COVID-19 Global Trends and Analyses

Volume 2:

- Vaccines and Viral Variants Update
- COVID-19 Global Snapshots

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SUMMARY

Vaccines

- As of 27 March, 508 million people (6.4 per cent of the world's population) have been vaccinated with at least one dose of an approved COVID-19 vaccine. 54 per cent of these doses were administered in just four countries -- the US, UK, China and Brazil. The countries with the highest rate of doses per 100 people are Israel (114), Seychelles (96), UAE (78), Chile (49), UK (47) and the US (40).
- Australia has been slow in the rollout of the two approved vaccines, Pfizer/BioNTech and AstraZeneca. Australia currently ranks #92 in the world for doses per 100 people at 1.6, behind Rwanda (2.7), Mongolia (7.8), and Maldives (42). But Australia's rate is higher than South Korea (1.5), New Zealand (0.9) and Japan (0.6).
- Three new vaccines have announced their safety and efficacy results of Phase 3 trials:
    - The Phase 3 **Janssen/Johnson and Johnson** study demonstrated the vaccine was 85 per cent effective in preventing severe disease across all regions studied and showed protection against COVID-19 related hospitalisation and death, beginning 28 days after vaccination.
    - The first interim analysis of the **Bharat Biotech** vaccine (Covaxin) is based on 43 cases, of which 36 cases of COVID-19 were observed in the placebo group versus 7 cases observed in the BBV152 group, resulting in a point estimate of vaccine efficacy of 80.6 per cent.
    - **Novavax** reported that overall, its vaccine had 96 per cent efficacy after two doses in protecting people from mild, moderate or severe COVID-19 disease if they were infected with SARS-CoV-2 virus that closely matches the vaccine sequence. Vaccine efficacy was reduced to 86 per cent in protecting against disease if people were infected with the B.1.1.7 strain of the virus.
- On 22 March, **AstraZeneca** released interim results of its clinical trial conducted in the USA. Vaccine efficacy of preventing symptomatic COVID-19 was 79 per cent and 100 per cent for preventing severe disease and hospitalisation. However, 2 days later, the efficacy was revised from 79 per cent to 76 per cent.
- By 16 March, at least 20 European countries had suspended or limited inoculations with the **AstraZeneca** vaccine due to a higher-than-expected number of thromboembolic events. On 18 March, the EMA's safety 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.
- Real-world data on effectiveness of approved vaccines:
    - Public Health England data show one dose of the **Pfizer/BioNTech** vaccine reduces the risk of being infected by more than 70 per cent, rising to 85 per cent after the second dose.
    - Results of a study by Health Scotland, which analysed data for 1.1 million people, showed that by the fourth week after the initial dose, the **Pfizer and AstraZeneca** vaccines were found to reduce the risk of hospitalisation by up to 85 per cent and 94 per cent, respectively.
    - An Israeli study found that **Pfizer's** vaccine effectiveness for outcomes at days 14 through 20 after the first dose and at 7 or more days after the second dose was as follows: for documented infection, 46 per cent and 92 per cent; for symptomatic COVID-19, 57 per cent and 94 per cent; for hospitalisation, 74 per cent and 87 per cent; and for severe disease, 62 per cent and 92 per cent, respectively.

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), P1 (Brazil), B.1.427 and B.1.429 (California), and B.1.526 (New York).
- The **B.1.1.7 variant**, first found in the UK, is spreading significantly in 27 European countries monitored by the WHO and is dominant in at least 10 countries: Britain, Denmark, Italy, Ireland, Germany, France, the Netherlands, Israel, Spain and Portugal. Globally, the B.1.1.7 variant has spread to more than 80 countries, including Australia, and has been doubling every ten days in the US, where it is expected to soon become the dominant variant. A number of studies in the UK have found that this variant is more transmissible than the original strain and is also associated with increased risk of hospitalisation and death.
- The **B.1.351 variant** was first identified in Nelson Mandela Bay, South Africa, in samples dating back to the beginning of October 2020, and cases have since been detected outside of South Africa, including the United States, a number of European countries and most Southern African countries.

  The steep rise in cases between November and February led to an increased burden on the South African health care system; however, the variant does not appear to cause more severe disease. According to a computer model, B.1.351's spread can be explained by the variant being 50 per cent more transmissible or 20 per cent better at evading the immune response in previously infected people, when compared with previous variants. On 7 February, South Africa put its AstraZeneca vaccine roll-out on hold after a small study suggested that it doesn't provide protection against mild or moderate illnesses caused by the B.1.351 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 has since been detected in the US, UK and a number of European countries. Researchers tracking P.1 found that by early January, the variant made up 87 per cent of samples in Manaus. By February it had taken over completely. Like B.1.1.7, P.1 is more transmissible than earlier strains. The researchers concluded that P.1's mutations had led to a second wave of infections in Manaus even though a study of blood donors had indicated that more than 70 per cent of the city's residents had antibodies to the original strain.
- The **B.1.427 and B.1.429 variants**, which were first identified in California, appear to be more transmissible and heighten patients' risk of admission to ICU and death. One study sequenced genomes from virus samples in 44 California countries between 1 September 2020 and 29 January 2021. The new variants accounted for 21.3 per cent of these sequences. A review of medical records found that, compared with patients who had other viral strains, those carrying the variants were 4.8 times more likely to be admitted to the ICU and more than 11 times more likely to die. The study also found that viral load in the nasopharynx was twice that of comparable patients infected with earlier strains.
- The variant known as **B.1.526** began showing up in samples collected in New York City in November 2020. By the middle of this month, it accounted for about one in four viral sequences appearing in a database shared by scientists. The emergence of this variant might be associated with a surge in new COVID-19 cases in north-eastern US states. A study by Columbia University observed a steady increase in the detection rate of the variant from late December to mid-February, with an alarming rise to 12.3 per cent in the first two weeks of February.
- The emergence of variants of concern affirms the need for **ongoing sequencing of viral genomes** around the world to monitor the evolution of SARS-CoV-2 and for the support of LMICs to have high testing rates and perform sequencing of viral genomes.

GLOBAL SCIENTIFIC UPDATES

SARS-CoV-2 Vaccines Update

Global Rollout of Vaccines

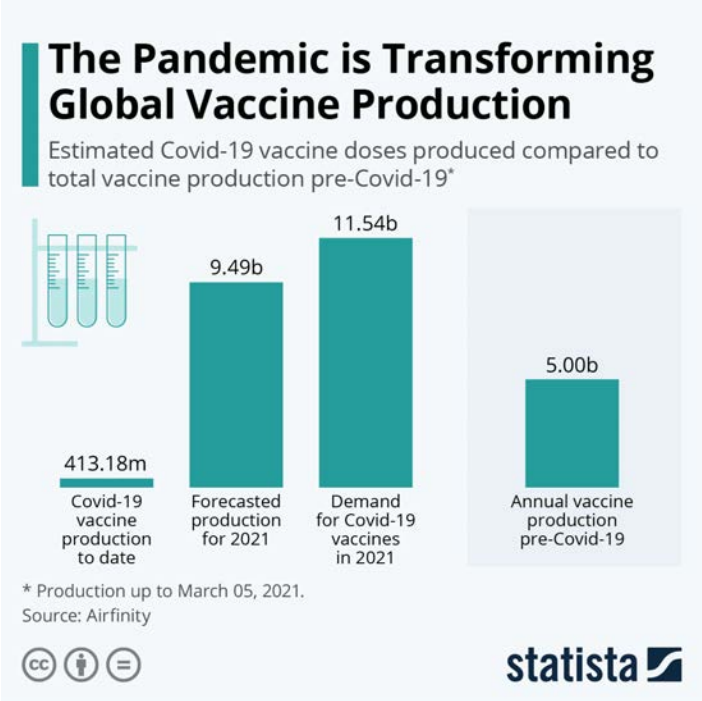
As of 27 March, 508 million people (6.35% of the world's population) have been vaccinated with at least one dose of an approved COVID-19 vaccine. 54 per cent of these doses were administered in just four countries -- the US, UK, China and Brazil. The countries with the highest rate of doses per 100 people are Israel (114), Seychelles (96), UAE (78), Chile (49), UK (47) and the US (40).

