# COVID-19: variants and vaccines

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In the latter part of 2020, two key events shifted the course of the COVID-19 pandemic: the availability of vaccines and the emergence of variants of concern.

A key question that rose up the agenda for policy makers — to what extent can vaccines mitigate the impacts of COVID-19, especially in the context of variants of concern?

Due to the many nuances and uncertainties in estimating the future impacts of vaccination, ongoing monitoring of SARS-CoV-2 epidemiology in Australia while vaccines continue to roll out is critical to adaptive policy making.

One of my roles in the COVID-19 response is to help provide epidemic situational assessment to Australian states and territories. As part of this, I have been coordinating (with Dr David Price) weekly (at least) situation reports submitted to the Communicable Disease Network of Australia (CDNA) and the Australian Health Protection Principal Committee (AHPPC) since April 2020. Each week the content of these reports represents a huge team effort – led by Professor James McCaw, an expert member of AHPPC (see the first essay in this series [3]). A large nationally distributed group of mathematical and statistical modellers conduct analyses of trends in population behaviours (using mobility data from technology companies and anonymous population surveys), the effective reproduction number (using case data) and forecasts of daily case counts and hospital occupancy. We also estimate the propensity for the virus to spread based on behavioural data and the biological characteristics of SARS-CoV-2 [2]. A weekly summary is published in the government's Common Operating Picture [1].

It has been an enormous privilege to develop new analyses and metrics alongside policymakers to meet information needs specific to our context — for example, understanding the risk of epidemic activity during sustained periods of zero cases and an ongoing risk of importation(s).

Over the past six months, the situational assessment teams have been continually adapting and extending their models to account for the differential impacts of new variants and vaccine products, and multiple co-circulating variants.

Vaccines can act on multiple elements of transmission and/or disease. They can reduce:

- Susceptibility to infection
- The probability of onward transmission from immunised infected individuals
- The probability of developing symptoms given infection
- The probability of developing severe disease and death given infection

The COVID-19 vaccines registered for use in Australia are highly effective at reducing susceptibility to infection and onward transmission from immunised infected individuals for the **Alpha variant**. The resulting overall reductions in transmissibility are estimated to be >90%.

These vaccines also dramatically reduce the probability that immunised infected individuals will develop severe disease ($>$ 85% estimated reduction) or die from their infection (also $>$ 85% estimated reduction). However, vaccine efficacy is specific to each

vaccine product and pathogen strain. At the time of writing, the **Delta variant** was set to become the dominant circulating SARS-CoV-2 strain globally. Early data shows decreased efficacy of our vaccines against the Delta variant (more on this later).

Above and beyond the direct benefits of vaccination, everyone—vaccinated and unvaccinated—indirectly benefits from reduced exposure because others are vaccinated. This protection is a consequence of the reduction in disease transmission brought by the depletion of fully susceptible people (see the first essay in this series by Professor James McCaw [3] for an explanation on the role of susceptible depletion).

This indirect protection is important because even highly effective vaccines are imperfect; there is still a chance of severe disease and death for fully vaccinated people. Further, some people are unable to be vaccinated, due to underlying health issues for example.

The level of vaccination coverage required to prevent sustained disease transmission is the critical vaccination or 'herd immunity' threshold. This threshold will vary according to pathogen transmissibility, vaccine efficacy, the population groups prioritised for vaccination, and levels of population mixing, among other factors. Higher pathogen transmissibility will increase the required level of coverage, while higher vaccine efficacy will decrease the required level of coverage.

More specifically, the proportion of a homogeneously mixing population that would need to be vaccinated to prevent sustained transmission is given by $(1 - 1/R_0)/\varepsilon$, where $R_0$ is the "basic reproduction number", the number of secondary cases arising from an index case in an otherwise fully susceptible population, and $\varepsilon$ is the proportional vaccine efficacy at reducing transmission.

