COVID-19 Global Trends and Analyses

Volume 2:

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

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- Currently, eight vaccines have been approved in at least one country, all of which require two doses, and just over 172 million people have received their first dose (as of 16 February)[1].
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    - AstraZeneca/Oxford - 41 countries
    - Moderna - 27 countries
    - Sinopharm Beijing - 10 countries
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- The US-based company Novavax announced on 28 January that NVX-CoV2373, its protein-based COVID-19 vaccine candidate, met the primary endpoint, with a **vaccine efficacy of 89.3 per cent**, in its Phase 3 clinical trial conducted in the United Kingdom (UK).
- A Phase 2b clinical trial of Novavax underway in South Africa (n = 4,400), has shown **60 per cent efficacy** (95% CI: 19.9 – 80.1) for the prevention of mild, moderate and severe COVID-19 disease in HIV-negative participants.
- Janssen/Johnson and Johnson have released the results of their one-dose vaccine trial. Overall, the **vaccine was 66 per cent effective** at preventing moderate to severe disease 28 days after vaccination. But efficacy differed depending on geography. The vaccine was 72 per cent effective among volunteers in the U.S, but 66 per cent among those in Latin America, and just 57 per cent among those in South Africa. The vaccine reduced severe disease alone by 85 per cent.
- AstraZeneca/Oxford announced that in trials in the UK, Brazil and South Africa, vaccine efficacy after a single standard dose (SD) of vaccine from day 22 to day 90 post vaccination was **76 per cent** (59%, 86%), and modelled analysis indicated that protection did not wane during this initial 3 month period.
- Data from Israel indicate that the Pfizer/BioNTech vaccine reduced the rate of symptomatic infection during days 15–28 after the first dose by 85 per cent.
- Pfizer/BioNTech announced on 19 February that the **vaccine can be stored in a standard freezer up to two weeks**.

SUMMARY

Variants of Concern

- The New and Emerging Respiratory Virus Threats Advisory Group recently concluded that infection with the B.1.1.7 variant is associated with a significantly increased risk of hospitalisation, ICU admission and death compared with the earlier strain. This conclusion was based on a number of studies where the increased risk of death ranged from **35 per cent to 71 per cent**.
- However, a number of vaccines have been shown to be effective in preventing symptomatic infection with the UK variant. They include Novavax, Pfizer, Moderna and AstraZeneca.
- The B.351 variant appears to be better able to evade neutralising antibody responses by the body. Recent results from the Novavax vaccine trials support this concern: while the vaccine had 95.6 per cent efficacy against the original coronavirus and 85.6 per cent against the UK variant, it had an efficacy of only 60 per cent against the South African variant.
- The P.1 variant has an "escape mutation" known as E484K, 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. This is confirmed by reports of large numbers of reinfections in Manaus, Brazil, where the variant was first identified.
- The B.1525 variant is the subject of a report by researchers at the University of Edinburgh, who say it has been detected through genome sequencing in 10 countries including Denmark, the US and Australia. There is no evidence yet that this variant increases infectivity or severity.
- Since October, the CAL.20C/B.1.427 variant's prevalence has increased in California state and Southern California, where on 22 January 2021, it accounted for 35 per cent (86 of 247) and 44 per cent (37 of 85) of all samples collected in January, respectively.

GLOBAL SCIENTIFIC UPDATES

SARS-CoV-2 Vaccines Update

Currently, eight vaccines have been approved in at least one country, all of which require two doses, and just over 172 million people have received their first dose (as of 16 February)[1]. They are Pfizer/BioNTech (61 countries), AstraZeneca/Oxford (41), Moderna (27), Sinopharm Beijing (10), Gamaleya/Sputnik V (9), Sinovac (6), Sinopharm Wuhan (two) and Bharat Biotech (only India). The following updates include two new vaccines – Novavax and Janssen/Johnson and Johnson.

