

# Australian Technical Advisory Group on Immunisation (ATAGI)

## Clinical guidance on use of COVID-19 vaccine in Australia in 2021 (v7.0)

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*This clinical guidance is for COVID-19 immunisation providers and program staff and is updated based on currently available data. It provides recommendations on the use of the Comirnaty (Pfizer) COVID-19 vaccine and COVID-19 Vaccine AstraZeneca. Recent changes from previous versions of ATAGI Clinical guidance on COVID-19 vaccines in Australia include:*

- *Spikevax (Moderna), an mRNA COVID-19 vaccine, is registered for use in people aged  $\geq 18$  years.*
- *Updated information about serious adverse events that may warrant the use of an alternative vaccine brand for subsequent doses*
- *ATAGI's recommended schedule for Spikevax is 2 doses, 28 to 42 days (4-6 weeks) apart.*
- *The absolute minimum interval for 2 doses of any COVID-19 vaccine to be considered valid is 14 days. ATAGI will provide further guidance regarding a repeat dose after an unacceptably short interval when more information about the use of a third dose becomes available.*

## Key points

- The overarching goal of Australia's COVID-19 vaccination program is to protect all people in Australia from the harm caused by SARS-CoV-2, through preventing serious illness and death, and, as much as possible, disease transmission.
- Delivery of vaccine has been prioritised initially for population groups at increased risk of exposure to SARS-CoV-2 or of severe COVID-19, or occupational groups critical to societal functioning. These are: quarantine and border workers; frontline healthcare workers; aged care and disability care staff and residents; older adults (initially ≥80 years with progression to lower age brackets); people aged ≥12 years with underlying medical conditions associated with an increased risk of severe COVID-19; Aboriginal and Torres Strait Islander adults and adolescents and critical and high-risk workers, including defence, police, fire, emergency services, operators of critical infrastructure and others.
- COVID-19 vaccine is currently recommended for all people aged ≥ 16 years, and for the following groups:
  - Children aged 12-15 years with specified medical conditions that increase their risk of severe COVID-19
  - Aboriginal and Torres Strait Islander children aged 12-15 years
  - All children aged 12-15 in remote communities, as part of broader community outreach vaccination programs.
- Comirnaty (Pfizer Australia Pty Ltd) is provisionally registered by the TGA in people aged ≥12 years and is given in a two-dose schedule. Efficacy against symptomatic COVID-19 is about 95% from seven days after the second dose.
- Spikevax (Moderna Australia Pty Ltd) is provisionally registered in people aged ≥18 years and is given in a two-dose schedule. Efficacy against symptomatic COVID-19 is approximately 94% from two weeks after the second dose.
- COVID-19 Vaccine AstraZeneca (AstraZeneca Pty Ltd) is provisionally registered in people aged ≥18 years and is given in a two-dose schedule. Efficacy against symptomatic COVID-19 ranges from about 62% to 73%, with the higher efficacy seen after a longer interval (12 weeks) between doses. Efficacy from day 22 after the first dose up until 12 weeks is about 73%.
- The effectiveness of all 3 vaccines against symptomatic infection with the Delta strain of SARS-CoV-2 is reduced compared with earlier strains, however protection against hospitalisation is maintained.
- ATAGI recommends completing the vaccination course with the same vaccine. Mixed (heterologous) schedules using 2 different vaccines to complete the primary vaccination course are only recommended in special circumstances such as for those with serious vaccine-attributed adverse events after the first dose and in those who were partially vaccinated overseas with a brand not available in Australia.
- COVID-19 Vaccine AstraZeneca is associated with a rare risk of thrombosis with thrombocytopenia syndrome (TTS). The risk of TTS appears higher in younger adults than in older adults, and is higher after the first dose than the second. Comirnaty and Spikevax are not associated with a risk of TTS.
- mRNA vaccines (i.e., Comirnaty or Spikevax) are the preferred vaccines over COVID-19 Vaccine AstraZeneca in people aged <60 years, and in pregnant people. COVID-19 Vaccine AstraZeneca continues to be recommended in people aged 18 to <60 years when the benefits outweigh risks, including in outbreak settings.
- Pregnant women and adolescents aged ≥12 years are a priority group for vaccination. Either Comirnaty or Spikevax should be routinely offered to pregnant people at any stage of pregnancy.
- Either Comirnaty or Spikevax is recommended in people with a past history of certain precautionary conditions for COVID-19 Vaccine AstraZeneca; cerebral venous sinus thrombosis

(CVST), heparin induced thrombocytopenia (HIT), idiopathic splanchnic (mesenteric, portal, splenic) vein thrombosis, and antiphospholipid syndrome with thrombosis. Comirnaty or Spikevax are recommended for the second dose for people in these groups who have received a first dose of COVID-19 Vaccine AstraZeneca.

- Contraindications to COVID-19 Vaccine AstraZeneca include anaphylaxis to a previous dose or to an ingredient; history of capillary leak syndrome; thrombosis with thrombocytopenia after a previous dose, or any other serious adverse event attributed to a previous dose.
- Contraindications to Comirnaty or Spikevax include anaphylaxis to a previous dose or to an ingredient of an mRNA COVID-19 vaccine; myocarditis and/or pericarditis attributed to a previous dose, or any other serious adverse event attributed to a previous dose.
- Precautions to vaccination include a history of generalised (non-anaphylactic) reaction to a prior dose or an ingredient, past anaphylaxis to medications/vaccines which may contain polyethylene glycol (relevant for Comirnaty and Spikevax) or polysorbate 80 (relevant for COVID-19 Vaccine AstraZeneca), and a history of confirmed mastocytosis (a mast cell disorder) with recurrent anaphylaxis which requires treatment.
- Precautionary conditions specific to Comirnaty and Spikevax include a recent history of inflammatory cardiac illness within the past 6 months, e.g., myocarditis, pericarditis, endocarditis; acute rheumatic fever (i.e., with active myocardial inflammation) or acute rheumatic heart disease; complex or severe congenital heart disease; acute decompensated heart failure or a history of cardiac transplant. People with these conditions **can still receive Comirnaty or Spikevax**, however consultation with a GP, immunisation specialist or cardiologist is recommended prior to vaccination to discuss the best timing of vaccination and to consider if any additional precautions are needed.
- Co-administration of a COVID-19 vaccine with other vaccines is not routinely recommended. A minimum 7-day interval is advised between administration of a COVID-19 vaccine and any other vaccine, including influenza vaccine. This interval can be shortened (including to same day administration) in special circumstances.
- Recording of COVID-19 vaccine administration in the Australian Immunisation Register (AIR) is mandatory.
- Notification of adverse events following immunisation should be made through the specified reporting mechanisms for your state or territory, or to the Therapeutic Goods Association (TGA).

## Additional Resources

The following resources are available for providers and consumers:

### **Resources for providers**

- [COVID-19 Vaccine training](#)
- [Information for providers: COVID-19 vaccination consent and FAQs](#)
- [Information for immunisation providers on thrombosis with thrombocytopenia syndrome \(TTS\) following COVID-19 vaccination](#)
- [Provider guide to COVID-19 vaccination of people with immunocompromise](#)
- [Consent form for COVID-19 vaccination](#)
- [Guidance on the use of multi-dose vials for COVID-19 vaccination](#)
- [Product Information for Comirnaty available at the Therapeutic Goods Administration \(TGA\) website](#)
- [Product Information for COVID-19 Vaccine AstraZeneca at the Therapeutic Goods Administration \(TGA\) website](#)
- [Product Information for Spikevax available at the Therapeutic Goods Administration \(TGA\) website](#)
- [ATAGI clinical advice on use of a different COVID-19 vaccine as the second dose in special circumstances](#)
- [Primary Care Approach to Thrombosis with Thrombocytopenia Syndrome \(TTS\) after COVID-19 Vaccine AstraZeneca](#)
- [Joint ATAGI-CSANZ Guidance on Myocarditis and/or Pericarditis after mRNA COVID-19 Vaccines](#)

### **Shared decision guides**

- [COVID-19 vaccination decision guide for women who are pregnant, breastfeeding, or planning pregnancy](#)
- [COVID-19 vaccination decision guide for frail older people, including those in residential aged care facilities](#)
- [COVID-19 vaccination decision guide for people receiving palliative or end-of-life care](#)
- [COVID-19 vaccination decision guide for people with immunocompromise](#)
- [COVID-19 vaccination – Weighing up the potential benefits against risk of harm from COVID-19 Vaccine AstraZeneca](#)

### **Resources for consumers**

- [Preparing for COVID-19 vaccination](#)
- [Information on COVID-19 Pfizer \(COMIRNATY\) vaccine](#)
- [After your Pfizer \(COMIRNATY\) vaccine](#)
- [Information on COVID-19 Moderna \(Spikevax\) vaccine](#)
- [After your Moderna \(Spikevax\) vaccine](#)
- [Information on COVID-19 Vaccine AstraZeneca](#)
- [After your AstraZeneca vaccine](#)
- [Patient information sheet on AstraZeneca COVID-19 vaccine and thrombosis with thrombocytopenia syndrome \(TTS\)](#)

Additional resources are available at [www.health.gov.au](http://www.health.gov.au), including 'easy read' and translated versions of patient fact sheets.

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## The virus: SARS-CoV-2

The pandemic of coronavirus disease (COVID-19) is caused by the severe acute respiratory coronavirus 2 (SARS-CoV-2), a virus first identified in December 2019. Bats appear to be the reservoir of SARS-CoV-2. SARS-CoV-2 is a single-stranded RNA betacoronavirus in the same subgenus as the severe acute respiratory virus syndrome (SARS) virus, and is more distantly related to the Middle East respiratory syndrome (MERS) virus.<sup>1</sup>

SARS-CoV-2 contains four main structural proteins: spike (S) glycoprotein, small envelope (E) glycoprotein, membrane (M) glycoprotein and nucleocapsid (N) protein.<sup>2</sup> Most COVID-19 vaccines target the spike protein, which contains two subunits: S1 and S2. S1 contains the receptor binding domain, which binds to the angiotensin converting enzyme 2 receptor on host cells, facilitating entry.<sup>3</sup>

Several SARS-CoV-2 variant strains have been identified. Some variants are associated with higher transmissibility and increased severity or duration of disease. These variants are classified as a Variant of Concern (VOC) or Variant of Interest depending on their attributes.<sup>4</sup>

As of July 2021, four VOCs have been identified: Alpha, first identified in the United Kingdom; Beta, first identified in South Africa; Gamma, first identified in Brazil, and Delta, first identified in India.<sup>4</sup> These variants are more transmissible than the wild type of SARS-CoV-2, and they have become the predominant strains in their countries of origin and in other settings.<sup>5</sup> The Delta variant has been shown to be more transmissible than other variants. In many countries, it has replaced Alpha as the dominant variant of SARS-CoV-2.<sup>6</sup> Some early surveillance data also suggests that it causes a higher rate of severe outcomes compared to other variants.<sup>7,8</sup>

Immunogenicity and efficacy/effectiveness of current COVID-19 vaccines against some variant strains of SARS-CoV-2 is reduced compared to the ancestral strain. For the Delta variant, vaccine effectiveness of both Comirnaty and COVID-19 Vaccine AstraZeneca against symptomatic infection has been reduced compared to Alpha but is maintained against hospitalisation.<sup>9</sup> Refer to the **Vaccine Information** section for further information.

Clinically significant variations in the efficacy/effectiveness of different vaccines against these emerging strains will continue to be monitored to determine if any changes to vaccines or to vaccine policy are needed.

## The disease: COVID-19

SARS-CoV-2 causes asymptomatic or mild disease in 81% of cases; severe illness (with dyspnoea, hypoxia or >50% lung involvement on imaging within 48 hours) in 14%; and critical illness in 5%.<sup>10</sup> The most common symptoms are fever and cough.<sup>11</sup> Other common symptoms include myalgia, headache, dyspnoea, sore throat, diarrhoea and nausea/vomiting. Loss of smell or taste and rhinorrhoea occur in fewer than 10% of cases.

Older age is an important risk factor for severe COVID-19, as shown in several international systematic reviews. In comparison with those aged <50 years, the risk of death from COVID-19 progressively increases throughout each decade of age, from about 2 times high for those aged 50–59 years to >10 times higher for those aged ≥80 years.<sup>12</sup> Findings were similar when results were adjusted for other risk factors.<sup>13</sup> In Australia, prior to the implementation of the COVID-19 vaccination program, the COVID-19 case fatality ratio increased substantially with age, from 0.6% in those aged 50–64 years, to 7.0% in those aged 65–79 years and 33.8% in those aged ≥80 years.<sup>14</sup>

Certain medical conditions are associated with an increased risk of severe illness from COVID-19. Refer to **Box 1** for a list of specified medical conditions.

There are certain occupational and environmental settings that may place individuals at higher risk of COVID-19 exposure either because of a higher risk of infected individuals being present and/or because the conditions enable rapid spread of the virus. These include healthcare facilities; aged care and disability care facilities; border and quarantine facilities; and some industries such as meat processing. Refer to the **Recommendations** section for further information.

Further information about COVID-19 is available in the [COVID-19 CDNA National Guideline for Public Health Units](#). Information about Australian epidemiology is available on the [Department of Health website](#), including regular epidemiological reports.

## **The COVID-19 vaccination program**

The aim of the COVID-19 vaccination program in Australia is to reduce COVID-19 related harm by preventing serious illness and death, and, as much as possible, disease transmission. Information on COVID-19 vaccination program implementation in Australia is available on the [Department of Health website](#).

The epidemiology of COVID-19 is a key determinant informing the most appropriate use of COVID-19 vaccines, in addition to the characteristics and availability of COVID-19 vaccines.

In Australia, outbreak control measures (including contact tracing, testing and isolation; border control and quarantine; and physical distancing) have been successful in limiting the spread of COVID-19 in the community.<sup>15</sup> However, disease outbreaks continue to occur following virus introduction from international travellers and then transmission in the community.

In settings where there is no sustained SARS-CoV-2 community transmission, the initial focus of a vaccine program is to prevent importation of cases and demonstrate reciprocity to critical (particularly frontline) workers at highest risk of exposure to SARS-CoV-2.<sup>16</sup> Subsequent priority groups include older adults, particularly those living in residential aged care or disability care facilities, and those with medical risk factors for severe illness or death from COVID-19.



## Vaccine, doses and administration

The following COVID-19 vaccines have been provisionally approved for use in Australia. The [TGA website](#) provides access to the TGA-approved Product Information for each vaccine. Key information from the Product Information is extracted below.

