are highly effective transmitters of SARS-CoV-2.[18] However, the role children play in transmitting SARS-CoV-2 is still unclear and could change as new variants evolve. Notably, in household settings, secondary attack rates have been found to be higher when the index case has been a child.[19]

5.2.2 Risk groups

Risk factors for severe disease include older age, male, smoking,[20] obesity and chronic medical conditions, including type 2 diabetes mellitus, cancer, chronic lung disease, cardiovascular disease, chronic kidney disease and being immunocompromised.[21] 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).[21]

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.[22] In Scotland, one-sixth of the COVID-19 cases admitted to hospital were health care workers and their household members.[22] Health care workers have also been implicated in the spread of SARS-CoV-2 within health and long-term care facilities.[22, 23, 24] However, the use of personal protective equipment (PPE) and other measures aimed at reducing nosocomial viral transmission have been shown to be effective. Where COVID-19 is prevalent in the community, health care workers are more likely to catch COVID-19 from an infected household member.[14]

Pregnant women

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.[25, 26] While the absolute risk of severe outcomes among pregnant women is low compared with absolute risk due to advanced age, the rate of ICU care for COVID-19 has been found to be over three-fold higher for pregnant women than for non-pregnant women, and the case-fatality rate in one United States study was 13.6-fold higher for pregnant women.[26] Obesity, hypertension, asthma, autoimmune disease, diabetes and older age are also associated with severe COVID-19 in pregnant women.

Infants of mothers with COVID-19 are at increased risk of preterm birth and neonatal ICU admission.[27] Early studies do not suggest intrauterine transmission, but vertical transmission has been shown in around 3 percent of neonates, predominantly from asymptomatic or mildly symptomatic mothers.[28]

5.2.3 Post-infection complications

Longer lasting effects of infection have been reported, described as 'long-COVID'. Long-COVID appears to affect around 10 percent of those infected, particularly those with at least five symptoms in the first week of illness.[29, 30, 31] Post-acute manifestations include cardiovascular, pulmonary and neurological effects, including chronic fatigue, dyspnoea, specific organ dysfunction and depression.[32] Paediatric multisystem inflammatory syndrome (PIMS-TS) has been temporally and rarely associated with largely asymptomatic SARS-CoV-2 infection in children and adolescents.[33, 34]

5.2.4 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 irrespective, the greater numbers of people becoming infected is increasing the burden of the disease.[7, 8]

5.3 Epidemiology

5.3.1 Global burden of disease

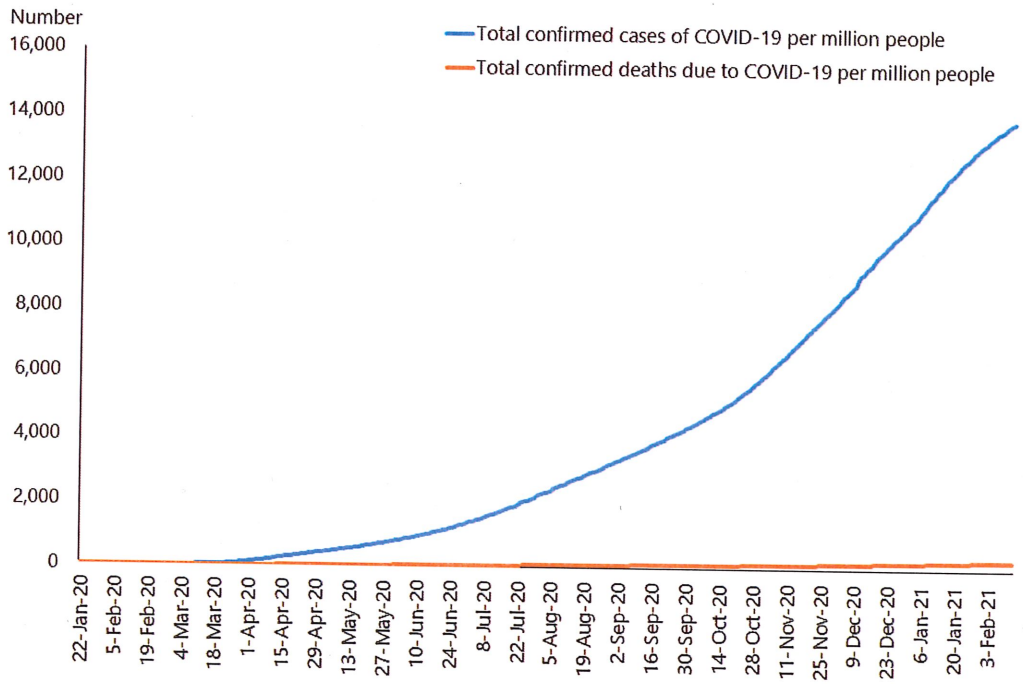
Clusters of distinctive pneumonia cases were observed in Wuhan, China during December 2019. The cause was identified in January 2020 as a novel coronavirus that had genetic and clinical similarity to the coronavirus causing the severe acute respiratory syndrome (SARS) epidemic from 2002 to 2004. Consequently, 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 1 million by late September 2020.

