COVID-19 Global Trends and Analyses

Volume 2: Vaccines and Viral Variants Update

June 2021 | Update 1 | Vol 2
Publication Date: 5 July 2021

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Burnet Institute
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This report can be cited as:

COVID-19 Global Trends and Analysis - Global Epidemiology and Global Snapshots (Public Health Report).
Toole M, Drummer H, Tachedjian G, Umali S, Majumdar S. Know-C19 Burnet Institute. 2021 June; Volume 2:1-21

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SUMMARY

Vaccines

- As of 1 July, more than 3.08 billion vaccine doses had been administered worldwide, equal to 40 doses for every 100 people. But the distribution across countries is highly uneven. If vaccines were distributed according to caseload, the greatest needs are in South and Central Asia, Southern Africa, and South America.
- 85 per cent of doses given worldwide have been administered in high- and upper-middle-income countries. Only 0.3 per cent of doses have been administered in low-income countries. Africa has the slowest vaccination rate of any continent, with some countries yet to start mass vaccination campaigns.
- Only seven African nations, most of them small, are expected to meet WHO's goal that every country worldwide vaccinate 10 per cent of its people against the coronavirus by September.
- In Australia, by 30 June, more than 7.8 million doses of COVID-19 vaccines had been administered, equivalent to 29 per 100 people. Around 6 per cent of the population are fully vaccinated. At the current pace of roughly 808,000 doses a week, we can expect to reach the 40 million doses needed to fully vaccinate Australia's adult population in early April 2022.
- Australia's coverage of fully vaccinated people is the lowest in the OECD.
- COVAX has so far shipped over 91 million COVID-19 vaccines to 133 countries. This is far short of the goal of delivering two billion doses in 2021. The ban on exports of the Indian manufactured AstraZeneca (CoviShield) has been a major blow to the program.
- A global survey was carried out by Imperial College London and YouGov between March and May 2021. The survey included more than 68,000 people in 15 countries. The UK had the highest share of respondents who reported trust in COVID-19 vaccines (87%), while Japan had the lowest (47%). Over half (59%) of respondents in Australia stated they trust COVID-19 vaccines.
- A new survey in Australia found 48 per cent of adults had one or two doses or had registered to be vaccinated. Another 26 per cent say they are likely to be vaccinated in the months ahead. The proportion of adults unlikely to get vaccinated was 26 per cent, down from 29 per cent in the previous survey.
- Researchers in the UK found efficacy of AstraZeneca vaccine against asymptomatic COVID-19 to be 62 per cent, much higher than the estimate of 22 per cent reported in an earlier paper.
- A study of people over 80 in Birmingham found that extending the interval between doses of Pfizer from 3 to 12 weeks led to a 3.5 fold increase in neutralising antibody but a reduced cellular response.
- In the UK where both Pfizer and AstraZeneca vaccines are used, effectiveness of two doses against the Alpha and Delta variants is 88 and 80 per cent, respectively, for the prevention of symptomatic disease.
- Moderna has announced that Delta was susceptible to its mRNA vaccine, although the antibody response was reduced compared to the original strain.
- Novavax's Phase 3 trial demonstrated overall efficacy of 90.4 per cent. All cases observed in the vaccine group were mild. Ten moderate cases and four severe cases were observed, all in the placebo group, yielding a vaccine efficacy of 100 per cent against moderate or severe disease.
- The UK reports that the incidence of TSS after the AstraZeneca vaccine is 20.2 per million doses in those aged 18-49 years compared to 10.7 per million doses in those aged 50 years and over.
- Australia has reported 64 confirmed and probable TSS cases with an incidence of 3.1 per 100,000 in those <50 years and 1.8 per 100,000 in those ≥50 years. Three people have died (one in the UK).

- The US CDC has reported a higher-than-expected number of young men experiencing heart inflammation after their second dose of Pfizer/BioNTech and Moderna. Israel and the EU have also reported these cases of myocarditis and pericarditis. Warnings have been issued.
- The evidence base for COVID-19 vaccination and effectiveness in immunocompromised individuals is limited. However, a number of studies have demonstrated reduced efficacy of vaccines in solid organ transplant recipients on immunosuppressive medications. A French study found a significantly higher antibody response after a third dose of Pfizer given within 60 days of the second dose.

Variants of Concern

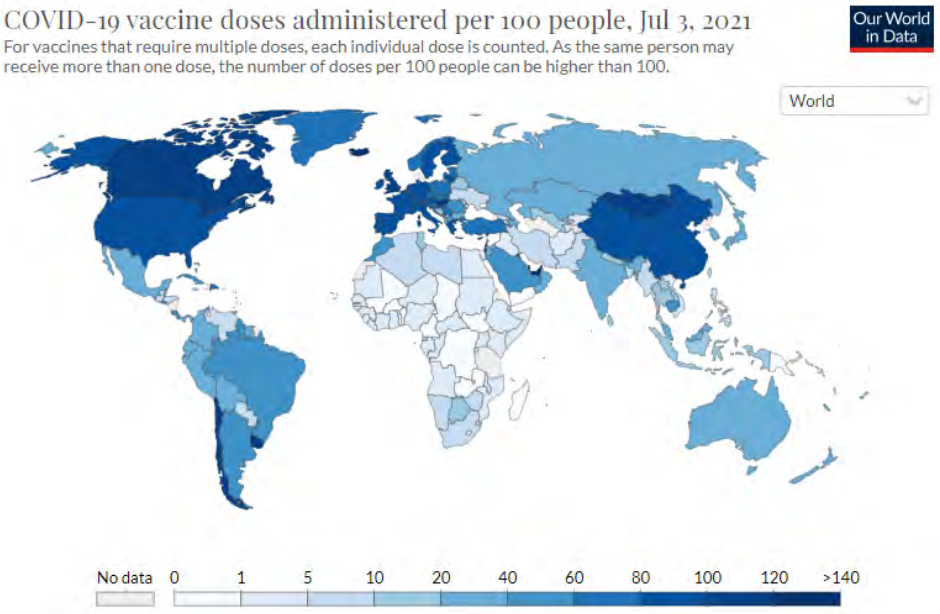
- According to WHO, the current SARS-CoV-2 variants of concern are Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Delta (B.1.617.2), and variants of interest are Epsilon (B.1.427 and B.1.429) Zeta (P2), Eta (B1.525), Theta (P3), Iota (B.1.526), Kappa (B1.617.1) and Lambda (C.37).
- The SARS-CoV-2 Alpha lineage virus is more transmissible than the original Wuhan strain, may lead to greater clinical severity, and results in modest reductions in antibody neutralisation. Since it was first detected in the UK late last year, the Alpha variant has spread around the world to become the dominant form of SARS-CoV-2 in most countries, although it is being replaced by Delta in some countries, including the UK. Some studies show that Alpha's ability to outstrip previously circulating variants could stem from mutations in its spike protein that allow it to enter cells more efficiently.
- A recent study suggests that Alpha also has properties linked to mutations outside the spike protein. These mutations probably mean that within hours of infecting a person, Alpha suppresses the rapid-response defence that the body mounts against all invaders. By blocking this 'innate immune response', the virus buys itself more opportunities to infect other people.
- First reported in October 2020, SARS-CoV-2 lineages Delta and Kappa have been increasingly detected in India and other countries. In just a few weeks, the Delta variant has become the dominant strain across India and has spread to about 96 nations, including the United Kingdom, Russia, Portugal, Myanmar, Nepal, Fiji, Vietnam and Singapore. It has caused community outbreaks in Australia, in Melbourne, Sydney, Darwin and Perth.
- In the UK, the most recent data show 99 per cent of sequenced and genotyped cases across the country are the Delta variant. The increase is primarily in younger age groups, a large proportion of which were unvaccinated.
- According to the Zoe COVID-19 Symptom app, initial symptoms associated with infection by the Delta strain in the UK are different from those experienced with earlier strains. The top five symptoms, in order, are headache, sore throat, runny nose, fever and cough. Loss of smell comes in at number 9 and shortness of breath comes far down the list at number 30.
- Data from Public Health England (PHE) show an increased risk of hospitalisation with Delta compared to Alpha, although PHE's analysis shows that two doses of a vaccine give a high degree of protection against hospitalisation, estimated to be more than 90 per cent.
- An analysis in Scotland found that Delta cases were associated with an 85 per cent increased risk of COVID-19 hospital admission when compared to non-Delta cases, after adjusting for age, sex, deprivation, temporal trend, and comorbidities.
- Also in Scotland, compared to those unvaccinated, the Pfizer vaccine offered very good protection, at least 14 days after the second dose: 92 per cent Alpha, 79 per cent Delta. Protection associated with the AstraZeneca vaccine was, however, substantial but reduced: 73 per cent for Alpha, 60 per cent for Delta.
- A Singapore study found that the serial interval between a person infected with Delta and infection of household contacts was not significantly reduced compared with Alpha.

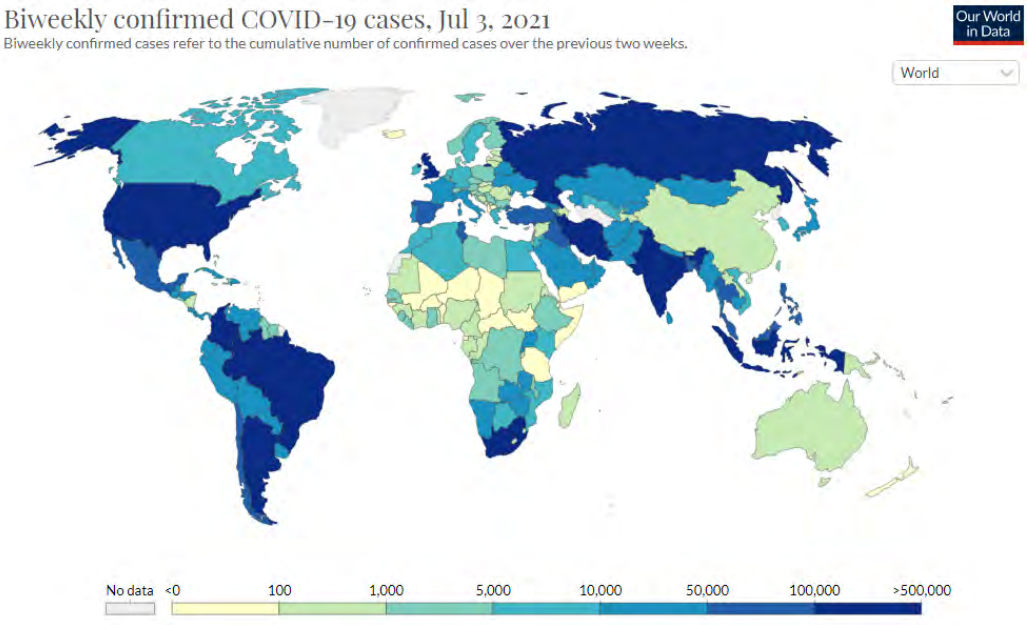
GLOBAL SCIENTIFIC UPDATES

SARS-CoV-2 Vaccines Update

Global Rollout of Vaccines

As of 1 July, more than 3.08 billion vaccine doses had been administered worldwide, equal to 40 doses for every 100 people. But the distribution across countries is highly uneven. **The map on the top shows** the per cent of people who have received at least one dose of vaccine. **The map underneath** shows the cases per 100,000 people in the past 14 days. If vaccines were distributed according to caseload, the greatest needs are in South and Central Asia, Southern Africa, and South America.