### **Comirnaty (generic name BNT162b2)**

Sponsor:	Pfizer Australia Pty Ltd
Approved age for use:	≥12 years
Presentation:	Multi-dose vial without preservative, each vial containing 6 doses in 0.45 mL. <b>Requires dilution</b> with 1.8 mL of sterile 0.9% NaCl without preservative into each multi-dose vial.
Volume/strength:	0.3 mL (30 µg) per dose
Schedule:	2 doses at least 21 days apart
Administration route:	Intramuscular injection into deltoid muscle
Ingredients:	Each 0.3mL dose contains 30 mcg mRNA encoding the SARS-CoV-2 spike glycoprotein  List of excipients: <ul style="list-style-type: none"><li>- ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate) (ALC-0315)</li><li>- 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide (ALC-0159)</li><li>- Distearoylphosphatidylcholine (DSPC)</li><li>- Cholesterol</li><li>- Potassium chloride</li><li>- Monobasic potassium phosphate</li><li>- Sodium chloride</li><li>- Dibasic sodium phosphate dihydrate</li><li>- Sucrose</li><li>- Water for injections</li></ul>

### **Spikevax (generic name Elasmoran or mRNA-1273)**

Sponsor:	Moderna Australia Pty Ltd
Approved age for use:	≥18 years
Presentation:	Multi-dose vial without preservative, each vial containing 10 doses in 5 mL.
Volume/strength:	0.5 mL per dose
Schedule:	2 doses, 28 days apart
Administration route:	Intramuscular injection, preferably into deltoid muscle
Ingredients:	Each 0.5 mL dose contains 100 µg mRNA encoding the SARS-CoV-2 spike glycoprotein  List of excipients: <ul style="list-style-type: none"><li>- Heptadecan-9-yl 8-[2-hydroxyethyl-(6-oxo-6-undecyloxyhexyl)amino]octanoate</li><li>- Cholesterol</li><li>- Distearoylphosphatidylcholine</li><li>- 1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG)</li><li>- Trometamol</li><li>- Trometamol hydrochloride</li><li>- Acetic acid</li><li>- Sodium acetate trihydrate</li><li>- Sucrose</li><li>- Water for injection</li></ul>

### COVID-19 Vaccine AstraZeneca

Sponsor:	AstraZeneca Pty Ltd
Approved age for use:	≥18 years
Presentation:	Multi-dose vial without preservative, each vial containing either 8 doses in 4 mL or 10 doses in 5 mL.
Volume/strength:	0.5 mL per dose
Schedule:	2 doses, 4 to 12 weeks apart
Administration route:	Intramuscular injection into deltoid muscle
Ingredients:	Each 0.5 mL dose contains $5 \times 10^{10}$ viral particles of ChAdOx1-S <sup>a</sup>  List of excipients: <ul style="list-style-type: none"><li>- Histidine</li><li>- Histidine hydrochloride monohydrate</li><li>- Sodium chloride</li><li>- Magnesium chloride hexahydrate</li><li>- Disodium edetate (EDTA)</li><li>- Sucrose</li><li>- Ethanol absolute</li><li>- Polysorbate 80</li><li>- Water for injection</li></ul>

a. Recombinant, non-replicating chimpanzee adenovirus vector encoding the SARS-CoV-2 Spike glycoprotein

## Recommendations

COVID-19 vaccination is recommended for all people aged ≥16 years to protect against COVID-19. Additionally, ATAGI currently recommends that the following children aged 12-15 years be prioritised for vaccination:

- Children with specified medical conditions that increase their risk of severe COVID-19 [**Box 1**]
- All Aboriginal and Torres Strait Islander children aged 12-15 years
- All children aged 12-15 in remote communities, as part of broader community outreach vaccination programs that provide vaccines for all ages (≥12 years).

Recommendations for use in all other children aged 12-15 years will be made in updated advice within the coming weeks.

There is a limited supply of COVID-19 vaccines in the initial phases of the COVID-19 vaccination program. Therefore, vaccine allocation is being determined based on several factors, such as timing of supply, priority target groups and logistical considerations. The following population groups are prioritised initially:

#### People with occupational risk of exposure to SARS-CoV-2

People in certain occupations are at increased risk of being infected with SARS-CoV-2 and/or transmitting the virus to vulnerable people who have risk factors for severe illness. These include:

- frontline healthcare workers, who have a seven-fold increased risk of severe COVID-19 compared with non-essential workers (RR 7.42; 95% CI: 5.52–10.00)<sup>17</sup>
- quarantine and border workers
- aged care and disability care staff
- critical and high-risk workers including defence, police, fire and emergency services; certain laboratory staff; meat processing workers; and select others.

#### Residents of aged care and disability care facilities

Aged care facilities have been the setting for a number of serious COVID-19 outbreaks in Australia.<sup>18</sup>

#### Older adults

Older age is by far the strongest risk factor associated with morbidity and mortality from COVID-19.<sup>10,13,19</sup>

### All Aboriginal and Torres Strait Islander people aged ≥ 12

Aboriginal and Torres Strait Islander people are at increased risk of severe illness and death from COVID-19 due to multiple factors, including a high prevalence of underlying chronic health conditions associated with severe COVID-19 and a greater likelihood of living in communities where social distancing cannot be practised.<sup>20</sup>

While the impact of COVID-19 on Aboriginal and Torres Strait Islander people to date has been mitigated by existing control measures (especially restriction of movement into communities), the factors above warrant prioritisation for vaccination.

### People aged ≥ 12 with medical conditions that increase their risk of severe COVID-19

People aged ≥ 12 years with certain underlying chronic medical conditions, outlined in **Box 1**, are at increased risk of severe illness with COVID-19 and should be prioritised for vaccination, particularly older adults and those who have multiple comorbidities.

### Pregnant women and pregnant adolescents aged ≥ 12 years

Compared to non-pregnant women, pregnant women who contract COVID-19 have an increased risk of severe illness, including increased odds of intensive care admission (OR 2.13, 1.53 – 2.95; I<sup>2</sup> 71.2%), need for invasive ventilation (OR 2.59, 2.28 – 2.94<sup>2</sup> 0%).<sup>21</sup> Compared to pregnant women who did not have COVID-19, women who had COVID-19 during pregnancy may have a higher risk of stillbirth (OR 2.84, 95% CI 1.25 to 6.45), neonatal death (OR 2.77, 95% CI 0.92 to 8.37), need for admission to the neonatal intensive care unit (odds ratio 4.89, 95% CI 1.87 to 12.81, I<sup>2</sup>=96.2%).<sup>21</sup>

## Box 1: Conditions associated with increased risk of severe COVID-19

Conditions	Notes
<b>Immunocompromising conditions</b>	
Haematological diseases or cancers	<b>Including</b> leukaemia, lymphoma or myeloma resulting in immunocompromise  Recommend discussion with specialist regarding optimal timing of vaccination
Solid organ transplant recipients who are on immune suppressive therapy	Recommend discussion with specialist regarding optimal timing of vaccination
Bone marrow transplant recipients or chimeric antigen receptor T-cell (CAR-T) therapy recipients or those with graft host disease	Recommend discussion with specialist regarding optimal timing of vaccination
Non-haematological cancer	Diagnosed within the past 5 years or on chemotherapy, radiotherapy, immunotherapy or targeted anti-cancer therapy (active treatment or recently completed) or with advanced disease regardless of treatment
Survivors of childhood cancers	
Chronic inflammatory conditions requiring medical treatments	<b>Including:</b> systemic lupus erythematosus, rheumatoid arthritis, Crohn's disease, ulcerative colitis, and similar who are being treated with disease modifying anti-rheumatic drugs (DMARDs) or immune-suppressive or immunomodulatory therapies.  <b>Generally not inclusive</b> of people living with osteoarthritis, fibromyalgia, myalgic encephalomyelitis/chronic fatigue syndrome or similar non-immunocompromising inflammatory conditions.
Primary or acquired immunodeficiency	<b>Including</b> congenital causes of immunodeficiency and HIV/AIDS
<b>Other underlying conditions</b>	
Chronic renal (kidney) failure with a eGFR of <44mL/min	<b>Does not include</b> mild-moderate chronic kidney disease

Heart disease	<b>Including</b> ischaemic heart disease, valvular heart disease, cardiomyopathies and pulmonary hypertension, and complex congenital heart disease
Chronic lung disease	<b>Including</b> chronic obstructive pulmonary disease, cystic fibrosis, interstitial lung disease and severe asthma (defined as requiring frequent hospital visits or the use of multiple medications).  <b>Does not include</b> Mild or moderate asthma
Diabetes	
Obesity	Defined for adults as severe obesity with BMI $\geq 40\text{kg/m}^2$ ; and for children as BMI $\geq 95^{\text{th}}$ percentile for age
Chronic liver disease	
Chronic neurological conditions	<b>Including</b> stroke, dementia, multiple sclerosis, motor neurone disease, Parkinson's disease, cerebral palsy and epilepsy. <b>Generally not inclusive</b> of migraine or cluster headaches
Poorly controlled blood pressure (defined as two or more pharmacologic agents for blood pressure control, regardless of readings)	
Those living with significant disability requiring frequent assistance with activities of daily living	<b>Including</b> Down syndrome, muscular dystrophy, traumatic brain and spinal cord injury, severe intellectual disability
Those with severe mental health conditions	<b>Including</b> schizophrenia and bi-polar disorder
Children with complex chronic disease	
Pregnant people	

## Vaccine preference recommendations

Comirnaty or Spikevax are preferred over COVID-19 Vaccine AstraZeneca in people aged < 60 years. This is based on the higher risk and observed severity of thrombosis and thrombocytopenia syndrome (TTS), a rare adverse event associated with COVID-19 Vaccine AstraZeneca, in people < 60 years compared to those  $\geq 60$ , and the higher risk of severe disease with increasing age among those who get COVID-19. However, COVID-19 Vaccine AstraZeneca can be used in adults aged < 60 years if the person has made an informed decision based on an understanding of the risks and benefits. In outbreak settings, adults <60 years of age should strongly consider COVID-19 Vaccine AstraZeneca if they are unable to access Comirnaty or Spikevax.

People of any age who have received their first dose of COVID-19 Vaccine AstraZeneca without any serious adverse events attributable to the first dose and without any new contraindications should receive a second dose of COVID-19 Vaccine AstraZeneca. This is supported by data indicating a substantially lower rate of TTS following a second COVID-19 Vaccine AstraZeneca dose in the United Kingdom (UK).

mRNA COVID-19 vaccines (Comirnaty or Spikevax) are also the recommended vaccines for pregnant women. Pregnant women who have already received a first dose of COVID-19 Vaccine AstraZeneca can receive either an mRNA COVID-19 vaccine or COVID-19 Vaccine AstraZeneca for their second dose, although an mRNA COVID-19 vaccine is preferred.

For those aged 60 years and above, the individual benefits of receiving a COVID-19 vaccine are greater than in younger people. The risks of severe outcomes with COVID-19 increase with age and are particularly high in older unvaccinated individuals. The benefit of vaccination in preventing COVID-19 with COVID-19 Vaccine AstraZeneca outweighs the risk of TTS in this age group and underpins its ongoing use in this age group.

## Considerations for special populations

### People who are immunocompromised

COVID-19 vaccine is recommended for people who are immunocompromised because of their increased risk of severe illness with COVID-19.<sup>22</sup> There are many causes and varying degrees of immunocompromise, and the risk of COVID-19 will vary according to the number and type of underlying conditions, medical management and other factors.

Immunogenicity studies in immunocompromised populations are limited and the population who are immunocompromised are clinically diverse. As there is no clear correlate of protection from immunogenicity data, translating findings from immunogenicity studies to predict anticipated protection against asymptomatic or symptomatic infection, hospitalisation, or severe disease is difficult. Post-vaccination antibody geometric mean titres have been generally lower among people with higher degrees of immunosuppression such as solid organ transplant and haematological malignancies<sup>23-28</sup> and those with B cell depleting therapies (anti-CD20 monoclonal antibodies).<sup>29-31</sup> Early studies in small numbers (n=12-54) of people with HIV infection have shown antibody responses similar to healthy people.<sup>32-34</sup> Fewer studies have evaluated T cell responses (cellular immunity) with some<sup>35</sup> finding reduced responses and others relatively preserved cellular immunity

Some early pre-print vaccine effectiveness studies suggest that immunocompromising conditions may be associated with a reduction in protection against COVID-19 compared immunocompetent individuals. This finding, however, has not been consistently demonstrated and these studies have some limitations. Overall, vaccine effectiveness against COVID-19 was around 70-90% in immunocompromised,<sup>37-40</sup> compared with effectiveness of around 84-94% in the general population. One preprint study by Whitaker et al (2021)<sup>40</sup> examined both Comirnaty and COVID-19 Vaccine AstraZeneca in the United Kingdom to 13 June 2021 and estimated vaccine effectiveness in a general immunocompromised population against medically attended PCR-confirmed COVID-19 after 2 doses of Comirnaty at 73.0% (33.9-89.0%) and COVID-19 Vaccine AstraZeneca at 74.6% (18.7-92.1%) at least 4 weeks post vaccination.

Effectiveness studies<sup>39,40</sup> in immunocompromised individuals confirm that it is essential to receive 2 doses of a COVID-19 vaccine, as protection may be suboptimal after a single dose; estimates have ranged from 4-43%<sup>39-41</sup> in partially vaccinated immunocompromised individuals. These studies were conducted prior to the widespread dominance of the Delta variant and may reflect effectiveness against older strains.

At this time, given the reassuring level of protection provided by two doses, ATAGI does not recommend additional vaccine doses for immunocompromised people. However, consideration on this topic is ongoing and will be informed by evolving evidence. For further information refer to the [COVID-19 vaccination decision guide for people with immunocompromise](#) and [Provider guide to COVID-19 vaccination in people with immunocompromise](#).

### Children

COVID-19 vaccine is currently recommended for children aged 12-15 in the following groups:

- Those with specified medical conditions that increase their risk of severe COVID-19 [**Box 1**]
- All Aboriginal and Torres Strait Islander children aged 12-15 years
- All children aged 12-15 in remote communities, as part of broader community outreach vaccination programs that provide vaccines for all ages (≥12 years).

Recommendations for use in all other children in this age group will be made in updated advice within the coming weeks.

