



# COVID-19 Global Trends and Analyses

Volume 2:  
Vaccines and Viral  
Variants Update

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# SUMMARY

## Vaccines

- As of 1 May, 1.13 billion doses of COVID-19 vaccines had been administered worldwide, equivalent to 15 per cent of the world's population. Of these doses, 39 per cent have been given in the world's 27 wealthiest countries and a further 35 per cent in China and India. The world's poorest 85 countries have received just 1.3 per cent of the vaccine doses.
- The countries with the highest rates of vaccination (per 100 people) are Seychelles, Israel, UAE, Chile, Bahrain and Bhutan. In the Asia-Pacific, Bhutan, Singapore, Mongolia and Cambodia have the highest rates.
- In Australia, the seven-day moving average of daily vaccinations has declined since the recommendation that people under 50 not receive the AstraZeneca vaccine from 61,400 on 10 April to 46,300 on 30 April. At the current pace of roughly 324,000 doses a week, the 40 million doses needed to fully vaccinate Australia's adult population will not be reached until late July 2023.
- COVAX has delivered 49 million doses to 121 countries across six continents. However, it has delivered only about two per cent of the two billion doses it hopes to deliver worldwide this year. Of the 121 economies reached, 66 are among the 92 lower-income economies receiving vaccines funded through the facility.
- The European Medicines Agency has revised the estimated frequency of clotting events associated with the AstraZeneca vaccine. The EMA puts the incidence of the clotting syndrome at around 20 cases per million for people in their 20s, 30s and 40s. The rate halves to about 10 in every million for those in their 50s and 60s, and then halves again to about five cases in every million for those aged 70 and above.
- Injections of Johnson & Johnson's coronavirus vaccine came to a halt across the US on 13 April as federal health agencies examined blood-clotting disorders. The rollout of the vaccine was halted in Europe. On 23 April, the US CDC's Advisory Committee on Immunisation Practices (ACIP) advised that the US could resume administering the vaccine. ACIP investigated 15 cases; all were women with 13 between 18-and 49-years-old. The EMA and FDA placed a warning on the vaccine and the rollout has resumed in Europe.
- Under real-world conditions, the US CDC found that mRNA vaccine effectiveness of full immunisation ( $\geq 14$  days after second dose) was 90 per cent against SARS-CoV-2 regardless of symptom status.
- In a large study of English aged care home residents, both Pfizer and AstraZeneca vaccines reduced the risk of infection by about 56 per cent at 28-34 days after the first dose, and 62 per cent at 35-48 days.
- In a Phase 3 trial conducted by Pfizer/BioNTech of 2,260 participants aged 12 to 15 in the US, the vaccine elicited strong antibody responses one month after the second dose -- exceeding those demonstrated in people aged 16 to 25 in previous trials. The vaccine had an efficacy of 100 per cent.
- Pfizer and BioNTech announced that their vaccine is about 91 per cent effective at preventing the disease, citing updated trial data. The analysis of 46,307 trial participants confirms previously released data and demonstrates strong protection against COVID-19 through six months post-second dose.
- A post-hoc analysis of the efficacy of the AstraZeneca vaccine among 8,534 study participants in the UK found that clinical vaccine efficacy against symptomatic PCR positive infection was 70.4 per cent for B.1.1.7 and 81.5 per cent for non-B.1.1.7 lineages.

- A case-control study of Israelis who had been vaccinated with the Pfizer vaccine with documented SARS-CoV-2 infection found that among people who had received two doses of the vaccine, the B.1.351 variant's incidence was eight times higher than those unvaccinated - 5.4 versus 0.7 per cent.
- An inactivated virus vaccine developed by the French company Valneva has shown promising results in Phase 1/2 trials. More than 4,000 people have been recruited in a Phase 3 trial where the control arm is being given the AstraZeneca vaccine. Australian authorities are negotiating purchase of the vaccine.
- A US CDC study of more than 35,000 women who received the Pfizer-BioNTech or Moderna vaccine during or shortly before pregnancy found that pregnant participants reported the same general pattern of side effects that non-pregnant ones did. Rates of miscarriage, prematurity, low birth weight and birth defects were consistent with those reported in pregnant women before the pandemic.

## Variants of Concern

- The current SARS-CoV-2 variants of concern are B.1.1.7 (originally detected in the UK), B.1.351 (South Africa), P.1 (Brazil), B.1.427 and B.1.429 (California), B.1.526 (New York) and B.1.617 (India).
- The B.1.1.7 variant of coronavirus first identified in England is more infectious but does not cause more severe disease than the original COVID-19, two new peer reviewed UK-based studies have found. These studies, which cover the period from September to December 2020, are in contrast to earlier studies which found higher rates of hospitalisations in people infected with the variant.
- The B.1.17 variant has now been detected in 114 countries and territories, including Australia. By late March, the B.1.17 variant accounted for almost 100 per cent of new cases in the UK, Ireland and Poland and more than 50 per cent in most other western European countries. It is also the dominant strain in some Indian states, such as Punjab.
- In the US, the B.1.1.7 variant has been spreading rapidly. By 27 March, it accounted for 44 per cent of all genomically sequenced samples. The variant has been reported in 52 states and territories, and is the predominant strain in seven states. In the Canadian province of Ontario, the B.1.17 variant has quickly become the main strain and is affecting young people and children more than the earlier lineage.
- Research conducted by a Brazilian public health institute has found new mutations in the spike region of the virus that is used to enter and infect cells. Those changes could make the virus more resistant to vaccines with potentially grave implications for the severity of the outbreak in Latin America's most populous nation.
- The P.1 variant has been identified in 37 countries, including Australia. In addition to Brazil, there has been community transmission in Colombia, Mexico, Canada and the US. The variant has been detected in 31 states in the US. This variant has been associated with a high proportion of new cases in British Columbia and Minnesota.
- The Indian SARS-CoV-2 Consortium on Genomics has identified two important mutations in a new variant (B.1.617). The first is the E484Q mutation, which is similar to the E484K mutation identified on the Brazilian and South African variants, which can change parts of the coronavirus spike protein. The second is the L452R mutation, which has also been found in a variant thought to be responsible for outbreaks in California. This variant has been detected in at least 10 other countries, including the US, UK, Fiji, Australia and New Zealand. Public Health England has found that B.1.617 is the fastest growing variant of concern in England.

# GLOBAL SCIENTIFIC UPDATES SARS-CoV-2 Vaccines Update

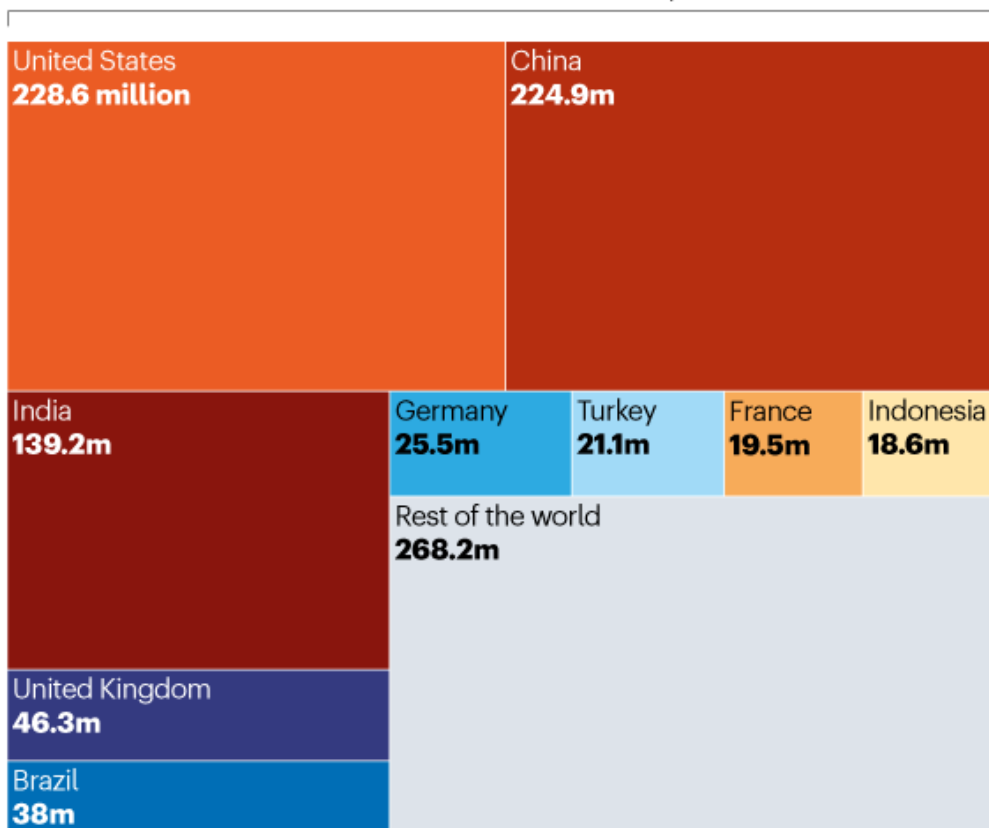
## Global Rollout of Vaccines

On 27 April, the world reached the milestone of administering [1 billion doses](#) of COVID-19 vaccines (to 570 million people), just four months after the World Health Organization (WHO) approved the first emergency use vaccine. This is equivalent to 7.3 per cent of the world's population of 7.79 billion. The second billion milestone is very likely to be reached sooner as delivery systems are established and improved. This is an unprecedented scientific and global health achievement given this is 16 months after the identification of a novel pathogen. However, the telling tale is the striking inequity in distribution.