Australia has been slow in the rollout of the two approved vaccines, Pfizer/BioNTech and AstraZeneca. Australia currently ranks #92 in the world for doses per 100 people at 1.6, behind Rwanda (2.7), Mongolia (7.8), Turkey (16.9) and Maldives (42). But Australia's rate is higher than South Korea (1.5), New Zealand (0.9) and Japan (0.6).

Vaccine Production Ramps Up

Soaring demand for COVID-19 vaccines has resulted in massive changes in vaccine production. Companies have drastically ramped up production and 413 million doses of nine different vaccines had been produced by early March, according to an analysis by predictive science intelligence company Airfinity. Out of that total, 43 per cent have been mRNA, 35 per cent are whole virus and 22 per cent are viral vector. With 119 million doses, Pfizer is the company that has produced the highest quantity of COVID-19 vaccine, ahead of Sinovac with 91 million and AstraZeneca with 83 million.

Airfinity's data show that an estimated 9.5 billion doses of COVID-19 vaccines will be produced in 2021. Putting that number into perspective, it is nearly twice the volume of the five billion vaccine doses of all types produced across the world before the pandemic struck. Despite the scale of that figure, it is still less than the 11.5 billion doses of COVID-19 vaccine needed to meet global demand this year.



Vaccine Export Bans

The greatest threat to global vaccination programs is the looming bans on the export of AstraZeneca vaccine by both the **EU and India**, between them the largest sources of that vaccine.

There has been a dispute between the EU and the UK over access to vaccines. While the UK has administered 46.7 doses per 100 people, Germany has administered just 14.2, according to figures compiled by Our World in Data. France has given just 13.8 doses per 100 people and Italy 14.5. At the same time, Europe had exported 77 million doses to 33 countries. The EU has singled out the Anglo-Swedish company AstraZeneca, which has slashed its projected EU vaccine delivery by June from 300 million to 100 million. Europe has ordered 400 million doses of the AstraZeneca vaccine, but the company has encountered delays at a factory in Belgium, affecting its ability to fulfil its commitments on the continent. This is affecting **Australia**, which had expected 3.8 million doses by the end of March but has received only 700,000 doses. The EU has stopped short of a total ban on exports of COVID-19 vaccines manufactured in member countries but the threat remains real.

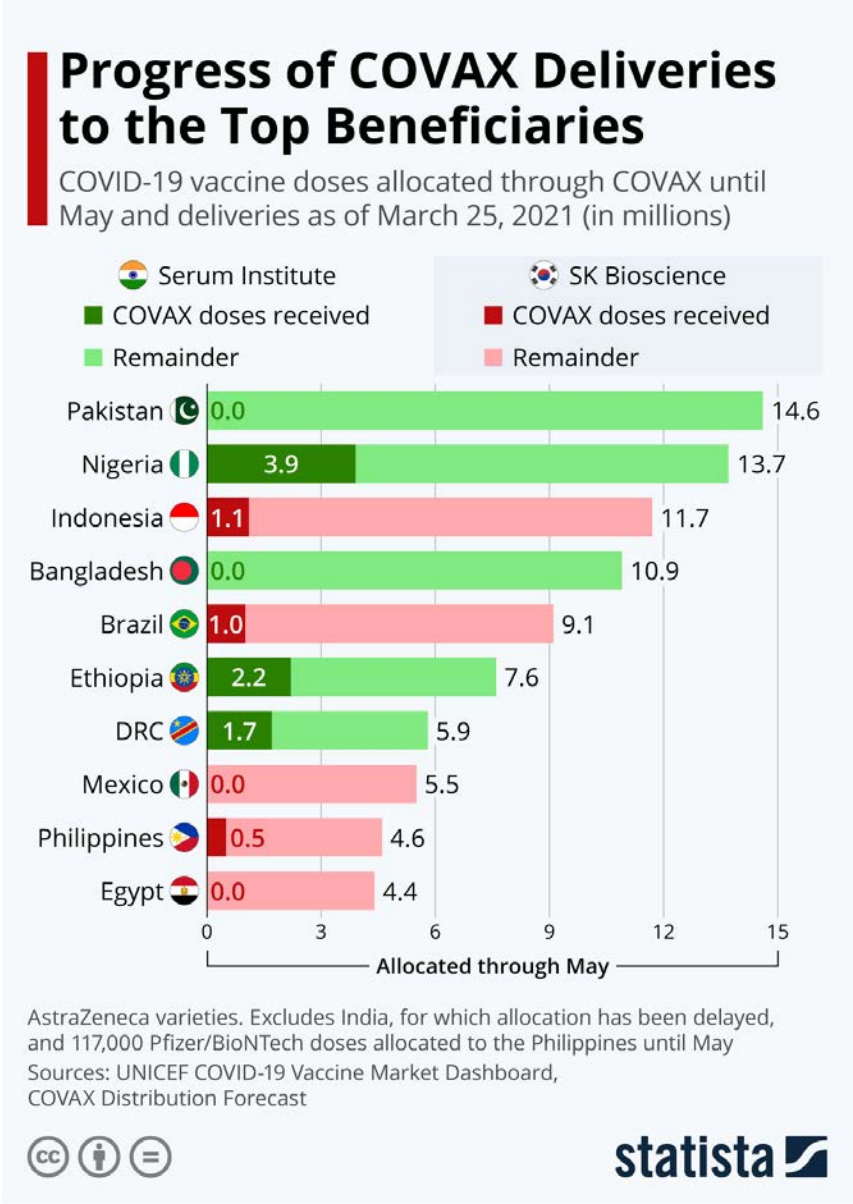
However, with its own battle against the coronavirus taking a sharp turn for the worse, **India** has severely curtailed exports of COVID-19 vaccines, triggering setbacks for vaccination drives in many other countries. The government of India is now holding back nearly all of the 2.4 million doses that the Serum Institute of India, the company that is one of the world's largest producers of the AstraZeneca vaccine, makes each day. Just a few weeks ago, India was a major exporter of the vaccine. More than 70 countries received vaccines made in India, with a total of more than 60 million doses. But the size of its shipments abroad has greatly diminished in the past two weeks, according to data from India's foreign ministry. And COVAX, the program set up by donor agencies to purchase vaccines for poorer nations, said on 26 March that it had told those countries that nearly 100 million doses expected in March and April would face delays because of increased demand for COVID-19 vaccines in India.

COVAX Progress

Deliveries by COVID-19 Vaccines Global Access – or COVAX – started up at the end of February but have already hit a barrier after only approximately 32 million doses have been shipped. India, which delivers domestically made doses of the AstraZeneca vaccine under the COVAX initiative, has slowed down exports after a new wave of infections in the country. The initiative, which aims to provide equitable access to COVID-19 vaccines, is planning to ship out almost 188 million doses of vaccines until the end of May, mainly from India and South Korea.

Among the ten biggest beneficiaries of the initiative, Nigeria has received the largest delivery. The 3.9 million doses shipped on 2 March make up approximately 30 per cent of the vaccine doses pledged for delivery to the country until the end of May. Shipments to Ethiopia and the Democratic Republic of the Congo were equally large in relation to expected shipments over this time period. By comparison, deliveries to Indonesia, Brazil and the Philippines made up only between 9 and 11 per cent of the delivery pledge. All three countries have received additional doses outside of COVAX, but amounts differ. Indonesia has received at least 38 million doses which were purchased from China (14 per 100 population) and Brazil has so far had access to approximately 20 million doses of the Chinese Sinovac variety which is produced locally in part (9.5 per 100 population).