Preliminary evidence suggests that children and adolescents have a lower susceptibility to SARS-CoV-2 compared to adults and play a lesser role in transmission at a population level.<sup>42</sup> Children and adolescents with COVID-19 are commonly asymptomatic or have mild or moderate symptoms. A systematic review that included data on illness severity in 1,475 children with COVID-19 reported asymptomatic infection in 15%, mild illness in 42%, moderate illness in 39%, severe illness in 2% and critical illness in 0.7%.<sup>43</sup>

A rare but serious condition associated with COVID-19 in children is Paediatric Inflammatory Multisystem Syndrome Temporally associated with SARS-CoV-2 (PIMS-TS), which can present with features similar to those of Kawasaki disease or toxic shock syndrome.<sup>44</sup>

Severe illness from COVID-19 in children is uncommon but is more likely in those with certain pre-existing medical conditions.<sup>45-47</sup>

Efficacy of COVID-19 vaccination has been demonstrated in adolescents. A phase II-III trial of Comirnaty which included 2260 adolescents aged 12 to 15 years found a vaccine efficacy against symptomatic COVID-19 in this age cohort of 100% (95% CI 75.3 – 100) from 7 days after the second dose, and an acceptable safety profile.<sup>48</sup> The most common adverse event was injection site pain (79-86%), followed by fatigue (60-66%) and headache (55-65%). Fever occurred in 20% of participants who received Comirnaty, and was slightly more frequent in those aged 12-15 (37%) than in those aged 16-25 (32%). Systemic adverse events were more common after the second dose. No vaccine-related serious adverse events were reported. Trials of Comirnaty and other COVID-19 vaccines in younger cohorts are underway.

### Women and adolescents who are pregnant, breastfeeding or planning pregnancy

Pregnant people are a priority group for COVID-19 vaccination and should be routinely offered an mRNA COVID-19 vaccine (Comirnaty or Spikevax) at any stage of pregnancy. Pregnant women with COVID-19 have an increased risk of severe illness and adverse pregnancy outcomes.

mRNA vaccines (Comirnaty or Spikevax) are the preferred COVID-19 vaccines for people who are pregnant. This is based on the growing body of evidence supporting the safety of mRNA vaccines in pregnancy, while there are still very limited data on the safety of viral vector vaccines (such as COVID-19 Vaccine AstraZeneca) in pregnancy. However pregnant women who cannot access an mRNA vaccine can consider vaccination with COVID-19 Vaccine AstraZeneca if the benefits to the individual outweigh the potential risks. Pregnant women who received a first dose of COVID-19 Vaccine AstraZeneca can receive either an mRNA COVID-19 vaccine (Comirnaty or Spikevax) or COVID-19 Vaccine AstraZeneca for their second dose, although an mRNA vaccine is preferred.

Women who are breastfeeding or planning pregnancy are preferred to have an mRNA COVID-19 vaccine because of their age (i.e. mRNA vaccines are the preferred vaccines for all people under 60) and because post-marketing studies demonstrate safety of these vaccines in pregnancy. However, there are no theoretical safety concerns associated with the use of COVID-19 Vaccine AstraZeneca specific to breastfeeding or planning pregnancy, and women in these groups who cannot access an mRNA COVID-19 vaccine should consider vaccination with COVID-19 Vaccine AstraZeneca, particularly in outbreak settings.

Refer to the [Shared decision making guide for women who are pregnant, breastfeeding or planning pregnancy](#) for further information.

Pregnant women with COVID-19 have a higher risk of intensive care admission (OR 2.13, 95% CI 1.53 - 2.95), invasive ventilation (2.59, 95% CI 2.28 - 2.94), need for extra corporeal membrane oxygenation (OR 2.02, 95% CI 1.22 - 3.34) and preterm birth (OR 1.47, 95% CI 1.14 – 1.91) compared to non-pregnant reproductive aged women<sup>21</sup> with COVID-19. Factors which increase the risk of severe illness and death from COVID-19 during pregnancy include increased maternal age, high body mass index and pre-existing co-morbidities. Infants born to mothers with COVID-19 are more likely to require admission to the neonatal intensive care unit (OR 4.89, 95% CI 1.87 – 12.81) versus those without COVID-19.

In a prospective cohort study of over 35,000 pregnant women who received an mRNA COVID-19 vaccine (54% received Comirnaty, 46% received Spikevax), the adverse event profile was similar to that of non-pregnant women.<sup>49,50</sup> Pregnant women were slightly more likely to report injection site pain, and less likely to report generalised symptoms such as fever or tiredness. Fever of 38°C or above was reported by fewer than 1% of pregnant women after the first dose of Comirnaty or Spikevax, and fewer than 5% after the second dose of Comirnaty, and 11.8% after the second dose of Spikevax. Fever of 39°C occurred in < 0.05% of pregnant

participants after the first dose, and 0.5% after the second dose. The findings from this large study are supported by other smaller observational studies.<sup>49-51</sup>

The same study reported on pregnancy and neonatal outcomes in 827 women who received an mRNA COVID-19 vaccine in pregnancy, and did not identify any safety concerns.<sup>52</sup> Complications such as preterm delivery, stillbirth, small for gestational age infants and congenital anomalies occurred at a similar rate to what is seen in the general population. In the clinical trial for Comirnaty, 23 women became pregnant during the study period, of which 11 had received Comirnaty.<sup>53</sup> In the clinical trial for Spikevax, 13 individuals were unknowingly pregnant or became pregnant during the trial, of which six received the vaccine.<sup>54</sup> Information about the outcomes of their pregnancies is awaited. Animal studies of Comirnaty and Spikevax have not shown any negative effects on fertility or pregnancy.<sup>54,55</sup> A phase 2/3 randomised controlled trial of Comirnaty in pregnant women is underway in the US.<sup>56</sup>

Evidence of vaccine effectiveness of mRNA COVID-19 vaccines in pregnant women is also emerging. A retrospective cohort study that included 15,060 pregnant women in Israel, including 7,530 who received Comirnaty, estimated effectiveness against PCR-confirmed SARS-CoV-2 infection from  $\geq 28$  days post vaccination to be 78% (95% CI 57-89%).<sup>57</sup>

## People with a past SARS-CoV-2 infection

Past infection with SARS-CoV-2 is not a contraindication to vaccination; however, it is recommended that vaccination be deferred for up to six months after the acute illness in those who have had PCR-confirmed SARS-CoV-2 infection. Evidence suggests that past infection reduces the risk of reinfection for at least 6 months.<sup>58</sup> Individuals who have prolonged symptoms from COVID-19 beyond six months can be vaccinated on a case-by-case basis.

In the phase II/III trial of Comirnaty, the vaccine was administered to a small number of people with serological evidence of previous SARS-CoV-2 infection. There were no specific safety issues reported among these individuals. A similarly high overall efficacy was shown when participants who had had previous SARS-CoV-2 infection were also included for analysis, but a separate estimate of efficacy for these individuals was not reported.

In the phase III trial of Spikevax, a small number of participants had evidence of current or prior SARS-CoV-2 infection based on RT-PCR or serology testing (n = 680).<sup>59</sup> Adverse reactions among this population occurred at lower or similar rates compared to individuals without prior SARS-CoV-2 infection and no specific safety concerns were observed.<sup>54</sup> A separate analysis of vaccine efficacy in this subgroup was not performed (only one previously infected individual in the placebo group subsequently developed COVID-19 in the study period).<sup>54,59</sup> In the pooled analysis of phase II/III trials of COVID-19 Vaccine AstraZeneca, 718 participants (3%) were found to be seropositive, and the safety profile was consistent across participants with or without prior evidence of SARS-CoV-2 infection at baseline. Seropositive participants had increased anti-spike antibody responses after the first dose, but no further increase after the second.<sup>60</sup>

Serological testing or other testing to detect current or previous infection with SARS-CoV-2 before vaccination is neither necessary nor recommended before vaccination.

## Timing of administration of other vaccines, including influenza vaccine

The preferred minimum interval between receipt of a COVID-19 vaccine and any other vaccine, including influenza vaccine, is 7 days. A shorter interval (i.e., less than 7 days, including co-administration) is acceptable in the following settings:

- Increased risk of COVID-19 or another vaccine-preventable disease (e.g., COVID-19 outbreak, influenza outbreak, tetanus-prone wound)
- Logistical issues e.g., difficulty scheduling visits to maintain the 7-day interval

This also means that a person may be able to receive another vaccine in between their two doses of a COVID-19 vaccine, if appropriate.

As with any other vaccine, vaccination should be deferred if the recipient is acutely unwell. If a person experiences a short term expected adverse event such as fever following vaccination, other vaccines should not be administered until the adverse event has resolved.

Co-administration or near administration (e.g., within days) of two or more vaccines can sometimes lead to a higher frequency of mild to moderate adverse events or make the attribution of potential adverse events to vaccination more challenging.

This advice is based on the current absence of data on the immunogenicity and safety of these vaccines when co-administered, and may change as further information becomes available.

If co-administration of an influenza vaccine and COVID-19 vaccine occurs, revaccination is not required for either vaccine. The patient should be informed of the possibility of an increased likelihood of common adverse effects and be asked to [report any untoward adverse events](#).

## Co-administration of antipyretics/analgesics

Prophylactic use of paracetamol or ibuprofen is not recommended before receiving a COVID-19 vaccine. Antipyretics and analgesics can be taken after vaccination for management of vaccine-related side effects such as fever and myalgia, if required.

## Recommended schedule

### Comirnaty and Spikevax

The recommended interval between two doses for Comirnaty is 21 to 42 days (3 - 6 weeks). The recommended interval between two doses for Spikevax is 28 to 42 days (4 - 6 weeks). This interval range allows time for logistical considerations, including supply and timing of access to vaccine at the individual and clinic levels, and is extrapolated from data on the intervals applied in clinical trials.

Although Comirnaty and Spikevax may provide partial protection against COVID-19 as soon as 12 days after the first dose, this protection is likely to be short lived. A two-dose course is recommended for optimal protection.

ATAGI advises that the absolute minimum interval between the first and second dose for the second dose to be considered as acceptable and valid as fully vaccinated in the Australian Immunisation Register (AIR) is 14 days. The immune response and clinical protection with this shortened interval may be sub-optimal. If two doses have inadvertently been given at a shorter than the minimum acceptable interval, it is not currently recommended that a vaccine dose is repeated. There is still a likelihood of clinical protection in that individual in the short term. ATAGI will provide further guidance on repeat doses after an unacceptably short interval when more information about the use of a third dose becomes available.

Longer intervals between first and second doses of Comirnaty or Spikevax, e.g., 8-12 weeks may need to be recommended during program rollout if epidemiological considerations warrant a change (e.g., during an outbreak response to ensure available doses are provided as first doses to as many people as possible). This requires local decision-making taking into account information on supply, logistics and disease epidemiology.

If the second dose of Comirnaty or Spikevax is administered later than the recommended interval, no further doses are required.

### COVID-19 Vaccine AstraZeneca

The recommended interval between two doses of COVID-19 Vaccine AstraZeneca is 12 weeks.

The minimum interval between doses is 4 weeks. Shortening the interval from 12 weeks to no less than 4 weeks between doses is acceptable and may be appropriate in certain circumstances, for example, imminent travel or anticipated risk of COVID-19 exposure. In an outbreak setting, ATAGI recommends an interval of 4 to 8 weeks between doses. In clinical trials, the timing of administration of COVID-19 Vaccine AstraZeneca ranged from approximately 4 weeks up to 26 weeks. In a post-hoc analysis, vaccine efficacy following the second dose of ATAGI Clinical Guidance on COVID-19 Vaccine in Australia\_v7.0



COVID-19 Vaccine AstraZeneca progressively increased with a longer interval between doses and appeared to be greatest when the interval was  $\geq 12$  weeks. Short-term efficacy from 3 weeks after the first dose, before the second dose and up to 12 weeks post vaccination was about 73% (95% CI: 48.8–85.8).<sup>61</sup> Also refer to the **Vaccine information** section for further information. Short term efficacy from 22 days until 90 days after a single dose was 76% (95% CI: 59.3–85.9). The duration of protection after a single dose has not yet been established, and a second dose is recommended for optimal protection.

If a dose has been inadvertently given before the minimum 4-week interval, it is not currently recommended that the vaccine dose be repeated. ATAGI advises that the absolute minimum interval between the first and second dose is 14 days for the second dose to be considered as acceptable and valid as fully vaccinated in the Australian Immunisation Register (AIR), acknowledging that the immune response and clinical protection with this shortened interval may be sub-optimal. If two doses have inadvertently been given at a shorter than the minimum acceptable interval, it is not currently recommended that a vaccine dose is repeated. There is still a likelihood of clinical protection in that individual in the short term. ATAGI will provide further guidance regarding a repeat dose after an unacceptably short interval when more information about the use of a third dose becomes available.

If the second dose of COVID-19 Vaccine AstraZeneca is administered later than the recommended interval, no further doses are required.

### Mixed (heterologous) schedules

Based on current evidence, ATAGI recommends using the same COVID-19 vaccine for the two doses of the primary course. Emerging (preprint) data demonstrates that mixed schedules (e.g., COVID-19 Vaccine AstraZeneca as dose 1 and either Comirnaty or Spikevax as dose 2 or, in one small randomised controlled trial, Comirnaty as first dose followed by COVID-19 Vaccine AstraZeneca as the second dose), are immunogenic. They also have an acceptable safety profile in the small cohorts vaccinated with these heterologous schedules.<sup>62-65</sup> Furthermore, preprint data from a large Danish population cohort study indicates that heterologous schedules (either COVID-19 Vaccine AstraZeneca dose 1 and Comirnaty dose 2 or COVID-19 Vaccine AstraZeneca dose 1 and Spikevax dose 2) led to good vaccine effectiveness against PCR-confirmed SARS-CoV-2 infection (88% [95% CI: 83-92%]) from day 14 after dose 2 onwards, and against COVID-19 related hospitalisation and death (VE estimated 100%; no confidence interval estimable due to no COVID-19 related hospitalisations or death seen after dose 2).<sup>66</sup> Larger studies and longer term follow up are required to confirm the safety of this approach.

In the following special circumstances, an alternate brand (or an alternative platform i.e. mRNA versus non mRNA) may be recommended for the second dose:

- People with serious vaccine-attributable adverse events after dose 1 that warrant the use of an alternate vaccine brand for dose 2:
  - anaphylaxis to the first dose of a COVID-19 vaccine (note: anaphylaxis to a previous dose of an mRNA COVID-19 vaccine [Comirnaty or Spikevax] is a contraindication to further doses of either vaccine), OR
  - thrombosis with thrombocytopenia following the first dose of COVID-19 Vaccine AstraZeneca, OR
- any other serious adverse event attributed to a previous dose of a COVID-19 vaccine (and without another cause identified) that:
  - has been reported to state adverse programs and/or the TGA, AND
  - has been determined following review by, and/or on the opinion of, an experienced immunisation provider/medical specialist taking into account whether repeat vaccine doses would be associated with a risk of recurrence of the serious adverse event.\*
- People with a precautionary condition for which the use of Comirnaty or Spikevax are recommended instead of COVID-19 Vaccine AstraZeneca:
  - history of cerebral venous sinus thrombosis (CVST)
  - history of heparin-induced thrombocytopenia

- history of idiopathic splanchnic (mesenteric, portal, splenic) venous thrombosis
- history of anti-phospholipid syndrome (APLS) with thrombosis.
- People given an incomplete course of a COVID-19 vaccine brand not available in Australia.