### DIVIDED BY DOSES

More than three-quarters of all doses of COVID-19 vaccines given so far have been administered in just ten nations. People in more than 170 other nations and territories have had to share the remainder.

Total vaccine doses administered as of 25 April **1.03 billion**



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As of 1 May, 1.13 billion doses of COVID-19 vaccines had been administered worldwide, equivalent to 15 per cent of the world's population. Of these doses, 39 per cent have been given in the world's 27 [wealthiest countries](#) and a further 35 per cent in China and India. The world's poorest 85 countries have received just 1.6 per cent of the vaccine doses.

The [ten countries with the highest rates](#) of vaccination coverage (and have received around 75% of all vaccinations), and selected Asia-Pacific countries, are as follows.

**Green** is high income, **orange** upper middle-income and **yellow** low- and lower-middle-income.

Country, classified by income	Doses per 100 people	Fully vaccinated	Population	Number of doses administered	COVID-19 cases per 1,000 population
<b>Seychelles</b>	130	61%	98,828	126,840	59
<b>Israel</b>	116	56%	9,197,590	10,497,355	91
<b>UAE</b>	108	n/a	9,984,665	10,547,584	52
<b>Chile</b>	78	35%	19,245,815	14,767,327	63
<b>Bahrain</b>	75	33%	1,747,847	1,235,170	102
<b>Maldives</b>	75	19%	548,000	397,875	56
<b>UK</b>	73	22%	68,168,000	48,748,962	65
<b>US</b>	72	31%	332,537,000	240,159,677	100
<b>Malta</b>	66	21%	442,474	331,438	69
<b>Bhutan</b>	63	n/a	778,313	480,422	1.5
<b>Singapore</b>	39	15%	5,886,695	2,213,888	10
<b>Mongolia</b>	37	11%	3,319,867	1,208,619	12
<b>China</b>	19	n/a	1,439,323,776	265,064,000	0.06
<b>Cambodia</b>	14	5.7%	16,901,000	2,284,788	0.9
<b>India</b>	11	1.8%	1,390,716,914	151,998,107	14
<b>Australia</b>	8.6	n/a	25,733,000	2,179,544	1
<b>Indonesia</b>	7.4	2.8%	275,805,497	20,068,537	6
<b>South Korea</b>	6.9	0.4%	51,304,000	3,554,402	2.4
<b>Bangladesh</b>	5.3	1.7%	166,042,950	8,625,350	4.6
<b>New Zealand</b>	4.7	1.2%	5,002,000	232,588	0.5
<b>Japan</b>	2.8	0.8%	126,169,398	3,489,719	5
<b>Vietnam</b>	0.5	n/a	98,030,000	506,435	0.03

## Country snapshots

### Australia

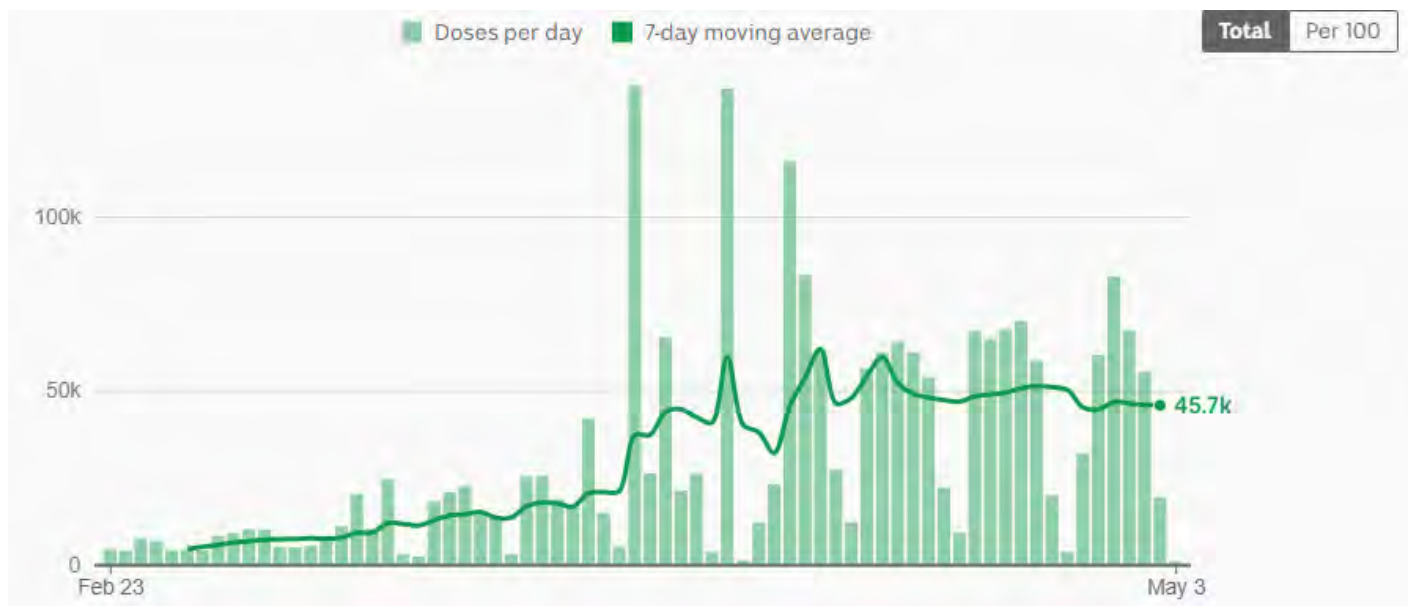
Australia has administered just over 2 million doses of two vaccines -- Pfizer and AstraZeneca -- the equivalent of 8.6 doses per 100 people. The number of fully vaccinated persons is unknown. State health departments have been responsible for vaccinating frontline health, quarantine, and other essential workers. The Federal Government is responsible for the rollout by GPs and for aged care and disability home residents and staff.

On 8 April, the Australian Technical Advisory Group on Immunisation ([ATAGI recommended](#)) that people under the age of 50 should be offered [an alternative](#) to the AstraZeneca vaccine. This was due to the age-related risk vs benefit of vaccine induced thrombotic thrombocytopenia (VITT – see section below). The Government immediately accepted this advice and subsequently adjusted the vaccination program such that all Australians over the age of 50 can access the AstraZeneca vaccine regardless of which priority category they belong to. Several states, such as Victoria and New South Wales, have established mass vaccination hubs to accommodate these people.

The seven day moving average of daily vaccinations [has declined](#) since the ATAGI decision, from 61,400 on 10 April to 46,300 on 30 April. At the current pace of roughly 324,000 doses a week, the 40 million doses needed to fully vaccinate Australia's adult population will not be reached until late July 2023.

The Victorian Government has committed [\\$50 million](#) towards establishing a facility to manufacture mRNA coronavirus vaccines domestically. This could enable licensing agreements with Pfizer and Moderna to manufacture these vaccines in Victoria. The mRNA coronavirus vaccines from Pfizer and Moderna have continually yielded strong results in clinical trials with growing evidence suggesting they will be much easier to reconfigure to cover new viral variants than more conventional inoculations such as AstraZeneca, which is being made in Australia by CSL.

Australian Vaccine Rollout



## Bhutan

It took less than two weeks for the Himalayan kingdom of Bhutan to vaccinate almost all of its eligible population. The country's vaccination campaign was launched on 27 March. By 8 April, according to the [Ministry of Health](#), 93 per cent of eligible adults had received their first dose. Officials said 472,139 people aged between 18 and 104 had been vaccinated as of that date, and they urged other eligible individuals to follow suit. Overall, roughly 63 per cent of Bhutan's 735,553 residents have been vaccinated so far.

Health officials said second doses will be administered after eight to 12 weeks. The country received 550,000 doses of the AstraZeneca vaccine, known locally as Covishield, in two batches in January and March donated by India. Bhutan launched its vaccination campaign at the end of last month to coincide with "auspicious dates in Buddhist astrology," according to the [Bhutan Times](#). The vaccines were distributed to more than [1,200 sites](#) across the country using cold-chain storage that was used during earlier vaccination drives. Nearly 3,300 health workers and 4,400 volunteers known as *desuups* were deployed across the country to help with the rollout.

## Maldives

Maldives has administered at least one dose of vaccine to 73 per cent of its population. That includes [90 per cent](#) of its frontline tourism workers. Maldives will soon offer visitors vaccinations on arrival as part of its three-pronged initiative aimed at reviving the country's hard hit travel sector. At present, visitors to Maldives must provide a negative PCR test and proof of hotel booking to gain entry. Around 67 per cent of its GDP is derived directly and indirectly from the tourism sector.

The country has received vaccine donations from India, China, and the COVAX scheme. Maldives has also ordered additional supplies from Singapore. The country has a target of 1.5 million tourist arrivals and 10 million bed nights during 2021. Already this year, Maldives has received 350,000 arrivals, as holidaymakers — primarily from nearby India — take advantage of the country's limited entry requirements.

## Cambodia

Cambodia is in the midst of its worst surge in cases since the pandemic began and there is a sense of urgency to roll out the vaccination program. So far, 13 per cent of the population has received at least one dose and 5 per cent are fully vaccinated. The Government intends to inoculate ten million of its citizens, initially with AstraZeneca and Chinese-made vaccines. Priority groups include health workers, and essential workers involved in the vaccination roll-out effort, elderly populations and adults with co-morbidities.