Some countries that have received none of their COVAX allotments so far have also purchased substantial amounts of vaccines, among them Bangladesh and Mexico. Others, like Egypt and Pakistan, have received very few additional doses relative to their population size.



Janssen/Johnson and Johnson (J&J)

The vaccine is known as Ad26.COV2.S, and uses adenovirus 26 as a vector to deliver double-stranded DNA encoding the SARS-CoV-2 spike protein. The World Health Organization (WHO) has approved this one dose vaccine for emergency use. This vaccine is also approved for emergency use in the US, EU, South Africa, Bahrain and Saudi Arabia.

The Phase 3 ENSEMBLE study demonstrated the vaccine was 85 per cent effective in preventing severe disease across all regions studied and showed protection against COVID-19 related hospitalisation and death, beginning 28 days after vaccination. The study enrolled a total of 43,783 participants. The trial, conducted in eight countries across three continents, includes a diverse and broad population including 34 per cent of participants over age 60. In preventing mild to moderate disease, efficacy varied by region. In the United States, for example, the vaccine was found to be 72 per cent effective. In Latin America, where the variant P.1 has cropped up, the vaccine was found to be 66 per cent effective. In studies in South Africa, where the variant B.1.351 is circulating, effectiveness was lower: 64 per cent.

Bharat Biotech (Covaxin)

On 4 March, the Indian drug company Bharat Biotech announced that initial results from clinical trials showed that the vaccine was both safe and effective. BBV152 contains a whole virion inactivated SARS-CoV-2 vaccine, which is produced in Vero cells. It is stable at 2 to 8°C (refrigerated) and is shipped in a ready-to-use liquid formulation that permits distribution using existing vaccine supply chain channels. BBV152 has a 28-day open vial policy as a unique product characteristic, thus reducing vaccine wastage by approximately 10-30 per cent.

The Phase 3 study enrolled 25,800 participants between 18-98 years of age, including 2,433 over the age of 60 and 4,500 with comorbidities. The primary endpoint of Phase 3 clinical trial is based on the first occurrence of PCR-confirmed symptomatic (mild, moderate, or severe) COVID-19 with onset at least 14 days after the second study vaccination in serologically negative (to SARS-CoV-2) adult participants at baseline. The first interim analysis is based on 43 cases, of which 36 cases of COVID-19 were observed in the placebo group versus 7 cases observed in the BBV152 group, resulting in a point estimate of vaccine efficacy of 80.6 per cent.

An additional interim analysis is planned for 87 cases, and the final analysis is planned for 130 cases. All data from the second interim and final analyses will be shared via prepublication servers as well as submitted to a peer-reviewed journal for publication.

European Countries Temporarily Suspend AstraZeneca/Oxford Vaccine

In early March 2021, concerns emerged regarding reports of a rare thromboembolic or clotting condition in healthy people who had received the AstraZeneca/Oxford vaccine. This was specifically, clots in the venous system around the brain, called cerebral venous sinus thrombosis (CVST), reported in younger, healthy people.

By 16 March, at least 20 European countries had suspended or limited inoculations with this vaccine. Austria moved first, halting the use of a single batch of the AstraZeneca vaccine on 7 March after one person, under the age 50, was reported to have died with blood clots after receiving the vaccine. Denmark, Iceland and Norway followed suit by halting AstraZeneca vaccinations altogether after further so-called thromboembolic events, including the death of one woman in Denmark. Germany, France, Italy and Spain announced suspension of use of the vaccine on 16 March. Germany announced that seven cases of CVST had been reported among 1.6 million people vaccinated with AstraZeneca, three of whom died. This exceeded their baseline of two cases per million. According to data published by the European Centre for Disease Prevention, AstraZeneca accounted for three in ten doses administered across the European Economic Area's 30 member states in the week ended 7 March.

The UK, India and Australia continued to use the vaccine and both WHO and the European Medicines Agency (EMA) declared that the vaccine is safe. The AstraZeneca vaccine has not yet been approved by the US Food and Drug Administration. According to the company, the number of reports from the ongoing vaccine program in the UK and EU, which includes more than 17 million individuals vaccinated to date, is just 37.

On 18 March, the EMA's safety committee released the findings of its investigation of the thromboembolic 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;
- the vaccine is not associated with an increase in the overall risk of blood clots (thromboembolic events) in those who receive it;
- there is no evidence of a problem related to specific batches of the vaccine or to particular manufacturing sites;
- however, the vaccine may be associated with very rare cases of blood clots associated with thrombocytopenia, i.e. low levels of blood platelets (elements in the blood that help it to clot) with or without bleeding, including rare cases of clots in the vessels draining blood from the brain (CVST).
- the EMA is continuing to investigate the matter and is convening another expert panel on 29 March.

Soon after the release of the report, France, Germany, Spain and Italy announced that they would resume administering the AstraZeneca vaccine. A number of smaller EU countries have followed suit.

A group of German researchers have said that the complication resembles a rare side effect of the blood thinner heparin, called heparin-induced thrombocytopenia (HIT). It is not clear yet as to the mechanism this occurs, although it is being postulated that it is related to the production of antibodies against platelet factor 4.

Australia did not suspend AstraZeneca vaccine. The Australian Technical Advisory Group in Immunisation (ATAGI) released statements on 19 March and 25 March, concluding the benefits of the vaccine far outweigh the risk. However, as a precautionary measure, they did recommend deferral of any COVID-19 vaccine in people with a confirmed medical history of CVST and/or HIT.

Real-World Data on Effectiveness of Approved Vaccines

1. Early data from Public Health England's (PHE) SIREN study in a pre-print paper show a promising impact on infection in healthcare workers aged less than 65 years. Healthcare workers in the study are tested for coronavirus (COVID-19) every 2 weeks – whether or not they have symptoms. Data show **one dose of the Pfizer/BioNTech** vaccine reduces the risk of being infected by more than 70 per cent, rising to 85 per cent after the second dose.

   PHE's analysis of routine testing data also shows that one dose is 57 per cent effective against symptomatic COVID-19 disease in those aged over 80. This effect occurs from about 3 to 4 weeks after the first dose. Early data suggests the second dose in over 80s improves protection against symptomatic disease by a further 30 per cent, to more than 85 per cent.

2. Results of a study (preprint) by Health Scotland, which analysed data for 1.1 million people, showed that by the fourth week after the initial dose, the **Pfizer and AstraZeneca vaccines were found to reduce the risk of hospitalisation by up to 85 per cent and 94 per cent, respectively**.

   The first dose of the BNT162b2 vaccine (Pfizer) was associated with a vaccine effect of 85 per cent for preventing COVID-19 related hospitalisation at 28-34 days post-vaccination. Vaccine effect at the same time interval for the ChAdOx1 vaccine (AstraZeneca) was 94 per cent. Results of combined vaccine effect for prevention of COVID-19 related hospitalisation were comparable when restricting the analysis to those aged ≥80 years at 28-34 days post-vaccination.

3. In this peer-reviewed study, data from Israel's largest health care organisation were used to evaluate the effectiveness of the BNT162b2 mRNA vaccine (**Pfizer**). Each study group included 596,618 persons. Estimated vaccine effectiveness for the study outcomes **at days 14 through 20 after the first dose and at 7 or more days after the second dose** was as follows: for documented infection, 46 per cent and 92 per cent; for symptomatic COVID-19, 57 per cent and 94 per cent; for hospitalisation, 74 per cent and 87 per cent; and for severe disease, 62 per cent and 92 per cent, respectively. Estimated effectiveness in preventing death from COVID-19 was 72 per cent for days 14 through 20 after the first dose. Estimated effectiveness in specific subpopulations assessed for documented infection and symptomatic COVID-19 was consistent across age groups.

