ARTICLE

# COVID-19 vaccines in 2023

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## SUMMARY

Most Australian adults now have hybrid immunity to the SARS-CoV-2 virus, referring to a combination of protection from previous vaccine doses and past infection.

Protection from both vaccination and past infection wanes over time. Booster doses are recommended to ensure that those who are at increased risk of severe COVID-19 remain protected. The optimal timing of future booster doses to maintain adequate protection against severe illness is not yet known.

Older age remains the most important risk factor for severe COVID-19, including in the current Omicron variant era.

The original COVID-19 vaccines are monovalent vaccines based on the ancestral strain of the SARS-CoV-2 virus. Bivalent vaccines have been developed based on earlier Omicron subvariants (BA.1 or BA.4-5) and the ancestral strain. These provide enhanced protection against severe illness from Omicron compared with the original monovalent vaccines.

Updated monovalent vaccines based on a more recent Omicron subvariant (XBB.1.5) have been developed.

COVID-19 vaccines have an excellent safety record, and serious adverse events are extremely rare.

## Introduction

COVID-19 vaccines have played an essential role in the pandemic response, protecting individuals from severe illness and enabling the easing of public health measures, such as lockdowns and mandatory use of face masks in public areas.

As the virus responsible for COVID-19, SARS-CoV-2, continues to evolve, vaccines are being updated. To address waning protection from vaccination, policymakers are reviewing the optimal timing of future booster doses to maintain adequate protection against severe illness, particularly for older adults.

## Natural, vaccine-induced and hybrid immunity to the SARS-CoV-2 virus

Both vaccine-induced immunity and natural immunity (from past infection with the SARS-CoV-2 virus) provide strong protection against severe illness from subsequent SARS-CoV-2 infection and reduce the likelihood of requiring hospitalisation or intensive care admission. In particular, the high vaccine coverage achieved in Australia before high rates of transmission of the virus helped reduce the rate of severe outcomes. The strongest protection comes from hybrid immunity, which is immunity developed from a combination of vaccination and past infection.[1]

Serosurveys have found that more than two-thirds of Australian residents have evidence of previous infection with SARS-CoV-2.[2,3] With over 95% of people aged older than 16 years having had at least 2 vaccine doses,[4] most Australian adults now have hybrid immunity against SARS-CoV-2. However, both vaccine-induced immunity and natural immunity against reinfection are temporary. Protection against reinfection wanes rapidly (within weeks to months), but protection against severe illness is sustained and wanes over many months.[1] As protection against severe illness is the aim of the COVID-19 vaccination program, the waning of this protection provides the rationale for additional booster doses.

## Evolving variants and updated vaccines

Omicron has been the dominant variant of the SARS-CoV-2 virus circulating globally since 2022; previously seen variants are no longer being detected. Several subvariants of Omicron have been described.

Lower rates of severe illness have been reported with Omicron than previous variants.[5] Severe illness still occurs, and is more likely in people who are unvaccinated, older adults, and people with certain medical conditions. Severe illness is very rare in healthy children and young adults.[6]

COVID-19 vaccines are being updated to address the evolution of the SARS-CoV-2 virus. For an overview of COVID-19 vaccines currently in use, see COVID-19 Vaccines in Australia—A3 poster.


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The original COVID-19 vaccines are monovalent vaccines based on the ancestral strain of SARS-CoV-2. The most recently available COVID-19 vaccines in Australia are bivalent messenger RNA (mRNA) vaccines, based on both the ancestral strain as well as either the BA.1 or BA.4-5 Omicron subvariants. The BA.1-based bivalent vaccines are approved for use in adults only while the BA.4-5-based bivalent vaccines are approved for use in people aged 12 years and older. These vaccines can be used for both the primary course and for booster doses in their approved age groups. The bivalent vaccines provide enhanced protection against severe illness from Omicron compared with the original monovalent vaccines.[7]

Omicron subvariants showing significant spread during 2023 include XBB.1.5 and XBB.1.16, themselves both recombinants of BA.2.10.1 and BA.2.75 subvariants. BA.2.86 is a newer Omicron subvariant with a high number of mutations that could potentially assist it to evade immunity, though this has not yet been confirmed.[8] Monovalent vaccines based on the XBB.1.5 subvariant have been developed and are currently being reviewed by the Australian Therapeutic Goods Administration and overseas regulators.[9,10] Preliminary reports suggest that these vaccines will also elicit an immune response against the BA.2.86 subvariant.[11]

## Current primary vaccination recommendations

The Australian Technical Advisory Group on Immunisation (ATAGI) currently recommend primary COVID-19 vaccination for all people aged 5 years and older. In children aged 6 months to younger than 5 years, primary vaccination is recommended for those with severe immune compromise, disability, or those who have complex or multiple medical conditions that increase the risk of severe COVID-19.[7] For more detail on medical risk factors, see ATAGI COVID-19 clinical guidance.