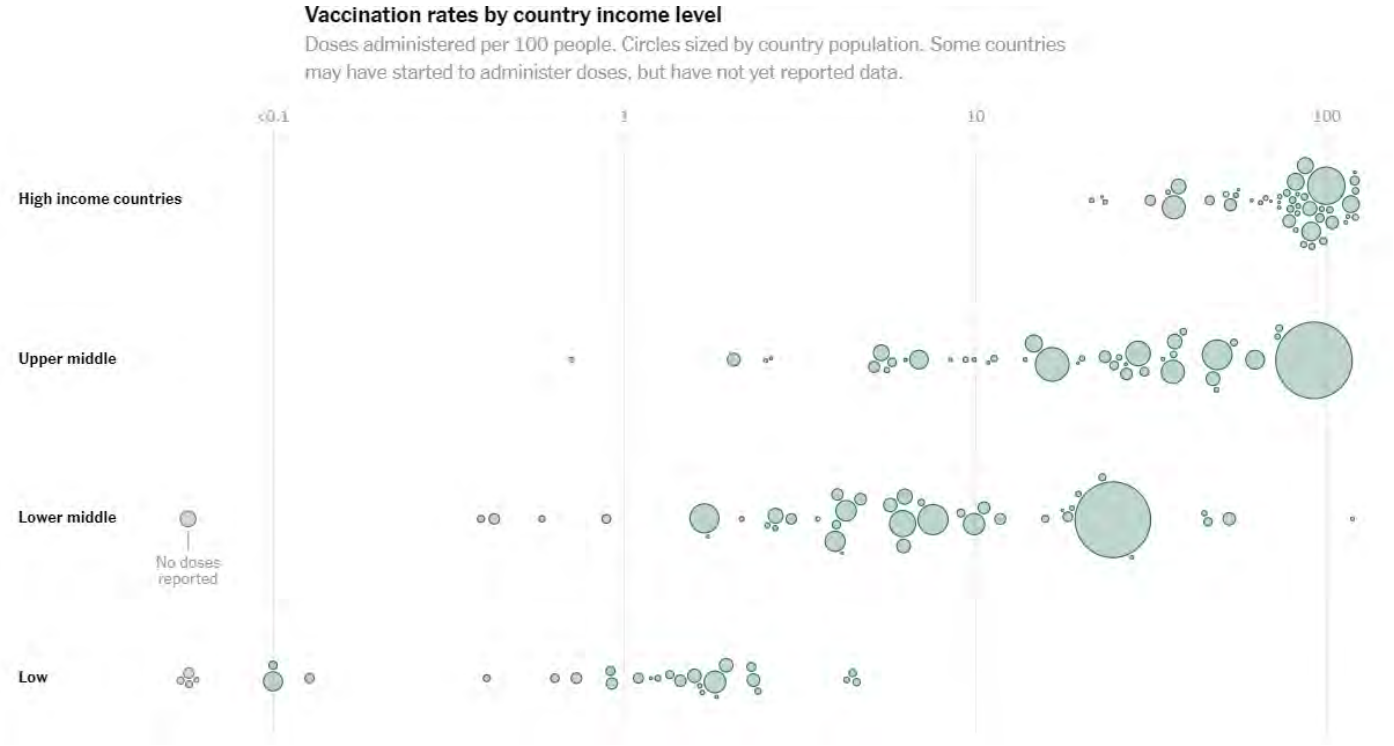


High Performers

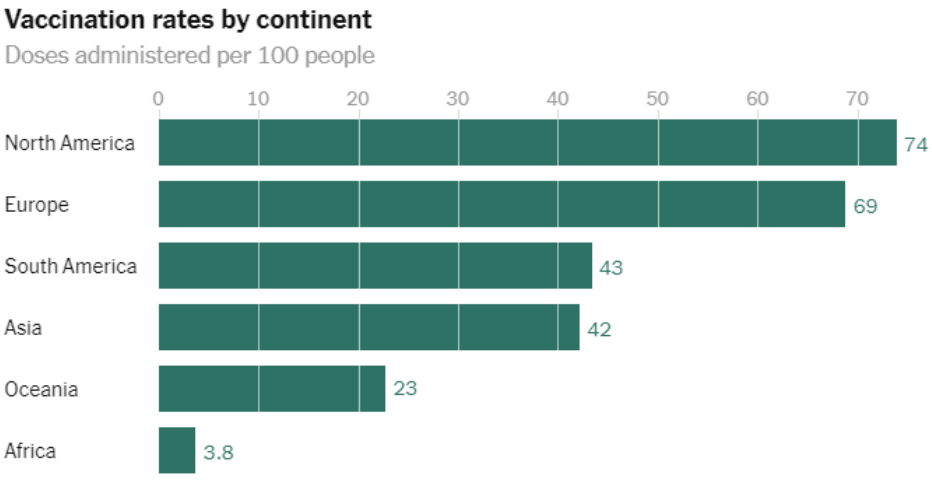
The threshold for COVID-19 vaccine coverage to achieve population (or 'herd') immunity is still unknown but expert estimates range between 70 and 90 per cent. **Seychelles** is vaccinating its people faster than any other nation. About 69 per cent of the population has received the two doses needed to be fully vaccinated. (Almost all the vaccines currently being used internationally require two doses several weeks apart. People are not fully vaccinated until they receive the second dose.) It is followed by Malta (62%), Bahrain (59%), Israel (57%), Chile (55%), Mongolia (54%), Hungary (50%), the UK (49%) and the US (46%).

Global Vaccine Inequity

The global distribution of COVID-19 vaccines has been marked by inequality. 85 per cent of doses given worldwide have been administered in high- and upper-middle-income countries. **Only 0.3 per cent of doses have been administered in low-income countries.** The following figure indicates the gap in coverage (doses per 100) by income levels.



There is also a striking divide between continents. Africa has the slowest vaccination rate of any continent, with some countries yet to start mass vaccination campaigns.