The recommended interval for administration of a second COVID-19 vaccine dose using any of the alternative brand is 4 to 12 weeks after the first dose, regardless of first dose brand. An interval longer than 12 weeks is acceptable if the second dose cannot be administered during this time window. Further advice is available in [ATAGI clinical advice on use of a different COVID-19 vaccine as the second dose in special circumstances](#)

\* Assessment of adverse events following immunisation requires detailed information on the event, a determination of the likelihood of a causal link with vaccination, as well as the severity of the condition. Serious adverse events are generally defined as those which require hospitalisation (e.g., thrombosis with thrombocytopenia following the first dose of COVID-19 Vaccine AstraZeneca); are medically significant (e.g., immune thrombocytopenia purpura, myocarditis), are potentially life threatening (e.g., anaphylaxis) and/or result in persistent or significant disability (e.g., Guillain-Barre Syndrome). These reactions do not typically include expected local or systemic reactions known to occur within the first few days after vaccination. Attributing a serious adverse event to a previous dose of a COVID-19 vaccine may require discussion with the individual's GP, local immunisation service or relevant medical specialist.

## Repeat vaccination

Additional or booster doses beyond the two-dose course are not currently recommended.

Data on the real-world effectiveness and duration of protection from Comirnaty, Spikevax and COVID-19 Vaccine AstraZeneca are emerging, including against current and emerging strains (variants) of SARS-CoV-2, and will inform future recommendations regarding the need for and timing of booster doses.

In the same way that the influenza vaccines are modified to protect against newly circulating strains each season, COVID-19 vaccines may in future be adapted to protect against SARS-CoV-2 variant strains. Moderna has released preliminary immunogenicity data indicating both a booster with the original Wuhan strain Spikevax vaccine and their booster formulation designed to target against the Beta variant of concern effectively increases neutralising antibody titres approximately six months following original vaccination.<sup>67</sup> The clinical significance of this is as yet unclear.

## Contraindications

Contraindications to COVID-19 Vaccine AstraZeneca are:

- anaphylaxis after a previous dose
- anaphylaxis to any component of the vaccine, including polysorbate 80
- history of capillary leak syndrome
- thrombosis with thrombocytopenia occurring after a previous dose
- any other serious adverse event attributed to a previous dose of COVID-19 Vaccine AstraZeneca (and without another cause identified) that has been reported to state adverse programs and/or the TGA, and, has been determined following review by, and/or on the opinion of, an experienced immunisation provider/medical specialist taking into account whether repeat vaccine doses would be associated with a risk of recurrence of the serious adverse event\*

Contraindications to Comirnaty or Spikevax are:

- anaphylaxis to a previous dose of an mRNA COVID-19 vaccine (Spikevax or Comirnaty) is a contraindication to further doses of either vaccine
- anaphylaxis to any component of the vaccine, including polyethylene glycol (PEG)
- myocarditis and/or pericarditis attributed to a previous dose of either Comirnaty or Spikevax
- any other serious adverse event attributed to a previous dose of Comirnaty or Spikevax (and without another cause identified) that has been reported to state adverse programs and/or the

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TGA, and, has been determined following review by, and/or on the opinion of, an experienced immunisation provider/medical specialist taking into account whether repeat vaccine doses would be associated with a risk of recurrence of the serious adverse event\*

\* Assessment of adverse events following immunisation requires detailed information on the event, a determination of the likelihood of a causal link with vaccination, as well as the severity of the condition. Serious adverse events are generally defined as those which require hospitalisation (e.g., thrombosis with thrombocytopenia following the first dose of COVID-19 Vaccine AstraZeneca); are medically significant (e.g., immune thrombocytopenia purpura, myocarditis), are potentially life threatening (e.g., anaphylaxis) and/or result in persistent or significant disability (e.g., Guillain-Barre Syndrome). These reactions do not typically include expected local or systemic reactions known to occur within the first few days after vaccination. Attributing a serious adverse event to a previous dose of a COVID-19 vaccine may require discussion with the individual's GP, local immunisation service or relevant medical specialist.

## Anaphylaxis after COVID-19 vaccines

The observed rate of anaphylaxis after Comirnaty administration in the United States in early 2021 was 4.7 cases per million doses administered, and the rate of anaphylaxis after Spikevax administration in the same period was 2.5 cases per million doses, based on passive reporting to the Vaccine Adverse Event Report System (VAERS).<sup>68</sup> 89% of cases after the administration of both mRNA vaccines occurred within 30 minutes of vaccination.<sup>68</sup> Comirnaty and Spikevax contain polyethylene glycol (PEG), and it is possible that this component is implicated in anaphylaxis.<sup>69,70</sup> However, anaphylaxis following PEG is reported to be extremely rare (37 case reports between 1977 and 2016).<sup>69</sup>

Anaphylaxis to polysorbate 80, which is an excipient in COVID-19 Vaccine AstraZeneca and is also included in many other vaccines, is rare.<sup>71</sup> Anaphylaxis to COVID-19 Vaccine AstraZeneca is rare. The rate of reported anaphylaxis after COVID-19 Vaccine AstraZeneca in Australia appears similar to the overall rate for other vaccines.

## Precautions

### Specific allergies

The following individuals should be assessed for suitability for vaccination, if necessary, in consultation with an allergist/immunologist or specialist immunisation clinic:

- people with immediate (within 4 hours) and generalised symptoms of a possible allergic reaction (e.g., urticaria/hives), without anaphylaxis, to a previous dose of a COVID-19 vaccine
- people with a generalised allergic reaction (without anaphylaxis) to any component of the COVID-19 vaccine to be administered (e.g., PEG in Comirnaty and Spikevax, or polysorbate 80 in COVID-19 Vaccine AstraZeneca)
- people with a history of anaphylaxis to previous vaccines and/or multiple drugs (injectable and/or oral) where ingredients such as PEG or polysorbate 80 may conceivably be the cause
- people with a history of confirmed mastocytosis with recurrent anaphylaxis that requires treatment.

People in these categories may require vaccination in a facility with medical staff in attendance, observation for at least 30 minutes following administration of a COVID-19 vaccine dose, or vaccination with an alternate brand of COVID-19 vaccine. Refer to [ASCIA Guide: Allergy and COVID-19 Vaccination](#) for more information.

All other vaccine recipients, including those with a history of allergy; anaphylaxis to food, drugs, venom or latex; or allergic conditions, including asthma, atopic dermatitis (eczema) or allergic rhinitis (hay fever), should be observed for at least 15 minutes following administration of the vaccine at the clinic site in accordance with the current recommendations in the Australian Immunisation Handbook. It is important that all providers are trained in [anaphylaxis management](#).

For individuals suspected to have had an allergic reaction to their first dose of a COVID-19 vaccine, seek advice from the state/territory specialist immunisation service or a specialist allergist/immunologist. These individuals may need a clinical assessment prior to the second vaccine dose. Before and during each vaccination session, providers should check that up-to-date protocols, equipment, medicines and trained staff to manage anaphylaxis are available. Refer to the [Preparing for vaccination](#) section of the Australian Immunisation Handbook.

## Precautionary conditions for COVID-19 Vaccine AstraZeneca

Comirnaty or Spikevax are recommended instead of COVID-19 Vaccine AstraZeneca in people of any age with:

- a history of cerebral venous sinus thrombosis (CVST)
- a history of heparin-induced thrombocytopenia (HIT)
- a history of idiopathic splanchnic (mesenteric, portal, splenic) thrombosis
- a history of antiphospholipid syndrome with thrombosis.

For people in the above groups who have received a first dose of COVID-19 Vaccine AstraZeneca, Comirnaty or Spikevax is recommended for the second dose.

People who develop immune thrombocytopenia (ITP) within 42 days after receiving COVID-19 Vaccine AstraZeneca should consult a haematologist regarding whether to proceed with the second dose using the same or an alternate vaccine, and the timing of the second dose.

## Precautionary conditions for Comirnaty and Spikevax

People with a history of any of the following conditions **can receive Comirnaty or Spikevax** but advice should be sought from a GP, immunisation specialist or cardiologist about the best timing of vaccination and whether any additional precautions are recommended:

- Recent (i.e., within the past 6 months) inflammatory cardiac illness e.g., myocarditis, pericarditis, endocarditis
- Acute rheumatic fever (i.e., with active myocardial inflammation) or acute rheumatic heart disease
- People aged 12-29 years with dilated cardiomyopathy
- Complex or severe congenital heart disease including single ventricle (Fontan) circulation
- Decompensated heart failure
- Cardiac transplant recipients.

Vaccination should be deferred in people with ongoing cardiac inflammation, or an alternative vaccine (e.g., COVID-19 Vaccine AstraZeneca) considered in people aged  $\geq 60$  years. People who develop myocarditis and/or pericarditis after receiving Comirnaty or Spikevax should defer further doses and discuss options of further COVID-19 vaccination with their treating doctor.

For further information, refer to the [Joint ATAGI-CSANZ Guidance on Myocarditis and/or Pericarditis after mRNA COVID-19 Vaccines](#)

## Acute illness

Vaccination should be deferred in people with an acute illness, including febrile illness (axillary temperature  $\geq 38.5^{\circ}\text{C}$ ). This is a general precaution for all vaccines and will avoid potential misattribution of symptoms from the acute illness as being due to the vaccine or vice-versa.

## People with bleeding disorders

People with bleeding disorders and people who are receiving anticoagulant therapy may develop haematomas at intramuscular injection sites. Before vaccination, the recipient should be informed about this risk. Comirnaty, Spikevax and COVID-19 Vaccine AstraZeneca should be administered by intramuscular injection. Subcutaneous administration is not recommended, as no data are available on the safety or immunogenicity of COVID-19 vaccines given via this route.

When administering an intramuscular injection to an individual with a bleeding disorder, a 23 or 25 gauge needle should be used, and firm pressure applied to the site without rubbing for at least 2 minutes.<sup>72</sup>

For further information on how to safely administer vaccines intramuscularly to people with bleeding disorders, refer to the [Vaccination for people with bleeding disorders](#) section in the Australian Immunisation Handbook.

## Adverse events

### Comirnaty

In the phase II/III trial of Comirnaty, adverse events within 7 days following vaccination were very common but generally mild to moderate and well tolerated.

Injection site reactions were very common (refer to **Table 1**). Injection site pain was reported with similar frequency after dose 1 and dose 2, and was more common in people aged 16 to 55 years (83% post dose 1 and 78% post dose 2) than in people aged >55 years (71% and 66 %, respectively). It also occurred at similar rates in people aged 12 to 15 years (86% post dose 1 and 79% post dose 2), and those aged 16-25 (83% and 78% respectively).<sup>48</sup> Injection site redness and swelling occurred in <10% of all participants. These local reactions were generally mild to moderate, had a median onset on the day following vaccination, and resolved within 1 to 2 days.

Systemic adverse events were more common following the second dose of Comirnaty than the first dose (refer to **Table 1**). The median onset of systemic adverse events was 1–2 days after vaccine receipt, with resolution in a median of 1 day.<sup>73</sup> Adverse events were generally milder and less frequent in adults aged >55 years than in those aged 16–55 years. It also occurred at similar rates in people aged 12 to 15 years (e.g. fatigue 60% post dose 1 and 66% post dose 2; headache 55% post dose 1 and 65% post dose 2), and those aged 16-25 (fatigue 60% and 66%, respectively; headache 54% and 61% respectively).<sup>48</sup> Most adverse events were mild to moderate severity and did not affect daily activities. The reported rates of diarrhoea and vomiting did not differ between vaccine and placebo recipients.

The median duration of follow-up for adverse events was 2 months after the second dose. Lymphadenopathy, though uncommon (<1%), was more common in vaccine recipients than in placebo recipients (64 cases [0.3%] versus 6 cases [<0.1%]) and is likely related to the expected immune response to the vaccine. The cases of lymphadenopathy were generally mild to moderate and resolved after a median time of 10 days.

There were four cases of Bell's palsy (acute peripheral facial paralysis) in the vaccination group (with onset at 3, 9, 37 and 48 days after a dose respectively), and no cases in the placebo group.<sup>73</sup> However, this observed frequency was consistent with the expected background rate of Bell's palsy in the general population and thus may not have a causal relationship to vaccination.

There were no substantive differences in the frequency of adverse events overall observed in the clinical trial by age, sex, race, ethnicity or baseline SARS-CoV-2 status. There was no evidence of enhanced COVID-19 disease in vaccinated individuals who developed SARS-CoV-2 infection after completing vaccination, with only one severe case in the eight vaccine failures.<sup>74</sup>

Anaphylaxis after Comirnaty has been reported rarely. Refer to **Contraindications** for further information.

Myocarditis and pericarditis have been reported following Comirnaty. Refer to section below on **Myocarditis and pericarditis after mRNA COVID-19 vaccines**.

Table 1: Frequency of select common adverse events reported within 7 days following each dose of Comirnaty in phase II/III trial<sup>73</sup>

	12 – 15 years of age		16–55 years of age		>55 years of age	
			Dose 1	Dose 2	Dose 1	Dose 2
<b>Injection site pain</b>	86%	79%	83%	78%	71%	66%
<b>Fever</b>	10%	20%	4%	16%	1%	11%
<b>Fatigue</b>	60%	66%	47%	59%	23%	51%
<b>Headache</b>	55%	65%	42%	52%	25%	39%
<b>Chills</b>	28%	42%	14%	35%	6%	23%
<b>Muscle pain</b>	24%	32%	21%	37%	14%	28%
<b>Joint pain</b>	10%	16%	11%	22%	9%	19%
<b>Required paracetamol</b>	37%	51%	28%	45%	20%	38%

## Spikevax

In the phase III trial of Spikevax that included participants aged ≥18 years, adverse reactions in the first seven days following vaccination were very common but generally mild to moderate and well tolerated.<sup>59</sup>

Adverse reactions at the injection site were very common after both the first and second dose of the vaccine. Injection site pain was the most frequently reported after both the first (84%) and second (88%) vaccine dose and was more common in participants aged 18-64 years than those aged 65 years or over, (Table 2). Axillary lymphadenopathy (swelling of the lymph nodes) within 7 days from vaccination occurred in 10% and 14% of vaccine recipients after the first and second doses, respectively. Injection site redness occurred in less than 10% of participants with injection site swelling in 6% after the first dose, and 12% after the second dose. Most local adverse reactions were grade 1 (not interfering with activities) or 2 (some interference with activities or repeated use of over-the-counter pain relief) in severity, with the proportion of grade 2 reactions higher after the second than the first dose. The mean duration 3 days after both dose 1 and dose 2. Delayed-onset injection site reactions that started after the first 7 days, including pain, redness or swelling, occurred in 0.8% after the first dose, and 0.2% after the second dose. These reactions resolved after a mean 4-5 days.<sup>59</sup>

Systemic adverse reactions were also more frequent after the second (79%) than the first dose (55%) of Spikevax, and more common in participants aged 18-64 years compared to those aged 65 years or over (Table 2). The most frequently reported were fatigue, headache and myalgia. The majority of systemic reactions were grade 1 or 2 in severity, with the proportion of grade 2 and 3 systemic reactions higher after dose 2 as compared to dose 1. The mean duration of systemic reactions was 3 days.