On 2 March, [324,000 doses](#) of the AstraZeneca vaccine licensed to the Serum Institute of India arrived in Cambodia, the first batch provided by the COVAX facility in Asia. These 324,000 doses are the first of a total of 1.1 million doses that are expected to be provided in batches by the COVAX facility by the end of May.

Australia has emerged as its biggest donor with a pledge of US\$28 million to help vaccinate 1.5 million people through the COVAX facility. China initially promised one million doses of its Sinopharm vaccine, enough to inoculate 500,000 Cambodians (the vaccine requires two jabs for each person). A second batch [has been promised](#) while 1.5 million doses of Sinovac are being purchased.



## India

In India, the world's biggest vaccine producer, millions of people are waiting for COVID-19 vaccines amid a devastating second wave of infections. India typically produces more than 60 per cent of all vaccines sold globally and is home to the Serum Institute of India (SII), the world's largest vaccine manufacturer. Under the initial agreement with COVAX [announced last year](#), SII would manufacture up to 200 million doses for up to 92 countries. India had provided [28 million doses](#) of the AstraZeneca vaccine so far, and was scheduled to deliver another 40 million doses in March and 50 million in April.

But the situation in India is markedly different from just a few months ago. Its [second wave](#) began in March, quickly surpassing the first, which had peaked last September at more than 97,000 coronavirus cases a day. In the past week, India has reported more than 300,000 cases daily. Since beginning its vaccine rollout in January, India has administered 147 million doses, equivalent to 11 per cent of its population; 1.8 per cent have been fully vaccinated.

India is administering two vaccines domestically:

1. Oxford-AstraZeneca also known as Covishield, and
2. Covaxin, developed jointly by Bharat Biotech and the Indian Council of Medical Research.

The country started its vaccination program in January for health care workers and priority groups, with the goal of fully inoculating 300 million people by August. But the program had a sluggish start, facing logistical issues, as well as vaccine hesitancy among the population -- especially towards Covaxin, which was approved for emergency use before the efficacy data of its third phase trial were released.

In the face of an escalating crisis, the government and SII have shifted focus from supplying vaccines to COVAX to prioritising their own citizens at home. Vaccine shortages have been reported in a number of Indian states. In Odisha, nearly 700 vaccination centres had to close in mid-April due to shortages, health authorities wrote a letter to the central government warning the state would soon exhaust its available stock. Several districts in Maharashtra, the worst-hit state, had to temporarily suspend vaccination drives, including more than 70 centres in Mumbai that shut last week.

Production of both Covishield and Covaxin has been delayed by a global shortage of raw materials because supply chains have been disrupted during the pandemic. The US has placed a temporary ban on exporting raw materials critical for vaccine production; however, on 27 April the US announced that it would send raw materials to India. India is also trying to source raw materials from neighbouring countries, such as Singapore.

The escalating second wave of cases in India, the problems with vaccine production and the desire of the Indian Government to direct all its vaccines to the Indian people will not only affect India's path out of the pandemic but will affect many low-income countries, especially in Africa, which rely on Indian vaccines for their programs.

## South Africa

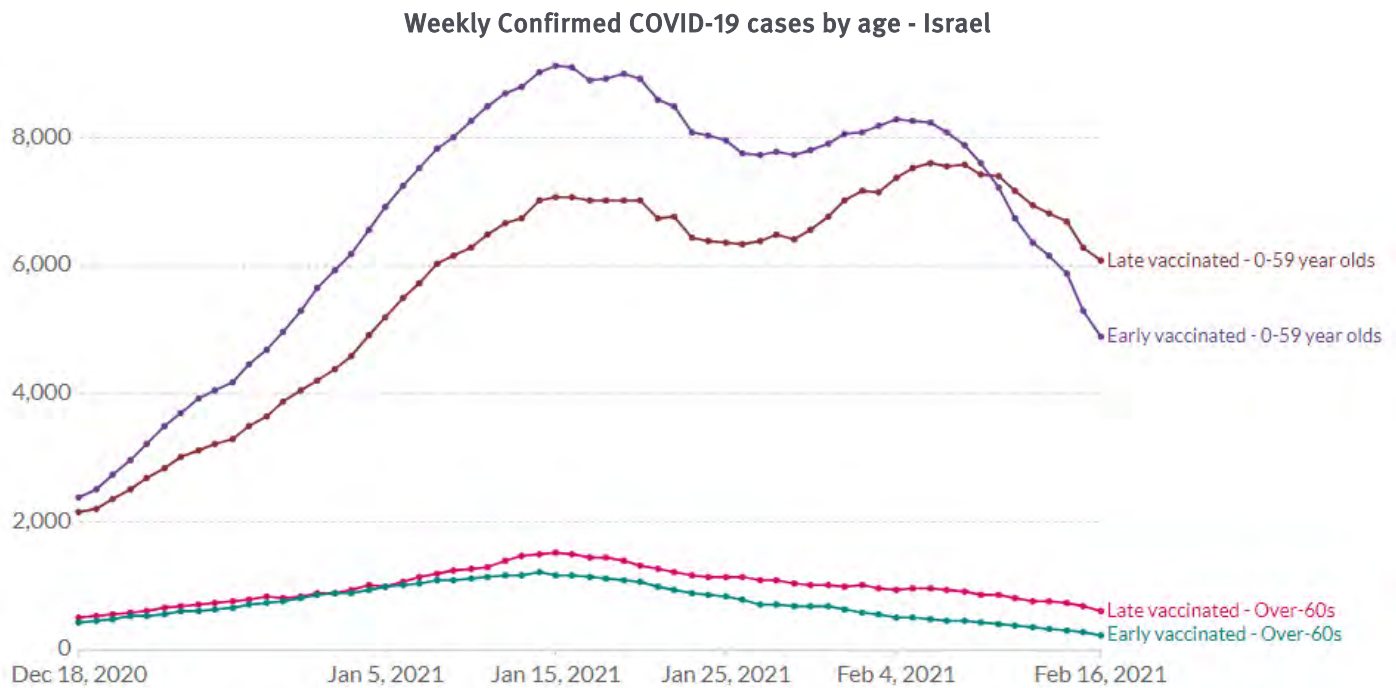
South Africa, which has recorded the highest number of COVID-19 cases on the African continent, hit a second roadblock in its attempt to roll out vaccines. Having already stopped using the AstraZeneca vaccine because of poor results in a clinical trial, the country suspended the use of the Johnson and Johnson vaccine because of reported blood clotting events associated with the vaccine in the US. The rollout of Johnson & Johnson [resumed](#) on 29 April. With 30 million doses of Johnson & Johnson and 30 million doses of Pfizer secured, the goal of fully vaccinating 20 million South Africans this year could be achieved.

## Israel

In Israel, more than half of its residents have been fully vaccinated and an additional 830,000 people have tested positive for the virus in the past, which should give them some natural immunity. Some commentators are suggesting that Israel may be reaching a level of population – or herd – immunity that would protect the country from future

outbreaks. [Professor Eyal Leshem](#), a Director at Israel's largest hospital, the Sheba Medical Centre, said herd immunity was the "only explanation" for the fact that cases continued to fall even as more restrictions were lifted. Cases are falling in all age groups including children, even though under-16s are not generally being vaccinated.

An analysis by [Eran Segal](#), a computational biologist at Israel's Weizmann Institute of Science, reported that since a January peak in infections, the country had seen daily drops of 96 per cent in cases, 90 per cent in critically ill patients and 85 per cent in deaths.



Source: Rossman, Shilo, Meir, Gorfine, Shalit & Segal (2021). Patterns of COVID-19 pandemic dynamics following deployment of a broad national immunization program. CC BY

## Serbia – vaccine diplomacy

Serbia has administered at least one vaccine dose to 49 per cent of the population and 20 per cent have been fully vaccinated. This is the [fourth highest rate](#) in Europe after the UK, Malta and Hungary. The country chose to diversify the type of vaccines on offer – they currently provide the Western-made Pfizer-BioNTech and AstraZeneca, China's Sinopharm and Russia's Sputnik V. Serbia has become a vaccine tourism hub. At the end of March, thousands of residents from neighbouring countries, including North Macedonia, Montenegro, and Bosnia and Herzegovina, among others, [travelled to Serbia](#) to get a COVID-19 shot. Unlike Serbia – which is not a member of the EU – other countries in the Balkans have struggled to secure any vaccine supplies. They have placed their hopes on the EU or the international COVAX scheme. In January 2021, Serbia became the first European country to use Chinese-developed COVID-19 vaccine for mass roll-out and has commenced manufacturing the Sputnik V vaccine.

## COVAX Progress

More than one hundred countries have received COVID-19 vaccines from COVAX, the global mechanism for equitable access to COVID-19 vaccines. The milestone came 42 days after the first COVAX doses were shipped and delivered internationally, to Ghana on 24 February 2021. So far, [COVAX has delivered](#) 49 million doses to 121 countries across six continents, supplied by three manufacturers: AstraZeneca, Pfizer-BioNTech and the Serum Institute of India (SII). To put these figures in context, the total number of doses delivered by COVAX is the equivalent of the number administered in the UK. It has delivered only about two per cent of the two billion doses it hopes to deliver worldwide this year. Of the 121 economies reached, 66 are among the 92 lower-income economies receiving vaccines funded through the [COVAX](#)

[Advance Market Commitment](#). The COVAX initiative has so far delivered vaccine doses to 36 African countries, according to the WHO.