For most people, a primary vaccination course consists of 2 doses given 8 weeks apart. A third primary dose is recommended for people aged 6 months or older with severe immune compromise.[7]

Bivalent mRNA vaccines are preferred for the primary course in people aged 12 years and older. Either a BA.1- or BA.4-5-based bivalent vaccine can be used, depending on the patient's age. If the primary course was started with an original monovalent COVID-19 vaccine, it is recommended that the course be completed with a bivalent mRNA vaccine.

In children aged 6 months to 11 years, currently only an age-approved original monovalent COVID-19 vaccine is recommended for primary vaccination.[7]

## Current booster recommendations

Booster doses of COVID-19 vaccines are given after the primary course to maintain protection against severe illness, and are of most benefit in people at high risk of severe COVID-19. For more detail on medical risk factors for severe illness, see ATAGI COVID-19 clinical guidance.

The following recommendations for boosters are from ATAGI.[12,13] Boosters are not currently recommended in children younger than 5 years.[12]

### *First 2023 booster dose*

A 2023 dose of COVID-19 vaccine is **recommended** for the following individuals whose last vaccine dose was at least 6 months ago (regardless of the number of previous vaccine doses received):

- adults aged 65 years and older
- adults aged 18 to 64 years who have medical comorbidities that increase their risk of severe COVID-19, or disability with significant or complex health needs.

A 2023 dose of COVID-19 vaccine can be **considered** for the following individuals whose last vaccine dose was at least 6 months ago (regardless of the number of previous vaccine doses received):

- all other adults
- children aged 5 to 17 years who have medical comorbidities that increase their risk of severe COVID-19, or disability with significant or complex health needs.

For patients in whom a 2023 dose can be considered, the decision should be based on an individual assessment of potential benefits and harms, and risk factors for severe COVID-19. Although the risk of severe illness in the context of younger age and previous vaccination may be low, other factors should be considered, such as individual preferences, medical history, history of SARS-CoV-2 infection (people who have never been infected do not have protection from hybrid immunity) and overseas travel. Also consider what the optimal timing of the dose would be for that person.

### *Additional 2023 booster dose*

An additional 2023 dose of COVID-19 vaccine is **recommended** for adults aged 75 years and older if it has been at least 6 months since their first 2023 dose.

An additional 2023 dose of COVID-19 vaccine can be **considered** for adults aged 65 to 74 years, and for adults aged 18 to 64 years with severe immune compromise, if it has been at least 6 months since their first 2023 dose. People who have no known history of SARS-CoV-2 infection, have medical risk

factors for severe COVID-19, or reside in an aged care facility are likely to benefit the most from an additional dose.

### *Vaccine choice for booster*

In people aged 12 years and older, bivalent mRNA vaccines are preferred for booster doses, regardless of which vaccine(s) were used for previous doses.[14] For adults, ATAGI does not specify a preference between BA.1- and BA.4-5-based bivalent vaccines, as both types provide a similar level of protection against severe illness from Omicron[7]. In children aged 12 to 17 years, only BA.4-5-based bivalent vaccines are approved for use.

In children aged 5 to 11 years, currently only an age-approved original monovalent vaccine is recommended for booster doses.

## Future booster recommendations

The optimal timing of future COVID-19 vaccine booster doses to maintain adequate protection against severe illness is not yet known. Annual vaccination coinciding with influenza vaccination would be a convenient strategy to alleviate the burden on health resources in winter. However, whether this is the optimal strategy for COVID-19 vaccination depends on the epidemiology of the SARS-CoV-2 virus. Unlike influenza, the seasonality of SARS-CoV-2 is not yet well characterised and, in Australia, 'waves' of COVID-19 have occurred during both summer and winter months, driven by waning immunity and/or new subvariants with increased immune escape potential.

Internationally, many countries have booster recommendations similar to ATAGI's advice, where groups at high risk for severe COVID-19 are recommended to receive a booster dose several months (e.g. between 6 and 9 months) after their most recent vaccine dose.