Novavax

US-based company Novavax announced on 28 January that NVX-CoV2373, its protein-based COVID-19 vaccine candidate, met the primary endpoint, with a vaccine efficacy of 89.3 per cent, in its Phase 3 clinical trial conducted in the United Kingdom (UK).[2] Novavax also announced successful results of its Phase 2b study conducted in South Africa. NVX-CoV2373 contains a full-length, prefusion spike protein made using Novavax's recombinant nanoparticle technology and the company's proprietary saponin-based Matrix-M adjuvant. The purified protein is encoded by the genetic sequence of the SARS-CoV-2 spike protein and is produced in insect cells. It is stable at 2°C to 8°C (refrigerated) and is shipped in a ready-to-use liquid formulation that permits distribution using existing vaccine supply chain channels.

UK Phase 3 Results: 89.3 per cent efficacy

The study enrolled more than 15,000 participants between 18-84 years of age, including 27 per cent over the age of 65. The primary endpoint of the UK Phase 3 clinical trial was based on the first occurrence of PCR-confirmed symptomatic (mild, moderate or severe) COVID-19 with onset at least 7 days after the second dose. The interim analysis is based on 62 cases (61 mild, 1 severe), of which 56 cases of COVID-19 were observed in the placebo group (1 severe) versus 6 cases observed in the NVX-CoV2373 group, which estimates vaccine efficacy of 89.3 per cent (95% CI: 75.2 – 95.4). Analysis by strain estimates **95.6 per cent efficacy against the original COVID-19 strain and 85.6 per cent against the B.1.1.7 variant** strain.

South Africa Results: Approximately 90 per cent of COVID-19 cases attributed to South Africa escape variant

A Phase 2b clinical trial underway in South Africa (n = 4,400), has shown **60 per cent efficacy** (95% CI: 19.9 – 80.1) for the prevention of mild, moderate and severe COVID-19 disease in HIV-negative participants, with 29 cases in the placebo group (one severe) and 15 in the vaccine group. All other cases were mild or moderate. The clinical trial also achieved its primary efficacy endpoint in the overall trial population, including HIV-positive and HIV-negative subjects (efficacy of 49.4%; 95% CI: 6.1 – 72.8). The reduced efficacy in South Africa compared with results obtained in the UK is attributed to the prevalence of the B.1.351 variant, detected in 92 per cent of infections (interim result).

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[1] https://www.statista.com/chart/24191/number-of-countries-using-selected-covid-19-vaccines/?utm_source=Statista+Global&utm_campaign=424fc3bbd6-All_InfographTicker_daily_COM_AM_KW05_2021_Fr_COPY&utm_medium=email&utm_term=0_afecd219f5-424fc3bbd6-309237453

[2] https://ir.novavax.com/news-releases/news-release-details/novavax-covid-19-vaccine-demonstrates-893-efficacy-uk-phase-3

Janssen/Johnson and Johnson (J&J)

The vaccine is known as JNJ-78436735 or Ad26.COV2.S, and uses adenovirus 26 as a vector to deliver double-stranded DNA encoding the SARS-CoV-2 spike protein. The results are based on a single dose of the vaccine, which can be stored at refrigerator temperatures.

The J&J results are from an interim analysis of a study of 44,783 volunteers in which 468 symptomatic cases of COVID-19 occurred. Volunteers came from the U.S. (44%), Central and South America (41%) and South Africa (15%).

Overall, the **vaccine was 66 per cent effective** at preventing moderate to severe disease 28 days after vaccination. But efficacy differed depending on geography. The vaccine was 72 per cent effective among volunteers in the U.S, but 66 per cent among those in Latin America, and just 57 per cent among those in South Africa. The vaccine reduced severe disease alone by 85 per cent. The trial did not result in any significant safety concerns about the vaccine. Fevers occurred in 9 per cent of those who received the vaccine, and fevers of more than 40 degrees occurred in 0.2 per cent of vaccine recipients. Serious adverse events were more common among those who received placebo than the vaccine.

J&J is running another large study, enrolling 30,000 volunteers, testing two doses of the vaccine given 57 days apart. In **South Africa**, after stopping use of the AstraZeneca vaccine, a prospective study of J&J will be conducted among 80,000 healthcare workers who will receive the J&J vaccine. Protection against infection and illness will be studied; no-one will receive a placebo.