Despite [reduced supply availability](#) in March and April – the result of vaccine manufacturers scaling and optimising their production processes in the early phase of the rollout, as well as increased demand for COVID-19 vaccines in India – COVAX expects to deliver doses to all participating economies that have requested vaccines in the first half of the year. Although most of the first doses available will be delivered to low- and middle-income countries, some will be sent to high-income countries such as Canada, [which has defended](#) its decision to draw on COVAX's early supply.

COVAX has an agreement for 340 million doses of the Oxford-AstraZeneca vaccine and about 1.2 million doses of the Pfizer-BioNTech vaccine. In early March, COVAX shipped its first Pfizer-BioNTech doses, with Rwanda among the first to receive a batch. Health care workers, the elderly and the vulnerable are first in line to receive inoculations. But COVAX is facing serious problems in reaching its 2021 objective of delivering two billion doses. Wealthy countries have jumped the queue to ensure they can procure enough doses for their own populations.

Export bans may have a huge impact on the ability of COVAX to obtain enough vaccines. Of greatest concern is the reduction in exports of CoviShield (under licence from AstraZeneca) by India. Before India suspended exports during its massive second wave of infections, more than [70 nations](#) received CoviShield, totalling more than 60 million doses. Many went to low- and middle-income countries through the COVAX facility; African countries are especially dependent on vaccines produced in India.

Even before India's halt in shipments, Africa was experiencing the slowest vaccine rollout of any continent. As of 21 April, African nations, with a total population of 1.3 billion, had acquired more than 36 million vaccine doses but administered only about 15 million, [according to the Africa Centres for Disease Control and Prevention](#). Just six million doses have been administered in all of sub-Saharan Africa – fewer than in [many individual US states](#). The prospect of reduced supplies further complicates what was, for many African nations, an already daunting logistical challenge.

Countries like Rwanda and Ghana, which were among the first to receive doses from COVAX, are about to exhaust their initial supplies. In Botswana, inoculations were [temporarily halted](#) in some areas this month after the allotted doses were finished. And Kenya, which has [almost run out of its initial one million doses](#), said this week that it would seek to acquire Johnson & Johnson and Pfizer vaccines to continue its inoculation campaign.

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

### AstraZeneca-Oxford Vaccine

The AstraZeneca-Oxford (ChAdOx1 nCoV-19) vaccine has been deployed against COVID-19 in **at least 115 countries**, some of them for several months now. In early March 2021, reports were emerging of a rare but serious side effect involving thrombosis (clotting) with thrombocytopenia (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). Women were affected more frequently than men.

This syndrome has been called several names - thrombosis with thrombocytopenia syndrome (TTS), vaccine induced prothrombotic immune thrombocytopenia (VIPIT); vaccine associated thrombosis and thrombocytopenia (VATT) and vaccine induced immune thrombotic thrombocytopenia (VITT).

By 16 March, at least 20 European countries had suspended or limited inoculations with this vaccine. On 18 March, the European Medicines Agency's safety committee released the findings of its investigation of the thrombotic events temporally associated with vaccination. The Committee confirmed that the benefits of the vaccine in combating the still widespread threat of COVID-19 (which itself results in clotting problems and may be fatal) continue to outweigh the risk of side effects.

On 7 April, the **European Medicines Agency** (EMA) issued a [second report](#) saying it has found a "possible link" between the AstraZeneca COVID-19 vaccine and "very rare cases" of blood clots. But it nevertheless maintained the benefits of the vaccine outweigh the risks of side effects. The determination came after a review of 169 cases in Europe, 25 per cent of which were fatal. The reported cases of unusual blood clots were mostly observed in women under the age of 60 but the EMA committee did not conclude that age and gender were clear risk factors. The UK's Joint Committee on Vaccines and Immunisation (JCVI) reported that there had been 79 reported cases of blood clots in the UK, out of more than 20 million doses of the AstraZeneca vaccine administered. Nineteen of them have died. The EMA said that about 34 million people had received the AstraZeneca vaccine in the EU and Britain and that the clotting problems were appearing at a rate of about one in 100,000 recipients. [Denmark](#) has since reported an incidence of one per 40,000 vaccine recipients.

In **Australia**, there have been six cases of VITT judged by the Advisory Committee on the Safety of Vaccines (ACSV) as associated with the AstraZeneca-Oxford vaccine for an incidence of one in 183,000 shots. One of the six patients died.

On 23 April, EMA released a [third report](#) revising the estimated frequency of clotting events associated with the AstraZeneca vaccine. The EMA puts the incidence of the clotting syndrome at around 20 cases per million for people in their 20s, 30s and 40s. This is double the incidence reported in the UK which was the basis for ACSV to recommend that people under the age of 50 not get the AstraZeneca vaccine. The rate halves to about 10 cases in every million for those in their 50s and 60s, and then halves again to about five cases in every million for those aged 70 and above.

The [New England Journal of Medicine](#) has published three separate studies (9 and 6 April from [Germany/Austria](#), [Norway](#) and the [UK](#)) that describe 39 persons with this newly described syndrome, VITT. The people developed thrombosis and thrombocytopenia 5 to 24 days after vaccination with the AstraZeneca vaccine and were healthy and largely without any previous thrombosis or risk factors. Most were women younger than 50 years of age. A remarkably high percentage of the patients had thromboses at unusual sites —cerebral venous sinus thrombosis or thrombosis in the portal, splanchnic, or hepatic veins. Other patients presented with deep venous thrombi, pulmonary emboli, or acute arterial thromboses. Approximately 40 per cent of the patients died.

So far, researchers have not identified any underlying medical conditions among the vaccine recipients who developed severe clotting issues that would help explain their susceptibility. The researchers found that vaccine recipients who developed the clotting disorder had produced [antibodies that activated their platelets](#) and led to the clots. The authors concluded that vaccination with ChAdOx1 nCov-19 can result in the rare development of immune thrombotic thrombocytopenia mediated by platelet-activating antibodies against PF4, which clinically mimics autoimmune heparin-induced thrombocytopenia.

Screening and testing for this syndrome is likely possible using assays for PF4, however, validation is needed. Management options include immune modulation with intravenous immune globulin and high dose steroids; and non-heparin anti-clotting agents if required. [Australia-NZ guidelines](#) are being updated regularly.

Experts have speculated that some unknown component of a COVID-19 vaccine can, in very rare situations, spur an autoimmune reaction against platelet factor 4. [One potential culprit](#) is the all-important spike protein—the one used by coronaviruses to infect cells and involved in every available COVID-19 vaccine as a target for the immune system. As it happens, the structure of the platelet factor 4 molecule has some similarities, in its curves and crevices, with that of the spike protein. In other words, training up the body to go after the spike protein could yield antibodies that stick to clotting-related proteins too. But there is no general agreement on this theory. Other experts have commented that if this were true, we would expect to see clotting events associated with the mRNA vaccines.

Following the EMA and UK reports, countries around the world have taken various precautionary actions. Germany, the Netherlands, the Philippines, Portugal and Spain have recommended that the AstraZeneca vaccine be given only to people over 60. Canada and France have limited it to those over 55; Australia, over 50; and Belgium, over 56. Britain, where the AstraZeneca vaccine was developed, announced that it would begin offering alternative vaccines to people under 30. As of 17 April, Denmark, Norway and Cameroon had stopped using the vaccine altogether, and the Democratic Republic of Congo delayed the start of its inoculation program.

## Johnson & Johnson (J&J)/Janssen vaccine

Injections of Johnson & Johnson's coronavirus vaccine came to a sudden halt across the US on 13 April after federal health agencies called for a pause in the vaccine's use as they examine blood-clotting disorders that emerged in six recipients. More than seven million people in the United States have received the J&J vaccine so far. All six patients were women aged between 18 and 48, and all developed the illness within one to three weeks of vaccination. One woman died, and a second woman has been hospitalised in critical condition. Five of the six patients have been tested for antibodies to platelet factor 4—and all were positive.

While they framed the move as a recommendation to health practitioners, the impact was immediate. By the next day, every state and territory had announced a pause in J&J vaccine injections. Beyond the US, Johnson & Johnson said it would delay the rollout of its vaccine in Europe, where several countries were poised to start administering it. The European Medicines Agency investigated four reported cases of blood clots with low platelets in people who have received the J&J vaccine. South Africa, devastated by a more infectious variant, suspended use of the vaccine. Australia announced it would not purchase any doses.

On 20 April, Johnson & Johnson said that it would resume the rollout of its coronavirus vaccine in Europe after the [EMA said that a warning](#) should be added to the product indicating a possible link to rare blood clots, but that the vaccine's benefits outweigh the risks.

[On 23 April](#), the US CDC's Advisory Committee on Immunisation Practices (ACIP) advised that the US could resume administering the vaccine. The FDA announced that a warning would be added. ACIP investigated 15 cases; all were women and thirteen of the cases were between 18 and 49 years old. There were seven cases per million doses in that age group.

## Gamaleya/Sputnik V vaccine

Like the AstraZeneca and J&J vaccines, the Gamaleya vaccine employs an adenovirus vector. It uses two different human adenoviruses in each of the two doses. In a [15 April statement](#), the Gamaleya Centre said a “comprehensive analysis of adverse events during clinical trials and over the course of mass vaccinations with the Sputnik V vaccine showed that there were no cases of cerebral venous sinus thrombosis (CVST).”

The EMA is investigating the deaths of four people who recently died after taking the Sputnik V vaccine in Russia. Three of the deceased were women aged 51, 69, and 74. Six other Russians have also had medical complications after taking the vaccine, according to internal case files from [RosPotrebNadzor](#), a Russian body responsible for administering vaccinations. Those clinical details which are available do not point to clotting events. They suffered a range of symptoms, including breathing difficulties, convulsions, swelling, muscle weakness, high blood pressure, headaches, dizziness, and fevers after their inoculations. Several EU countries, including Serbia and Italy, are keen to buy and produce the vaccine.