By the end of January 2021, over 2.2 million deaths and over 100 million confirmed cases were reported to the WHO, with around 4 million new cases in a week. The Americas and Europe had the highest numbers of recorded cases (44.2 million in the Americas and 33.5 million in Europe, with the Western Pacific experiencing 1.38 million).

See the **WHO Coronavirus Disease (COVID-19) Dashboard** for the latest official data. Actual rates are expected to be considerably higher than officially reported rates.

The infection-fatality rate, while still high particularly in the older age groups, has reduced since the start of the pandemic, with improved clinical recognition and management and the use of therapies of demonstrated value, such as dexamethasone (see Figure 5.1.).[35, 36]

Figure 5.1: Total confirmed COVID-19 deaths and cases per million people, World (as of 14 February 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. By 31 January 2021, almost 100 million COVID-19 vaccinations had been given worldwide.

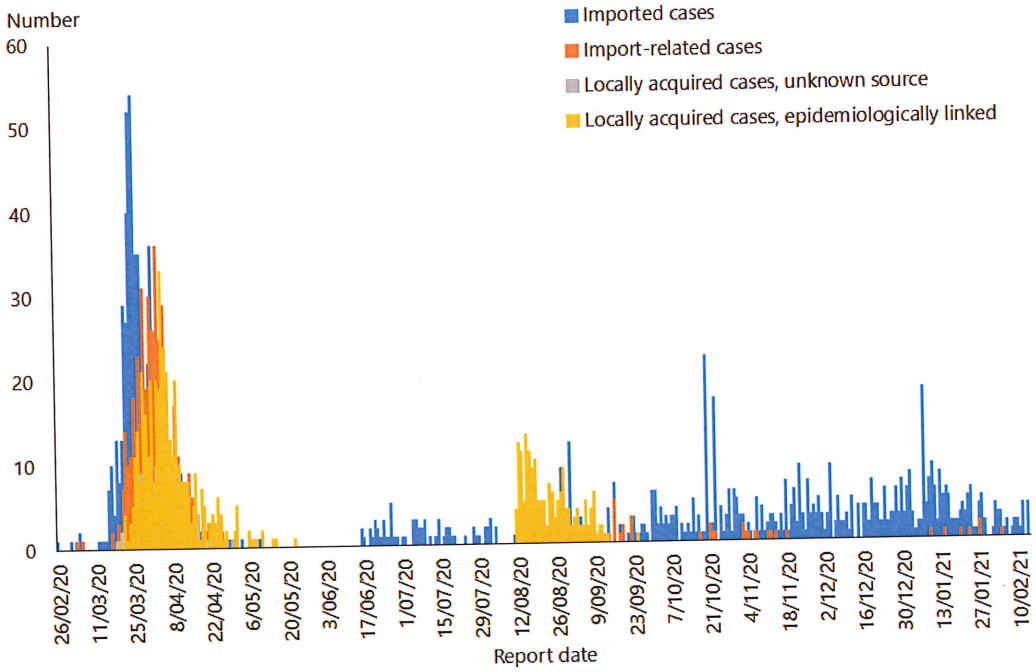
See the **Our World in Data** website for the latest figures.