AstraZeneca/Oxford

In a pre-print article, not yet peer-reviewed, data were presented from phase 3 efficacy trials of ChAdOx1 nCoV-19 in the United Kingdom and Brazil, and Phase I/II clinical trials in the UK and South Africa, against symptomatic disease caused by SARS-CoV-2[3]. The data cut-off date for these analyses was 7 December 2020. 17,177 baseline seronegative trial participants were eligible for inclusion in the efficacy analysis, 8,948 in the UK, 6,753 in Brazil and 1,476 in South Africa, with 619 documented PCR positive infections of which 332 met the primary endpoint of symptomatic infection >14 days post dose 2.

Vaccine efficacy after a single standard dose (SD) of vaccine from day 22 to day 90 post vaccination was **76 per cent** (59%, 86%), and modelled analysis indicated that protection did not wane during this initial 3-month period. In the SD/SD group, after the second dose, efficacy was higher with a longer prime-boost interval: VE 82.4 per cent (62.7%, 91.7%) at 12+ weeks, compared with VE 54.9 per cent (32.7%, 69.7%) at <6 weeks. In summary, ChAdOx1 nCoV-19 vaccination programs aimed at vaccinating a large proportion of the population with a single dose, with a second dose given after a 3-month period are an effective strategy for reducing disease and may be the optimal for rollout of a pandemic vaccine when supplies are limited in the short term.

South Africa

South Africa has halted its rollout of the AstraZeneca vaccine after disappointing results against the B1.351 COVID-19 variant. The B.1.351 variant is responsible for about 90 per cent of new infections in South Africa. A study, which has not yet been published, of 2,000 HIV-negative individuals, mean age of 31 years, found that the vaccine did not prevent mild or moderate COVID-19 illness (VE 22%)[4]. The study lacked the power to assess prevention of severe illness.

WHO emergency authorisation

WHO has granted an emergency authorisation to AstraZeneca's coronavirus vaccine, a move that should allow the UN

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[3] https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3777268

[4] https://www.bmj.com/content/372/bmj.n372

agency's partners to ship millions of doses to low- and middle-income countries as part of the COVAX program[5]. In a statement on 15 February, the WHO said it was clearing the AstraZeneca vaccines made by the Serum Institute of India and South Korea's AstraZeneca-SKBio. The AstraZeneca vaccine has already been authorised in more than 50 countries, including the UK, India, Argentina, Australia and Mexico. It is cheaper and easier to handle than the Pfizer-BioNTech vaccine, which needs deep-cold storage that is not widespread in many developing nations.

Pfizer/BioNTech Vaccine (Comirnaty®)

Israel was the first country to roll out Comirnaty®, the BNT162b2 vaccine, and has provided at least one dose to 40 per cent of its population. Under an agreement with Pfizer, the Israeli Government is sharing its data on the rollout with the company and globally in the public domain. Israel's largest healthcare provider (Clalit) has reported a 94 per cent drop in symptomatic COVID-19 infections and 92 per cent fewer severe infections among 600,000 people who received two doses of the Pfizer vaccine in the country's biggest study to date[6]. The comparison was against a group of the same size, with matching medical histories, who had not received the vaccine. Researchers at the Weizmann Institute of Science, who have been tabulating national data, reported that a sharp decline in hospitalisation and serious illness identified earlier among the first age group to be vaccinated - aged 60 or older - was seen for the first time in those aged 55 and older.

High efficacy after one dose

In a paper recently published in The Lancet, researchers in **Israel** found a high-rate reduction of symptomatic infection during days 15–28 after the first dose[7]. Researchers followed 9,109 HCWs in the Sheba Medical Centre as a vaccination program was implemented. By 24 January 2021, 7,214 (79%) had received a first dose and 6,037 (66%) had received the second dose. 5,505 (91%) fully vaccinated HCWs received the second dose on days 21 or 22 after the first dose. Compared with a symptomatic COVID-19 rate of 5.0 per 10,000 person-days in unvaccinated HCWs, disease rates were 2.8 and 1.2 per 10,000 person-days on days 1–14 and days 15–28 after the first dose of the vaccine, respectively. Adjusted rate reductions of COVID-19 disease were 47 per cent (95% CI 17–66) and **85 per cent** (71–92) for days 1–14 and days 15–28 after the first dose, respectively.