## mRNA vaccines (Pfizer and Moderna)

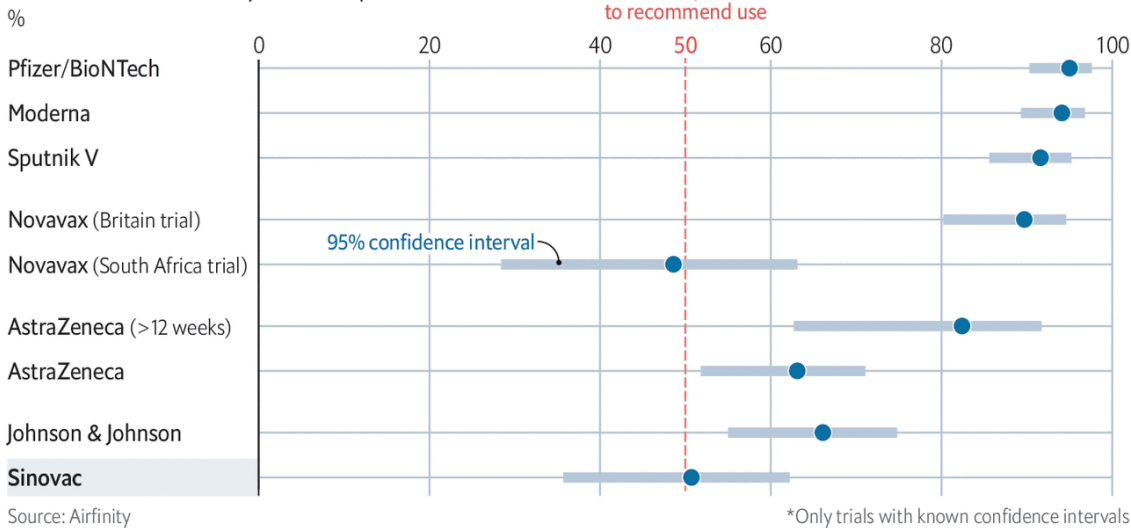
Whilst VITT has not been reported in the mRNA vaccines (Moderna [mRNA-1273] and Pfizer–BioNTech [BNT162b2]), cases of [low platelets and bleeding](#), without clotting have. This was first noted and investigated after a Miami physician died of a brain haemorrhage after developing immune thrombocytopenic purpura (ITP) following vaccination with Pfizer. A study from the USA, where over 20 million people had received the mRNA vaccines, found 17 cases of ITP in people without any pre-existing condition. The authors comment that this rate is comparable to background rates of ITP in the population and they are unable to distinguish or attribute causality at this time.

## Updates on leading vaccine candidates

### Summary of vaccine efficacies (does not include Sinopharm)

#### Making the cut

Covid-19 vaccine efficacy results in phase-three trials\*



Source: Airfinity

\*Only trials with known confidence intervals

The Economist

### Pfizer and Moderna vaccines 90 per cent effective after two doses in the US

In a [study](#) published by the US CDC of prospective cohorts of 3,950 health care personnel, first responders, and other essential and frontline workers completed weekly SARS-CoV-2 testing for 13 consecutive weeks. Under real-world conditions, mRNA vaccine effectiveness of full immunisation ( $\geq 14$  days after second dose) was 90 per cent against SARS-CoV-2 infections regardless of symptom status. Vaccine effectiveness of partial immunisation ( $\geq 14$  days after first dose but before second dose) was 80 per cent. The CDC concluded that authorised mRNA COVID-19 vaccines are effective for preventing SARS-CoV-2 infection in real-world conditions. COVID-19 vaccination is recommended for all eligible persons.

### Effectiveness of Pfizer and AstraZeneca vaccines after one dose in English aged care facilities

Researchers tracked more than [10,400 aged care home residents](#) in England (with an average age of 86) between December and March, comparing the number of infections occurring in vaccinated and unvaccinated groups – using data retrieved from routine monthly PCR testing. Both Pfizer and AstraZeneca vaccines reduced the risk of infection by about 56 per cent at 28-34 days after the first dose, and 62 per cent at 35-48 days. The effect is maintained for at least seven weeks, the authors concluded in their analysis, which has not yet been peer-reviewed.

These data are significant, given older adults with underlying illnesses have largely been excluded from vaccine trials. It also supports the UK's decision to extend dose intervals beyond what was studied in clinical trials. The beneficial impact on transmission was further bolstered by the findings of a lower viral load in positive tests post-vaccination, which suggests a lower level of infectiousness.

### Safety and efficacy of Pfizer/BioNTech vaccine in adolescents

In a [Phase 3 trial](#) conducted by the company of 2,260 participants aged 12 to 15 in the US, the vaccine elicited strong antibody responses one month after the second dose – exceeding those demonstrated in people aged 16 to 25 in previous trials. The vaccine was well tolerated by participants. Researchers observed 18 COVID-19 cases among the 1,129 participants who were given a placebo, and none among the 1,131 volunteers who received the vaccine. The data have yet

to be peer reviewed. Pfizer/BioNTech added that the side effects seen in the young teens were similar to those seen among 16 to 25-year-olds. Common side effects include pain at the injection site, fatigue and fever. The participants will be monitored for protection and safety for two years after their second dose.

Researchers can define a number of antibodies that are a correlate of the protection seen in adults, and then look for that level of antibodies in paediatric participants to know that the vaccine is providing protection. That's why the COVID-19 vaccine trials in children and adolescents have generally required fewer volunteers than the adult trials. The companies plan to submit these data to FDA as a proposed amendment to their emergency use authorisation in the coming weeks and to other regulators around the world, with the hope of starting to vaccinate this age group before the start of the next northern school year.

A separate Phase 1/2/3 study of the Pfizer/BioNTech vaccine in children aged 6 months to 11 years was launched in March, when the first children aged 5 to 11 received their first dose. Pfizer/BioNTech has also begun trialling 2 to 5-year-olds in April and will work its way down to participants aged 6 months to 2 years. The company aims to enrol 4,644 children in the trial and expects results by the end of 2021.

### **Updated efficacy data by Pfizer/BioNTech including against the B.1.351 variant**

Pfizer and BioNTech [announced](#) that their COVID-19 vaccine is about 91 per cent effective at preventing the disease, citing updated trial data. Results from this analysis of 46,307 trial participants build upon and confirm previously released data and demonstrate strong protection against COVID-19 through six months post-second dose. From the 927 confirmed symptomatic cases of COVID-19 in the trial, 850 cases of COVID-19 were in the placebo group and 77 cases were in the BNT162b2 group, corresponding to vaccine efficacy of 91.3 per cent.

While the new overall efficacy of 91.3 per cent is lower than the 95 per cent originally reported in November, a number of variants have become more prevalent around the world since then. The updated result includes data on more than 12,000 people fully inoculated for at least six months. The vaccine was 100 per cent effective in preventing severe disease as defined by the US CDC.

In **South Africa**, where the B.1.351 lineage is prevalent and 800 participants were enrolled, nine cases of COVID-19 were observed, all in the placebo group, indicating vaccine efficacy of 100%. In an exploratory analysis, the nine strains were sequenced and six of the nine were confirmed to be of the B.1.351 lineage. These data support previous results from immunogenicity studies demonstrating that BNT162b2 induced a robust neutralising antibody response to the B1.351 variant, and although lower than to the wild-type strain, it does not appear to affect the high observed efficacy against this variant.

Pfizer and BioNTech plan to submit detailed data for scientific peer review and potential publication in the near future.

### **COVID-19 vaccine coverage in health care workers in England and effectiveness of the Pfizer vaccine against infection (SIREN study)**

The SIREN study is a prospective cohort study among staff (aged  $\geq 18$  years) working in publicly funded hospitals in the UK. Participants were assigned into either the positive cohort (antibody positive or history of infection [indicated by previous positivity of antibody or PCR tests]) or the negative cohort (antibody negative with no previous positive test) at the beginning of the follow-up period.

Participants had fortnightly asymptomatic SARS-CoV-2 PCR testing and monthly antibody testing, and all tests (including symptomatic testing) outside SIREN were captured. The primary outcomes were vaccinated participants (binary ever vaccinated variable; indicated by at least one vaccine dose recorded by at least one of the two vaccination data sources) for the vaccine coverage analysis and SARS-CoV-2 infection confirmed by a PCR test for the vaccine effectiveness analysis. Results [were published](#) in *The Lancet* in late April.

A total of 23,324 participants from 104 sites (all in England) met the inclusion criteria for this analysis and were enrolled, of whom 8,203 (35%) were assigned to the positive cohort at the start of the analysis period, and 15,121 (65%) assigned to the negative cohort. Total follow-up time was two calendar months and 1,106,905 person-days (396,318 vaccinated and 710,587 unvaccinated). Vaccine coverage was 89 per cent on 5 February 2021, 94 per cent of whom had the BNT162b2 (Pfizer/BioNTech) vaccine.

During follow-up, there were 977 new infections in the unvaccinated cohort, an incidence density of 14 infections per 10,000 person-days. The vaccinated cohort had 71 new infections 21 days or more after their first dose, an incidence density of eight infections per 10,000 person-days, and nine infections seven days after the second dose (incidence density four infections per 10,000 person-days).