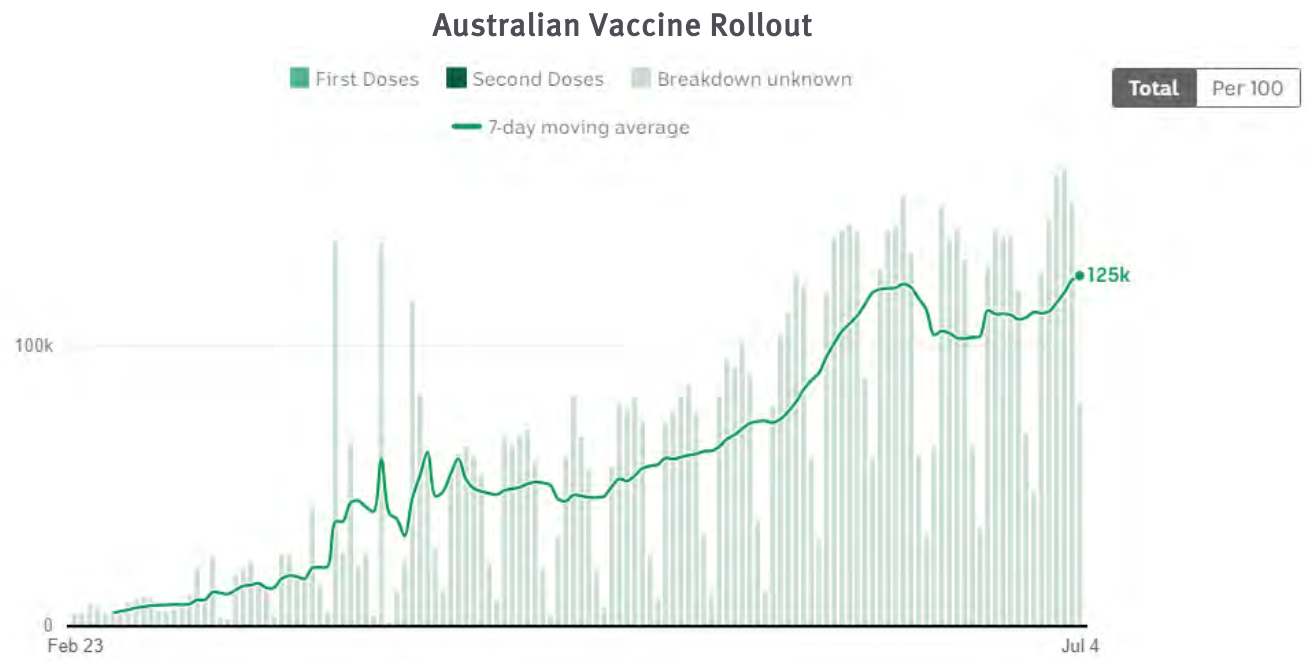


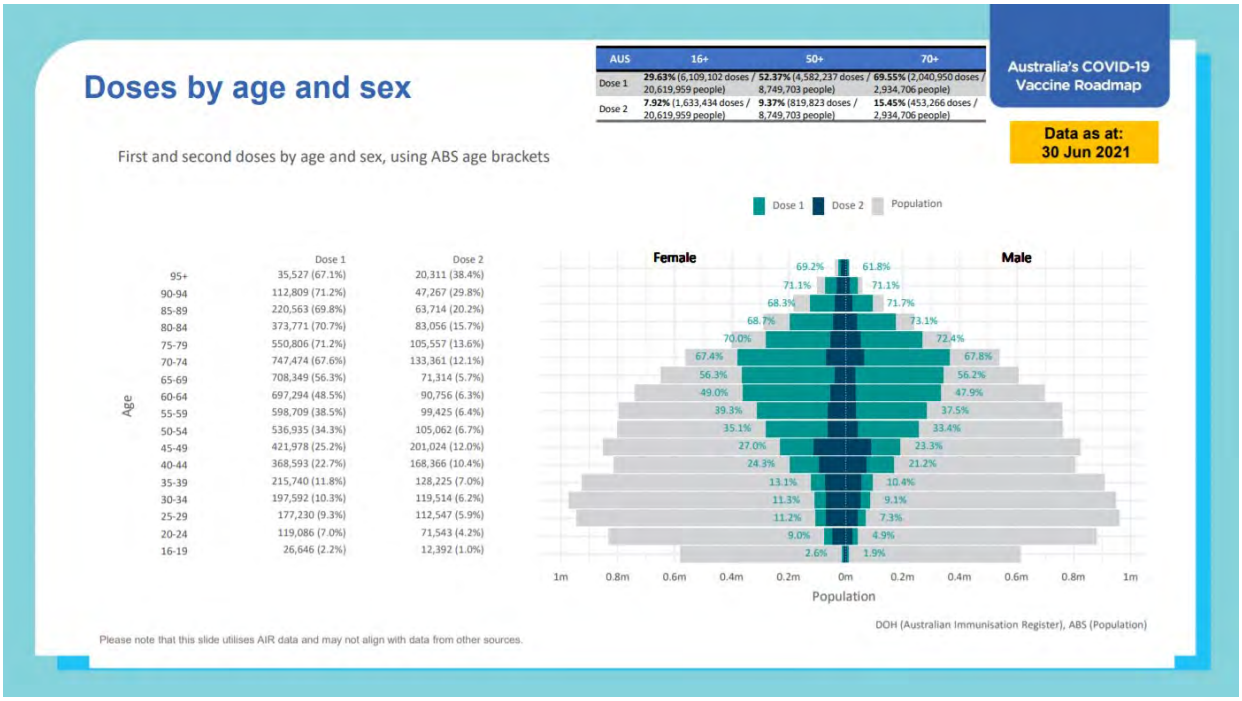
Australia | Vaccine Rollout and Trends

By 30 June, more than 7.8 million doses of COVID-19 vaccines had been administered, equivalent to 29 per 100 people. Around 6 per cent of the population are fully vaccinated. Vaccinations reached an all-time peak of 153,000 doses a day (moving average) on 11 June during Melbourne's lockdown and has since declined to 115,000 doses per day on 1 July.

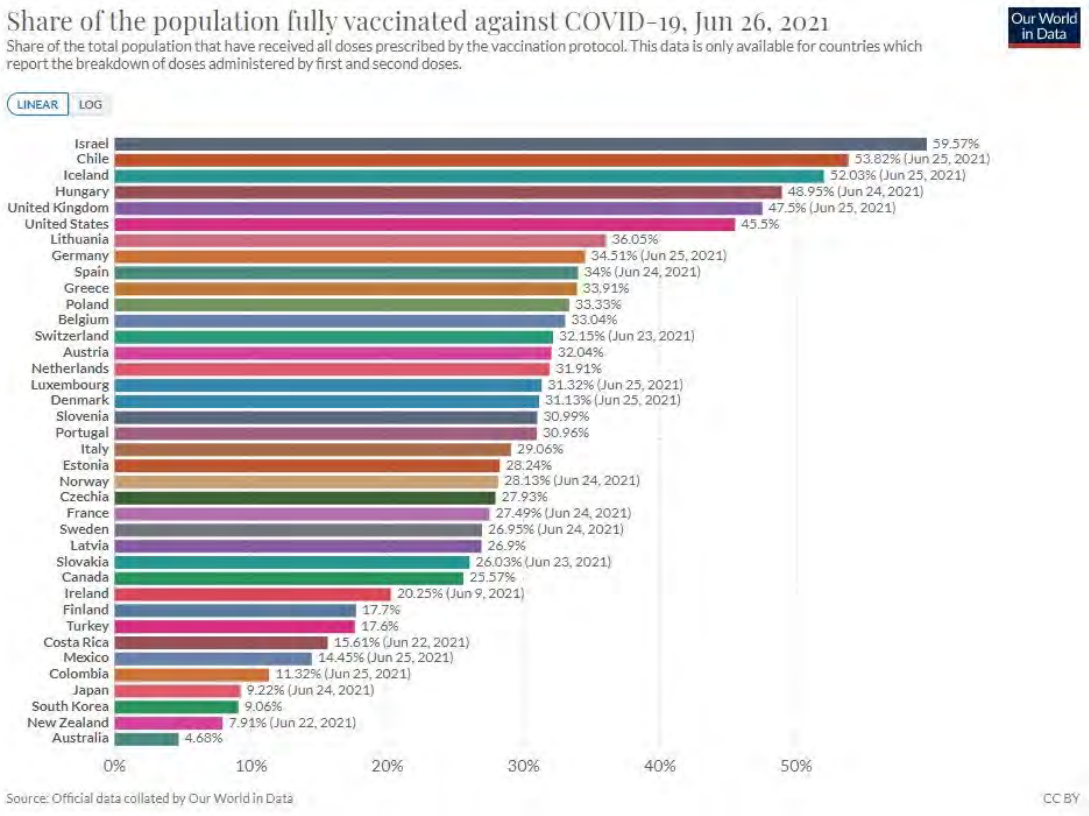
At the current pace of roughly 808,000 doses a week, we can expect to reach the 40 million doses needed to fully vaccinate Australia's adult population [in early April 2022](#).

Ongoing monitoring of rare side effects as a result of AstraZeneca vaccinations resulted in a change of advice from ATAGI on the 17 June 2021 to increase the age of eligibility to receive an AZ vaccine in people 60 years and over; the Pfizer vaccine is preferred for those 16 - 59 years of age.





Australian Vaccine Coverage Compared with Other High- and Upper-Middle-Income Countries



South Asia | Vaccine Rollout and Trends

So far, **India** has provided at least one dose to 23 per cent of the population. Just over 4 per cent have been fully vaccinated. In South Asia, tiny **Bhutan** has the highest rate of vaccinations having administered at least one dose to 64 per 100 but **Maldives** has the highest rate of fully vaccinated at 36 per cent.

Country	At least one dose per 100	Per cent fully vaccinated
Bhutan	64	-
Maldives	60	36
India	23	4
Sri Lanka	12	4.3
Nepal	9.1	2.6
Pakistan	5	1.6
Bangladesh	3.6	2.6
Afghanistan	1.7	0.5

Southeast Asia | Vaccine Rollout and Trends

As COVID-19 cases continue to surge in several Southeast Asian countries, such as Myanmar, Thailand, Malaysia, Cambodia, Vietnam and Indonesia, vaccination rates remain low with the exception of Singapore (which is 36 per cent fully vaccinated).

Other than Singapore, Cambodia (25%) has the highest rate of one vaccine dose, followed by Malaysia (18%), Indonesia (11%), Thailand (9.7%), Vietnam (3.5%) and Myanmar (3.4%). In Timor-Leste, which is just recovering from its largest surge of infections, 15.4 per cent of the population has received one dose of vaccine.

Africa | Vaccine Rollout and Trends

Only seven African nations, most of them small, are expected to meet WHO's goal that every country worldwide vaccinate 10 per cent of its people against COVID-19 by September. It is a dire prospect for a continent where vaccine supplies are being quickly depleted, and governments are battling resurgences in infections. WHO said on 10 June that inoculation coverage remained at about 2 per cent continent-wide — and about 1 per cent in sub-Saharan Africa — even as some rich nations across the world have administered shots to a majority of their people. The seven countries likely to meet the goal are Comoros, Equatorial Guinea, Mauritius, Morocco, Sao Tome and Principe, the Seychelles and Zimbabwe. An additional six countries — Eswatini, formerly known as Swaziland, Ghana, Kenya, Lesotho, Rwanda and Tunisia — could reach the target if they receive enough supply to keep up with their current pace of vaccination, WHO said.

As of 1 July, across the 54 countries on the African continent, at least one dose of vaccine has been administered to 2.7 per cent of the population. Only 1.04 per cent has been fully vaccinated. The highest coverage rate is in **Seychelles** where 62 per cent of the population has been fully vaccinated, followed by **Morocco**, which has fully vaccinated 25 per cent of the population. The only other African countries that have fully vaccinated more than one per cent of their populations are **Mauritius** (17%), **Equatorial Guinea** (8.4%), **Comoros** (4.8%), **Tunisia** (4.6%), **Zimbabwe** (3.7%), **Botswana** (2.9%), **Rwanda** (1.8%) and **Ghana** (1.3%). Not a single dose has been administered in Burundi, Central African Republic, Chad, Eritrea, Madagascar, Tanzania, Sahrawi Republic and Burkina Faso.

COVAX Progress | Vaccine Rollout and Trends

COVAX was created last year to ensure COVID-19 vaccines were made available around the world, with richer countries subsidising costs for poorer nations. The scheme hopes to distribute enough vaccines to protect at least 20 per cent of the population in 92 low- or medium-income countries - starting with healthcare workers and the most vulnerable groups. Its initial goal was to provide two billion doses of vaccines worldwide in 2021, and 1.8 billion doses to 92 poorer countries by early 2022.

COVAX has so far shipped over 91 million COVID-19 vaccines to 133 countries. This is far short of the goal of delivering two billion doses in 2021. The ban on exports of the Indian manufactured AstraZeneca has been a major blow to the program. Much depends on when the Novavax vaccine, which is the second largest planned source of vaccines for COVAX, will become available. Novavax has announced a delay in seeking authorisation until the third quarter of the year.