4. Israel's health ministry has recommended vaccinating some children if they suffer from underlying conditions that make them vulnerable to coronavirus. Israel has so far immunised around 600 children. No major side-effects were seen and minor ones were rare. The children, some of whom have cystic fibrosis, which affects the lungs, were not part of a clinical trial. Pfizer, Moderna and AstraZeneca are in the process of conducting safety trials in children.

Novavax

Novavax revealed the final results of its Phase 3 human trials of NVX-CoV2373 in a press release; the findings have not been submitted for peer-review in a scientific journal yet. The company reported that overall, its vaccine had 96 per cent efficacy after two doses in protecting people from mild, moderate or severe COVID-19 disease if they were infected with SARS-CoV-2 virus that closely matches the vaccine sequence. Vaccine efficacy was reduced to 86 per cent in protecting against disease if people were infected with the B.1.1.7 strain of the virus. In an ongoing, Phase 2B study of the vaccine in South Africa, where the B.1.351 variant is predominant, vaccine efficacy is 55 per cent in protecting against symptomatic COVID-19.

Sinopharm

The United Arab Emirates (UAE) and Bahrain were the first countries to approve the Sinopharm vaccine after releasing the results of their trials (UAE, n=31,000; Bahrain, n=7700). Both reported an efficacy of 86 per cent and the UAE reported that 99 per cent of those vaccinated with two doses developed neutralising antibodies to SARS-CoV-2 and that the vaccine prevented moderate and severe disease in everyone vaccinated.

However, health authorities in the UAE have recently begun administering a third dose of the Sinopharm vaccine to at least some residents, as doctors say the inoculations in some cases haven't generated enough protective antibodies. G42 Healthcare, the company that coordinated Sinopharm's Phase 3 clinical trials in the U.A.E., said a "select group of people are being administered a third shot to observe the immune system response" as part of a scientific study.

Gamaleya/Sputnik V

The Russian-developed vaccine is becoming a more popular option outside the country. Preliminary trial data (n=20,000) published in The Lancet demonstrated an overall efficacy of 91.6 per cent. The trial will continue until there are 40,000 participants. The vaccine uses two different adenovirus vectors in the first and second dose. Now, as European nations scramble to secure enough vaccines, some of Russia's staunchest critics are considering using Sputnik V as well.

The Sputnik V vaccine is already being used in dozens of countries across the Middle East, Africa, Asia and South America. Slovakia and Hungary have already taken deliveries of Sputnik V, bypassing the European Medicines Agency which has placed the vaccine under a 'rolling review'. Serbia (not an EU member) is also using the vaccine. Austria and the Czech Republic have also expressed an interest in using it. Even Germany – an outspoken critic of Russia – says it would be prepared to purchase the Sputnik V vaccine. However, the EU's Internal Market Commissioner Thierry Breton dismissed suggestions Europe needed Russia's assistance. "We have absolutely no need for Sputnik V," he told French television station TF1. "It's a strange statement," Vladimir Putin replied. What happens next will be interesting.

AstraZeneca

On 22 March, AstraZeneca released interim results of its clinical trial conducted in the USA. The study conducted in 32,449 individuals randomised vaccine to placebo 2:1 and accrued 141 symptomatic infections. Vaccine efficacy of preventing symptomatic COVID-19 was 79 per cent and 100 per cent for preventing severe disease and hospitalisation. In people aged over 65 years, efficacy against symptomatic infection was 80 per cent. The study comprised 79 per cent White/Caucasian, 8 per cent Black/African American, 4 per cent Native American and 4 per cent Asian. 22 per cent of participants were Hispanic, and 20 per cent of individuals were over 65 years of age. A close review of thrombotic events was performed including cerebral venous sinus thrombosis (CVST) with the assistance of an independent neurologist. No increased risk of thrombosis or events characterised by thrombosis among the 21,583 participants receiving at least one dose of the vaccine were observed. These results should reassure people of the safety and efficacy of the AstraZeneca vaccine.

However, the following day, the NIH Data and Safety Monitoring Board (DSMB), which monitors patient safety and the scientific validity of clinical trials, released a public letter claiming that the data published by AstraZeneca were "outdated" and that the efficacy published dated back to 24 February. When an additional month was taken into account, the effectiveness ranged from 69 per cent to 75 per cent. "The DSMB is concerned that AstraZeneca chose to use data that were already outdated and potentially misleading in their press release," the letter states. AstraZeneca released a statement promising that the full analysis of its data would be available within 48 hours and indicated the results would be consistent with the analysis released on 22 March.

Re-Analysis of Pfizer Vaccine Efficacy Following a Single Dose

In this pre-print paper, researchers re-analysed vaccine efficacy for the Phase 3 results of the Pfizer/BioNTech clinical trial. Using mathematical methods, the estimated efficacy over the period 11 to 28 days post first vaccination was 94 per cent and there was no detectable increase in efficacy following the second vaccination. The efficacy post first dose substantially preceded the development of detectable serum neutralising antibody. The results suggest that neutralising antibody may not be the sole predictor of vaccine efficacy and that additional antiviral mechanisms may be at play early in the immune response. Further, the resulting high vaccine efficacy is achievable at least in the short term following one vaccination allowing more flexibility in vaccination regimens, and the potential to provide a single dose where supply is limited.

What Level of Neutralising Antibody Protects from COVID-19?

In this pre-print paper, researchers modelled the relationship between in vitro neutralisation levels and observed protection from SARS-CoV-2 infection using data from seven current vaccines, as well as convalescent cohorts. The 50 per cent protective neutralisation level was estimated to be approximately 20 per cent of the average convalescent level. The estimated neutralisation level required for 50 per cent protection from severe infection was significantly lower – 3 per cent of the mean convalescent level. Modelling the decline in neutralisation titre over the first 250 days after immunisation predicted that a significant loss in protection from infection will occur, although protection from severe disease should be largely retained.

Acute Allergic Reactions to mRNA COVID-19 Vaccines

In this study of 69,000 employees of a Massachusetts hospital system who received their first dose of vaccine between December 2020 and February 2021, 40 per cent received the Pfizer-BioNTech vaccine and 60 per cent received the Moderna vaccine. At least one symptom survey was completed by 52,805 (81%). Acute allergic reactions were reported by 1,365 employees overall (2.10%), more frequently with the Moderna vaccine compared with Pfizer-BioNTech (2.20% vs 1.95%; P = .03). Anaphylaxis was confirmed in 16 employees (0.025%). Mean time to anaphylaxis onset was 17 minutes (SD, 28; range, 1-120). One patient was admitted to intensive care, 9 (56%) received intramuscular epinephrine, and all recovered.

Vaccine Confidence

Intention to get vaccinated reflects the political opinions of individuals in a number of countries, including the US and Australia. A recent poll in the US showed that nearly half of Republican men and 47 per cent of those who supported Trump in the 2020 election said they would not choose to be vaccinated, even if the coronavirus vaccines were made available to them. By contrast, only 10 per cent of supporters of President Biden said they would not choose to be vaccinated if offered one.