5.3.2 New Zealand epidemiology

As of 31 January 2021, New Zealand had 2,303 cases and 25 deaths associated with COVID-19 notified since 24 February 2020. Most cases were observed in those aged 20–34 years (803 cases, 34.9%), 35–49 years (499; 21.7%) and 50–64 years (456, 19.8%). This reflects the age groups most likely to be travelling to New Zealand and the proportion of cases arriving at the border being detected in managed quarantine facilities. In children, there were 253 cases (11.0%) aged 5–7 years and 56 cases (2.5%) aged under 4 years. To date, no child under 13 years of age has been hospitalised with COVID-19 in New Zealand.

Currently, most of the cases occur in managed facilities. As of 1 February 2021, 50 percent of total confirmed cases had been imported, 21 percent were related to an imported case and 25 percent were locally acquired from a known case (see Figure 5.2). According to the Ministry of Health, out of 1,535,292 tests conducted from 22 January 2020 (the date of the first test in New Zealand) to 1 February 2021, 1907 tests in the community and 721 tests in managed facilities were positive for SARS-CoV-2.

Figure 5.2: Daily confirmed COVID-19 cases by source, 26 February 2020 to 16 February 2021



Source: ESR

For the current case status, see the **NZ COVID-19 Dashboard** produced by the Institute of Environmental Science and Research (ESR), and for further information about current sources of cases, see the **Ministry of Health COVID-19** website.

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 4).

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. For further information about the country's alert system levels, see the **United against COVID-19** website.

These strategies were effective in containing the spread of SARS-CoV-2 in New Zealand (see case curve for 24 February to 8 June 2020 at **NZ COVID-19 Dashboard** for details. These restrictions were able to rapidly stop the spread of the virus within the country. Only 19 percent of the introductions of virus resulted in ongoing transmission or more than one additional case.[5]

5.4 Vaccines

5.4.1 Introduction

Clinical trials for COVID-19 vaccine candidates began shortly after the pandemic was announced in March 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 approval process is ongoing for each vaccine candidate. Provisional approval was granted on 3 February 2021 for using New Zealand's first COVID-19 vaccine, namely, a mRNA-based COVID-19 vaccine (mRNA-CV, trade name Comirnaty) manufactured by Pfizer/BioNTech.

Funded vaccines

The mRNA-CV consists of messenger ribonucleic acid (mRNA) encoding the full-length spike glycoprotein of the SARS-CoV-2 virus inside a lipid nanoparticle. 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.

mRNA-CV (Comirnaty, Pfizer/BioNtech)

Each 0.3 mL dose of mRNA-CV contains:

- 30 µg of 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-ditetradecylacetamid), distearoylphosphatidylcholine (DSPC)) and cholesterol. As well as buffers, mRNA-CV contains sucrose to protect the lipid during ultra-low temperature storage.

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.[37, 38]

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.[39, 40] Anti-receptor binding domain (anti-RBD) IgG antibodies also increased with dose.[41] 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.

Efficacy – clinical trial data

Efficacy of 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.[42] 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%); 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% without and 94.6% 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% of participants were obese, BMI ≥ 30) and the presence of at least one co-existing medical conditions (in 21%). Moderate early protection against COVID-19 was observed before the second dose.[42] 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.

Efficacy against transmission

Efficacy of mRNA-CV against transmission of SARS-CoV-2 is unclear. It is expected that, at the least, with fewer symptomatic people coughing and producing large quantities of virus, the spread of the virus will be reduced.

Efficacy against new virulent SARS-CoV-2 strains

Currently there is limited clinical data about the efficacy of mRNA-CV against the new virulent SARS-CoV-2 strains. In vitro study data has shown that sera from vaccine recipients are able to neutralise a pseudo-virus bearing variant spike proteins from the United Kingdom strain but are slightly less effective against the South African strain. It is anticipated that small differences in viral neutralisation are unlikely to lead to significant reduction in vaccine effectiveness against the latter variant.