Recent developments include:

- The US has announced plans to donate 500 million doses of the Pfizer vaccine to the scheme (it previously offered 60 million doses).
- Japan has pledged $1 billion.
- The EU has pledged €500million, plus additional loans of €500million, while other European countries have collectively pledged more than €1billion (£864million)
- Germany, the UK, France, Italy and Sweden have each promised at least 100 million doses.

Problems at Biggest Vaccine Maker Leave World Short of COVID-19 shots

The world's largest vaccine maker, the Serum Institute of India (SII), was last year named a top supplier of COVID-19 vaccines to COVAX, the GAVI and WHO-backed initiative aimed at securing an equitable global rollout. But the Indian company has been affected by setbacks, including a ban on exports and a factory fire, which have hampered its ability to fill orders. The company manufactures Covishield under licence from AstraZeneca. The CEO had promised that 400 million doses would be available by the end of 2020. In fact, only 70 million were produced.

COVAX has so far received only 30 million of the minimum 200 million doses – at US$3 per dose – it ordered from the SII, which was to provide the bulk of its early supply. The company has been unable to send any vaccine overseas since April, when the Indian government banned COVID-19 vaccine exports amid the country's devastating second wave. The shortages come as the WHO and public health experts warn that low levels of vaccination in poorer nations could fuel the emergence of dangerous variants and lengthen the global pandemic.

Neighbouring countries are suffering from the shortfalls. Nepal, a nation of 28 million people has received only 2.38 million doses: one million directly from the SII (although it ordered two million), another one million in grant aid from India, and the rest from COVAX. Nepal had been expecting 13 million doses altogether from COVAX. But those flows have dried up given COVAX was relying heavily on the SII for supply. Pakistan and Bangladesh have kept their vaccination drives going by securing the majority of their doses from China after COVAX delayed deliveries.

The other company supplying India's rollout, Bharat Biotech, has also only provided about 27 million of a promised one billion annual doses of its vaccine.

Vaccine Confidence and Hesitancy

Global attitudes towards COVID-19 vaccines

A global survey was carried out by Imperial College London and YouGov between March and May 2021. The survey included more than 68,000 people from Australia, Canada, Denmark, France, Germany, Israel, Italy, Japan, Norway, Singapore, South Korea, Spain, Sweden, the UK, and the US. The UK had the highest share of respondents who reported trust in COVID-19 vaccines (87 per cent), while Japan had the lowest (47 per cent). In all countries but two (South Korea and Japan), over 50 per cent of respondents reported trust in COVID-19 vaccines.

Confidence in health authorities varies: respondents from the UK had the highest level of confidence that their health authorities would provide them with an effective COVID-19 vaccine (70 per cent), whereas respondents in South Korea had the lowest (42 per cent).

Excluding not being eligible for vaccination, the top reasons for hesitancy across all 15 countries surveyed were 'concerns about side effects' and/or 'concerns that there has not been enough testing of vaccines'. When respondents who **had not yet received the vaccine** were asked which brand they trusted the most, Pfizer had the highest response rate across all age groups in nine of the 15 countries surveyed. It had the highest response rate among those under 65 in three additional countries.

Attitudes towards COVID-19 vaccines in Australia

As of mid-May 2021, according to the Imperial College/YouGov survey, over half (59%) of respondents in Australia stated they trust COVID-19 vaccines. Excluding not being eligible yet, the main reason for not having received a COVID-19 vaccine across all age groups was 'concerns about side effects', followed by 'concerns that there has not been enough testing of vaccines'. When asked which brand they trusted the most, Pfizer had the highest share of respondents. This rate has increased since March.

A new survey, published on 15 June, conducted for *The Sydney Morning Herald* and *The Age* by research company Resolve Strategic, finds majority support for vaccination but highlights the obstacles in signing up the last quarter of adults. More Australians are getting their first doses, completing two doses or registering with authorities to be vaccinated,

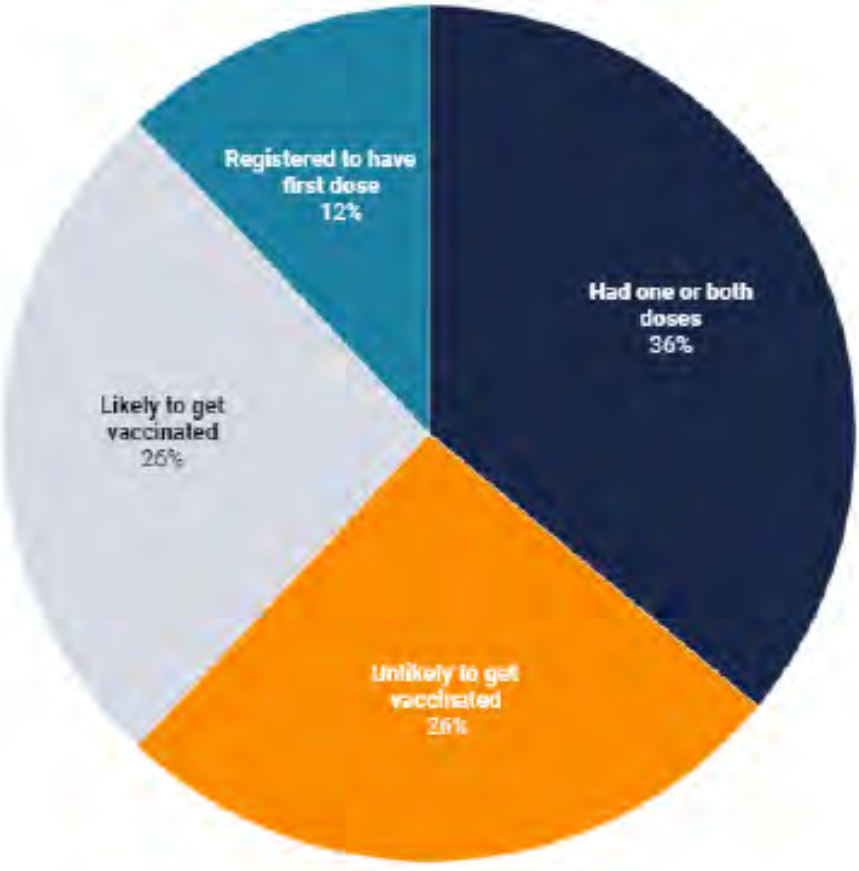
taking this group to 48 per cent of adults. Another 26 per cent say they are likely to be vaccinated in the months ahead. The proportion of adults **unlikely to get vaccinated was 26 per cent**, down from 29 per cent in the previous survey.

Outside those who have already had a vaccine or signed up for one, the survey found 8 per cent were “extremely likely” to be vaccinated, another 8 per cent were “very likely” and 11 per cent were “fairly likely” to do so. However, 12 per cent said they were “not very likely” and 14 per cent said they were “not at all likely” to be vaccinated. These results were down from 14 per cent and 15 per cent respectively one month ago.

The three most common reasons given for vaccine hesitancy were nervousness about side-effects in their age group (47 per cent), not knowing enough about the vaccines yet (43 per cent) and wanting to wait until more people get vaccinated (31 per cent). More than one reason could be given by respondents. Only 5 per cent said they were opposed to all vaccinations.

Vaccine status and uptake

Question: Have you been vaccinated yet?
If you were offered a vaccine appropriate to your age group in the next month or two, i.e. AstraZeneca for the over 50s and Pfizer for the under 50s, how likely would you be to take up the offer?



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Source: Resolve Political Monitor • Created with Datawrapper

Current Vaccines Update

AstraZeneca/Oxford (Vaxzevria)

AstraZeneca/Oxford vaccine: asymptomatic efficacy estimates

In a *Lancet* paper published in February, based on a meta-analysis of four separate trials, British researchers estimated that the efficacy of AstraZeneca vaccine increased from 55 per cent when the interval between doses was <6 weeks to 81 per cent when the interval was 12 weeks. Efficacy was calculated on the basis of prevention of symptomatic SARS-CoV-2 infection.

In a follow-up response published in *The Lancet* and using the original data table, the authors estimated efficacy against asymptomatic COVID-19 cases to be 61.9 per cent, which is much higher than the estimate reported in the original paper of 22.2 per cent. They concluded that this gives further confidence that the AstraZeneca vaccine provides substantial protection against asymptomatic infections. Real world data from Public Health England demonstrates that two doses of the Astra Zeneca vaccine reduce the risk of hospitalisation by up to 90 per cent with similar efficacy for both the Alpha and Delta variants.

Pfizer/BioNTech (Comirnaty)

Delaying the Pfizer vaccine's second dose boosts immune response

In a pre-print paper, not yet peer-reviewed, a study in Birmingham, UK, suggests that extending the interval between two doses enhances peak antibody generation in older people. In a population-based cohort study 172 people aged over 80 years of age received the Pfizer/BioNTech vaccination and were vaccinated with either a standard 3 week interval between doses or an extended interval schedule with the second dose at 12 weeks.

In those without evidence of previous infection the peak antibody response was 3.5-fold higher in people who had undergone delayed interval vaccination. But cellular immune responses were 3.6-fold lower. Extended interval vaccination may therefore offer the potential to enhance and extend humoral immunity. Further follow up is now required to assess long term immunity and clinical protection.

Real world data of vaccine effectiveness from Israel reveal that two doses of vaccine are required to achieve maximal effectiveness at preventing symptomatic disease, hospitalisation and severe disease, and effectiveness was similar across all age groups.

	14-20 days post 1st vaccination	>7 days post 2nd vaccination
Documented infection	46%	92%
Symptomatic infection	57%	94%
Hospitalisation	74%	87%
Severe disease	62%	92%
Death	72%	N/A

Neutralising antibody activity against SARS-CoV-2 Delta, Kappa and other variants by Pfizer vaccination

In this small US study published in *Nature*, the authors report that 20 human sera, drawn 2 or 4 weeks after two doses of Pfizer, neutralise Delta, Eta and Kappa variants of SARS-CoV-2. All sera tested neutralise the variant viruses at titres of at least 40. The susceptibility of these newly emerged variants to Pfizer vaccine-elicited neutralisation supports mass immunisation as a central strategy to end the COVID-19 pandemic across geographies.

In the United Kingdom where both Pfizer and Astra Zeneca vaccines are used, effectiveness of two doses against the Alpha and Delta variants is 88 and 80 per cent, respectively, for the prevention of symptomatic disease. This suggests there is only a modest reduction in efficacy towards the Alpha variant, while a more pronounced reduction in efficacy against the Delta variant.