Reduction of viral load

Data from researchers in **Israel,** published on a pre-print server, suggest the Pfizer/BioNTech vaccine is reducing viral load, a key signal that the intervention could diminish the spread of COVID-19[8]. To evaluate the impact of the vaccine on transmission, researchers compared data from people over 60 years old and those aged 40 to 60, evaluating data from 16,297 people who had tested positive for coronavirus between 1 December and 30 January. Israel's vaccine program began on 20 December. By the time of analysis, more than 75 per cent of those in the older group were likely to have received their first dose, as had about 25 per cent of the younger group. The researchers compared viral load in people who received Comirnaty® and developed a symptomatic infection following vaccination. In the first 11 days following vaccination, prior to the onset of immunity, viral loads were significantly higher than those observed 12 days after vaccination suggesting that once immunity develops, it rapidly controls viral replication and reduces the amount of virus in the respiratory tract.

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[5] https://www.who.int/news/item/16-02-2021-covax-statement-on-who-emergency-use-listing-for-astrazeneca-oxford-covid-19-vaccine

[6] https://mobile.reuters.com/article/amp/idUSKBN2AE0Q0

[7] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00448-7/fulltext

[8] https://www.medrxiv.org/content/10.1101/2021.02.06.21251283v1

Furthermore, they compared viral loads in age and sex matched unvaccinated patients and compared their viral loads to those of vaccinated people and found a significant reduction in viral loads in vaccinated individuals 12 days following vaccination. Although researchers did not know whether each person had been given their first vaccine dose, their hypothesis was that if the vaccine was reducing viral load, then evidence of that would begin to show up in late January but not before, because of the time required by the vaccine to stimulate the immune system. As expected, in the last two weeks of January the researchers noted a statistically significant fall in the viral load for the individuals aged over 60, compared with the 40-to-60 group.

The researchers used available demographic data and vaccination rates to estimate the effect of the first dose on viral load reduction, calculating that the vaccine **reduced the viral load 4-fold** for infections occurring 12-28 days after the first dose of vaccine. These reduced viral loads detected in oro-nasopharyngeal swabs suggest vaccination may reduce the ability of the virus to be transmitted, further increasing the benefit of vaccination. However, the researchers were unable to assess how much widespread mask use might be contributing to the drop in viral load.

Vaccines Approved in Australia

The Therapeutic Goods Administration has approved two vaccines – Pfizer/BioNTech vaccine for people over the age of 16 years and the AstraZeneca/Oxford vaccine for people over the age of 18. There are no upper age limits for either vaccine. The Pfizer vaccine will be the first rolled out to high-priority groups, such as border and hotel quarantine staff, HCWs, and residents of aged care facilities. The first batches of the AstraZeneca vaccine will be imported then it will be manufactured in Australia by CSL.

Pfizer/BioNTech announced on 19 February that the **vaccine can be stored in a standard freezer up to two weeks**.

Access to Vaccines in Low- and Middle-Income Countries (LMIC)

As of 22 February, around 200 million people worldwide have been vaccinated with at least one dose of a vaccine for COVID-19[9]. Israel has the highest vaccination rate having provided 78 doses per 100 population. The only LMIC in the top ten is Seychelles, which has delivered 63 doses per 100. Some large LMICs have begun the rollout of vaccines, including India, China, Brazil, Mexico, and Indonesia. So far, the only African countries conducting vaccinations are Morocco (AstraZeneca and Sinopharm), Egypt (Sinopharm), Algeria (Sputnik V), South Africa (Johnson & Johnson), the Seychelles (Sinopharm and AstraZeneca), Rwanda (Pfizer and Moderna), Mauritius (AstraZeneca) and Zimbabwe (Sinopharm). However, the Economist Intelligence Unit estimates that most middle-income countries won't achieve adequate vaccination coverage until late 2022 and most low-income countries won't do so until 2023[10]. The latter include almost every country in Africa. Some middle-income countries and most low-income countries will be relying on COVAX, an initiative led by the WHO and Gavi that aims to secure 6 billion doses of vaccine for poorer countries[11]. The first 2 billion of these will be given in 2021, mainly to healthcare workers (COVAX doses will cover only up to 20 per cent of the population of each country). However, COVAX supplies may be slow to arrive, especially if delays in the production for and delivery to richer countries push back delivery dates for poorer nations.