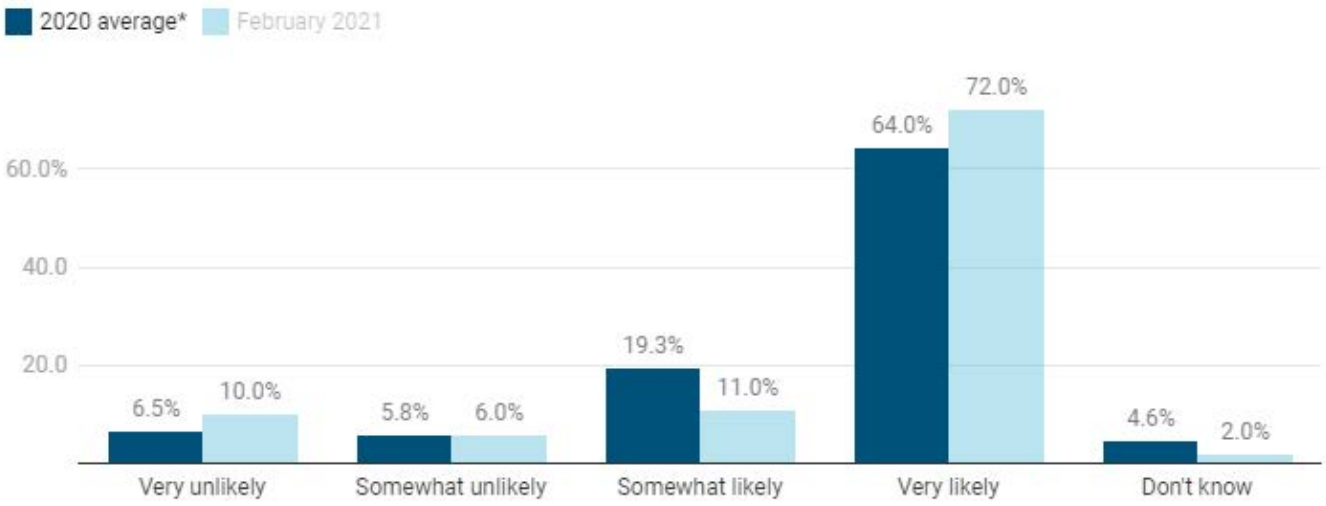
Overall, 30 per cent of polled Americans said they would not get vaccinated. There was no statistical significance between Black and White people. Other groups that had higher than average intentions not to be vaccinated included

White men without a college degree (40%), White evangelical Christians (38%), people under the age of 45 (37%) and rural dwellers (36%).

In Australia, a survey found that attitudes towards COVID-19 vaccination also differ on political lines. The survey, carried out by Vox Pop Labs for the ABC, took place over five days from 21 February — the day before Australia's vaccine rollout was launched. Of the 1,376 participants across Australia, 72 per cent said they were very likely to get vaccinated, close to the US figure and up 8 per cent from the 2020 average. However, those who said they were very unlikely to be vaccinated increased from an average of 6 per cent in 2020 to 10 per cent in February.

In late September — the last time the survey was conducted — 11 per cent of those people identifying to the right side of politics said they were 'very unlikely' to take the vaccine, compared to 6 per cent of those in the 'centre' and 5 per cent for those on the 'left'. The latest survey now shows substantial growth in that figure, with 19% on the right now saying they're 'very unlikely' to take the vaccine. That compares to 8 per cent of those identifying with the 'centre' and 4 per cent for those on the 'left'.

Percentage of Australians likely to get the vaccine when it becomes available to them



** The ABC, through Vox Pop Labs, conducted 20 surveys through 2020 asking Australians about COVID-19. The surveys started in April and finished in October. This figure is the average of those responses.*

Source: Vox Pop Labs • Get the data

The Role of Faith Leaders in Promoting Vaccine Confidence

The role of religious leaders in promoting public health programs, including immunisation, has long been recognised. For example, in the final stages of the global polio eradication initiative, positive fatwas by Islamic scholars and supportive messages by Imams have been crucial in maintaining community support for polio vaccination and countering misinformation.

In the case of COVID-19, a number of influential religious leaders have publicly endorsed vaccination. The Grand Mufti of Saudi Arabia Shaikh Abdul Aziz Aal-ash Shaikh received the vaccine in early January and has urged Muslims to be vaccinated. Pope Francis was vaccinated in January. "I believe that ethically everyone should take the vaccine," the Pope said in an interview with TV station Canale 5. The influential Buddhist leader the Dalai Lama has been vaccinated in India and after receiving the injection, he urged people to be "brave and come forward to be vaccinated". After claims on social media that the vaccine was 'not halal', a group of Imams in Australia issued a fatwa stating that both the Pfizer and AstraZeneca vaccines are halal for Muslims. Adel Salman, spokesperson from the Islamic Council of Victoria, says without the engagement of community leaders the vaccine rollout will fail.

Are New COVID-19 Vaccine Trials Ethical?

The authorisation of three highly effective COVID-19 vaccines for emergency use in the United States and four others elsewhere poses an ethical dilemma for researchers conducting ongoing clinical trials or planning trials of new vaccines. Researchers are currently testing **78 vaccines** in clinical trials on humans, and 22 have reached the third phase of testing. At least 77 preclinical vaccines are under active investigation in animals.

The first question that has been raised is "Should all trial participants who received the placebo be offered the vaccine tested in their trial once proven to be effective?" A paper by US bioethicists argues that only those participants who meet the existing eligibility criteria should be vaccinated and others in the placebo group should continue to be followed along with the vaccinated group, providing valuable additional data such as the long-term safety of the vaccines. Careful statistical adjustments would have to be made for removing participants in the placebo group, perhaps with an 'intent-to-continue' analysis of only those who are not eligible for vaccination outside the trial. Others argue that there is a duty of care to the control arm participants and that they should not continue to be exposed to a risk of infection that may have severe consequences.

The second ethical reason given in this paper against offering vaccine to all participants in the placebo groups of the trials is that this would yield lower health and health equity gains from vaccination overall if participants do not belong to the identified priority groups. Thus, if all participants in the placebo groups in the Pfizer-BioNTech trial (n = 43,651; placebo group, n = 21,828) and Moderna trial (n = 30,000; placebo group, n = 15,000) were offered vaccine, this would mean that currently up to 36,828 health care personnel or other individuals who have higher priority than the participants could not be vaccinated. The resulting loss of benefits could be significant.

Another paper looks at vaccine trial ethics once efficacious vaccines have been developed and are available. It has long been recognised that an ethical dilemma arises when one effective vaccine has been successfully developed against an epidemic disease and researchers seek to test the efficacy of another vaccine for the same pathogen in clinical trials involving human subjects. On the one hand, there are compelling reasons why it would be unethical to trial a novel vaccine when an effective product exists already. First, it is a firm principle of medical ethics that an effective treatment or vaccine should not be withheld from patients if their life may depend on it. Second, since epidemic outbreaks often emerge in settings with less-resourced health systems, there is a pronounced risk that any trial withholding an effective vaccine would disproportionately affect the vulnerable populations that historically have been exploited for biomedical research. Limitations on current COVID-19 treatment options mean that it is in each individual's interests to receive the first vaccine found to be safe and efficacious, rather than participate in vaccine trials where they might receive placebo or an unproven vaccine candidate.

In the case of COVID-19 vaccines, a counter argument is that we are aiming to eventually vaccinate the world's population of almost 8 billion people and that there are just not enough of the current vaccines to go around. Given the challenges of manufacturing sufficient supply for so many people, and given that different vaccine candidates may be efficacious in different populations numerous vaccines may be needed to meet the global need. This highlights the potential social value of conducting additional trials after one or more vaccine candidates are found to be safe and efficacious.

There is no algorithm for determining how much social value a given clinical trial has and whether its social value justifies the risks participants face. As a result, ethics committees tend to focus on ensuring that a trial has the potential to collect important data and that the risks of substantial harm are low. Even when a vaccine candidate is found to be safe and efficacious, there are likely to be good reasons to study others. Another vaccine candidate might be more effective, generate longer-lasting immunity, work better in certain subpopulations, provide greater protection against severe disease, or prevent infection better. Other candidates may also be superior with respect to cost or other practical considerations, such as storage. These may be important factors to justify clinical trials of new vaccines developed and manufactured in low and middle income countries, such as Cuba, Vietnam, Thailand and India.

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).