Certain unsolicited adverse reactions up to 28 days after either dose of the Spikevax vaccine were more common than after administration of placebo in the phase III trial.<sup>54</sup> This includes lymphadenopathy, which occurred in 1.1% of vaccine recipients and 0.6% of placebo recipients overall. While plausibly linked to the vaccine due to temporal association, most lymphadenopathy was mild to moderate and resolved within 1-2 days. Hypersensitivity-related adverse reactions were more common in vaccine as compared to placebo recipients (1.5% versus 1.1%). However, there were no anaphylactic or severe hypersensitivity reactions in close temporal relationship with the vaccine dose.

There was a small imbalance in the number of participants with Bell's palsy (3 in the vaccine arm on day 22, 28 and 32 versus 1 in the placebo arm on day 17). All cases were unrelated to the administration of either the vaccine or placebo. Two participants, both with a history of facial dermal filler cosmetic injection, experienced facial swelling within two days from vaccine receipt.

There were no reported differences in the occurrence of adverse reactions in this clinical trial by race, ethnicity, medical comorbidities, or prior SARS-CoV-2 infection.<sup>54</sup>

**Table 2: Frequency of select common adverse events reported within 7 days following each dose of Spikevax in phase III trial<sup>59</sup>**

	18-64 years of age		≥65 years of age	
	Dose 1	Dose 2	Dose 1	Dose 2
<b>Injection site pain</b>	87%	90%	74%	83%
<b>Lymph node swelling at the axilla</b>	12%	16%	6%	9%
<b>Fever</b>	0.9%	17%	0.3%	10%
<b>Fatigue</b>	38%	68%	33%	58%
<b>Headache</b>	35%	63%	25%	46%
<b>Chills</b>	9%	49%	5%	31%
<b>Myalgia</b>	24%	62%	20%	47%
<b>Arthralgia</b>	17%	46%	16%	35%
<b>Nausea/vomiting</b>	9%	21%	5%	12%

Myocarditis and pericarditis have been reported following Spikevax. Refer to section below on **Myocarditis and pericarditis after mRNA COVID-19 vaccines**.

### Myocarditis and Pericarditis after mRNA COVID-19 vaccines

Myocarditis and pericarditis have been reported following vaccination with Comirnaty and Spikevax vaccine.<sup>75,76</sup> These conditions can occur separately or together (myopericarditis). Most reported cases have been mild, self-limiting and recovered quickly, although longer-term follow-up of these cases is ongoing. Cases have been reported predominantly after the second dose and mainly in younger males (aged < 30 years), including in adolescents.<sup>77</sup> This association is based on data from the USA and Europe, where mRNA COVID-19 vaccines have been extensively used.<sup>75,76,78-81</sup> In an analyses of myocarditis cases reported after mRNA vaccines in the US Vaccine Adverse Events Reporting System (VAERS) which met the CDC's case definition, 76% of the 323 cases were in males and the median age was 19 years (range 12-29).<sup>82</sup> Any difference between the rate of myocarditis/pericarditis after Comirnaty compared with Spikevax is still being examined. COVID-19 Vaccine AstraZeneca has not been associated with an increased risk of myocarditis/pericarditis.

Symptoms typically appear within 1-5 days (median 2 days) following vaccination and include chest pain, pressure or discomfort, palpitations, syncope and shortness of breath.<sup>82</sup>

Comirnaty and Spikevax continue to be recommended for people with a history of most chronic cardiovascular conditions and **can be given** to people in the following groups without any specific precautions:

- Prior myocarditis, pericarditis or endocarditis (i.e. > 6 months prior to vaccination)
- Coronary artery disease
- Myocardial infarction
- Stable heart failure

- Arrhythmias
- Prior history of rheumatic heart disease (RHD)
- Kawasaki disease
- Most congenital heart disease
- People with implantable cardiac devices

People with a history of the following conditions **can receive** Comirnaty or Spikevax, however are recommended to consult a GP, immunisation specialist or cardiologist about the best timing of vaccination and whether any additional precautions are recommended:

- Recent (i.e. within the past 6 months) or current inflammatory cardiac illness e.g., myocarditis, pericarditis, endocarditis
- Acute rheumatic fever (i.e., with active myocardial inflammation) or acute rheumatic heart disease
- People aged 12-29 years with dilated cardiomyopathy
- Complex or severe congenital heart disease including single ventricle (Fontan) circulation
- Acute decompensated heart failure
- Cardiac transplant recipients

For further information, refer to the [Joint ATAGI-CSANZ Guidance on Myocarditis and/or Pericarditis after mRNA COVID-19 Vaccines](#)

## COVID-19 Vaccine AstraZeneca

### Thrombosis with thrombocytopenia syndrome

A newly identified, rare condition called thrombosis with thrombocytopenia syndrome (TTS) has been reported after COVID-19 Vaccine AstraZeneca in several countries including Australia, and appears to be causally linked to vaccination. TTS involves thrombosis *with* thrombocytopenia. The onset of symptoms is around 4 to 42 days post vaccination. The site of thrombosis varies, and reported presentations include cerebral venous sinus thrombosis (CVST), thrombosis in the splanchnic (mesenteric, portal, splanchnic) circulations, deep vein thrombosis, pulmonary embolism and arterial thrombosis. Although very rare, TTS can cause disability and even death, with a fatal outcome in about one fifth of the cases reported in the UK to date.<sup>83</sup>

The overall estimated rate of TTS is around 1-2 cases per 100,000 doses administered, however this estimate is based on a relatively small number of cases, especially in young adults, reported in Australia to date and is therefore imprecise.<sup>84</sup> The estimated rate is higher in younger adults (<60 years of age), therefore younger age appears to be a risk factor for TTS. No other specific risk factors have been identified. In Australia, higher number of severe outcomes have been observed in younger women than in younger men. No sex differences are being observed in older individuals.

There is no evidence that a past history of clots or of any clotting tendencies increases the risk of TTS, and people with the following conditions *can receive* COVID-19 Vaccine AstraZeneca:

- History of blood clots in typical sites
- Increased clotting tendency that is not immune-mediated
- Family history of blood clots
- History of ischaemic heart disease or stroke
- Current or past thrombocytopenia (low platelet count)
- Those receiving anticoagulation therapy

There is a theoretical concern that certain rare conditions may increase the risk of TTS, and therefore Comirnaty is recommended for people with a history of these conditions:

- Cerebral venous sinus thrombosis (CVST)
- Heparin-induced thrombocytopenia (HIT)



- Idiopathic splanchnic (mesenteric, portal, splenic) vein thrombosis
- Antiphospholipid syndrome with thrombosis.

The great majority of reported cases of TTS have been after the first vaccine dose. As of July 2021, 44 cases were reported out of 22.8 million second doses administered in the UK. This translates to a rate of 1.9 cases per million doses<sup>83</sup>

TTS requires specific haematological investigations as part of the diagnostic workup.<sup>85</sup> Antibodies to platelet factor 4 are reported in most, but not all, cases. For further information about TTS, refer to [Information for Immunisation Providers on Thrombosis with Thrombocytopenia Syndrome \(TTS\) following COVID-19 vaccination](#).

### Other adverse events reported after COVID-19 Vaccine AstraZeneca

In the phase II/III trials of COVID-19 Vaccine AstraZeneca, adverse events reported within 7 days following vaccination were very common (86%) but the majority were mild or moderate.<sup>60</sup> Injection site tenderness (63.7%) and pain (54.2%) were the most commonly reported. Fatigue (53.2%) and headache (52.6%) were the most frequently reported systemic adverse events<sup>60</sup> (refer to **Table 2**).

Local or systemic solicited adverse events were most commonly reported on day 1 following vaccination. These reactions were generally mild to moderate and resolved within a few days. The most common systemic solicited adverse effects at day 7 were fatigue, headache and malaise.

Adults aged  $\geq 65$  years reported fewer local or systemic solicited adverse events, and fewer  $\geq$ grade 3 solicited adverse events, than younger adults.<sup>60,74</sup> Most adverse events did not affect daily activities. Adverse events reported after the second dose were milder and less frequent than those after the first dose.

Reports on unsolicited adverse events were collected through to 28 days following a dose of the COVID-19 Vaccine AstraZeneca. Most of the unsolicited adverse events were mild to moderate in severity and consistent with adverse events commonly observed following vaccination with other vaccines.<sup>60</sup>

In a combined interim analysis of four clinical trials, one case of transverse myelitis was reported in the vaccine arm, which occurred 14 days after dose 2.<sup>61</sup> This case was reviewed by an independent neurological committee and the likely diagnosis was revised to be idiopathic short segment spinal cord demyelination. Two additional cases of transverse myelitis were considered unlikely to be related to vaccination, with one case subsequently attributed to pre-existing but previously unrecognised multiple sclerosis, and the other case reported in the control group.

The first dose of COVID-19 Vaccine AstraZeneca has been found to be associated with a small risk of immune thrombocytopenia (ITP).<sup>86</sup> Two other serious but rare adverse events have been reported after COVID-19 Vaccine AstraZeneca, for which a causal association has not yet been confirmed. These are Guillain Barre syndrome and capillary leak syndrome.<sup>87,88</sup>

Anaphylaxis after COVID-19 Vaccine AstraZeneca has been reported rarely. Refer to **Contraindications** for further information.

Table 3: Frequency of select common adverse events reported within 7 days following at least one dose of COVID-19 Vaccine AstraZeneca in phase II/III trial in people aged >18 years<sup>89</sup>

	18–55 years		56–69 years		≥70 years	
	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 2
<b>Injection site pain</b>	61%	49%	43%	34%	20%	10%
<b>Injection site tenderness</b>	76%	61%	67%	59%	49%	47%
<b>Fatigue</b>	76%	55%	50%	41%	41%	33%
<b>Headache</b>	65%	31%	50%	34%	41%	20%
<b>Muscle pain</b>	53%	35%	37%	24%	18%	18%
<b>Fever</b>	24%	0%	0%	0%	0%	0%

## Reporting adverse events

All notifications of adverse events following immunisation should be made through the [usual reporting mechanisms](#).

The safety of COVID-19 vaccines will be actively monitored by the TGA as well as state and territory governments.

## Vaccine information

### Vaccine efficacy in clinical trials

#### Comirnaty

A phase II/III trial of Comirnaty is ongoing with >43,000 individuals aged ≥12 years enrolled. An interim analysis, with an observation period of 2 months post dose 2, reported vaccine efficacy (VE) of 95.0% (95% CI: 90.3–97.6) in preventing symptomatic laboratory-confirmed COVID-19 in people aged ≥16 years (median age 52 years, range 16–89 years for vaccine recipients) without evidence of prior infection with SARS-CoV-2.<sup>74</sup> There is also evidence of VE against severe illness, although the estimate is imprecise due to the lower number of people overall who developed severe disease (VE 88.9% after first dose [95% CI: 20.1–99.7]).<sup>74</sup>

No data are currently available to assess efficacy for prevention of asymptomatic infection, although serological data are awaited. The duration of protection has not been determined.

In this interim analysis, short-term VE after a single dose was 52.4% (95% CI: 29.5–68.4), with protective effect observed starting 12 days after dose 1.

#### **People aged ≥ 65 years**

Sub-group analyses demonstrated similarly high efficacy in adults aged ≥65 years (VE 94.7% [95% CI: 66.7–99.9]) and in adults with at least one medical comorbidity or obesity (VE 95.3% [95% CI: 87.7–98.8]).<sup>49</sup>

#### **Children aged <16 years**

Preliminary results of an ongoing study involving more than 2000 adolescents aged 12–15 years showed that VE against COVID-19 occurrence at least 7 days after dose 2 in participants with or without evidence of previous infection was 100% (95%CI 78.1-100) with no cases in the vaccine arm. After dose 1 and before dose 2, 3 COVID-19 cases were noted (within 11 days after dose 1) among vaccine recipients, compared with 12 cases

among placebo recipients (VE:75% (95% CI: 7.6 to 95.5)). No cases of severe COVID-19 were observed in this age cohort. The neutralising antibody response after 2 doses was higher among those aged 12–15 years compared with those aged 16–25 years.<sup>48</sup>

### **People with specified medical conditions**

This ongoing phase II/III trial also includes participants with well-controlled chronic medical conditions. An interim sub-analysis of data on those with some specified medical conditions showed a similar VE to those without such conditions (95.3% [95% CI: 87.7–98.8] versus 94.7% [95% CI: 85.9–98.6]<sup>74</sup>).

Data on safety, immunogenicity or efficacy of Comirnaty in people living with stable HIV have not yet been published.

## **Spikevax**

There is an ongoing phase III trial of Spikevax that enrolled >30,000 individuals aged ≥18 years (mean age 51.4 years [range: 18-95 years];<sup>90</sup> about a quarter were aged ≥65 years, and about one-fifth of adults aged 18–64 years had a medical condition with increased risk of severe COVID-19). Preliminary results of this trial to two months after the second dose, reported a vaccine efficacy of 94.1% (95% CI: 89.3 to 96.8%) in preventing symptomatic laboratory-confirmed COVID-19 in participants not previously been infected with SARS-CoV-2. All 30 severe COVID-19 cases occurred in the placebo group, resulting in a vaccine efficacy estimate of 100% (95% confidence interval unable to be estimated). One death due to SARS-CoV-2 infection occurred in the placebo group.

Short-term vaccine efficacy against symptomatic laboratory-confirmed COVID-19, from 14 days after the first dose and prior to the second dose, was 92.1% (95% CI: 68.8 to 99.1%).

The duration of protection is yet to be determined. The phase I trial indicates that vaccine-induced antibodies lasted for at least 6 months after dose 2.<sup>91</sup>

### **People aged ≥ 65 years**

In the ongoing phase III trial, 24.8% of participants were aged 65 years or over.<sup>59</sup> In this subgroup, vaccine efficacy against symptomatic disease was estimated to be 86.4% (95% CI: 61.4 to 95.2%), as compared to 95.6% (95% CI: 90.6 to 97.9%) among patients aged 18-64 years.

### **People with specified medical conditions**

The ongoing phase III trial enrolled individuals with stable medical conditions that put them at increased risk of severe COVID-19. An analysis of this subgroup demonstrated vaccine efficacy similar to the efficacy estimated in those without risk factors for severe disease (90.9% [95% CI: 74.7 to 96.7%) vs. 95.1% [95% CI: 89.6 to 97.7%]).