On 20 February, the G7 group of rich nations pledged US$7.5 billion to COVAX, including a $4 billion contribution by the new US Administration and $1.6 billion by the EU. Several countries, including France, Germany and the UK pledged to divert 5 per cent of their own vaccine stocks to 6.5 million HCWs in Africa. The most preferred vaccine in LMICs is the AstraZeneca vaccine because it is relatively cheap and can be stored in a regular refrigerator. Both Russia and China

[9] https://github.com/owid/covid-19-data/blob/master/public/data/vaccinations/vaccinations.csv

[10] https://www.eiu.com/n/85-poor-countries-will-not-have-access-to-coronavirus-vaccines/

[11] https://www.who.int/initiatives/act-accelerator/covax

have offered vaccines produced in their country to LMICs at discount prices or at no cost. However, there are severe concerns about the limited production capacity for Russia's Sputnik V vaccine.

Vaccine Confidence

Attitudes towards COVID-19 vaccines seem to be improving in some parts of the world, according to a survey of thousands of people in 15 countries[12]. In November — before countries began to approve COVID-19 vaccines — only around 40 per cent of respondents said they would get a COVID-19 vaccine if they were offered one during the week that they took the survey, and more than half were worried about potential side effects. In January, more than half the respondents agreed that they would get a vaccine if it was available during the week of the survey. And the share of people who said they worry about the vaccines' side effects had dropped to 47 per cent.

The **United Kingdom** had the highest share of people who were willing to receive a vaccine (78%) — and for 11 of the 15 countries, this figure increased, sometimes considerably. In Spain, for example, the proportion of respondents willing to be immunised had increased from 28 per cent in November 2020 to 52 per cent by mid-January. However, the figure remains below 50 per cent in **France, Russia and Japan**.

In **Australia**, just 64 per cent of Australians will "definitely" get a COVID-19 vaccine while more than one quarter (27%) are unsure, according to government research reported in the Guardian[13]. Some 9 per cent of Australians aged over 16 said they will "definitely not" get the vaccine, according to the poll of 4,001 people commissioned by the Federal Health Department. However, a series of Essential Polls found that the proportion of Australians who would "never get vaccinated" rose from 8 per cent in August to 11 per cent in January[14]. The proportion who would get vaccinated "as soon as possible" fell from 56 per cent to 42 per cent in the same period. In the January 2021 survey, 51 per cent of males intended to get vaccinated as soon as possible compared to just 34 per cent of females. The top three reasons for vaccine hesitancy were that long-term side effects are still unknown, that "vaccines have been developed too quickly" and concerns about having an allergic reaction.

Reports of Anaphylaxis after Receipt of mRNA COVID-19 Vaccines in the US

A review published in *JAMA* provides rates and clinical details of anaphylactic reactions reported to and verified by the US CDC in the first month of use of the Pfizer-BioNTech and Moderna COVID-19 vaccines in the US[15]. During 14 December 2020 through 18 January 2021, a total of 9,943,247 doses of the Pfizer-BioNTech vaccine and 7,581,429 doses of the Moderna vaccine were reported administered in the US. CDC identified 66 case reports received that met Brighton Collaboration case definition criteria for anaphylaxis (levels 1, 2 or 3): 47 following Pfizer-BioNTech vaccine, for a reporting rate of 4.7 cases/million doses administered, and 19 following Moderna vaccine, for a reporting rate of 2.5 cases/million doses administered.

Cases occurred after receipt of doses from multiple vaccine lots. Anaphylactic reactions occurred a median of ten minutes after injection. CDC physician reviewers concluded that the clinical characteristics of anaphylaxis cases following both vaccines were similar. Common signs and symptoms in anaphylaxis cases were generalized urticaria,

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[12] https://www.nature.com/articles/d41586-021-00368-6

[13] https://www.theguardian.com/australia-news/2021/feb/16/two-thirds-of-australians-definitely-want-covid-vaccine-while-27-are-unsure?CMP=Share_AndroidApp_Other

[14] https://essentialvision.com.au/uptake-of-a-covid-19-vaccine-2

[15]https://jamanetwork.com/journals/jama/fullarticle/2776557?utm_source=silverchair&utm_campaign=jama_network&utm_content=covid_weekly_highlights&utm_medium=email

diffuse erythematous rash, angioedema, respiratory and airway obstruction symptoms, and nausea. 32 per cent of the case reports noted a prior episode of anaphylaxis from other exposures. 92 per cent of patients received epinephrine and all cases recovered.