Moderna announces its vaccine protects against Delta strain

Moderna has announced that Delta was susceptible to its mRNA vaccine, although the antibody response was reduced compared to the original strain.

In a pre-print article, sera from participants immunised on a prime-boost schedule with the mRNA-1273 COVID-19 vaccine were tested for neutralising activity against several SARS-CoV-2 variants of concern (VOCs), compared to neutralisation of the wild-type SARS-CoV-2 virus (designated as D614G). Results showed minimal effects on neutralisation titres against the Alpha variant (1.2-fold reduction compared with D614G); other VOCs such as Beta, Delta, and Gamma showed decreased neutralisation titres ranging from 2.1-fold to 8.4-fold reductions compared with D614G, although all remained susceptible to mRNA-1273–elicited serum neutralisation.

Sinopharm and Sinovac

China is currently the world's leading exporter of coronavirus vaccines. It has delivered more than 250 million doses to more than 90 countries around the world, with many of them in Latin America and the Asia-Pacific region. The WHO has given emergency authorisation to two of China's vaccines — one from the state-owned company Sinopharm, and the other from Sinovac, a private company based in Beijing. But the Chinese vaccines have recently come under scrutiny after cases rose in places like Bahrain, Mongolia and Seychelles — countries where large per centages of the population had been inoculated with the Sinopharm vaccine.

Both are inactivated virus vaccines. This means they're made from viral particles produced in a lab, which are then inactivated so they can't infect a recipient with COVID-19. Many other vaccines use similar platforms, including injectable polio, Hepatitis A and flu vaccines. Both companies use similar technology, and the vaccines are mixed with an adjuvant, which is a substance added to vaccines to stimulate a stronger immune response. The vaccines contain many proteins the immune system can respond to, stimulating the production of antibodies to fight COVID-19.

Sinovac's efficacy at preventing symptomatic infection was 51 per cent in Brazil, 67 per cent in Chile, 65 per cent in Indonesia, and 84 per cent in Turkey. The differences in results may be due to different variants circulating in each country at the time and differences in the populations included in the studies. Sinopharm's efficacy in preventing symptomatic infection was 78 per cent in UAE, Bahrain, Egypt and Jordan combined.

As with all the COVID-19 vaccines for which data are available, efficacy against the more severe outcomes is greater. Efficacy against hospitalisation for Sinovac in Chile, Brazil and Turkey was 85 per cent, 100 per cent and 100 per cent, respectively.

The Sinovac vaccine is 50 per cent effective against the gamma variant in Brazil. Sinopharm has said that a small-scale study showed that it could protect against the beta variant, which first appeared in South Africa, but there was some unspecified reduction in the protection.

Data published in April from a large real-world study in Chile suggests Sinovac is 67 per cent effective in preventing symptomatic COVID-19 infection. It's effectiveness against hospitalisation was 85 per cent, ICU admission 89 per cent, and death 80 per cent. Sinopharm's effectiveness against symptomatic infection in Bahrain was 90 per cent.

The main problem with these vaccines, especially Sinovac, is that a very high coverage will be needed to achieve herd immunity and may indeed not be attainable against the beta or gamma variants if this is the sole vaccine used in any country. While China's vaccine rollout was slow initially it has recently been accelerating reaching around 20 million doses per day. By 16 June, 63 per cent of the population had received at least one dose of vaccine.

Vaccines in Development

Novavax

Novavax COVID-19 vaccine demonstrates 90 per cent overall efficacy and 100 per cent protection against moderate and severe disease in Phase 3 trial.

In a media release, the company announced the results of the Phase 3 trial of its vaccine (NVX-CoV2373), a recombinant nanoparticle protein-based COVID-19 vaccine The study enrolled 29,960 participants across 119 sites in the US and Mexico to evaluate efficacy, safety and immunogenicity, with an emphasis on recruiting a representative population of communities and demographic groups most impacted by the disease.

In the placebo-controlled study randomised 2:1, NVX-CoV2373 demonstrated overall efficacy of 90.4 per cent, achieving its primary endpoint. Seventy-seven cases were observed: 63 in the placebo group and 14 in the vaccine group. All cases observed in the vaccine group were mild as defined by the trial protocol. Ten moderate cases and four severe cases were observed, all in the placebo group, yielding a vaccine efficacy of 100 per cent against moderate or severe disease.

Against variants of concern (VoC) and variants of interest (VoI), which represented 82 per cent of the cases, vaccine efficacy was 93.2 per cent. Thirty-eight of the VoC/VoI cases were in the placebo group and six were in the vaccine group.

However, in a Phase 2a-b study conducted in South Africa in 6,234 people and published in the New England Journal of Medicine reveals a post-hoc analysis of efficacy for the beta variant of 51 per cent among HIV negative individuals.

The company plans to seek regulatory authorisation In the US in the third quarter and is on track to reach manufacturing capacity of 100 million doses per month by the end of the third quarter and 150 million doses per month by the end of the fourth quarter of 2021. **Australia** has ordered 51 million doses of Novavax.

Valneva

Inactivated COVID-19 vaccine candidate launches Phase 3 trial.

France-based Valneva has completed the recruitment of 4,000 volunteers in the UK for the Phase 3 trial of its inactivated, adjuvanted COVID-19 vaccine candidate, VLA2001. VLA2001 is currently the only inactivated COVID-19 vaccine in clinical trials in Europe. It is intended for active immunisation of at-risk populations to prevent carriage and symptomatic infection with COVID-19 and potentially later for routine vaccination, including addressing new variants. The UK-based trial "Cov-Compare" will be conducted at 26 sites and will compare Valneva's VLA2001 against AstraZeneca's conditionally approved vaccine, Vaxzevria. Results are expected in September 2021.

Valneva recently announced that it is participating in the world's first COVID-19 vaccine booster trial in the UK. The "COV-Boost" trial will look at seven different COVID-19 vaccines and provide vital data on how effective a booster of each vaccine protects individuals from the virus. Initial findings for the COV-Boost study are also expected in September 2021.

BCG-adjuvanted COVID-19 Vaccine

A single dose, BCG-adjuvanted vaccine provides sterilising immunity against SARS-CoV-2 infection in mice.

In a pre-print paper, Melbourne researchers report that they employed the immunostimulatory properties of bacille Calmette-Guérin (BCG), the existing tuberculosis vaccine, to deliver a vaccination regimen (BCG:CoVac) with potent SARS-CoV-2-specific protective immunity. Combination of BCG with a stabilised, trimeric form of SARS-CoV-2 spike antigen promoted rapid development of virus-specific IgG antibodies in the blood of vaccinated mice, which was further augmented by the addition of alum.

Vaccination of mice with a single dose of BCG:CoVac almost completely annulled disease after SARS-CoV-2 challenge, with minimal inflammation and no detectable virus in the lungs of infected animals. Boosting BCG:CoVac-primed mice with a heterologous vaccine further increased SARS-CoV-2-specific antibody responses, which effectively neutralised the Alpha and beta SARS-CoV-2 variants of concern.

Benefits of Vaccination

Six months of COVID-19 vaccines: what have 1.7 billion doses taught us?

A paper in *Nature* explores key questions about the vaccines that countries are racing to deliver while viral variants spread around the world.

1. Real-world data have come in from several countries, and much of the news has been positive about how well vaccines perform in the general population. A nationwide vaccination campaign in Israel found the Pfizer–BioNTech vaccine to be 95 per cent effective against SARS-CoV-2 infection seven days or more after the second dose. The Gamaleya Centre in Moscow announced that the Sputnik V vaccine has been 97 per cent effective in almost 4 million people in Russia. And in May, Public Health England reported that the Pfizer and AstraZeneca vaccines are both 85–90 per cent effective in preventing symptomatic disease after two doses.

2. Among older adults who received the Pfizer vaccine, Israel has seen 94 per cent protection from SARS-CoV-2 infection in people over 85 years old. Similarly, a UK study found that the Pfizer and AstraZeneca vaccines were both 80 per cent effective at preventing COVID-19 hospitalisations in people aged 70 or older.

3. At the other end of the age spectrum, Pfizer and Moderna have recently completed clinical trials of their vaccines in adolescents, showing 100 per cent and 93 per cent protection in those aged 12–15 and 12–17, respectively.

4. Initial laboratory tests suggested that antibodies raised by the Pfizer vaccine were less effective against the beta variant identified in South Africa, but it was unclear how that would affect protection against disease. In May, researchers in Qatar published reassuring data showing that people who received two doses of the Pfizer vaccine were 75 per cent less likely to develop COVID-19 from infection with beta and were almost completely protected from severe disease.

   The AstraZeneca vaccine did not fare as well in another study: in South Africa, a small clinical trial suggested that the vaccine did little to prevent infections of the beta variant that, by that point, was causing most infections there.

5. Six months is not much time to collect data on how durable vaccine protection will be, but data could soon emerge from clinical-trial participants who had their first doses last July. In the meantime, some researchers are looking to natural immunity as a guide. A study in more than 25,000 healthcare workers in the UK found that a SARS-CoV-2 infection reduced the risk of catching the virus again by 84 per cent for at least 7 months.

   But viral immunologists at Emory University in Atlanta, Georgia, found that antibody levels declined faster in those who were vaccinated with the Moderna vaccine than in those who had been infected by SARS-CoV-2.

6. The UK Government is funding a study of seven different COVID-19 vaccines given as boosters at least 10–12 weeks after the second dose of an initial vaccine. Early findings are expected in September. The US NIH is also studying boosters in study participants who received their first vaccine dose in an early clinical trial that began in March 2020.

7. Key clinical trials for currently authorised vaccines determined whether the inoculations could safely avert symptomatic disease in individuals. But blocking transmission of the virus is also crucial for ending a pandemic, and most of those clinical trials did not track asymptomatic infections that could fuel the virus's spread.

   Researchers have been trying to fill this gap, and, so far, the data look promising. Results announced by Johnson & Johnson from clinical trials suggest that its vaccine is 74 per cent effective against asymptomatic infections. Researchers studying deployment of the Pfizer vaccine in Israel have also reported that vaccination reduces the amount of virus found in infected individuals by up to 4.5-fold, suggesting that they could be less likely to shed that virus into the environment, where it might infect someone else.