Duration of immunity

There has been insufficient time since the commencement of clinical trials to assess how long immunity lasts following immunisation or natural infection. It is unknown whether booster vaccinations will be required to maintain immunity.

5.4.4 Transport, storage and handling

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

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 six months.

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 5 days (120 hours) once thawed.

Thawed vaccines will be shipped to vaccination sites as per the standard cold chain, as detailed in the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* available at: **www.health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**.

Store undiluted vials at +2°C to +8°C for up to five days (120 hours) or 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.

5.4.5 Dosage and administration

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 age 16 years or older.

Each multi-dose vial 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 five or six 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 20 minutes is recommended (see section 5.6.2). This is to ensure that any anaphylactic-type reactions can receive prompt treatment.

5.5 Recommended immunisation schedule

5.5.1 Recommended and funded

The vaccine will only be available according to a prioritisation schedule for defined groups.

Individuals from the age of 16 years are recommended to received two doses of given at least 21 days apart.

The safety and efficacy of mRNA-CV in children and adolescents aged under 16 years have not yet been established. The vaccine is not currently approved for this age group but is expected to be efficacious and may be deployed in high-risk situations, such as in response to a school-based outbreak of the disease.

5.5.2 Spacing of COVID-19 vaccination and other vaccines

In view of the absence of data on concomitant delivery, and to minimise confusion with any associated reactions, a gap of two weeks is generally recommended between giving mRNA-CV after any other vaccine. However, based on first principles of how these vaccines work, adverse impacts on immunogenicity or safety are unlikely with a shorter gap, so if it is clinically important to deliver in a shorter time, do not delay.

- If it is not practicable to keep a two-week gap between vaccines, then do not delay.
- If a live vaccine has been administered, wait four weeks before giving a COVID-19 vaccine but if not practicable, then do not delay.
- If a COVID-19 vaccine is administered first, then maintain a two-week gap before any other vaccines.

Note: the second mRNA-CV dose is given at least 21 days after the first dose.

5.5.3 Previous history of COVID-19

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 regardless of history of disease. Viral or serological testing is not required before vaccination.

5.5.4 Previous COVID-19 vaccination

Individuals who have had one dose of mRNA-CV should receive a second dose of the same mRNA-CV to complete the vaccination course. There is no data available on the interchangeability between COVID-19 vaccines, and as such, other vaccines should not be substituted to complete the course.

5.5.5 Breastfeeding

While lactating women were not included in phase III studies, as with all schedule vaccines, there are no safety concerns about giving mRNA-CV to lactating women.

5.5.6 Individuals receiving immunosuppressive agents

There are no safety concerns around administering mRNA-CV to individuals who are receiving immunosuppressive agents. As with other non-live vaccines, the antibody response to mRNA-CV may be reduced and protection may be suboptimal but, it is likely to be adequate to protect against severe disease.

5.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines, section 2.1.4 for general contraindications for all vaccines and section 4.3.2 for immune checkpoint inhibitor (immunostimulant) therapy, particularly for oncology patients.

Specialist advice should be sought before administering any vaccine to individuals who are currently being treated with immune checkpoint inhibitors (nivolumab, pembrolizumab, atezolizumab and ipilimumab) or who have discontinued treatment within the past six months (see section 4.3.2).

5.6.1 Contraindications

A history of anaphylaxis to any component or previous dose of mRNA-CV 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 mRNA-CV. 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 mRNA-CV and observation extended to 30 minutes after vaccination in health care settings, where anaphylaxis can be immediately treated with adrenaline.