Given an $R_0$ value in many countries for **wildtype** SARS-CoV-2 of between 3 and 4, if we assume that vaccine efficacy is 90%, then the critical vaccination coverage becomes 75-85%. The **Alpha** variant is estimated to be around 50% more transmissible than wild type. This increases the critical vaccination threshold to 85–95%.

Early evidence suggests that the **Delta** variant is between 30 and 60% more transmissible than Alpha and may partially evade vaccine- and naturally-derived immunity. The critical vaccination threshold for a strain exhibiting such characteristics is nearing 100%, though we would expect significant population protection at lower vaccination levels and effective management of transmission. Due to the relatively short circulation period of Delta, very limited evidence is available on clinical severity and vaccine effectiveness against clinical outcomes. Early available data suggests lower vaccine effectiveness against the Delta variant compared to Alpha for most outcomes.

The above simple calculations ignore important population heterogeneities that would make estimates higher or lower in specific settings. There are uncertainties in the transmissibility of Delta, indeed of any SARS-CoV-2 variant, including how it might vary geographically (even within Australia).

An important part of our research is to adapt the above calculations to include a range of age-specific heterogeneities. The level of transmission reduction and protection against clinical outcomes achievable for a given population level of coverage depends on which sub-populations are prioritised for vaccination and differences in disease characteristics and social behaviours across different groups.

The probability of hospitalisation, ICU admission and death given SARS-CoV-2 infection increases sharply with age, which is why vaccination programs in many countries have initially prioritised the oldest age groups.

Groups at the highest risk of severe outcomes receive indirect protection through the vaccination of key transmitting population groups. Not all age groups contribute equally to transmission. Contributions vary because of different social contact rates, susceptibilities to infection and symptomatic fractions (which affect infectiousness) by age. For SARS-CoV-2, evidence suggests that susceptibility to infection and propensity to develop symptoms increases with age. Younger people and working age groups typically have more social contacts than older people.

After accounting for all these factors, key transmitting ages for SARS-CoV-2 are estimated to be those aged 20–60 years. Whilst people under 20 have the highest numbers of contacts, they are less likely to spread SARS-CoV-2 to those contacts. People over 60

are more likely to spread SARS-CoV-2 to their contacts but typically have fewer contacts. People aged 20–60 have both relatively high numbers of contacts and ability to spread the disease. Thus, high coverage in these age groups is important for mitigating transmission and clinical outcomes.

Future emerging variants are a key uncertainty in our ongoing management of COVID-19. With the emergence of each novel variant of concern, an early priority is to gather information on critical epidemiological indicators. What is its relative transmissibility compared to existing variants? What is the probability of severe illness given infection with the new variant? Does this vary by age group? What is the effectiveness of vaccines against the new variant? Does this differ by vaccine product?

Estimating these quantities is extremely difficult in the early stages of variant emergence when information is scarce and detection efforts are highly varied and rapidly changing. Yet response planning/decisions are required before complete information is available. To support these decisions, analyses are made using the limited available data and must be continually reviewed and updated as evidence emerges.

Ongoing global circulation of COVID-19, and global vaccine inequity mean that new variants will continue to emerge. Some of these variants will likely exhibit some combination of higher transmissibility, higher clinical severity and/or immune evasion. New vaccines/boosters will likely be needed to protect against such future variants. Response planning is designed to be adaptable to this continually evolving situation and many possible futures. For now, vaccination programs globally will continue to reduce transmission and harms related to COVID-19, together with public health and social measures.

# References


[1] *Coronavirus (COVID-19) common operating picture*, https://www.health.gov.au/resources/collections/coronavirus-covid-19-common-operating-picture

[2] Nick Golding et al, *Situational assessment of COVID-19 in Australia Technical Report 15 March 2021 (released 28 May 2021)*, https://www.doherty.edu.au/uploads/content_doc/Technical_Report_15_March_2021_RELEASED_VERSION.pdf

[3] James McCaw, *Informing the COVID-19 response: mathematicians' contributions to pandemic planning and response*, https://austms.org.au/informing-the-covid-19-response-mathematicians-contributions-to-pandemic-planning-and-response/