In the unvaccinated cohort, 543 (56%) participants had typical COVID-19 symptoms and 140 (14%) were asymptomatic, compared with 29 (36%) with typical COVID-19 symptoms and 15 (19%) asymptomatic in the vaccinated cohort.

A single dose of BNT162b2 vaccine showed vaccine effectiveness of 70 per cent 21 days after first dose and 85 per cent seven days after two doses in the study population.

### **Real world data on the efficacy of the Pfizer vaccine against the B.1.351 variant in Israel**

In a pre-print paper, [Israeli researchers](#) report reduced efficacy of the Pfizer vaccine against the B.1.351 variant that was originally identified in South Africa. They performed a case-control study that examined whether BNT162b2 vaccinees (Pfizer/BioNTech) with documented SARS-CoV-2 infection were more likely to become infected with B.1.1.7 or B.1.351 compared with unvaccinated individuals. The South African variant, B.1.351, was found to make up about one per cent of all the COVID-19 cases across all the people studied. But among patients who had received two doses of the vaccine, the variant's prevalence rate was eight times higher than those unvaccinated - 5.4 per cent versus 0.7 per cent.

This suggests the vaccine is less effective against the B.1.351 variant, compared with the original coronavirus and the B.1.1.7 variant that has come to comprise nearly all COVID-19 cases in Israel.

### **Efficacy of the AstraZeneca/Oxford vaccine against the B.1.1.7 variant**

A post-hoc analysis of the efficacy of the adenoviral vector vaccine, ChAdOx1 nCoV-19, against the B.1.1.7 variant was [published](#) in *The Lancet* on 10 April. Volunteers (aged ≥18 years) who were enrolled in phase 2/3 vaccine efficacy studies in the UK, and who were randomly assigned (1:1) to receive ChAdOx1 nCoV-19 or a meningococcal conjugate control vaccine, provided upper airway swabs on a weekly basis and also if they developed symptoms of COVID-19 disease.

Swabs were tested by nucleic acid amplification test (NAAT) for SARS-CoV-2. Neutralising antibody responses were measured using a live-virus microneutralisation assay against the B.1.1.7 lineage. The efficacy analysis included symptomatic COVID-19 in seronegative participants with a NAAT positive swab more than 14 days after a second dose of vaccine.

Of 8,534 participants in the primary efficacy cohort, 520 participants developed SARS-CoV-2 infection. 1,466 NAAT positive nose and throat swabs were collected from these participants during the trial. Of these, 401 swabs from 311 participants were successfully sequenced. Laboratory virus neutralisation activity by vaccine-induced antibodies was lower against the B.1.1.7 variant than against the other lineages. Clinical vaccine efficacy against symptomatic NAAT positive infection was 70.4 per cent for B.1.1.7 and 81.5 per cent for non-B.1.1.7 lineages.

### **Real-world efficacy data on CoronaVac (Sinovac) vaccine**

Phase-three trials, which were conducted on health care workers in Brazil, yielded an efficacy rate of 50.7 per cent, just barely above the 50 per cent threshold set by WHO for COVID-19 vaccines. CoronaVac clinical trials in Turkey and Indonesia found efficacies of 83.5 per cent and 65 per cent, respectively. The results of a [real-world trial](#) in Brazil released in April were about the same as the clinical trial: the vaccine was estimated to be 49.6 per cent effective against



symptomatic COVID-19 cases. When asymptomatic infections were included, this figure dropped to 35.1 per cent.

The recent study involved health care workers in Manaus, a city in the Amazon region that is the epicentre of the P.1 variant. The mutant virus now accounts for 75 per cent of all positive test results in the city, where the health system is collapsing because of COVID-19. The researchers focused on 2,656 health workers who had taken RT-PCR tests beginning in January, with the initial rollout of the vaccine, through March. They identified 786 people with apparent COVID-19 symptoms, whom they divided into two groups of 393 each: those who tested positive and negative for the virus. Then, the researchers checked the proportion of vaccinated and unvaccinated people in both groups. In the positive group, 18.6 per cent were vaccinated; in the negative group, the proportion was 24.4 per cent. Using the unvaccinated people as a reference, the researchers calculated the risk of infection by SARS-CoV-2 14 days after the first dose.

The Chilean government [released a report](#) that found two doses of the vaccine were 67 per cent effective in preventing symptomatic infection, 85 per cent effective in preventing hospitalisations and 80 per cent effective in preventing deaths. The Chilean study looked at the impact of the vaccine among people in the public health system between 2 February – 1 April, adjusting for age, sex, comorbidities, income and nationality. It compared people who were not inoculated, individuals 14 days or more after receiving one dose and more than 14 days after receiving a second dose. Protection against the virus was far higher after the second dose.

### **Valneva vaccine shows promise**

The Australian Government is in talks with the [French biotech firm Valneva](#) over the potential to import their vaccine. Valneva has developed a vaccine from chemically inactivated coronaviruses, using an adjuvant from [Dynavax](#). The vaccine, called VLA2001, is currently the only inactivated-virus vaccine being developed in Europe. On 16 December, Valneva [launched](#) a Phase 1/2 trial in the UK, and in April the company announced that the trial had delivered positive results. On 22 April, Valneva [launched a Phase 3 trial](#) on 4,000 volunteers in the UK. The trial is different from the first wave of studies on COVID-19 vaccines, in which some volunteers got a vaccine, and the others received a placebo. With a growing number of vaccines now authorised for use in Britain, such randomised clinical trials are no longer ethical. Instead, Valneva will give VLA2001 to half the volunteers, while the others will receive the AstraZeneca vaccine. The company hopes to submit VLA2001 for authorisation in late 2021. The British Government has already reached an agreement to purchase 100 million doses of the vaccine should it prove safe and effective, with an option to acquire a further 90 million.

### **Antibody and cellular responses to a single dose of Pfizer/BioNTech and AstraZeneca/Oxford vaccines**

In a [pre-print paper](#), researchers described recruiting 165 participants aged 80+ years that had received a single dose of either BNT162b2 mRNA or ChAdOx1 adenovirus vaccine and studied adaptive immune responses after 5 weeks. Antibody responses against spike protein were detectable in 93 per cent and 87 per cent of mRNA or ChAdOx1 recipients, respectively, with median antibody titres that were not statistically different. Spike-specific T cell responses were observed in 12 per cent and 31 per cent of mRNA and ChAdOx1 recipients, respectively, and median responses were 3-fold higher in ChAdOx1 vaccine recipients. Evidence of previous natural infection was seen in eight participants and associated with 691-fold and 4-fold increase in humoral and cellular immune responses, respectively.

### **Spike antibody levels of aged care home residents three weeks after a single Pfizer/BioNTech dose**

In a recently [peer-reviewed paper](#) published in JAMA, researchers compared IgG antibody levels after a single dose of BNT162b2 (Pfizer-BioNTech) vaccine in residents of six aged care home in Montpellier, France with or without prior COVID-19.

During an outbreak of COVID-19 In 2020, all residents in a number of facilities were repeatedly tested with RT-PCR until no new cases were diagnosed. Six weeks after the end of the outbreak, all residents underwent blood testing for levels of IgG antibody against the SARS-CoV-2 nucleocapsid (N) protein. All residents were offered a first vaccine dose in

January 2021. Three weeks later, all residents underwent blood testing to quantitatively assess IgG antibody levels against the SARS-CoV-2 spike (S) protein and N protein.

Of the 102 residents, 60 had no prior SARS-CoV-2 infection and 36 had a positive RT-PCR result and were seropositive for SARS-CoV-2 N-protein IgG in June 2020. Of these 36 residents, 26 remained seropositive in January-February 2021 (72.2%). All 36 residents with prior COVID-19 were seropositive for S-protein IgG after one vaccine dose vs 29 of 60 residents (49.2%) without prior COVID-19.

Among residents with prior COVID-19, the median level of S-protein IgG was 40,000 AU/mL or greater vs 48.0 AU/mL in those without prior COVID-19 ( $P < .001$ ).

This preliminary study suggests that a single dose of BNT162b2 vaccine may be sufficient to obtain a high level of S-protein IgG antibody in nursing home residents previously diagnosed with COVID-19 based on RT-PCR results. Measuring S-protein IgG antibody levels just before the second vaccine dose could be useful in determining whether a second dose is required in individuals whose infection history is unknown.

### **No evidence that Pfizer and Moderna vaccines unsafe during pregnancy in the US**

COVID-19 poses serious risks during pregnancy. Pregnant women who develop symptoms of the disease [are more likely to become seriously ill](#), and more likely to die, than non-pregnant women with symptoms.

In an [early analysis](#) of coronavirus vaccine safety data published in the *New England Journal of Medicine*, researchers at the US CDC have found no evidence that the Pfizer-BioNTech or Moderna vaccines pose serious risks during pregnancy. The findings are preliminary and cover just the first 11 weeks of the U.S. vaccination program. But the study, which included self-reported data on more than 35,000 women who received one of the vaccines during or shortly before pregnancy, is the largest yet on the safety of the coronavirus vaccines in pregnant people.

Participants in the program use a smartphone app to complete regular surveys about their health, and any side effects they might be experiencing, after receiving a COVID-19 vaccine. The researchers analysed the side effects reported by V-safe participants who received either the Pfizer or Moderna vaccine between 14 December 2020, and 28 February 2021. They focused on 35,691 participants who said that they had been pregnant when they received the vaccine or became pregnant shortly thereafter.

After vaccination, pregnant participants reported the same general pattern of side effects that non-pregnant ones did, the researchers found: pain at the injection site, fatigue, headaches and muscle pain. Women who were pregnant were slightly more likely to report injection site pain than women who were not, but less likely to report the other side effects. They were also slightly more likely to report nausea or vomiting after the second dose.