Technical Vaccine Update

Vaccine Safety

Since early March 2021, reports have emerged in many countries of a rare but serious side effect involving thrombosis (clotting) with thrombocytopaenia (low blood platelet count) in young healthy people who had received the AstraZeneca-Oxford vaccine. Most cases involved clotting in a large vein such as in the brain, called cerebral venous sinus thrombosis (CVST). This clotting syndrome is now commonly known as thrombosis with thrombocytopenia syndrome (TTS), and has been associated with only adenoviral vector vaccines (currently AstraZeneca and Johnson and Johnson).

Testing typically reveals low platelet count and low fibrinogen and very raised D-Dimer levels above the level typically expected in venous thromboembolism. Antibodies to platelet factor 4 (PF4) have been identified, hence there are similarities to heparin-induced thrombocytopenia despite the absence of prior exposure to heparin treatment.

Incidence in the UK

According to the UK Medicines and Healthcare products Regulatory Agency (MHRA), up to 9 June 2021, 390 cases of major thromboembolic events following vaccination with AstraZeneca had been reported in the UK. Twenty-seven of these events have been reported after a second dose. Of the 390 reports, 207 occurred in women, and 180 occurred in men aged from 18 to 93 years. The overall case fatality rate was 18 per cent with 71 deaths, four of which occurred after the second dose.

The estimated number of first doses of AstraZeneca administered in the UK by 9 June was 24.6 million and the estimated number of second doses was 17.7 million. The overall incidence after first or unknown doses was 14.8 per million doses. There is a higher reported incidence rate in the younger adult age groups following the first dose compared to the older groups (20.2 per million doses in those aged 18-49 years compared to 10.7 per million doses in those aged 50 years and over).

Incidence in Australia

In the week to 24 June, five additional cases of blood clots with low blood platelets have been assessed by the TGA as TTS likely to be linked to the AstraZeneca vaccine. The increase in the number of cases correlates with an increase in the number of doses of AstraZeneca vaccine administered during the reporting period. When assessed using the UK case definition, three cases were confirmed and two were deemed probable TTS. However, following reassessment of a previously reported case as being unlikely to be TTS, there is only a net increase of four cases. This brings **the total number of cases of TTS to 64**.

This takes the total Australian reports assessed as TTS following the AstraZeneca vaccine to 40 confirmed cases and 24 probable cases. Cases have most often occurred about two weeks after vaccination, although the time to onset (or diagnosis) has ranged from two days to 52 days. Approximately one in four TTS cases has required ICU treatment, although all but four patients have since been released from ICU. Although estimates of risk based on small numbers of cases are imprecise, the risk of TTS in Australia is estimated by ATAGI at around:

- 3.1 per 100,000 in those <50 years
- 1.8 per 100,000 in those ≥50 years.

There were no significant differences in estimated risk by sex in those ≥50 years of age.

ATAGI has since recommended that AstraZeneca should only be given to people over the age of 59 years In Australia, in line with most European countries.

Reported blood clotting with low platelet events associated with SARS-CoV-2 vaccines in Scotland

Scottish researchers estimated associations between exposure to first-dose AstraZeneca and Pfizer vaccinations and haematological and vascular adverse events. An almost six-fold increased risk of idiopathic thrombocytopenic purpura (ITP) was found after AstraZeneca vaccination 0–27 days after the first dose, with an estimated incidence of 1.13 cases per 100,000 doses. There was also an increased risk for arterial thromboembolic events. For haemorrhagic events 0–27 days after vaccination, there was a 1.5-fold increased risk. No positive associations were seen between the Pfizer vaccine and thrombocytopenic, thromboembolic and haemorrhagic events.

Cases of heart inflammation found in young men after Pfizer and Moderna vaccines

The US CDC has reported a higher-than-expected number of young men experiencing heart inflammation after their second dose of the mRNA COVID-19 shots from Pfizer/BioNTech (Comirnaty) and Moderna. The US agency has been investigating heart inflammation cases after Israel's Health Ministry reported that it had found a likely link to the condition in young men who received Pfizer's COVID-19 vaccine. The US Food and Drug Administration (USFDA) announced that it will add a warning of rare heart inflammation cases among adolescents and young adults to its fact sheets for Pfizer-BioNTech and Moderna COVID-19 vaccines. This comes after the US CDC advisory groups found that inflammation in adolescents and young adults is likely linked to vaccines, but that the benefits of the vaccines appeared to clearly outweigh the risk. The health regulator noted that those who report heart inflammation after vaccination generally recover from the symptoms.

According to an Israeli health ministry report in late April, out of more than 5 million people vaccinated at that time, 62 were diagnosed with myocarditis, inflammation of the heart muscle, within days of receiving their Pfizer dose, of which 56 were recorded after the second shot, chiefly in men under 30. Two of the patients, a 22-year-old woman and a 35-year-old man, died.

More than half of the cases reported to the US Vaccine Adverse Event Reporting System (VAERS) after people had received their second dose of either the Pfizer/BioNTech or Moderna vaccines were in people between the ages of 12 and 24 years. There were 283 observed cases of heart inflammation after the second vaccine dose in those aged 16 to 24, and just less than 80 per cent of the cases were men. The CDC said they would typically expect to find between 10 and 102 cases of the condition in that age range, based on US population background incidence rates.

According to the European Medicines Agency (EMA), as of the end of May 2021, cases of **myocarditis** reported in the EU were: 122 (Comirnaty), 16 (Moderna), 38 (Vaxzevria) and zero for Janssen/Johnson and Johnson. The exposure in the EU for each vaccine was around 160 million doses for Comirnaty, 19 million doses for Moderna, 40 million for Vaxzevria and 2 million for Janssen.

As of end of May 2021, cases of **pericarditis** reported in the EU were: 126 (Comirnaty), 18 (Moderna), 47 (Vaxzevria) and 1 (COVID-19 Vaccine Janssen). The exposure in the EU for each vaccine was around 160 million doses for Comirnaty, 19 million doses for Moderna, 40 million for Vaxzevria and 2 million for Janssen.

Effectiveness of COVID-19 vaccines in immunocompromised individuals

The evidence base for COVID-19 vaccination and effectiveness in immunocompromised individuals is limited. This is an important issue as immunocompromised people (1) are at high risk of severe outcomes from COVID-19; (2) may not mount an appropriate antibody response and remain at risk of infection and, therefore, also transmission to others and (3) if infected, there may be a higher chance of a variant emerging within that individual. This perspective from an immunocompromised healthcare worker highlights the uncertainty and risk, ongoing need for personal infection prevention measures and potential stigma. The Melbourne Vaccine Education Centre has a resource page for COVID-19 vaccines in immunocompromised people.

There have been several recent developments, noting the heterogeneity in immunosuppressive medications and conditions. Studies have been assessing antibody responses to vaccines; however, there is no established threshold for protective immunity. Therefore, routine antibody testing after vaccination is not currently recommended.

This study assessed antibody responses after two doses of an mRNA vaccine in 658 solid organ transplant recipients. It found that 54 per cent had detectable antibodies after the second dose, although the levels were lower in those who did not respond to the first dose. Poor response was associated with the use of antimetabolite immunosuppression agents (43 per cent had antibodies after dose 2), such as methotrexate, and azathioprine - also used in conditions such as rheumatoid arthritis and inflammatory bowel disease and certain cancer chemotherapy.

Strategies to address the lack of response include booster doses (a third dose) or increasing the dosing as has been done for hepatitis B and influenza vaccination in the immunocompromised. A small case series of 30 patients with solid organ transplants who had no (24 patients) or low (6 patients) response after two doses of mRNA vaccine, assessed antibody responses after a 3rd dose. The 3rd dose was an adenovirus vector vaccine (15 patients) or mRNA (15 patients). All six patients with low antibodies responded to the 3rd dose but only 33 per cent of the no response patients. There were no serious adverse effects.

In correspondence with the *NEJM*, researchers assessed the effectiveness of a recommendation by the French National Authority for Health to give a third dose of an mRNA vaccine to immunosuppressed patients. They report the humoral response in a group of 101 consecutive solid-organ transplant recipients who were given three doses of the Pfizer–BioNTech vaccine. The group included 78 kidney-transplant recipients, 12 liver-transplant recipients, eight lung-transplant or heart-transplant recipients, and three pancreas-transplant recipients. The first two doses were given one month apart, and the third dose was administered around 60 days after the second dose.

Among the 59 patients who had been seronegative before the third dose, 26 (44%) were seropositive at four weeks after the third dose. All 40 patients who had been seropositive before the third dose were still seropositive four weeks later; their antibody titres increased from 36±12 before the third dose to 2676±350 one month after the third dose.

This study showed that administration of a third dose of the Pfizer vaccine to solid-organ transplant recipients significantly improved the immunogenicity of the vaccine, with no cases of COVID-19 reported in any of the patients. However, a large proportion of the patients remain at risk for COVID-19. Barrier measures should be maintained, and vaccination of the relatives of these patients should be encouraged.

Antibody responses are important, but longer term studies are needed to determine the effectiveness. A multi-centre study from Israel assessed the effectiveness and safety of two dose mRNA vaccine in patients with autoimmune inflammatory rheumatic diseases (AIIRD), compared with the general population. The Pfizer vaccine was immunogenic in the majority of patients with AIIRD, with an acceptable safety profile. Following vaccination, the seropositivity rate and S1/S2 IgG levels were significantly lower among patients with AIIRD versus controls (86% (n=590) vs 100%). Treatment with glucocorticoids, rituximab, MMF, and abatacept was associated with a significantly reduced Pfizer-induced immunogenicity.

GLOBAL SCIENTIFIC UPDATES

Variants of Concern and Variants of Interest Update

Naming of SARS-CoV-2 Variants

On 1 June, the expert group convened by the WHO has recommended using labelled letters of the Greek Alphabet as a more practical way to discuss variants with non-scientific audiences. More information is available here.

Variants of Concern (VOC)

- Alpha is the B.1.1.7 lineage first detected in England in September 2020.
- Beta is the B.1.351 lineage first detected in South Africa in May 2020.
- Gamma is the P.1 variant first detected in Japan and Brazil in November 2020.
- Delta is the B.1.617.2 variant first detected In India in October 2020, which caused recent outbreaks in Melbourne and Sydney.