Pregnancy

Pregnancy is a precaution for mRNA-CV. To date, previous clinical studies have not investigated the mRNA vaccine in pregnancy – a phase II/III clinical trial is underway in the US. Based on how the vaccine works, it is unlikely to pose a specific risk when given to pregnant women. Increased risk of severe COVID-19 disease in pregnancy and adverse fetal outcomes have been documented.[26]

- It is recommended to delay vaccination until after delivery if the pregnant woman is at low risk of exposure, but for those at risk of exposure to SARS-CoV-2, vaccination can be offered with informed consent.
- Routine testing for pregnancy before COVID-19 vaccination is not recommended.
- Women who are trying to become pregnant do not need to avoid pregnancy after receiving mRNA-CV.

5.7 Potential responses and AEFIs

5.7.1 Potential responses

Commonly reported responses to mRNA-CV (during clinical trials and post-licensure) are 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 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.[42, 43] Paracetamol can be taken for pain and discomfort following vaccination.

5.7.2 AEFIs

Adverse events following immunisation (AEFIs) with mRNA-CV are being closely monitored during clinical trials and post marketing surveillance. A list of adverse events of special interest (AESI), including those previously associated with immunisation in general and with particular vaccine platforms, has been 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 the **Brighton Collaboration COVID-19** website. Global pharmacovigilance and active safety monitoring systems continue to watch for both AESI and unexpected AEFI. As of 16 January 2021, no AESI signals had been detected up to 21 days after vaccination by the Vaccine Adverse Event Reporting System (VAERS) in the US, following the administration of 121,000 doses of mRNA-CV (Comirnaty).[43]

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.[42] 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.[44] No safety signal has been detected for this condition as an AESI, and clinical trial safety monitoring is ongoing.

Following approval for use in the US, the VAERS detected 50 cases of anaphylaxis after administration of 9,943,247 doses (five cases per million doses) mRNA-CV (Pfizer/BioNTech). The median interval to symptom onset was 10 minutes (range <1–150 minutes), 90 percent occurred within 30 minutes of vaccination.[43] All were successfully treated with adrenaline. See section 5.6 for contraindications and precautions.

A follow-up, after approximately 2 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.[43] 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.[43] There are no added safety concerns about the use of this vaccine in the elderly.[43, 45]

5.8 Public health measures

There is an ongoing COVID-19 pandemic globally. New Zealand has implemented strict pandemic response control measures to prevent the spread of SARS-CoV-2 in the community. New Zealand has a four-level alert system to stipulate the measures that

the whole population needs to take (as described on the **Unite against COVID-19** website).

All individuals with symptoms of COVID-19 are expected to seek medical advice and be tested for infection. Rapid contract 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. The initial phases of the vaccination programme are aimed at protecting those at risk of exposure to SARS-CoV-2 at the border or in health care facilities and to prevent the spread of the virus into the community.

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 mRNA-CV for post-exposure prophylaxis or outbreak control.

5.9 Variations from the vaccine data sheet

None applicable.

References

1. V'Kovski P, Kratzel A, Steiner S, et al. 2020. Coronavirus biology and replication: implications for SARS-CoV-2. *Nature Reviews: Microbiology* 1–16.
2. Walls AC, Park YJ, Tortorici MA, et al. 2020. Structure, function, and antigenicity of the SARS-CoV-2 spike glycoprotein. *Cell* 181(2): 281–92 e6.
3. Lam TT, Jia N, Zhang YW, et al. 2020. Identifying SARS-CoV-2-related coronaviruses in Malayan pangolins. *Nature* 583(7815): 282–5.
4. Xiao K, Zhai J, Feng Y, et al. 2020. Isolation of SARS-CoV-2-related coronavirus from Malayan pangolins. *Nature* 583(7815): 286–9.
5. Geoghegan JL, Ren X, Storey M, et al. 2020. Genomic epidemiology reveals transmission patterns and dynamics of SARS-CoV-2 in Aotearoa New Zealand. *Nat Commun* 11(1): 6351.

6. Hussein M, Toraih E, Elshazli R, et al. 2021. Meta-analysis on serial intervals and reproductive rates for SARS-CoV-2. *Annals of Surgery* 273(3): 416–23.

7. Horby P, Huntley C, Davies N, et al. 2021. *NERVTAG note of B.1.1.7 severity*. Government U. URL: **https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/955239/NERVTAG_paper_on_variant_of_concern__VOC__B.1.1.7.pdf**. (accessed 5 February 2021).