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. The variant, first found in the UK, is spreading significantly in 27 European countries monitored by the WHO and is dominant in at least 10 countries: Britain, Denmark, Italy, Ireland, Germany, France, the Netherlands, Israel, Spain and Portugal. Globally, the B.1.1.7 variant has spread to more than 80 countries and has been doubling every ten days in the US, where it is expected to soon become the dominant variant.

A number of studies in the UK have found that this variant is more transmissible than the original strain and is also associated with increased risk of hospitalisation and death. One such study in England found that, based on 4,945 deaths with known spike gene target failure (SGTF) status, the hazard of death associated with SGTF is 55 per cent (95% CI 39–72%) higher after adjustment for age, sex, ethnicity, deprivation, care home residence, local residence and test date.

An Italian study confirmed that the viral load detected by nasopharyngeal swabs in people infected with the B.1.1.7 variant is significantly higher than with other lineages. In addition, there was a significant difference between the median values of the duration of RNA positivity: 16 days with the variant compared to 14 days with other lineages.

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. This variant was first identified in Nelson Mandela Bay, South Africa, in samples dating back to the beginning of October 2020, and cases have since been detected outside of South Africa, including the United States, a number of European countries and most Southern African countries.

The steep rise in cases between November and February led to an increased burden on the South African health care system; however, the variant does not appear to cause more severe disease. According to a computer model, B.1.351's spread can be explained by the variant being 50 per cent more transmissible or 20 per cent better at evading the immune response in previously infected people, when compared with previous variants.

On 7 February, South Africa put its AstraZeneca vaccine roll-out on hold after a small study suggested that it doesn't provide protection against mild or moderate illnesses caused by the B.1.351 variant. The study, conducted in 2,026 HIV-1 negative participants, concluded that the overall efficacy was 20.4 per cent at preventing mild-to-moderate COVID-19, and 10.4 per cent against the B.1.351 variant. AstraZeneca has since said that it could take six to nine months to produce and deploy a COVID-19 vaccine that works against B.1.351 and other new variants of the coronavirus. COVID-19 vaccines

produced by Novavax and Janssen/Johnson and Johnson are also less effective against B.1.351 than against other variants; however, they are both around 60 per cent effective at preventing mild or moderate infections.

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. The P.1 variant has since been detected in the US, UK and a number of European countries.

Researchers have been tracking P.1 from its earliest detection in December but have not yet published in peer-reviewed journals. By early January, the variant made up 87 per cent of samples in Manaus. By February it had taken over completely. Like B.1.1.7, P1 is more transmissible than earlier strains. The researchers estimate it is somewhere between 1.4 and 2.2 times more transmissible than other lineages of coronaviruses. Combining the data from genomes, antibodies and medical records in Manaus, they concluded that P.1's mutations had led to a second wave of infections in Manaus even though a study of blood donors had indicated that more than 70 per cent of the city's residents had antibodies to the original strain. This may be due to mutations that let it escape antibodies from previous coronavirus infections. They estimate that for every 100 people who were infected with non-P.1 lineages in Manaus last year, somewhere between 25 and 61 of them could have been reinfected if they were exposed to P.1 in Manaus.

In a Lancet pre-print paper posted on 1 March, Brazilian researchers reported mixing P.1 variant viruses with antibodies from Brazilians who had COVID-19 last year. They found that the effectiveness of their antibodies dropped sixfold against P.1 compared with other lineages of SARS-CoV-2. In another unpublished laboratory study, researchers also tested antibodies from eight people who received CoronaVac, a Chinese-made vaccine that has been used in Brazil. They found that the vaccine-generated antibodies were less effective at stopping the P.1 variant than other types. The researchers cautioned that what happens in a test tube does not necessarily predict what will happen in the real world.

B.1.427 and B.149 variants

These variants carry three mutations in the spike protein, including an L452R substitution. The variants, which were first identified in California, appear to be somewhat more transmissible and heighten patients' risk of admission to the intensive care unit (ICU) and death, according to a preprint reporting lab studies and epidemiological data. For their study, the authors sequenced 2172 genomes from virus samples obtained from patients in 44 California countries between 1 September 2020 and 29 January 2021. The new variants, which come in two forms labelled B.1.427 and B.1.429 that carry slightly differing mutations, accounted for 21.3 per cent of these sequences overall.

The medical records of 324 people with COVID-19 were reviewed. Adjusting for differences in age, gender, and ethnicity, they found that, compared with patients who had other viral strains, those carrying the variants were 4.8 times more likely to be admitted to the ICU and more than 11 times more likely to die. The study also found that viral load in the nasopharynx was twice that of comparable patients infected with earlier strains.

In lab studies, B.1.429 also impacted the effectiveness of antibodies: It was four times less susceptible than the original coronavirus to neutralising antibodies from the blood of people who recovered from COVID-19, and two times less susceptible to antibodies from the blood of people vaccinated with the Pfizer or Moderna vaccines.

B.1.526 variant

The variant known as B.1.526 began showing up in samples collected in New York City in November 2020. By the middle of this month, it accounted for about one in four viral sequences appearing in a database shared by scientists. The emergence of this variant might be associated with a surge in new COVID-19 cases in north-eastern US states. One study (pre-print) detected an emerging lineage of viral isolates that shares mutations with previously reported variants. The most common sets of spike mutations in this lineage are L5F, T95I, D253G, E484K or S477N, D614G, and A701V. E484K, which also exists in the B.1.351 and P.1 variants, has been found in lab experiments to help the coronavirus evade protective antibodies generated by earlier infections and possibly vaccines.

Another study from Columbia University designed PCR assays to identify viruses with two B.1.526 variant signature mutations, E484K and N501Y. They observed a steady increase in the detection rate from late December to mid-February, with an alarming rise to 12.3 per cent in the first two weeks of February. Patients with this novel variant came from diverse neighbourhoods in the New York metropolitan area, and they were on average six years older and more frequently hospitalised.

The emergence of variants of concern affirms the need for **ongoing sequencing of viral genomes** around the world to monitor the evolution of SARS-CoV-2 and for the support of LMICs to have high testing rates and perform sequencing of viral genomes.

SNAPSHOTS | DIAGNOSIS, EPIDEMIOLOGY AND INFECTION OUTCOMES

COVID-19: Highest death rates seen in countries with most overweight populations

A recent report by the World Obesity Federation states that COVID-19 mortality rates in countries where more than half of the population is overweight are ten times higher than other countries. The report analysed mortality data from over 160 countries from Johns Hopkins University and the WHO Global Health Observatory data on obesity. Of the 2.5 million COVID-19 deaths reported by the end of February 2021, 2.2 million were in countries where over half the population is classified as overweight—defined as a body mass index above 25. The report found linear correlations between a country's COVID-19 mortality and the proportion of adults that are overweight. There is not a single example of a country with less than 40 per cent of the population overweight that has high death rates (over 10 per 100,000), the report said. Similarly, no country with a death rate over 100 per 100,000 had less than 50 per cent of their population overweight.

Vietnam, for example, had the lowest death rate from COVID-19 in the world (0.04 per 100,000) and the second lowest levels of population overweight at 18.3 per cent. The UK has the third highest death rate globally (184 deaths per 100,000) and the fourth highest prevalence of overweight at 63.7 per cent. The United States has the next highest death rate at 153 deaths per 100,000 and 67.9 per cent of the population overweight.

A small number of countries seem to run against the trend including New Zealand, Australia, and several Gulf states, where prevalence of overweight among adults is high, but reported deaths from COVID-19 are low. The report said that this was likely to be due to national responses to the pandemic, including border controls.

In a comprehensive article in the New Yorker about why the pandemic has hit some countries harder than others, the author pondered why Mexico and India fared so differently. Both countries have similar demographic profiles and per capita GDP. However, Mexico has recorded a COVID-19 mortality rate of 152 per 100,000 compared to just 12 per 100,000 in India. This difference can perhaps be explained by the very different rates of overweight and obesity. The prevalence of overweight and obesity among adults in Mexico is 75 per cent while in India it's 20 per cent.