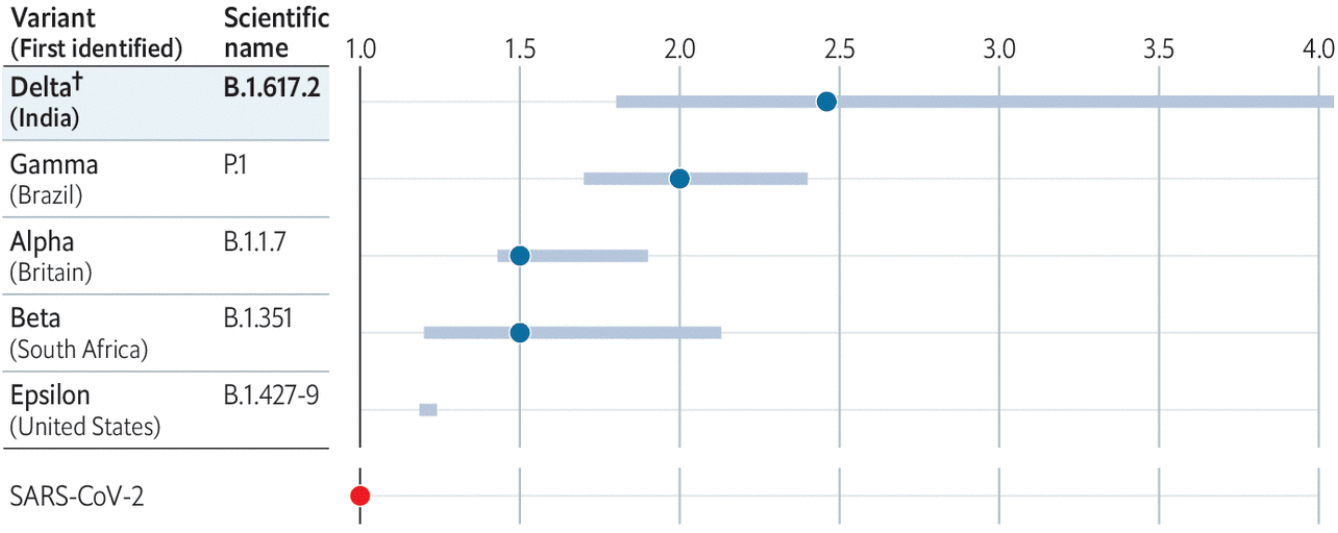
Variants of Interest (VOI)

- Epsilon is the B.1.427/B.1.429 lineage first detected in California in late 2020.
- Iota is the B.1.526 variant first identified in New York in November 2020.
- Kappa is the B.1.617.1 variant first detected in India in October 2020, which caused a recent outbreak in Melbourne.
- Lambda is the C.37 variant, which emerged in Peru in December 2020 and has been identified in 26 countries.

Estimated transmissibility of VOCs

Rate of change

Covid-19, estimated transmissibility* of variants compared with original SARS-CoV-2 virus



Sources: Davies et al. (2021); Pearson et al. (2021); Faria et al. (2021); Allen et al. (2021); Centres for Disease Control and Prevention; Public Health England

*Odds ratio of infection or relative R number
†Extrapolated from transmissibility relative to alpha variant

The Economist

Alpha (B.1.1.7) variant

A study posted on bioRxiv on 7 June suggests that Alpha has properties linked to mutations outside the spike protein. These mutations probably mean that within hours of infecting a person, Alpha suppresses the rapid-response defence that the body mounts against all invaders. By blocking this 'innate immune response', the virus buys itself more opportunities to infect other people.

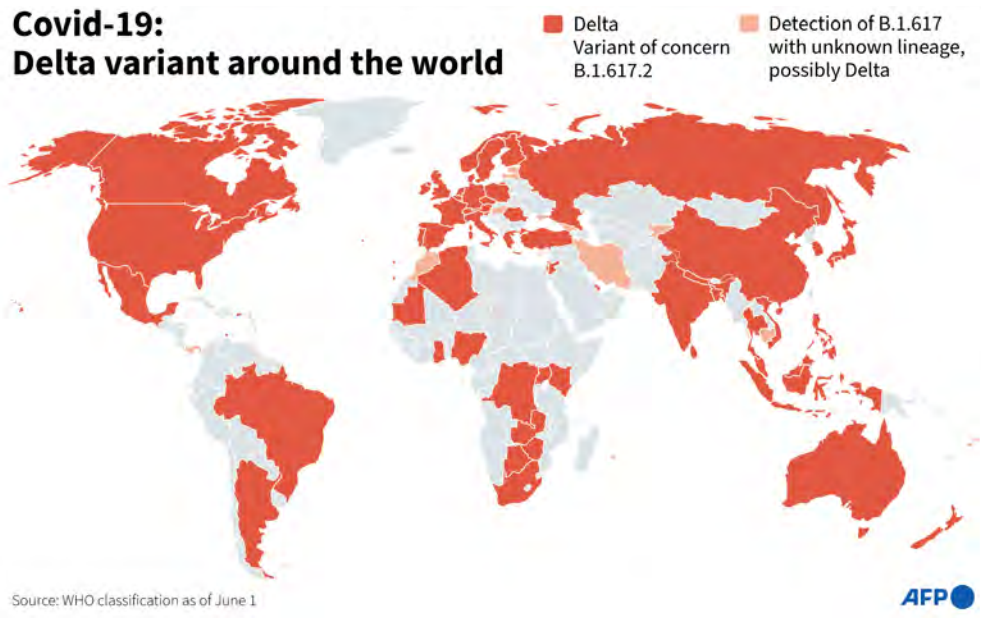
Krogan and colleagues examined how cells from the human airway produced interferon, an immune protein that kick-starts the body's defences on the arrival of a pathogen. The team found that cells infected with Alpha produce much less interferon than do cells infected with previously circulating SARS-CoV-2 variants. Alpha's suppression of interferon production helps the variant to linger for longer in the body. Alpha-infected cells also had much higher levels of viral RNA encoding the protein Orf9b, and of Orf9b itself. The researchers found that Orf9b dampens the body's defences by interfering with host proteins that typically activate interferon production and other genes important for the innate immune response.

In another study posted on bioRxiv, and also not yet peer-reviewed, researchers analysed viral samples from people infected with Alpha and found significantly higher levels of RNA expression — probably representing Orf9b production — than in people infected with previous variants. The authors attribute this over-expression to a mutation outside the spike protein, in genes that are important for viral replication.

Delta (B.1.617.2) variant

First reported in October 2020, SARS-CoV-2 lineages Delta and Kappa have been increasingly detected in India and other countries. In just a few weeks, the Delta variant has become the dominant strain across India and has spread to about 96 nations, including the United Kingdom, Russia, Portugal, Myanmar, Nepal, Fiji, Vietnam and Singapore. It has caused community outbreaks in Australia, in **Melbourne, Sydney, Darwin and Perth**.

The Indian SARS-CoV-2 Consortium on Genomics has identified two important mutations in the Delta variant. First, the **T478K** mutation is located on the SARS-CoV-2 spike protein. The mutation is structurally located in the region of interaction with human receptor ACE2. The second is the L452R **mutation**, which has also been found in a variant thought to be responsible for outbreaks in California. Scientists believe this mutation increases the spike protein's ability to bind to human host cells, thereby increasing its infectivity.



In the UK, PHE's most recent **weekly COVID-19 variant cases data** show that numbers of the Delta variant in England have risen by 33,630 since the previous week to a total of 75,953. The most recent data show 99 per cent of sequenced

and genotyped cases across the country are the Delta variant. The increase is primarily in younger age groups, a large proportion of which were unvaccinated but are now being invited to receive the vaccine.

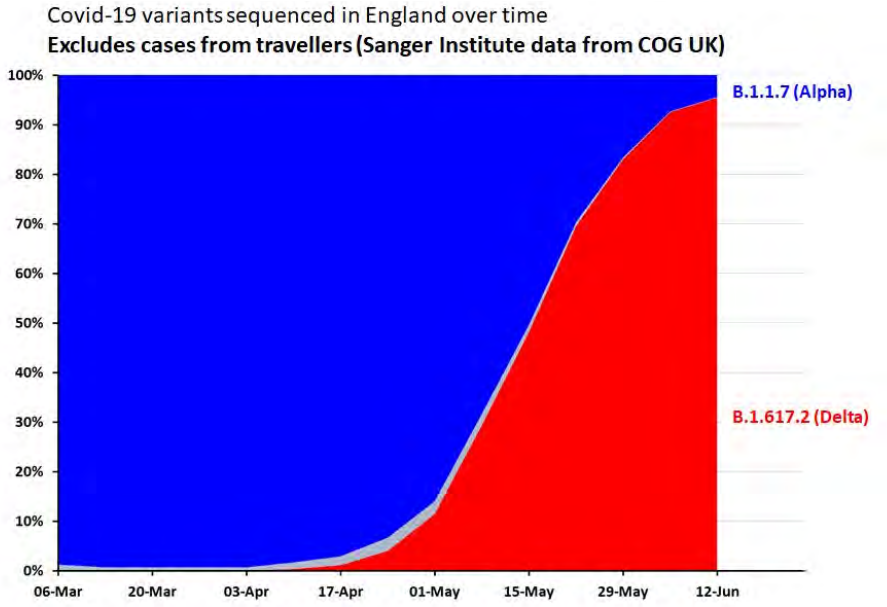
According to the Zoe COVID-19 Symptom app, which has almost 5 million subscribers, the initial symptoms associated with infection by the Delta strain are different from those experienced with earlier strains. The top five symptoms, in order, are headache, sore throat, runny nose, fever and cough. Loss of smell comes in at number 9 and shortness of breath comes far down the list at number 30, indicating the symptoms as recorded previously are changing with the evolving variants of the virus. Runny nose, for example, was a rare symptom with the original strain.

Data show an increased risk of hospitalisation with Delta compared to Alpha, although PHE's analysis shows that two doses of a vaccine give a high degree of protection against hospitalisation, estimated to be more than 90 per cent. According to PHE's latest variant technical briefing, a total of 806 people have been hospitalised with the Delta variant between 1 February and 14 June in England, an increase of 423 since the previous week. Of those:

- 527 (65%) people were unvaccinated.
- 135 (17%) were more than 21 days after their first dose of vaccine.
- 84 (10%) were more than 14 days after their second dose.