8. Public Health England. 2020. *Investigation of novel SARS-CoV-2 variant. Variant of Concern 202012/01. Technical briefing 2*. England PH. URL: **https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/949639/Technical_Briefing_VOC202012-2_Briefing_2_FINAL.pdf** (accessed 5 February 2021).

9. Cevik M, Tate M, Lloyd O, et al. 2021. SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis. *The Lancet Microbe* 2(1): e13–e22.

10. Zou L, Ruan F, Huang M, et al. 2020. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *New England Journal of Medicine* 382(12): 1177–9.

11. Singanayagam A, Patel M, Charlett A, et al. 2020. Duration of infectiousness and correlation with RT-PCR cycle threshold values in cases of COVID-19, England, January to May 2020. *Euro Surveillance* 25(32).

12. Bai Y, Yao L, Wei T, et al. 2020. Presumed asymptomatic carrier transmission of COVID-19. *JAMA* 323(14): 1406–7.

13. Liu Y, Yan LM, Wan L, et al. 2020. Viral dynamics in mild and severe cases of COVID-19. *Lancet Infectious Diseases* 20(6): 656–7.

14. Piccoli L, Ferrari P, Piumatti G, et al. 2021. Risk assessment and seroprevalence of SARS-CoV-2 infection in healthcare workers of COVID-19 and non-COVID-19 hospitals in Southern Switzerland. *The Lancet Regional Health – Europe* 1.

15. Whitcombe AL, McGregor R, Craigie A, et al. 2020. Comprehensive analysis of SARS-CoV-2 antibody dynamics in New Zealand. *medRxiv (preprint published online 11 December 2020)*.

16. Lumley SF, O'Donnell D, Stoesser NE, et al. 2021. Antibody status and incidence of SARS-CoV-2 infection in health care workers. *New England Journal of Medicine* 384(6): 533–40.

17. Viner RM, Mytton OT, Bonell C, et al. 2021. Susceptibility to SARS-CoV-2 infection among children and adolescents compared with adults: a systematic review and meta-analysis. *JAMA Pediatr* 175(2): 143–56.

18. Goldstein E, Lipsitch M, Cevik M. 2021. On the effect of age on the transmission of SARS-CoV-2 in households, schools and the community. *Journal of Infectious Diseases* 223(3): 362–9.

19. Lopez Bernal J, Panagiotopoulos N, Byers C, et al. 2020. Transmission dynamics of COVID-19 in household and community settings in the United Kingdom. *medRxiv* (preprint published online 22 August).

20. Reddy RK, Charles WN, Sklavounos A, et al. 2021. The effect of smoking on COVID-19 severity: a systematic review and meta-analysis. *Journal of Medical Virology* 93(2): 1045–56.

21. Williamson EJ, Walker AJ, Bhaskaran K, et al. 2020. Factors associated with COVID-19-related death using OpenSAFELY. *Nature* 584(7821): 430–6.

22. Shah ASV, Wood R, Gribben C, et al. 2020. Risk of hospital admission with coronavirus disease 2019 in healthcare workers and their households: nationwide linkage cohort study. *BMJ* 371: m3582.

23. Arons MM, Hatfield KM, Reddy SC, et al. 2020. Presymptomatic SARS-CoV-2 infections and transmission in a skilled nursing facility. *New England Journal of Medicine* 382(22): 2081–90.

24. Jefferies S, French N, Gilkison C, et al. 2020. COVID-19 in New Zealand and the impact of the national response: a descriptive epidemiological study. *Lancet Public Health* 5(11): e612–23.

25. Kotlar B, Gerson E, Petrillo S, et al. 2021. The impact of the COVID-19 pandemic on maternal and perinatal health: a scoping review. *Reprod Health* 18(1): 10.

26. Lokken E, Huebner E, Taylor GG, et al. 2021. Disease severity, pregnancy outcomes and maternal deaths among pregnant patients with SARS-CoV-2 infection in Washington State. *American Journal of Obstetrics and Gynecology*.