By the end of February, 827 of those enrolled in the pregnancy registry had completed their pregnancies, 86 per cent of which resulted in a live birth. **Rates of miscarriage, prematurity, low birth weight and birth defects were consistent with those reported in pregnant women before the pandemic.**

# GLOBAL

## SCIENTIFIC UPDATES

### Variants of Concern Update

The current SARS-CoV-2 variants of concern are B.1.1.7 (originally detected in the UK), B.1.351 (South Africa), P1 (Brazil), B.1.427 and B.1.429 (California), and B.1.526 (New York). In addition, a new variant has been identified in India (B.1.617).

#### **B.1.1.7 variant**

This variant has a mutation in the receptor binding domain of the spike protein at position 501, where the amino acid asparagine (N) has been replaced with tyrosine (Y). The shorthand for this mutation is N501Y. The N501Y mutation enables the virus's spike protein to more easily bind to human cells, which may make it more infectious.

#### **Severity of disease caused by the B.1.1.7 variant**

The B.1.1.7 variant of coronavirus first identified in England is more infectious but does not cause more severe disease than the original COVID-19, two new UK-based studies, published in *The Lancet Infectious Diseases* and *The Lancet Public Health*, have found. These studies, which cover the period from September to December 2020, are in contrast to [earlier studies](#) which found higher rates of hospitalisations in people infected with the variant.

The [first report](#) is a whole-genome sequencing study involving COVID-19 patients admitted to London's UCL London Hospital and North Middlesex University Hospital between 9 November and 20 December, 2020. This was a critical point when both the original and B.1.1.7 variants were circulating in the capital, and before the UK's mass vaccination program had begun to gather momentum.

The authors compared illness severity in 143 people with the original variant, and 198 infected with B.1.1.7, and calculated viral load: the amount of virus in an infected person's blood. They found no evidence of an association between the B.1.17 variant and worse symptoms. In total, 36 per cent of B.1.1.7 patients became severely ill or died compared to 38 per cent of those with a non-B.1.1.7 strain.

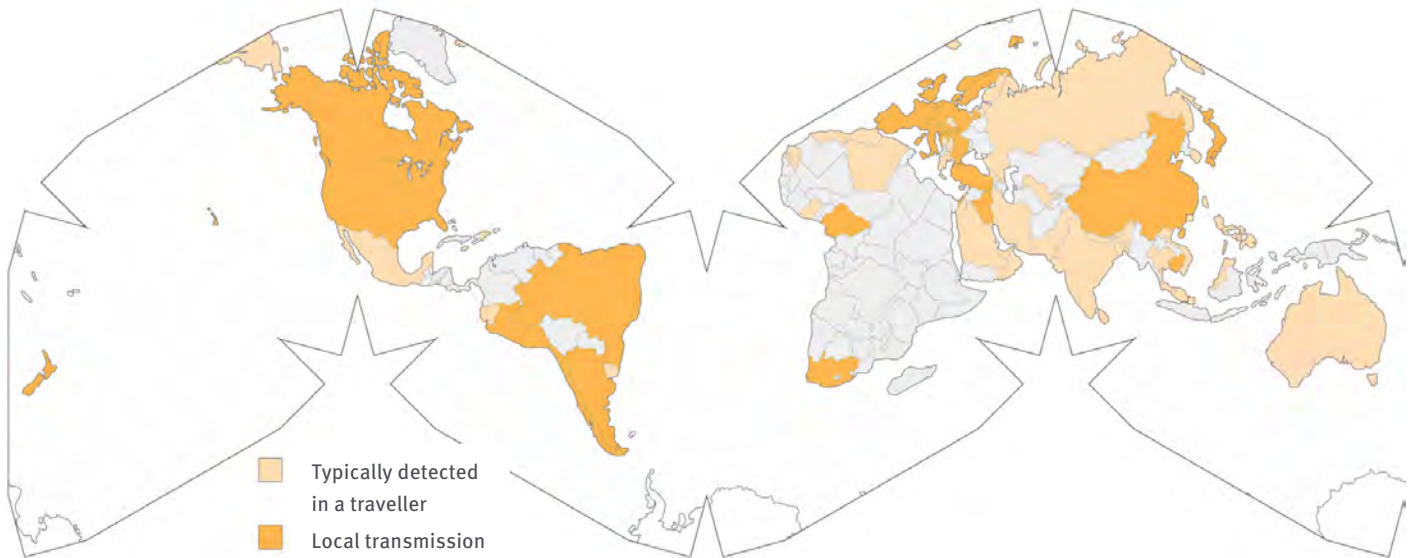
They did find that people infected with the variant tended to be younger, with 55 per cent of those infected aged under 60 compared to 40 per cent in the other cohort. In addition, the authors did find that the B.1.1.7 strain was likely to be more infectious. Samples collected by PCR tests from patients infected with the variant indicated higher amounts of virus in their noses and throats.

The [second observational study](#) used data logged by 36,920 UK users of a COVID-19 symptom self-reporting app, all of whom had tested positive between 28 September and 27 December, 2020. The authors combined their results and symptom reports with surveillance data from the COVID-19 UK Genetics Consortium and Public Health England. For each week and in each UK region, the authors calculated the proportion of users who reported any of the 14 officially recognised COVID-19 symptoms.

This analysis found no significant links between the proportion of B.1.1.7 in each region and the type of symptoms people said they experienced, or in the number of people who reported having long COVID. It also found no evidence that the reinfection rate – the proportion of people who tested positive for coronavirus before October 1, 2020, testing positive again more than 90 days later – was affected by the variant. But they did find that the new strain led to a slight increase in the  $R_0$  number: the average number of new people infected by a COVID-19 patient during their infectious period.

## Global spread of B.1.17 variant

The B.1.17 variant has now been detected in [114 countries](#) and territories, including Australia. Here is the [worldwide distribution](#) of the variant.



By late March, the B.1.17 variant accounted for almost [100 per cent of new cases](#) in the UK, Ireland and Poland and more than 50 per cent in all other western European countries except Lithuania and Slovenia.

In the United States, the B.1.17 variant has been spreading rapidly and by 27 March, it accounted for [44 per cent of all](#) genomically sequenced samples. The variant has been reported in 52 states and territories and is the [predominant strain](#) in seven states. In the Canadian province of Ontario, the B.1.17 variant has quickly become the main strain and is affecting young people and children more than the earlier lineage. This has forced Toronto to [close all schools](#).

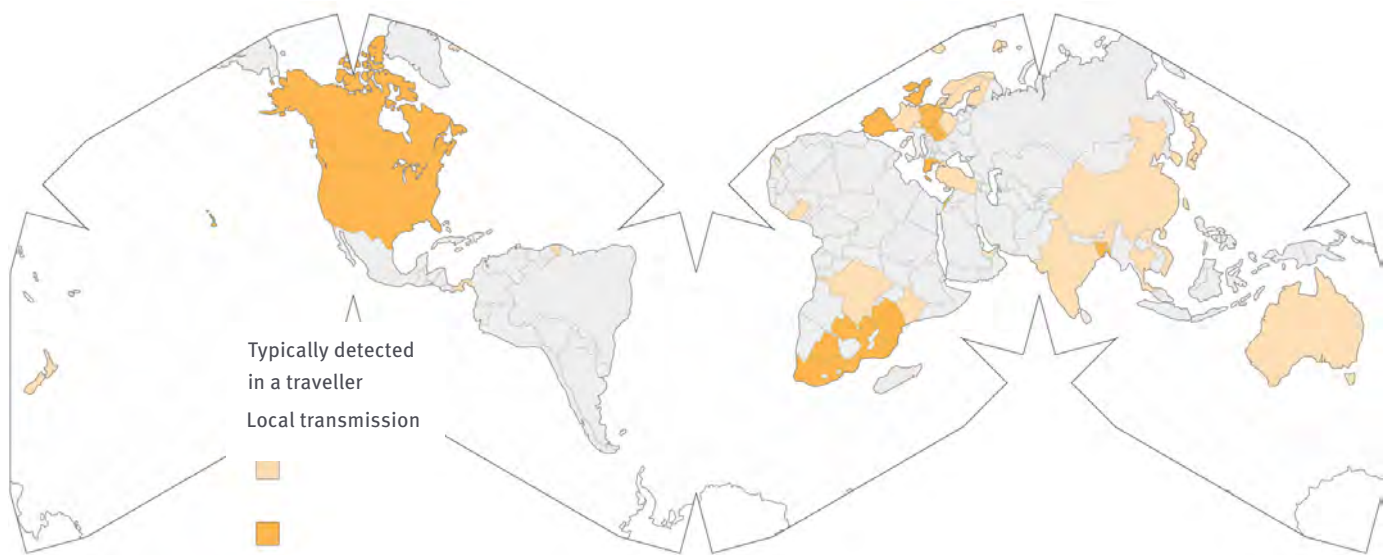
In India, which has been reporting more than 300,000 cases daily, the B.1.17 variant has also become the predominant strain in some states, such as [Punjab](#) where 81 per cent of samples sent for genomic testing were B.1.17. Nationally, the Ministry of Health and Family Welfare [reported](#) that 771 variants of concerns have been detected in a total of 10,787 positive samples shared by States. These include 736 samples (6.8%) positive for viruses of the UK (B.1.17) lineage. Doctors at New Delhi's All India Institute of Medical Sciences have found that one patient is now infecting up [to nine in 10 contacts](#), compared with up to four last year, which implies that variants are driving transmission.