The World Health Organization recommends a 6-month booster interval for the 'oldest' adults; the definition of this group is determined by individual countries, but generally refers to people older than 75 years. A 12-month booster interval is recommended for other groups at risk of severe COVID-19.[15]

The availability of new COVID-19 vaccines in the future (e.g. based on XBB.1.5 subvariants) may lead to new booster recommendations, particularly if clinical data show that they provide significantly better protection than currently available vaccines.

## Vaccine safety update

The safety of COVID-19 vaccines has been actively and intensively monitored in Australia and globally since their introduction. Most local and systemic adverse events are mild and transient, such as injection-site pain and fatigue.

Serious adverse events remain extremely rare. Because of the large number of vaccine doses given globally, important safety signals for serious adverse events have been promptly identified. One example is the rare association between adenoviral vector vaccines (e.g. Vaxzevria [AstraZeneca]) and thrombosis with thrombocytopenia syndrome (TTS). These vaccines are no longer available in Australia, and no association with TTS has been found with other vaccine types.

Anaphylaxis after COVID-19 vaccines is very rare and occurs at a rate similar to other common vaccines. A study assessing anaphylaxis reports after COVID-19 vaccines across Europe and the USA found an overall rate of 10.67 cases per million doses (range: 7.99 to 19.39 cases per million doses depending on the vaccine).[16]

All COVID-19 vaccines have a very rare risk of myocarditis and pericarditis, and the mechanism by which this occurs is still under investigation. The risk of myocarditis is higher in males than in females, and is higher in adolescents and young adults compared with older adults. Early evidence suggests that the risk is higher after a second dose than after a third dose.[17] In Australia, the highest rate of myocarditis was reported in males aged 12 to 17 years after a second dose of Spikevax (Moderna) (23.6 cases per 100 000 doses).[18] Pericarditis occurs more commonly in adults aged 18 to 39 years.[18]

Other less common serious adverse events (eg capillary leak syndrome following Spikevax [Moderna]) have also been reported. For more detail, refer to the product information for each vaccine.

The safety profile of bivalent mRNA COVID-19 vaccines appears similar to the original monovalent mRNA vaccines. Up-to-date information on COVID-19 vaccine safety in Australia, including rates of serious adverse events such as myocarditis and pericarditis, is available from:

- AusVaxSafety
- Therapeutic Goods Administration COVID-19 vaccine safety reports.

## Revaccination after an adverse event

People who have experienced myocarditis or pericarditis or another serious adverse event (whether immune-mediated or nonimmune-mediated) after a COVID-19 vaccine dose may still be able to receive further vaccine doses. This decision should be based on an assessment of the potential harms and benefits of further doses, as well as considering the optimal timing of vaccination and choice of vaccine.[19] Specialist immunisation services can be consulted to provide advice regarding individual cases.

True contraindications to COVID-19 vaccines are extremely rare and individuals who have a contraindication to one COVID-19 vaccine may be able to receive an alternative brand or vaccine type, depending on the nature of the contraindication. For example, ATAGI advises that both the monovalent and bivalent formulations of the mRNA vaccines, Comirnaty (Pfizer) and Spikevax (Moderna), are contraindicated in a person with a history of anaphylaxis to polyethylene glycol (PEG) or to a previous dose of these mRNA vaccines; however, the person may be able to be safely vaccinated with Nuvaxovid (Novavax), a protein-based vaccine.[20]

People with non-anaphylactic–hypersensitivity reactions (e.g. delayed hypersensitivity or mild immediate hypersensitivity) may consider revaccination with additional supervision (e.g. longer observation period postvaccination) or additional measures (e.g. prophylactic antihistamines). Specialist medical guidance (e.g. from an immunologist) is recommended.

## Conclusion

While the combination of a successful COVID-19 primary vaccination program and widespread past infection with SARS-CoV-2 has reduced the risk of severe illness from COVID-19 for most young, healthy people, additional doses are likely to be needed to maintain adequate protection for older adults and others at high risk of severe illness. The optimal timing for future doses is not yet known. As SARS-CoV-2 evolves, updated vaccines to new variants are likely to be required. ≺

*Declared interests: Ketaki Sharma is a member of the Australian Regional Immunisation Alliance. Both Ketaki and Jean Li-Kim-Moy contributed to the authorship of the Australian Immunisation Handbook and statements of the Australian Technical Advisory Group on Immunisation (ATAGI). They both assisted ATAGI in drafting COVID-19 vaccination advice as part of their roles at the National Centre for Immunisation Research and Surveillance.*

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