27. Allotey J, Stallings E, Bonet M, et al. 2020. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ* 370: m3320.

28. Adhikari EH, Moreno W, Zofkie AC, et al. 2020. Pregnancy outcomes among women with and without severe acute respiratory syndrome coronavirus 2 infection. *JAMA Netw Open* 3(11): e2029256.

29. Greenhalgh T, Knight M, A'Court C, et al. 2020. Management of post-acute covid-19 in primary care. *BMJ* 370: m3026.

30. Sivan M, Taylor S. 2020. NICE guideline on long COVID. *BMJ* 371: m4938.

31. Sudre C, Murray B, Varsavsky T, et al. 2020. Attributes and predictors of Long-COVID: analysis of COVID cases and their symptoms collected by the Covid Symptoms Study App. *medRxiv* (preprint published online 19 December).

32. Del Rio C, Collins LF, Malani P. 2020. Long-term health consequences of COVID-19. *JAMA*.

33. Carter MJ, Shankar-Hari M, Tibby SM. 2021. Paediatric inflammatory multisystem syndrome temporally-associated with SARS-CoV-2 infection: an overview. *Intensive Care Medicine* 47(1): 90–3.

34. Jiang L, Tang K, Levin M, et al. 2020. COVID-19 and multisystem inflammatory syndrome in children and adolescents. *Lancet Infectious Diseases* 20(11): e276–88.

35. Our World in Data. 2021. *Mortality Risk of COVID-19*. URL: **https://ourworldindata.org/mortality-risk-covid** (accessed 2 February 2021).

36. Roser M, Ritchie H, Ortiz-Ospina E, et al. 2020. *Coronavirus Pandemic (COVID-19)*. Published online at OurWorldInData.org. URL: **https://ourworldindata.org/coronavirus** (accessed 1 February 2021).

37. Callaway E. 2020. The race for coronavirus vaccines: a graphical guide. *Nature* 580(7805): 576-7.

38. Flanagan KL, Best E, Crawford NW, et al. 2020. Progress and pitfalls in the quest for effective SARS-CoV-2 (COVID-19) vaccines. *Frontiers in Immunology* 11: 579250.

39. Walsh EE, Frenck R, Falsey AR, et al. 2020. RNA-based COVID-19 vaccine BNT162b2 selected for a pivotal efficacy study. *medRxiv* (preprint published online 26 August).

40. Walsh EE, Frenck RW Jr, Falsey AR, et al. 2020. Safety and immunogenicity of two RNA-based Covid-19 vaccine candidates. *New England Journal of Medicine* 383(25): 2439–50.

41. Mulligan MJ, Lyke KE, Kitchin N, et al. 2020. Phase I/II study of COVID-19 RNA vaccine BNT162b1 in adults. *Nature* 586(7830): 589–93.

42. Polack FP, Thomas SJ, Kitchin N, et al. 2020. Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. *New England Journal of Medicine* 383(27): 2603–15.

43. Shimbabukuro T, CDC-COVID-19 Vaccine Task Force. 2021. *COVID-19 vaccine safety update* (ACIP) ACoIP. URL: **https://www.cdc.gov/vaccines/acip/meetings/slides-2021-1-27-21.html** (accessed 5 February 2021).

44. Pfizer New Zealand. 2021. *New Zealand Datasheet: Comirnaty COVID-19 vaccine*. Medsafe. URL: **https://www.medsafe.govt.nz/profs/Datasheet/c/comirnatyinj.pdf** (accessed 5 February 2021).

45. World Health Organization. 2021. *GACVS COVID-19 Vaccine Safety Subcommittee meeting to review reports of deaths of very frail elderly individuals vaccinated with Pfizer BioNTech COVID-19 vaccine, BNT162b2*. World Health Organization (WHO) [updated 22 January 2021]; URL: **https://www.who.int/news/item/22-01-2021-gacvs-review-deaths-pfizer-biontech-covid-19-vaccine-bnt162b2**.