Long COVID-19 gets a new name: post-acute sequelae of SARS-CoV-2

At a recent White House briefing, Anthony Fauci, MD, introduced a new name for what had been called 'long COVID.' Post-Acute Sequelae of COVID-19 (PASC) is the new term used to describe long-lingering effects of COVID-19. At the briefing, Fauci stressed that even patients with moderate cases of COVID-19 can develop PASC. "New symptoms sometimes arise well after the time of infection, or they evolve over time and persist for months," he explained. "They can range from mild or annoying to actually quite incapacitating." The National Institutes of Health have launched a new program to fund further studies of the phenomenon.

The most common symptoms of PASC include fatigue, gastrointestinal problems, mental health issues, sleep difficulties, impaired lung capacity, and what has been called COVID-19 brain fog. Loss of smell is also a well-recognised long-term effect, especially for healthcare workers. PASC has been reported in all age groups, including children. A recent preprint posted on medRxiv, which has yet to be peer reviewed, provides preliminary evidence that children may also have symptoms that last for months after their initial SARS-CoV-2 infection. In this Italian study, more than a half of paediatric

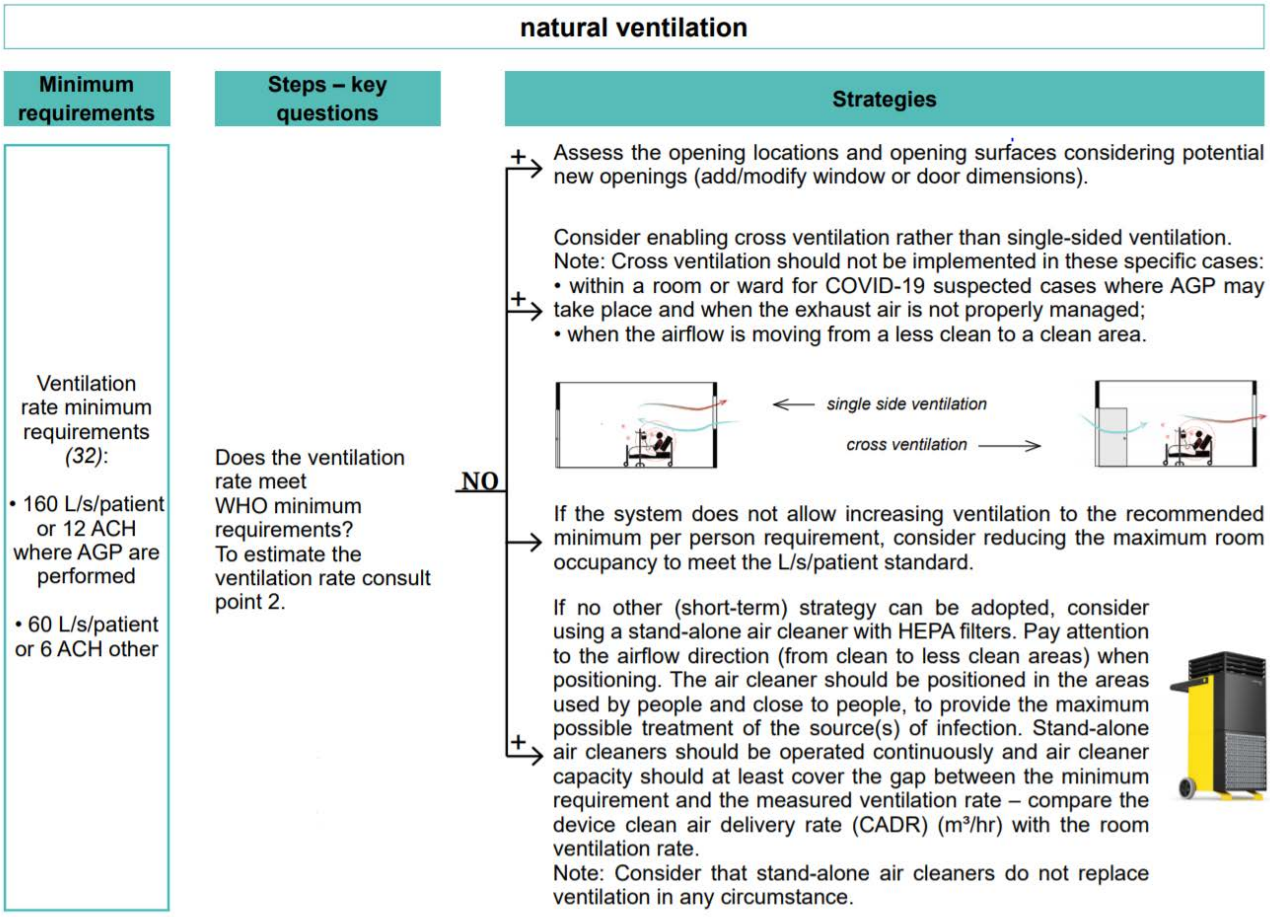
patients reported at least one persisting symptom 120 days after COVID-19 infection, with 42.6 per cent being impaired by these symptoms during daily activities. Symptoms like fatigue, muscle and joint pain, headache, insomnia, respiratory problems and palpitations were particularly frequent, as also described in adults.

WHO roadmap to improve and ensure good indoor ventilation in the context of COVID-19

In early March, WHO published their new guidelines to improve indoor ventilation. The roadmap was developed after conducting a scoping review of the available literature and an assessment of the available guidance documents from the major internationally recognised authorities on building ventilation. The available evidence and guidance were retrieved, collated and assessed for any discrepancies by international expert members of the WHO Environment and Engineering Control Expert Advisory Panel (ECAP) for COVID-19.

The roadmap is divided into three settings – health care, non-residential and residential spaces – and takes into account different ventilation systems (mechanical or natural). The roadmap is aimed at health care facility managers, building managers, as well as those members of the general public who are providing home care or home quarantine.

The Introduction states that a well-designed, maintained and operated system can reduce the risk of COVID-19 spread in indoor spaces by diluting the concentration of potentially infectious aerosols through ventilation with outside air and filtration and disinfection of recirculated air. Proper use of natural ventilation can provide the same benefits. The decision whether to use mechanical or natural ventilation should be based on needs, resource availability and the cost of systems to provide the best control to counteract the risks. Here is a short extract from the algorithm provided in the roadmap to assess and address ventilation issues. ACH = air changes per hour; AGP = aerosol generating procedures.



Changes in reported adherence to non-pharmaceutical interventions during the COVID-19 pandemic

Non-pharmaceutical interventions (NPIs) have been used to mitigate the effects of the COVID-19 pandemic. Reports have described an increasing attitude of apathy or resistance toward adherence to NPIs, termed pandemic fatigue. To better describe this phenomenon in the US, these researchers used national surveillance data to analyse reporting of adherence to protective behaviours identified as NPIs.

They analysed survey responses from 16 waves of the Coronavirus Tracking Survey (CTS) completed between 1 April 2020, and 24 November 2020. Every 14 days, each participant was asked to complete a wave of the CTS within the next 14 days. They constructed an NPI adherence index from 16 evidence-based protective behaviours that were included in all survey waves. 97 per cent of participants completed the first wave of the survey and 80 per cent completed the last wave. The analysis involved 7,705 participants.

The national NPI adherence index decreased substantially from 70.0 in early April, reaching a plateau in the high 50s in June. In late November, an increase to 60.1 in the final survey week remained significantly below the starting level in early April ($P < .001$). All US Census regions experienced decreases in the NPI adherence index from early April to late November.