## B.1.351 variant

This variant carries a mutation, called N501Y and contains other mutations of concern, including E484K and K417N. These two mutations are thought to explain why the B.1.351 variant appears to be better able to evade neutralising antibody responses elicited through natural infection or vaccination. Clinical trials of AstraZeneca, Johnson and Johnson and Novavax showed lower efficacies than in countries where the variant is not circulating. Currently there is no evidence to suggest that this variant has any impact on disease severity.

This variant was first identified in Nelson Mandela Bay, South Africa, in samples dating back to the beginning of October 2020. The variant spread from South Africa into Zambia and other neighbouring countries and was detected in the United States in January. It has been detected in at least 25 US states. It has since spread to at least 48 countries. The worldwide dispersion of this variant is less than for the B.1.17 variant.

## Global spread of B.1.351 variant



### P.1 variant

The P.1 variant was [first detected](#) in samples from Manaus in the Amazonas state in northern Brazil in mid-December 2020. The P.1 variant harbours the N501Y mutation in the spike protein and has an 'escape mutation' known as E484K, which also exists in the B.1.351 variant from South Africa and which in lab experiments has been found to help the coronavirus evade protective antibodies generated by earlier infections, as well as less susceptible to antibody-based drugs.

In a [pre-print paper](#), Brazilian researchers cross-referenced data from the national health surveillance system for hospitalisations and data on the prevalence of the P.1 variant in Manaus from December 2020 to February 2021, when the city was experiencing four times more cases than in the previous peak (April 2020). They found that the P.1 variant was 2.6 times as transmissible as non-P1 strains and they estimated that 28 per cent of cases in this period were due to reinfections. This was in a city where between 42 and 76 per cent of adults had been infected during the first wave. Their model did not demonstrate more severity of disease than with other strains.

### P.1 variant may be mutating further

Research conducted by the Brazilian public health institute Fiocruz into the variants circulating in Brazil has found [mutations in the spike region](#) of the virus that is used to enter and infect cells. Those changes, the scientists said, could make the virus more resistant to vaccines - which target the spike protein - with potentially grave implications for the severity of the outbreak in Latin America's most populous nation. The new changes appeared to be similar to the mutations seen in the B.1.351 variant, which has shown in South Africa to be more resistant to existing vaccines than other variants.

### P.1 variant around the world

The P1 variant has been identified in [37 countries](#), including Australia. In addition to Brazil, there has been community transmission in Colombia, Mexico, Canada and the US. The variant has been detected in around 500 samples in 31 states in the US. This variant has been associated with a high proportion of new cases in [British Columbia and Minnesota](#).

In Brazil, Canada and some US states, the P.1 variant is affecting younger people than earlier strains. In Brazil, COVID-19 cases among people in their 30s, 40s, and 50s are up by 565 per cent, 626 per cent, and 525 per cent respectively since the beginning of January, according to the [Oswaldo Cruz Foundation](#). Growing evidence shows that young people are not

only more likely to get infected with P.1 but also to die from it. The Brazilian Association of Intensive Care Medicine said that [the number of 18–45-year-olds](#) requiring intensive care for COVID-19 in February to March this year was three times greater than in September to November 2020 and coronavirus related deaths in that age group have almost doubled.

A [preliminary study](#) (pre-print) which compared case fatality rates in Manaus’s first wave of cases in April to May 2020 with the second wave in January 2021, found that deaths among people aged 20-39 were 2.7 times higher in the second wave than in the first. In the general population they were only 1.15 times higher.

### Emerging variant in India (B.1.617)

In late March, India’s National Centre for Disease Control, a division of the Ministry of Health and Family Welfare, announced that a [new variant](#) – dubbed a “double mutant” – had been identified in samples of saliva taken from people in Maharashtra, Delhi and Punjab. The Ministry says this new variant has not been found in sufficient numbers to account for the increase in COVID-19 cases across the country. In 15-20 per cent of samples from the Indian state of Maharashtra (the state accounting for 62 per cent of cases in the country) the new, [double mutation](#) in key areas of the virus was detected.

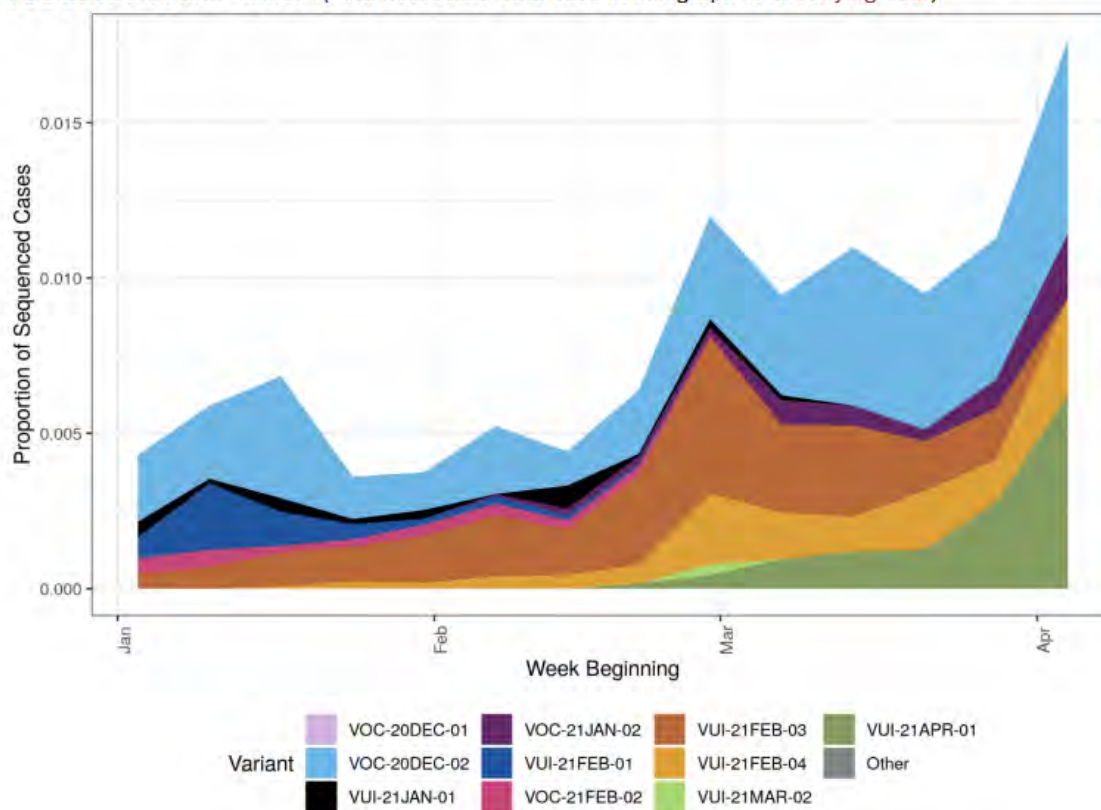
The Indian SARS-CoV-2 Consortium on Genomics has identified two important mutations in the new variant. First, the E484Q mutation, which is similar to the E484K mutation identified on the Brazilian and South African variants, can change parts of the coronavirus spike protein. The spike protein forms part of the coronavirus outer layer and is what the virus uses to make contact with human cells, bind to them, then enter and infect them.

The current vaccines have been designed to create antibodies which target the spike protein of the virus specifically. The concern is that if a mutation changes the shape of the spike protein significantly then the antibodies may not be able to recognise and neutralise the virus effectively. Scientists are investigating whether this may be the case for the E484Q mutation.

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. The study also suggests this mutation may aid the virus in evading the neutralising antibodies that both the vaccine and previous infection can produce, though this is still being investigated.

This variant has been detected in at least 10 other countries, including the US, the UK, Australia and New Zealand. As of 16 April, 408 sequences in the B.1.617 lineage have been detected of which 265 were found in India. A surveillance report by the UK Government said that it has found 77 cases in [England and Scotland](#) so far. Public Health England has found that B.1.617 is the fastest growing variant of concern in England. See Graph and Table below (B.1.617 = VUI-21APR-01).

**Figure 2. Variant prevalence for all England available case data from 1 February 2021 to 21 April 2021 excluding VOC-20DEC-01 and "Other" (Find accessible data used in this graph in [underlying data](#))**



**Growth rate of variants of concern and variants under investigation 1 January 2021 as of 20 April 2021**

Variant	Lineage	Growth rate (1/week) Set 1	Growth rate (1/week) Set 2
VOC-20DEC-02	B.1.351	0.076 (n=250, p=9.139e-06)	0.056 (n=141, p=0.014)
VOC-21JAN-02	P.1	0.27 (n=19, p=0.035)	0.17 (n=9, p=0.34)
VOC-21FEB-02	B.1.1.7 with E484K	-0.16 (n=33, p=0.06)	-0.23 (n=28, p=0.032)
VUI-21JAN-01	P.2	0.034 (n=22, p=0.70)	0.044 (n=22, p=0.62)
VUI-21FEB-01	A.23.1 with E484K	-0.19 (n=43, p=0.077)	-0.25 (n=46, p=0.022)
VUI-21FEB-03	B.1.525	0.051 (n=142, p=0.039)	0.0063 (n=77, p=0.84)
VUI-21FEB-04	B.1.1.318	0.16 (n=79, p=0.0001)	0.23 (n=54, p=4.65e-05)
VUI-21APR-01	B.1.617.1	0.81 (n=68, p=1.217e-12)	0.51 (n=21, p=0.006)

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