## **COVID-19 Vaccine AstraZeneca**

Phase II/III trials of COVID-19 Vaccine AstraZeneca are ongoing with >57,000 individuals aged ≥18 years enrolled. An interim analysis of pooled data was conducted as of 4 November 2020 from two ongoing randomised, blinded, controlled trials: a phase II/III study, COV002, in adults aged ≥18 years in the UK and a phase III study, COV003, in adults aged ≥18 years in Brazil. This analysis showed the overall VE was 70.4% (95% CI: 54.8–80.6) in preventing symptomatic laboratory-confirmed COVID-19 in people aged ≥18 years 15 or more days after the second dose in the primary efficacy study population.<sup>61</sup> The median duration of follow up from 15 or more days after the second dose was 48 days. This was based on 131 cases (30 among 5,807 who received COVID-19 Vaccine AstraZeneca versus 101 among 5,829 who received the control vaccine).<sup>61</sup>

COVID-19 Vaccine AstraZeneca was demonstrated to have reduced neutralisation activity against the B.1.1.7 variant than against a canonical (Victoria) lineage, however vaccine efficacy against B.1.1.7 was preserved with VE 70.4% (95% CI 43.6 – 84.5), compared to VE 81.5% (95% CI 67.9 – 89.4) for the Victoria lineage.<sup>92</sup> No efficacy data has been published on the VE against the Delta variant. Sera neutralisation studies show 4.3-fold

reduction in neutralisation of Delta after 2 doses of COVID-19 Vaccine AstraZeneca compared to wild type. After 1 dose COVID-19 Vaccine AstraZeneca, the sera barely inhibited Delta.

### **Number of doses and interval between the 2 doses**

Updated analysis of pooled data as of 7 December 2020 reported a VE of 63.09% (95% CI: 51.81–71.73) in preventing symptomatic laboratory-confirmed COVID-19 in people aged  $\geq 18$  years who received two standard doses.<sup>93</sup> This was based on 271 cases (74 among 7,201 who received COVID-19 Vaccine AstraZeneca versus 197 among 7,178 who received the control vaccine).<sup>61</sup> Efficacy from day 22 after the first dose until up to 12 weeks post vaccination was 76.0% (59.3–85.9).<sup>61</sup>

In clinical trials, the interval between the two doses of COVID-19 Vaccine AstraZeneca ranged from approximately 4 weeks up to 26 weeks. Among participants who received two standard recommended doses at an interval of 4 to 12 weeks, the overall VE for prevention of symptomatic laboratory-confirmed COVID-19 was 59.5% (95% CI: 45.8–69.7), based on 218 cases.<sup>94</sup> The VE varies with dose interval. The VEs for prevention of symptomatic laboratory-confirmed COVID-19 more than 14 days after the second dose with intervals of <6 weeks, 6–8 weeks, 9–11 weeks and  $\geq 12$  weeks between the first and second dose were 55.1% (95% CI 33.0 – 69.9), 59.9% (95% CI 32.0 – 76.4), 63.7% (95% CI 28.0 – 81.7) and 81.3% (95% CI 60.3 – 91.2) respectively.<sup>95</sup>

There were very few people with severe disease and hospitalisation in the interim analysis of clinical trials to assess VE against these outcomes. In the population who received two standard doses, there were 0 out of 4,440 participants who received COVID-19 Vaccine AstraZeneca who were hospitalised, and 4 out of 4,455 in the control group.<sup>96</sup>

### **People aged $\geq 65$ years**

Fewer than 6% of participants included in the interim analysis were aged  $\geq 65$  years.<sup>61</sup> In this cohort there were only four and eight cases of COVID-19 in recipients of COVID-19 Vaccine AstraZeneca and of control vaccine, respectively. However, there were no cases of COVID-19 hospitalisation, severe disease or COVID-19 deaths among trial participants aged  $\geq 65$  years.<sup>93</sup> These small numbers preclude the assessment of the efficacy of COVID-19 Vaccine AstraZeneca in this age group at this time. Participants aged  $\geq 65$  years who received two doses showed SARS-CoV-2 specific neutralising antibody levels comparable with those in serum samples from people who had recovered from COVID-19 (convalescent sera).

Additional information on the efficacy of COVID-19 Vaccine AstraZeneca in adults aged  $\geq 65$  years is anticipated from a phase III clinical trial underway in the USA and South America (NCT04516746) with over 30,000 participants, including at least 25% of participants aged  $\geq 65$  years.<sup>97,98</sup>

### **People with specified medical conditions**

An interim sub-analysis of data on people with specified medical conditions in the Phase II/III trials showed VE in this group was similar to that in people without such conditions. A total of 2,068 (39.3%) participants had at least one pre-existing comorbidity (defined as a BMI  $\geq 30$  kg/m<sup>2</sup>, cardiovascular disorder, respiratory disease or diabetes). A pooled data analysis (as of 7 December 2020) showed that participants who had one or more comorbidities had a VE of 58.3% (95% CI: 33.6–73.9).<sup>94</sup>

## **Vaccine effectiveness in post-licensure studies**

### **Comirnaty**

The effectiveness of Comirnaty has been studied in vaccination programs in countries such as Israel, USA, Canada and the UK.

In a study in Israel that included over 1.1 million people aged  $\geq 16$  years, effectiveness of Comirnaty from 7 days after 2 doses was 87% (95% CI: 55–100) against COVID-19 hospitalisations and 92% (95% CI: 75–100) against severe disease.<sup>38</sup> Data on the duration of protection from the vaccine are not available yet.

## Spikevax

The effectiveness of Spikevax has been assessed in vaccination programs in the USA and Canada.

In the US Mayo Clinic Health System study, Spikevax was found to be 92% (95% CI: 82-97%) effective against PCR-positive SARS-CoV-2 infection from day 14 after dose 2.<sup>99</sup> From seven days after the second dose, this vaccine was 86% (95% CI: 72-94%) effective against hospitalisation, and 100% (95% CI: 43-100%) against ICU admission.

In a large Canadian study, Spikevax was found to be 94% (95% CI: 86-97%) effective against laboratory-confirmed symptomatic SARS-CoV-2 infection from 7 days after dose 2, and 96% (95% CI: 74-100%) effective against severe outcomes, including hospitalisation and death, from the day of dose 2.<sup>100</sup>

## COVID-19 Vaccine AstraZeneca

Effectiveness data for COVID-19 Vaccine AstraZeneca are available from studies mainly in the UK. In a population-based cohort study in the UK, COVID-19 Vaccine AstraZeneca had 64% (95% CI: 55-70) effectiveness against PCR-positive SARS-CoV-2 infection 21 days after the first dose.<sup>101</sup> Effectiveness against symptomatic infection was marginally higher than against asymptomatic infection.

A prospective cohort study in Scotland found effectiveness of COVID-19 Vaccine AstraZeneca against COVID-19 hospitalisations was 94% for the first dose in 28 to 34 days after vaccination.<sup>102</sup>

Large population studies have also been done in the UK in period when the Delta variant has become dominant. Overall effectiveness of COVID-19 Vaccine AstraZeneca against PCR-positive SARS-CoV-2 infection irrespective of symptoms at the swab test was 18% (95% CI: 9-25)  $\geq$ 28 days after dose 1 and 60% (95% CI: 53-66)  $\geq$ 14 days after dose 2. When assessed against symptomatic infection, effectiveness estimates were 33% (95% CI: 23-41) and 61% (95% CI: 51-70) respectively.<sup>7</sup> Another study examined hospitalisation caused by Delta in the UK, vaccine effectiveness estimates were 71% (95% CI: 51-83) after dose 1 and 92% (95% CI: 78-97)  $\geq$  after dose 2.<sup>9</sup>

## Vaccine effectiveness against SARS-CoV-2 transmission

Data from studies in the UK shows that both Comirnaty and COVID-19 Vaccine AstraZeneca are effective in preventing onward transmission of the virus to close contacts in case of breakthrough infections. In one study among the UK general population the effectiveness against transmission from breakthrough infections to household contacts from 21 days after the first dose was 47% (95% CI :37-57%) for COVID-19 Vaccine AstraZeneca and 49% (95%CI:41-56%) for Comirnaty.<sup>103</sup> Another UK study reported that among healthcare workers, who predominantly had received Comirnaty, vaccination was associated with a 30% (95% CI: 22-37) reduction in transmission of SARS-CoV-2 to household contacts.<sup>104</sup>

Preliminary data from Finland also suggest that there is an indirect effect of both Comirnaty and Spikevax on close contacts of vaccine recipients.<sup>105</sup> Among healthcare workers, vaccine effectiveness against PCR-confirmed infection in their unvaccinated household contacts was 43% (95% CI: 22-58%) 10 weeks after the first vaccine dose. The Alpha (B.1.1.7) variant was the dominant strain in Finland at time of this study.

The National Institute of Allergy and Infectious Diseases (NIAID) in the USA is currently undertaking a clinical trial evaluating the effect of Spikevax on preventing transmission.<sup>106</sup>

## Vaccine effectiveness in older adults

In a single-centre case-control study in Bristol in the UK,<sup>107</sup> vaccine effectiveness against hospitalisation among adults aged  $\geq$ 80 years from 14 days after dose 1 was 71% (95% CI: 36-95) for COVID-19 Vaccine AstraZeneca 79% (95% CI: 47- 93) for Comirnaty.<sup>107</sup>

Other UK studies have reported effectiveness of first dose of *either* Comirnaty or COVID-19 Vaccine AstraZeneca of 76% (95% CI: 68-82) against overall SARS-CoV-2 infection in people aged  $\geq$ 75 years and 81% (95% CI: 65-90) against COVID-19 hospitalisation in people aged  $\geq$ 80 years.<sup>101,102,108</sup> Additionally, among long  
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term care facility residents aged  $\geq 65$  years, vaccine effectiveness against PCR-confirmed SARS-CoV-2 infection, regardless of the presence of symptoms, was estimated to be 62% (95% CI: 23–81%), with no difference between COVID-19 Vaccine AstraZeneca and Comirnaty.<sup>108</sup>

A Canadian study where both Comirnaty and Spikevax were used estimated the vaccine effectiveness against symptomatic infection from two to three weeks after dose 2 to be 85% (95% CI: 38–97%), and the vaccine effectiveness against severe outcome, including hospitalisation and death, to be 97% (95% CI: 86–99%) from the day of dose 2 among adults aged 70 years or over.<sup>100</sup>

VE data available for two doses of COVID-19 Vaccine AstraZeneca are still limited because of the 12-week interval between the two doses used in vaccination programs.<sup>101</sup>

## **Transporting, storing and handling vaccines**

### **Comirnaty**

Comirnaty vaccine vials have a shelf life of 6 months at  $-90^{\circ}\text{C}$  to  $-60^{\circ}\text{C}$ . Vials can be stored at domestic freezer temperatures ( $-25^{\circ}\text{C}$  to  $-15^{\circ}\text{C}$ ) for up to 2 weeks and can be returned to  $-90^{\circ}\text{C}$  to  $-60^{\circ}\text{C}$  within the original shelf life. Frozen vials should be thawed at  $2^{\circ}\text{C}$  to  $8^{\circ}\text{C}$ . A carton of 195 vials would require 3 hours to thaw. Frozen vials can also be thawed at room temperature (up to  $30^{\circ}\text{C}$ ) for 30 minutes, for immediate use. Once thawed, the vaccine should not be re-frozen. Refer to the product information for more detailed guidance regarding thawing of vials.

After thawing, the shelf life is 31 days at  $2^{\circ}\text{C}$  to  $8^{\circ}\text{C}$ . Undiluted vaccine vials can be stored at up to  $30^{\circ}\text{C}$  for 2 hours (including thawing time). After vial puncture and dilution, the vials and the prepared syringes with the vaccine dose must be kept at  $2^{\circ}\text{C}$  to  $30^{\circ}\text{C}$  and used within 6 hours from the time of dilution (not including the 2-hour maximum window for storage of an undiluted vial at up to  $30^{\circ}\text{C}$ ). Do not freeze the diluted vaccine. ATAGI recommends that, when possible, pre-drawn doses kept at room temperature be used within an hour to minimise any remote potential risk of infection.

Comirnaty is presented in a multi-dose vial containing 0.45 mL of undiluted vaccine and must be reconstituted by diluting with 1.8 mL of sterile 0.9% sodium chloride. The vaccine does not contain a preservative. Do not use bacteriostatic 0.9% sodium chloride. The total quantity after dilution will be 2.25 mL. Do not shake the vial. It is preferable to administer vaccine doses immediately after dilution.

During storage, minimise exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

For additional information refer to the National Vaccine Storage Guidelines [Strive for 5](#).

### **Spikevax**

The shelf life of Spikevax is 7 months frozen at  $-25^{\circ}\text{C}$  to  $-15^{\circ}\text{C}$  and in its original carton, protected from light. Spikevax vials cannot be stored on dry ice or at temperatures below  $-50^{\circ}\text{C}$ . Frozen vials can be thawed at  $2^{\circ}\text{C}$  to  $8^{\circ}\text{C}$  in a refrigerator in 2.5 hours, or at room temperature ( $15^{\circ}\text{C}$  to  $25^{\circ}\text{C}$ ) in one hour. Thawed vials should not be re-frozen. Refer to the product information for more detailed guidance regarding thawing of vials.

Spikevax is a white to off-white liquid, and is available in multi-dose vials of 5 mLs containing 10 doses of 0.5 mL. Spikevax does not contain a preservative. Dilution is not required. The vial should be swirled gently after thawing and before each withdrawal, but should not be shaken. Providers should confirm that the syringe containing the dose is not cold to touch prior to administration to minimize discomfort from receiving an injection of a chilled product.

Once thawed, the shelf life of an unpunctured vial is 30 days in a refrigerator ( $2^{\circ}\text{C}$  to  $8^{\circ}\text{C}$ ) protected from light, of which 12 hours can be used for transportation; and 24 hours in storage at  $8^{\circ}\text{C}$  to  $25^{\circ}\text{C}$ . Thawed vials can be handled in room light conditions.

Chemical and physical stability has been shown with storage of Spikevax for 19 hours at  $2^{\circ}\text{C}$  to  $25^{\circ}\text{C}$  after initial puncture. However, since this vaccine contains no antimicrobial preservatives, ATAGI recommends that opened ATAGI Clinical Guidance on COVID-19 Vaccine in Australia\_v7.0

vials should preferably be stored at 2°C to 8°C, and the cumulative storage time of opened vials at 2°C to 25°C should not exceed 6 hours. Additionally, as much as possible, pre-drawn doses kept at room temperature should be used within an hour to minimise any remote potential risk of infection.