Reported protective behaviours that had the largest decreases in weighted and adjusted adherence from early April to late November 2020 were remaining in residence except for essential activities or exercise (from 79.6% to 41.1%), having no close contact with non–household members (from 63.5% to 37.8%), not having visitors over (from 80.3% to 57.6%), and avoiding eating at restaurants (from 87.3% to 65.8%) (all $P < .001$). Reported **wearing of a mask** or other face covering showed a significant **increase** among participants (from 39.2% to 88.6%) ($P < .001$).

Higher airborne pollen concentrations correlated with increased SARS-CoV-2 infection rates

Pollen exposure weakens the immunity against certain seasonal respiratory viruses by diminishing the antiviral interferon response. The authors of this paper investigated whether the same applies to the pandemic SARS-CoV-2, which is sensitive to antiviral interferons, and whether infection waves coincide with high airborne pollen concentrations. To examine the potential effects of pollen–virus co-exposure, a large cross-sectional and longitudinal study was established, based on 248 airborne pollen monitoring sites, from 31 countries in all continents across the globe. The initiative started when, during 10 to 14 March 2020, a warm weather episode brought about higher airborne pollen concentrations across the Northern Hemisphere. This coincided with high SARS-CoV-2 infection rates characteristic of the early exponential infection phase. To explicitly investigate the effects of social contact, they additionally considered population density of each study area, as well as lockdown effects, in all possible combinations.

They found that airborne pollen, sometimes in synergy with humidity and temperature, explained, on average, 44 per cent of the infection rate variability. Infection rates increased after higher pollen concentrations most frequently during the four previous days. Without lockdown, an increase of pollen abundance by 100 pollen/m^3 resulted in a 4 per cent average increase of infection rates. Lockdowns halved infection rates under similar pollen concentrations.

COVID-19 disruptions led to the deaths of 228,000 children in South Asia

A recently released report by UNICEF estimates that the disruption in healthcare services caused by COVID-19 may have led to an estimated 239,000 maternal and child deaths in South Asia during 2020. The report focused on Afghanistan, Nepal, Bangladesh, India, Pakistan and Sri Lanka, home to some 1.8 billion people. It estimates that in 2020 there were 228,000 additional deaths of children under five, with 134,800 (59%) of these deaths in the neonatal period, in these six countries due to crucial services, ranging from nutrition benefits to immunisation, being halted. Overall in South Asia, child and maternal mortality is estimated to have increased in 2020 by 14 per cent and 16 per cent, respectively.

The number of children being treated for severe malnutrition fell by more than 80 per cent in Bangladesh and Nepal, and immunisation among children ‹5 years of age dropped by 35 per cent and 65 per cent in India and Pakistan, respectively. The report says that child mortality rose the highest in India in 2020 - up by 15.4 per cent - followed by Bangladesh at 13 per cent. Sri Lanka saw the sharpest increase in maternal deaths - 21.5 per cent followed by Pakistan's 21.3 per cent.

Across South Asia as a whole, an estimated 89,434 additional stillbirths are anticipated as a result of reduced coverage of essential sexual, reproductive, maternal, newborn and child health services. Due to the observed and expected reduction in coverage of modern contraceptive methods, more than 3.5 million additional unintended pregnancies are expected in South Asia, with the highest number likely in India (~3 million). The number of unsafe abortions is also expected to increase in the region, by more than 50 per cent.

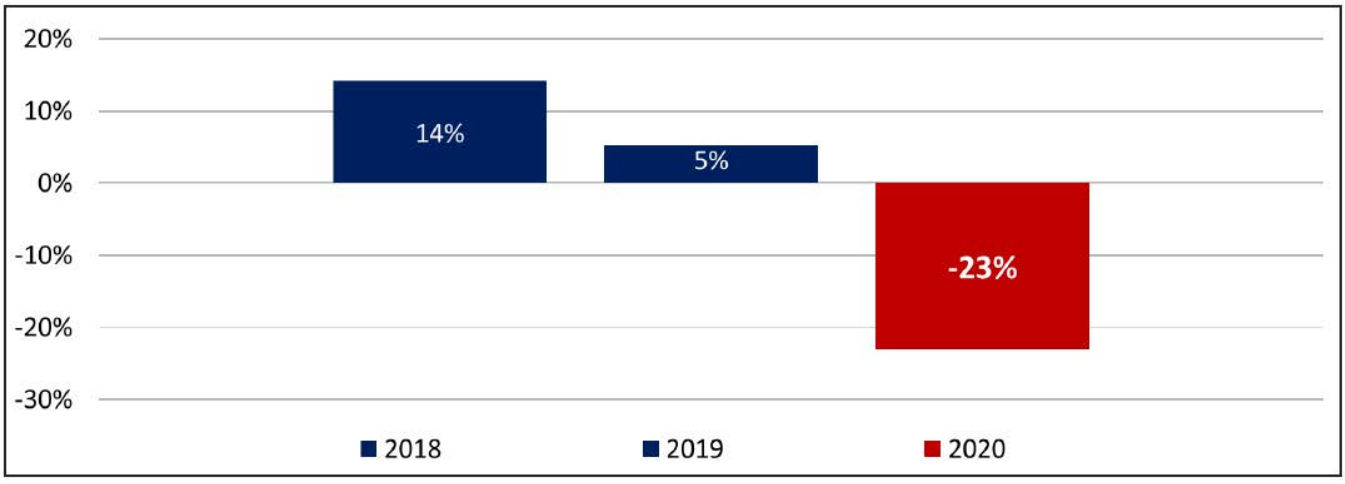
COVID-19 and Tuberculosis

World Tuberculosis (TB) Day is commemorated each year on the 24 March to increase public awareness about the consequences of the world's leading infectious disease killer. Each day, nearly 4,000 people lose their lives to TB and close to 28,000 people fall ill with this preventable and curable disease.

In addition to the direct consequences of the COVID-19 pandemic, its impact on essential health services and disease control programs, such as TB has been immense. It is estimated that disruptions to TB health services during 2020 may lead to an additional 6.3 million people developing TB and 1.4 million additional deaths by 2025, levels that have not been seen since between 2013 and 2016.

In 2020, 1.4 million fewer people were diagnosed and linked to TB care, a shortfall of 23 per cent. This has set back the progress made on TB by 12 years, back to 2008 levels. The countries with the biggest relative gaps were Indonesia (42%), South Africa (41%), Philippines (37% and India (25%).

Annual percentage change in TB diagnosis and enrollment for nine high-TB burden countries



Both TB and COVID-19 are airborne diseases that affect the respiratory tract. They both cause similar symptoms such as cough, fever and breathlessness. Synergies in the TB and COVID-19 response programs allow for integrated services across the continuum of care. The responses to COVID-19 such as testing, tracing, masking and isolating are not new and have been employed in the TB response. Integration in the responses can allow the world to recover from COVID-19, address the setback to TB responses and can help prepare for any future pandemic arising from an airborne disease.

The Stop TB Partnership has suggested that forward looking interventions that address current and future infectious disease should focus on:

- Implementing massive community and primary health care level screening. People with a cough and fever should be tested for both TB and COVID-19.
- Mobilise, create, develop and support networks of TB survivors and TB communities to address stigma and fears.
- Implement airborne infection prevention and control measures in all health care units and in congregation settings.
- Implement real-time surveillance data with early warning systems for data-drive and agile public health decision making.

This year's theme for World TB Day is 'The Clock is Ticking', sending a message of urgency to global leaders to act and commit to ending TB. Dr Lucica Ditiu, MD, Executive Director of the Stop TB Partnership stated: "There are ways forward. It is possible to recover from this. We just need the vision, power and the ambition to push the TB agenda and not allow COVID-19 mitigation measures and COVID-19 disease and pandemic to impact TB". COVID-19 has presented many challenges in the fight against TB, but it has also demonstrated what is possible with political will and global commitment to a cause.

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