As of 14 June, there had been 73 deaths in England of people who were confirmed as having the Delta variant and who died within 28 days of a positive test, and of these:

- 34 (47%) were unvaccinated.
- 10 (14%) were more than 21 days after their first dose of vaccine.
- 26 (36%) were more than 14 days after their second dose.



Recent data on Delta in Scotland

Published in *The Lancet*, sequencing data from Scotland has found that for 1 April to 6 June 2021, the latest date until which data were available, 97 per cent of *S* gene positive cases sequenced in Scotland were the Delta variant.

There were 19,543 confirmed SARS-CoV-2 infections over the period of interest, of whom 377 were admitted to hospital for COVID-19; 7,723 (39.5%) of these cases and 134 (35.5%) hospital admissions were in those who were S gene-positive. The analysis for time to hospital admission found that *S* gene-positive cases were associated with an 85 per cent increased risk of COVID-19 hospital admission when compared to *S* gene-negative cases, after adjusting for age, sex, deprivation, temporal trend, and comorbidities.

Compared to those unvaccinated, at least 14 days after the second dose, the Pfizer vaccine offered very good protection: 92 per cent *S* gene-negative, 79 per cent *S* gene-positive. Protection associated with the AstraZeneca vaccine was, however, substantial but reduced: 73 per cent for *S* gene-negative cases versus 60 per cent for those *S* gene-positive.

In summary, they showed that the Delta VOC in Scotland was found mainly in younger, more affluent groups. Risk of COVID-19 **hospital admission was approximately doubled** in those with the Delta VOC when compared to the Alpha VOC, with risk of admission particularly increased in those with five or more relevant comorbidities. Both the AstraZeneca and Pfizer vaccines were effective in reducing the risk of SARS-CoV-2 infection and COVID-19 hospitalisation in people with the Delta VOC, but these effects on infection appeared to be diminished when compared to those with the Alpha VOC. The AstraZeneca vaccine appeared less effective than the Pfizer vaccine in preventing SARS-CoV-2 infection in those with the Delta VOC.

Delta variant in English schools

In an opinion piece in the *BMJ*, PHE was criticised for a lack of transparency around the spread of the Delta variant in schools. Media reports suggested that this was at the insistence of the UK government. In a detailed technical report released on the 3 June, PHE only provided data on the number of "incidents" or outbreaks involving two or more students in schools. It did not provide numbers of Delta variant cases linked to schools, which had been specifically and repeatedly requested by unions and scientists and specified in the pre-action letter.

According to the report, 140 outbreaks of the Delta variant had been identified in educational settings up to 30 May, the largest number in any of the settings specified. According to the *BMJ* opinion piece, PHE has continued to put out contradictory claims. Just a day after reporting that infection rates were currently highest in 10-19 year olds, it claimed that cases among school-age children were low. This contradicted other Office of National Statistics data released the same day that showed rapid rises in prevalence in this age group, with this now being much higher than all other groups.

Data from Bolton in NW England, and several other places, where the Delta variant gained dominance suggested early on that infection spread first among school age children, and then to other age groups. It is likely that lack of mitigations in schools played an important role in this highly transmissible, more virulent, escape variant gaining dominance rapidly across England.

The opinion piece calls for urgent action to mitigate the COVID-19 risk in schools, including the reintroduction of masks, central investment in ventilation and air cleaning in schools, including CO2 monitors, and air filtration devices, to supplement ventilation where needed, and practical, financial, and remote learning support for families with children who are isolating.

Serial intervals observed in SARS-CoV-2 Delta (B.1.617.2) variant cases

The factors driving the recent rapid growth of COVID-19 cases could be attributed to shorten generation intervals or higher transmissibility (effective reproduction number, R), or both. In a pre-print article, researchers in Singapore analysed the serial interval of household transmission pairs (i.e. onset-to-onset delay) — a proxy for the generation interval — between pairs of a primary case and a secondary case occurring among household members.

Exposure histories were reviewed for all household transmission pairs involving COVID-19 cases infected between 27 April and 22 May 2021. The Delta variant was detected in 97 per cent of the sequenced samples from local COVID-19 cases identified in this period. For comparison, they identified household transmission pairs prior to the partial lockdown in Singapore on 7 April 2020 and applied the same exclusion criteria. This time period precedes the occurrence of the major global SARS-CoV-2 variants.

The median of the serial interval was two days for Delta cases and for all the recently notified cases and 2.8 days for cases prior to the April 2020 lockdown. After controlling for confounding factors, their findings suggest no significant changes in the serial intervals for SARS-CoV-2 cases infected with the Delta variant. This, in turn, lends support for the hypothesis of a higher R in such cases.

Delta variant in China

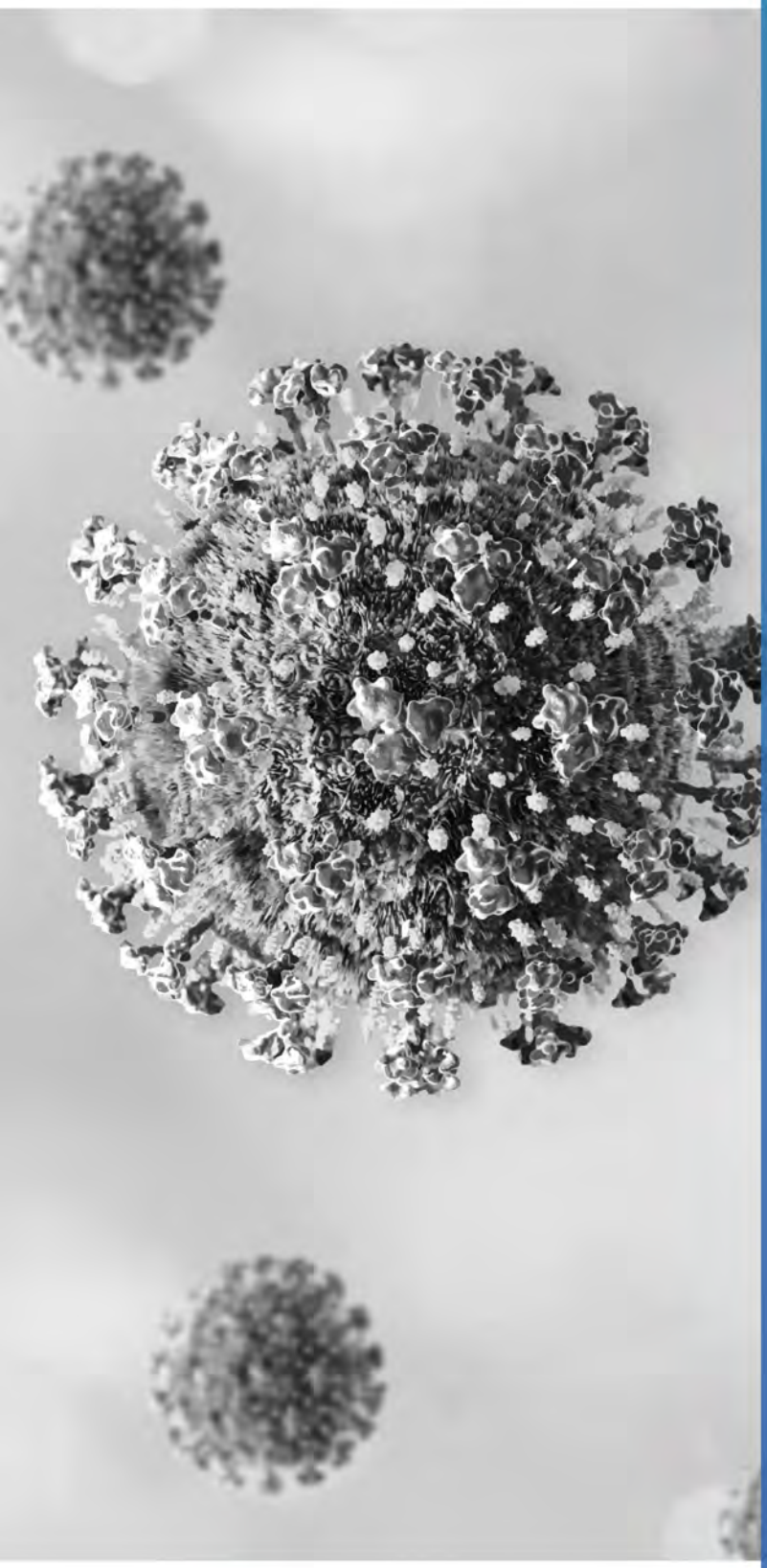
As the Delta variant of the coronavirus spreads in south-eastern China, doctors say they are finding that the symptoms are different and more severe than those they saw when the initial strain of the virus started spreading in late 2019 in the central city of Wuhan. The viral loads that are detected climb to levels higher than previously seen, and then decline only slowly, the doctors said.

Up to 12 per cent of patients become severely or critically ill within three to four days of the onset of symptoms, said Guan Xiangdong, director of critical care medicine at Sun Yat-sen University in the city of Guangzhou, where the outbreak has been centred. In the past, the proportion had been 2 per cent or 3 per cent, although occasionally up to 10 per cent, he said.

Delta's spread in south-eastern China focuses more attention on the effectiveness of China's vaccines. The Chinese authorities have not indicated how many of the new infections have occurred in people who had been vaccinated. As some other parts of the world still struggle to acquire and administer large numbers of coronavirus tests, south-eastern China has used its local production to conduct testing on a major scale. The authorities said that they had conducted 32 million tests in Guangzhou, which has 18 million people, and 10 million in the adjacent city of Foshan, which has seven million.

Vietnam variant

A coronavirus variant that Vietnamese authorities thought was a combination of the Alpha and Delta strains is not a new hybrid but part of the existing Indian variant according to the WHO. Genetic sequencing is now showing the strain circulating in Vietnam is a Delta variant that has developed some additional mutations. The details of which extra mutations are found in the Vietnam version of the Delta variant are not yet known. Whether this mutated variant is more infectious, and the degree to which it can be implicated in Vietnam's current surge of infections, is not yet certain.



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