## COVID-19 Vaccine AstraZeneca

COVID-19 Vaccine AstraZeneca does not need to be stored in a freezer and hence does not need to be thawed. It is stored in a refrigerator at 2°C to 8°C. The shelf life of COVID-19 Vaccine AstraZeneca is 6 months at 2°C to 8°C.

In Australia, COVID-19 Vaccine AstraZeneca is supplied in multi-dose vials, with either 8 doses in 4 mL or 10 doses in 5 mL. Unopened multi-dose vials are to be stored at 2°C to 8°C and in the outer carton, to protect from light. Dilution is not required.

After first opening, chemical and physical in-use stability has been demonstrated from the time of vial puncture to administration for no more than 6 hours at room temperature up to 30°C, or no more than 48 hours in a refrigerator at 2°C to 8°C. The vial can be re-refrigerated, but after first opening the cumulative storage time at room temperature must not exceed 6 hours, and the total cumulative storage time must not exceed 48 hours.

Although there are data supporting stability of vaccine doses after withdrawal into a syringe for up to 6 hours at room temperature (as reflected in the Astra Zeneca vaccine product information [PI]), ATAGI recommends that, when possible, pre-drawn doses kept at room temperature be used within an hour to minimise any remote potential risk of infection.

For additional information refer to the [National Vaccine Storage Guidelines Strive for 5](#).

## Transporting doses for home visits

When transporting COVID-19 Vaccine AstraZeneca or Comirnaty for a home visit, there are two options:

1. Where possible, transport the vial at 2-8°C and not exceeding the total maximum storage period of 6 hours and draw up the dose at the site of administration
2. A pre-drawn dose in a syringe can be transported if it can be appropriately stored (protecting from light and maintaining the cold chain) and can be administered as soon as practicable and not exceeding the total maximum storage period of 1 hour if at room temperature, and within 6 hours if at 2-8°C).

## Recording vaccination

It is mandatory to record every administered dose of COVID-19 vaccine on AIR.

This will assist in ensuring that the correct vaccine and interval are used for the second dose, and in identifying patients who are due for a second dose. This will also allow verification or provision of evidence of completion of COVID-19 vaccination, if required.

For more information, refer to the Services Australia website: [AIR for health professionals](#).

## Serological testing for immunity

Testing for anti-spike antibodies or neutralising antibodies to demonstrate immunity against SARS-CoV-2 in vaccinated individuals is not recommended. An immune correlate of protection has not yet been established for SARS-CoV-2 infection.<sup>109</sup>

## Impact of vaccination on future COVID-19 testing

Receipt of a COVID-19 vaccine will not affect the results of nucleic acid (PCR) testing or rapid antigen testing for diagnosis of SARS-CoV-2 infection.

Since Comirnaty, Spikevax and COVID-19 Vaccine AstraZeneca encode the spike protein of SARS-CoV-2, vaccination may affect any subsequent serological diagnostic testing and result in detection of antibody to the spike protein, but will not affect the results of anti-nucleocapsid antibody testing.

## Isolation or testing for COVID-19 following adverse events

Testing for SARS-CoV-2 infection or implementing (non-medically recommended) isolation of someone who develops symptoms of fever, headache, fatigue or other systemic symptoms within and lasting for <48 hours after receipt of a COVID-19 vaccine is not necessarily required. If a vaccine recipient develops typical vaccine-related adverse events (refer to **Adverse events** section) and there is complete absence of respiratory symptoms (including loss of smell), it is more likely that they have an expected vaccine response. However, vaccine-induced protection is not immediate, and it is possible that SARS-CoV-2 could be contracted within several days before or after vaccination (this would not constitute vaccine failure).

Local public health guidance should be followed irrespective of a history of vaccination. Criteria for SARS-CoV-2 testing vary and depend, in part, on local epidemiology and outbreak management.

For Comirnaty, the median time of onset of systemic adverse events was 1–2 days after vaccine receipt, with resolution in a median of 1 day. For Spikevax, the median onset of systemic adverse events was 0-1 days following vaccination for the majority of participants (70.2%), and symptoms continued for about 3 days on average.<sup>59</sup> For COVID-19 Vaccine AstraZeneca, local or systemic solicited adverse events were most commonly reported on day 1 following vaccination, and generally resolved within a few days.

## Post-exposure prophylaxis

COVID-19 vaccines are not recommended for post-exposure prophylaxis use, as no data are available to support such use. The median incubation period for SARS-CoV-2 is 5–6 days (with a range of 1 to 14 days in most people) and vaccination after exposure is unlikely to generate sufficient immunity within this period to prevent infection in a previously unvaccinated exposed individual.

However, local public health authorities may recommend prioritising COVID-19 vaccination for certain populations related to local outbreaks or settings with community transmission of COVID-19. For latest information refer to the CDNA [National guidelines for public health units](#) on COVID-19.



## References

1. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. *Nat Microbiol* 2020;5:536-44.
2. Dhama K, Khan S, Tiwari R, et al. Coronavirus Disease 2019-COVID-19. *Clin Microbiol Rev* 2020;33.
3. Amanat F, Krammer F. SARS-CoV-2 vaccines: status report. *Immunity* 2020;52:583-9.
4. World Health Organization (WHO). Tracking SARS-CoV-2 variants. Updated 6 July 2021. 2021. Available from: <https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/> (Accessed 20 July 2021).
5. World Health Organization (WHO). Weekly epidemiological update on COVID-19 - 13 April 2021. Available from: <https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---13-april-2021> (Accessed 26 April 2021).
6. Public Health England. SARS-CoV-2 variants of concern and variants under investigation in England, Technical Briefing 17. 25 June 2021. Available from: [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/1001354/Variants\\_of\\_Concern\\_VOC\\_Technical\\_Briefing\\_17.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1001354/Variants_of_Concern_VOC_Technical_Briefing_17.pdf) (Accessed 20 July 2021).
7. Sheikh A, McMenamin J, Taylor B, Robertson C. SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness. *The Lancet* 2021;397:2461-2.
8. Ong SWX, Chiew CJ, Ang LW, et al. Clinical and virological features of SARS-CoV-2 variants of concern: a retrospective cohort study comparing B.1.1.7 (Alpha), B.1.315 (Beta), and B.1.617.2 (Delta). *The Lancet* 2021.
9. Stowe J, Andrews NJ, Gower C, et al. Effectiveness of COVID-19 vaccines against hospital admission with the Delta (B.1.617.2) variant. 2021. Available from: [https://media.tghn.org/articles/Effectiveness\\_of\\_COVID-19\\_vaccines\\_against\\_hospital\\_admission\\_with\\_the\\_Delta\\_B.1.617.2.pdf](https://media.tghn.org/articles/Effectiveness_of_COVID-19_vaccines_against_hospital_admission_with_the_Delta_B.1.617.2.pdf) (Accessed 20 July 2021).
10. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *Jama* 2020;323:1239-42.
11. Stokes EK, Zambrano LD, Anderson KN, et al. Coronavirus disease 2019 case surveillance - United States, January 22-May 30, 2020. *MMWR Morbidity and Mortality Weekly Report* 2020;69:759-65.
12. Docherty AB, Harrison EM, Green CA, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *Bmj* 2020;369:m1985.
13. Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature* 2020;584:430-6.
14. COVID-19 National Incident Room Surveillance Team. COVID-19 Australia: Epidemiology Report 32: Four-week reporting period ending 3 January 2021. *Communicable Diseases Intelligence* 2021;45.
15. Price DJ, Shearer FM, Meehan MT, et al. Early analysis of the Australian COVID-19 epidemic. *Elife* 2020;9.
16. World Health Organization (WHO). WHO SAGE roadmap for prioritizing uses of COVID-19 vaccines in the context of limited supply. Geneva: World Health Organization; 2020. Available from: <https://www.who.int/publications/m/item/who-sage-roadmap-for-prioritizing-uses-of-covid-19-vaccines-in-the-context-of-limited-supply> (Accessed 26 April 2020).
17. Mutambudzi M, Niedwiedz C, Macdonald EB, et al. Occupation and risk of severe COVID-19: prospective cohort study of 120 075 UK Biobank participants. *Occup Environ Med* 2020.
18. Australian Government Department of Health. COVID-19 cases in aged care services – residential care, 2021. Canberra: Australian Government Department of Health; 2021. Available from: <https://www.health.gov.au/resources/covid-19-cases-in-aged-care-services-residential-care> (Accessed 26 April 2021).
19. Petrilli CM, Jones SA, Yang J, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *Bmj* 2020;369:m1966.
20. Yashadhana A, Pollard-Wharton N, Zwi AB, Biles B. Indigenous Australians at increased risk of COVID-19 due to existing health and socioeconomic inequities. *The Lancet Regional Health Western Pacific* 2020;1.
21. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *Bmj* 2020;370:m3320.
22. Gao Y, Chen Y, Liu M, Shi S, Tian J. Impacts of immunosuppression and immunodeficiency on COVID-19: a systematic review and meta-analysis. *Journal of Infection* 2020;81:e93-e5.
23. Boyarsky BJ, Werbel WA, Avery RK, et al. Antibody Response to 2-Dose SARS-CoV-2 mRNA Vaccine Series in Solid Organ Transplant Recipients. *Jama* 2021;325:2204-6.

24. Peled Y, Ram E, Lavee J, et al. BNT162b2 vaccination in heart transplant recipients: Clinical experience and antibody response. *Journal of Heart and Lung Transplantation* 2021;40:759-62.
25. Grupper A, Rabinowich L, Schwartz D, et al. Reduced humoral response to mRNA SARS-Cov-2 BNT162b2 vaccine in kidney transplant recipients without prior exposure to the virus. *American Journal of Transplantation* 2021.
26. Marion O, Del Bello A, Abravanel F, et al. Safety and Immunogenicity of Anti-SARS-CoV-2 Messenger RNA Vaccines in Recipients of Solid Organ Transplants. *Ann Intern Med* 2021.
27. Herishanu Y, Avivi I, Aharon A, et al. Efficacy of the BNT162b2 mRNA COVID-19 vaccine in patients with chronic lymphocytic leukemia. *Blood* 2021;137:3165-73.
28. Parry H, McIlroy G, Bruton R, et al. Antibody responses after first and second Covid-19 vaccination in patients with chronic lymphocytic leukaemia. *Blood Cancer J* 2021;11:136.
29. Moor MB, Suter-Riniker F, Horn MP, et al. Humoral and cellular responses to mRNA vaccines against SARS-CoV2 in patients with a history of CD20-B-cell depleting therapy. 2021. Available from: <https://doi.org/10.1101/2021.07.04.21259848> (Accessed 12 August 2021).
30. Deepak P, Kim W, Paley MA, et al. Glucocorticoids and B cell depleting agents substantially impair immunogenicity of mRNA vaccines to SARS-CoV-2. 2021. Available from: <https://doi.org/10.1101/2021.04.05.21254656> (Accessed 12 August 2021).
31. Apostolidis SA, Kakara M, Painter MM, et al. Altered cellular and humoral immune responses following SARS-CoV-2 mRNA vaccination in patients with multiple sclerosis on anti-CD20 therapy. 2021. Available from: <https://doi.org/10.1101/2021.06.23.21259389> (Accessed 12 August 2021).
32. Woldemeskel BA, Karaba AH, Garliss CC, et al. The BNT162b2 mRNA Vaccine Elicits Robust Humoral and Cellular Immune Responses in People Living with HIV. *Clinical Infectious Diseases* 2021.
33. Ruddy JA, Boyarsky BJ, Bailey JR, et al. Safety and antibody response to two-dose SARS-CoV-2 messenger RNA vaccination in persons with HIV. *Aids* 2021.
34. Frater J, Ewer KJ, Ogbe A, et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 in HIV infection: a single-arm substudy of a phase 2/3 clinical trial. *Lancet HIV* 2021;8:e474-e85.
35. Prendecki M, Thomson T, Clarke CL, et al. Comparison of humoral and cellular responses in kidney transplant recipients receiving BNT162b2 and ChAdOx1 SARS-CoV-2 vaccines. 2021. Available from: <https://doi.org/10.1101/2021.07.09.21260192> (Accessed 12 August 2021).
36. Mahil SK, Bechman K, Raharja A, et al. The effect of methotrexate and targeted immunosuppression on humoral and cellular immune responses to the COVID-19 vaccine BNT162b2: a cohort study. *Lancet Rheumatology* 2021.
37. Chodick G, Tene L, Rotem RS, et al. The effectiveness of the TWO-DOSE BNT162b2 vaccine: analysis of real-world data. *Clinical Infectious Diseases* 2021.
38. Dagan N, Barda N, Kepten E, et al. BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting. *New England Journal of Medicine* 2021;384:1412-23.
39. Young-Xu Y, Korves C, Roberts J, et al. Coverage and Effectiveness of mRNA COVID-19 Vaccines among Veterans. 2021. Available from: <https://doi.org/10.1101/2021.06.14.21258906> (Accessed 12 August 2021).
40. Whitaker HJ, Tsang RSM, Byford R, et al. Pfizer-BioNTech and Oxford AstraZeneca COVID-19 vaccine effectiveness and immune response among individuals in clinical risk groups. 2021. Available from: <https://khub.net/documents/135939561/430986542/RCGP+VE+riskgroups+paper.pdf/a6b54cd9-419d-9b63-e2bf-5dc796f5a91f> (Accessed 12 August 2021).
41. Khan N, Mahmud N. Effectiveness of SARS-CoV-2 Vaccination in a Veterans Affairs Cohort of Patients With Inflammatory Bowel Disease With Diverse Exposure to Immunosuppressive Medications. *Gastroenterology* 2021.
42. Viner RM, Mytton OT, Bonell C, et al. Susceptibility to SARS-CoV-2 infection among children and adolescents compared with adults: a systematic review and meta-analysis. *JAMA Pediatr* 2021;175:143-56.
43. Liguoro I, Pilotto C, Bonanni M, et al. SARS-COV-2 infection in children and newborns: a systematic review. *Eur J Pediatr* 2020;179:1029-46.
44. Jiang L, Tang K, Levin M, et al. COVID-19 and multisystem inflammatory syndrome in children and adolescents. *The Lancet Infectious Diseases* 2020;20:e276-e88.
45. Graff K, Smith C, Silveira L, et al. Risk factors for severe COVID-19 in children. *Pediatric Infectious Diseases Journal* 2021;40:e137-e45.
46. Kompaniyets L, Agathis NT, Nelson JM, et al. Underlying medical conditions associated with severe COVID-19 illness among children. *JAMA Netw Open* 2021;4:e2111182.
47. Ward JL, Harwood R, Smith C, et al. Risk factors for intensive care admission and death amongst children and young people admitted to hospital with COVID-19 and PIMS-TS in England during the first pandemic year medRxiv; 2021. Available from: <https://doi.org/10.1101/2021.07.01.21259785> (Accessed 30 July 2021).

48. French RW, Jr., Klein NP, Kitchin N, et al. Safety, immunogenicity, and efficacy of the BNT162b2 Covid-19 vaccine in adolescents. *New England Journal of Medicine* 2021;385:239-50.
49. Gray KJ, Bordt EA, Atyeo C, et al. Coronavirus disease 2019 vaccine response in pregnant and lactating women: a cohort study. *Am J Obstet Gynecol* 2021.
50. Collier AY, McMahan K, Yu J, et al. Immunogenicity of COVID-19 mRNA Vaccines in Pregnant and Lactating Women. *Jama* 2021.
51. Kadali RAK, Janagama R, Peruru SR, et al. Adverse effects of COVID-19 messenger RNA vaccines among pregnant women: a cross-sectional study on healthcare workers with detailed self-reported symptoms. *Am J Obstet Gynecol* 2021.
52. Shimabukuro TT, Kim SY, Myers TR, et al. Preliminary findings of mRNA COVID-19 vaccine safety in pregnant persons. *New England Journal of Medicine* 2021.
53. Perlman S. Another decade, another coronavirus. *New England Journal of Medicine* 2020;382:760-2.
54. United States Food and Drug Administration. Moderna COVID-19 vaccine: Emergency Use Authorization (EUA) for an unapproved product review memorandum. 2021. Available from: <https://www.fda.gov/media/144673/download> (Accessed 12 August 2021).
55. Bowman CJ, Bouressam M, Campion SN, et al. Lack of effects on female fertility and prenatal and postnatal offspring development in rats with BNT162b2, a mRNA-based COVID-19 vaccine. *Reproductive Toxicology* 2021;103:28-35.
56. ClinicalTrials.gov. Study to evaluate the safety, tolerability, and immunogenicity of SARS CoV-2 RNA vaccine candidate (BNT162b2) against COVID-19 in healthy pregnant women 18 years of age and older. United States of America: National Institutes of Health; 2021. Available from: <https://clinicaltrials.gov/ct2/show/NCT04754594> (Accessed 10 June 2021).
57. Goldshtein I, Nevo D, Steinberg DM, et al. Association Between BNT162b2 Vaccination and Incidence of SARS-CoV-2 Infection in Pregnant Women. *Jama* 2021.
58. Lumley SF, O'Donnell D, Stoesser NE, et al. Antibody status and incidence of SARS-CoV-2 infection in health care workers. *New England Journal of Medicine* 2021;384:533-40.
59. Baden LR, El Sahly HM, Essink B, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *New England Journal of Medicine* 2021;384:403-16.
60. Medicines and Healthcare Products Regulatory Agency. Public Assessment Report Authorisation for Temporary Supply. COVID-19 Vaccine AstraZeneca, solution for injection in multidose container COVID-19 Vaccine (ChAdOx1-S [recombinant]) December 2020. Available from: [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/963928/UKPAR\\_COVID\\_19\\_Vaccine\\_AstraZeneca\\_23.02.2021.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/963928/UKPAR_COVID_19_Vaccine_AstraZeneca_23.02.2021.pdf) (Accessed 26 April 2021).
61. Voysey M, Clemens SAC, Madhi SA, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *The Lancet* 2021;397:99-111.
62. Liu X, Shaw RH, Stuart ASV, et al. Safety and immunogenicity report from the Com-COV Study – a single-blind randomised non-inferiority trial comparing heterologous and homologous prime-boost schedules with an adenoviral vectored and MRNA COVID-19 vaccine. 2021. Available from: <https://ssrn.com/abstract=3874014> (Accessed 20 July 2021).
63. Shaw RH, Stuart A, Greenland M, et al. Heterologous prime-boost COVID-19 vaccination: initial reactogenicity data. *The Lancet* 2021;397:2043-6.
64. Normark J, Vikström L, Gwon YD, et al. Heterologous ChAdOx1 nCoV-19 and mRNA-1273 Vaccination. *New England Journal of Medicine* 2021.
65. Schmidt T, Klemis V, Schub D, et al. Immunogenicity and reactogenicity of heterologous ChAdOx1 nCoV-19/mRNA vaccination. *Nat Med* 2021.
66. Gram MA, Nielsen J, Schelde AB, et al. Vaccine effectiveness when combining the ChAdOx1 vaccine as the first dose with an mRNA COVID-19 vaccine as the second dose. 2021. Available from: <https://doi.org/10.1101/2021.07.26.21261130> (Accessed 12 August 2021).
67. Wu K, Choi A, Koch M, et al. Preliminary analysis of safety and immunogenicity of a SARS-CoV-2 variant vaccine booster. 2021. Available from: <https://doi.org/10.1101/2021.05.05.21256716>.
68. Shimabukuro TT, Cole M, Su JR. Reports of anaphylaxis after receipt of mRNA COVID-19 vaccines in the US-December 14, 2020-January 18, 2021. *Jama* 2021;325:1101-2.
69. Castells MC, Phillips EJ. Maintaining safety with SARS-CoV-2 vaccines. *New England Journal of Medicine* 2021;384:643-9.
70. Sellaturay P, Nasser S, Islam S, Gurugama P, Ewan PW. Polyethylene glycol (PEG) is a cause of anaphylaxis to the Pfizer/BioNTech mRNA COVID-19 vaccine. *Clinical and Experimental Allergy* 2021.
71. Wenande E, Garvey LH. Immediate-type hypersensitivity to polyethylene glycols: a review. *Clinical and Experimental Allergy* 2016;46:907-22.
72. National Center for Immunization and Respiratory Diseases. General recommendations on immunization — recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recommendations and Reports* 2011;60:1-64.

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73. United States Food and Drug Administration. Pfizer-BioNTech COVID-19 Vaccine (Comirnaty, PF-07302048) Vaccines and Related Biological Products Advisory Committee Briefing Document. Available from: <https://www.fda.gov/media/144246/download> (Accessed 10 December 2020).
74. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. *New England Journal of Medicine* 2020;383:2603-15.
75. Kim HW, Jenista ER, Wendell DC, et al. Patients With Acute Myocarditis Following mRNA COVID-19 Vaccination. *JAMA Cardiol* 2021.
76. Montgomery J, Ryan M, Engler R, et al. Myocarditis Following Immunization With mRNA COVID-19 Vaccines in Members of the US Military. *JAMA Cardiol* 2021.
77. Marshall M, Ferguson ID, Lewis P, et al. Symptomatic Acute Myocarditis in 7 Adolescents After Pfizer-BioNTech COVID-19 Vaccination. *Pediatrics* 2021.
78. Abu Mouch S, Roguin A, Hellou E, et al. Myocarditis following COVID-19 mRNA vaccination. *Vaccine* 2021;39:3790-3.
79. Rosner CM, Genovese L, Tehrani BN, et al. Myocarditis temporally associated with COVID-19 vaccination. *Circulation* 2021;144:502-5.
80. Larson KF, Ammirati E, Adler ED, et al. Myocarditis after BNT162b2 and mRNA-1273 vaccination. *Circulation* 2021;144:506-8.
81. UK Medicines & Healthcare products Regulatory Agency. Coronavirus vaccine - weekly summary of Yellow Card reporting. 2021. Available from: <https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting> (Accessed 18 August 2021).
82. Gargano JW, Wallace M, Hadler SC, et al. Use of mRNA COVID-19 vaccine after reports of myocarditis among vaccine recipients: update from the Advisory Committee on Immunization Practices - United States, June 2021. *MMWR Morbidity and Mortality Weekly Report* 2021;70:977-82.
83. Medicines and Healthcare Products Regulatory Agency. Coronavirus vaccine - weekly summary of Yellow Card reporting. 2021. Available from: <https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting> (Accessed 26 April 2021).
84. Australian Technical Advisory Group on Immunisation (ATAGI). ATAGI reinforce recommendations on use of COVID-19 vaccines following review of vaccine safety data and benefits  
Canberra, Australia: Australian Government Department of Health; 23 April 2021. Available from: <https://www.health.gov.au/news/atagi-reinforce-recommendations-on-use-of-covid-19-vaccines-following-review-of-vaccine-safety-data-and-benefits> (Accessed 29 April 2021).
85. Thrombosis and Haemostasis Society of Australia and New Zealand. Suspected Vaccine Induced Prothrombotic Immune Thrombocytopenia (VIPIT)/Vaccine induced immune thrombotic thrombocytopenia (VITT): THANZ Advisory Statement for Haematologists. 24 April 2021. Available from: <https://www.thanz.org.au/documents/item/577> (Accessed 29 April 2021).
86. Simpson CR, Shi T, Vasileiou E, et al. First-dose ChAdOx1 and BNT162b2 COVID-19 vaccines and thrombocytopenic, thromboembolic and hemorrhagic events in Scotland. *Nat Med* 2021;27:1290-7.
87. Maramattom BV, Krishnan P, Paul R, et al. Guillain-Barré Syndrome following ChAdOx1-S/nCoV-19 Vaccine. *Ann Neurol* 2021.
88. Allen CM, Ramsamy S, Tarr AW, et al. Guillain-Barré Syndrome Variant Occurring after SARS-CoV-2 Vaccination. *Ann Neurol* 2021.
89. Ramasamy MN, Minassian AM, Ewer KJ, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. *The Lancet* 2021;396:1979-93.
90. US National Library of Medicine. A study to evaluate efficacy, safety, and immunogenicity of mRNA-1273 vaccine in adults aged 18 years and older to prevent COVID-19. Identifier: NCT04470427. 2021. Available from: <https://clinicaltrials.gov/ct2/show/NCT04470427> (Accessed 12 August 2021).
91. Doria-Rose N, Suthar MS, Makowski M, et al. Antibody Persistence through 6 Months after the Second Dose of mRNA-1273 Vaccine for Covid-19. *New England Journal of Medicine* 2021;384:2259-61.
92. Emary KRW, Golubchik T, Aley PK, et al. Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 variant of concern 202012/01 (B.1.1.7): an exploratory analysis of a randomised controlled trial. *The Lancet* 2021;397:1351-62.
93. World Health Organization (WHO). AZD1222 vaccine against COVID-19 developed by Oxford University and Astra Zeneca: Background paper (draft). 10 February 2021. Available from: [https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE\\_recommendation-AZD1222-background-2021.1](https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-background-2021.1) (Accessed 26 April 2021).
94. European Medicines Agency. COVID-19 Vaccine AstraZeneca: Product Information as approved by the CHMP on 29 January 2021, pending endorsement by the European Commission. 29 January 2021. Available from: [https://www.ema.europa.eu/en/documents/product-information/covid-19-vaccine-astrazeneca-product-information-approved-chmp-29-january-2021-pending-endorsement\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/covid-19-vaccine-astrazeneca-product-information-approved-chmp-29-january-2021-pending-endorsement_en.pdf) (Accessed 26 April 2021).

95. Voysey M, Costa Clemens SA, Madhi SA, et al. Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials. *The Lancet* 2021;397:881-91.
96. Therapeutic Goods Administration (TGA). AusPAR: ChAdOx1-S - Australian Public Assessment Report. 2021. Available from: <https://www.tga.gov.au/auspar/auspar-chadox1-s> (Accessed 26 April 2021).
97. US National Institutes of Health. Phase III Double-blind, Placebo-controlled Study of AZD1222 for the Prevention of COVID-19 in Adults. 2021. Available from: <https://clinicaltrials.gov/ct2/show/NCT04516746> (Accessed 26 April 2021).
98. AstraZeneca. AZD1222 US Phase III primary analysis confirms safety and efficacy. 25 March 2021. Available from: <https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2021/azd1222-us-phase-iii-primary-analysis-confirms-safety-and-efficacy.html> (Accessed 29 April 2021).
99. Pawlowski C, Lenehan P, Puranik A, et al. FDA-authorized mRNA COVID-19 vaccines are effective per real-world evidence synthesized across a multi-state health system. *Medicine* 2021;<https://doi.org/10.1016/j.medj.2021.06.007>.
100. Chung H, He S, Nasreen S, et al. Effectiveness of BNT162b2 and mRNA-1273 COVID-19 vaccines against symptomatic SARS-CoV-2 infection and severe COVID-19 outcomes in Ontario, Canada: a test-negative design study. 2021. Available from: <https://doi.org/10.1101/2021.05.24.21257744> (Accessed 12 August 2021).
101. Pritchard E, Matthews PC, Stoesser N, et al. Impact of vaccination on SARS-CoV-2 cases in the community: a population-based study using the UK's COVID-19 Infection Survey. 2021. Available from: <https://doi.org/10.1101/2021.04.22.21255913> (Accessed 29 April 2021).
102. Vasileiou E, Simpson CR, Robertson C, et al. Effectiveness of first Dose of COVID-19 vaccines against hospital admissions in Scotland: national prospective cohort study of 5.4 million people (preprint). *The Lancet*.
103. Harris RJ, Hall JA, Zaidi A, et al. Impact of vaccination on household transmission of SARS-COV-2 in England. 2021. Available from: <https://khub.net/documents/135939561/390853656/Impact+of+vaccination+on+household+transmission+of+SA+RS-COV-2+in+England.pdf/35bf4bb1-6ade-d3eb-a39e-9c9b25a8122a?t=1619601878136> (Accessed 10 May 2021).
104. Shah ASV, Gribben C, Bishop J, et al. Effect of vaccination on transmission of COVID-19: an observational study in healthcare workers and their households (preprint). *medRxiv* 2021.
105. Salo J, Hägg M, Kortelainen M, et al. The indirect effect of mRNA-based Covid-19 vaccination on unvaccinated household members. 2021. Available from: <https://doi.org/10.1101/2021.05.27.21257896> (Accessed 12 August 2021).
106. US National Library of Medicine. A study of SARS CoV-2 infection and potential transmission in individuals immunized with Moderna COVID-19 vaccine (CoVPN 3006). Identifier: NCT04811664. 2021. Available from: <https://www.clinicaltrials.gov/ct2/show/NCT04811664> (Accessed 12 August 2021).
107. Hyams C, Marlow R. Assessing the Effectiveness of BNT162b2 and ChAdOx1nCoV-19 COVID-19 Vaccination in Prevention of Hospitalisations in Elderly and Frail Adults: A Single Centre Test Negative Case-Control Study (Pre-print). *The Lancet* 2021.
108. Shrotri M, Krutikov M, Palmer T, et al. Vaccine effectiveness of the first dose of ChAdOx1 nCoV-19 and BNT162b2 against SARS-CoV-2 infection in residents of long-term care facilities in England (VIVALDI): a prospective cohort study. *Lancet Infectious Diseases* 2021.
109. Poland GA, Ovsyannikova IG, Kennedy RB. SARS-CoV-2 immunity: review and applications to phase 3 vaccine candidates. *The Lancet* 2020;396:1595-606.