Vaccination of Pregnant and Breastfeeding Women

The **World Health Organization** (WHO) has recently updated its advice around pregnant women receiving the vaccine, stating only those who are at high risk of contracting COVID-19 through work, or who have underlying health conditions which predispose them to develop complications from the virus, should take the vaccine[16].

The authors of a paper recently published in JAMA suggested that pregnant women should be vaccinated because pregnant women with severe or critical COVID-19 infection are at increased risk for preterm birth and pregnancy loss[17]. In studies of hospitalised pregnant women with COVID-19, which have included between 240 and 427 infected women, the **risk for preterm delivery** (both iatrogenic and spontaneous) has ranged from 10 per cent to 25 per cent, with rates as high as 60 per cent among women with critical illness. In addition, pregnant women may be at higher risk for severe illness and death caused by COVID-19 compared with non-pregnant women. In an analysis of national surveillance data that included pregnancy status of 409,462 women with symptomatic COVID-19 illness through 3 October 2020, the adjusted risk ratio in pregnant women (vs those of similar age and not pregnant) was 3.0 for intensive care unit admission, 2.9 for mechanical ventilation, and 1.7 for death.

Israel became the first country to authorise use of the Pfizer vaccine in pregnant women and women needing or undergoing fertility treatment, particularly those at high-risk exposure or suffering underlying conditions.[18] The recommendation follows a rise in cases of pregnant women hospitalised for the virus in Israel; some of their lives are at risk, as well as those of their unborn babies.

On 16 December 2020, the **American** Society for Reproductive Medicine put out a statement that said: "Patients undergoing fertility treatment and pregnant patients should be encouraged to receive vaccination based on eligibility criteria. Since the vaccine is not a live virus, there is no reason to delay pregnancy attempts because of vaccination administration or to defer treatment until the second dose has been administered."[19] In the **United Kingdom** last month, the Royal College of Obstetricians and Gynaecologists put out a joint statement with the Royal College of Midwives stating: "There is no biologically plausible mechanism by which current vaccines would cause any impact on women's fertility. Evidence has not been presented that women who have been vaccinated have gone on to have fertility problems."[20] In fact, during the Pfizer study looking at the effectiveness of the vaccine, 23 of the participants became pregnant during the trial period. Only one of these women went on to have a miscarriage and she was in the placebo group.[21]

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[16] https://www.aljazeera.com/features/2021/2/15/coronavirus-vaccines-pregnancy-breastfeeding-and-fertility

[17]https://jamanetwork.com/journals/jama/fullarticle/2776449?utm_source=silverchair&utm_campaign=jama_network&utm_content=covid_weekly_highlights&utm_medium=email

[18] https://www.washingtonpost.com/world/2021/01/22/coronavirus-vaccine-pregnant-women-israel-risks/

[19] https://www.asrm.org/globalassets/asrm/asrm-content/news-and-publications/covid-19/covidtaskforceupdate11.pdf

[20] https://www.rcog.org.uk/en/news/RCOG-and-RCM-respond-to-misinformation-around-Covid-19-vaccine-and-fertility/

[21] https://www.nebraskamed.com/COVID/you-asked-we-answered-can-mrna-vaccines-cause-infertility

In **Australia,** the Department of Health published a decision guide on vaccination for women who are pregnant, breastfeeding and planning a pregnancy[22]. It was published after the approval of the Pfizer vaccine but before the AstraZeneca vaccine was approved. Overall, it says that it's safe for breastfeeding women and those planning a pregnancy to have the vaccine. However, pregnant women should consult with their doctor to weigh the risks of being vaccinated with the risks of being exposed to the coronavirus.

Variants of Concern Update

The main SARS-CoV-2 variants of concern continue to be B.1.1.7 (originally detected in South-eastern UK), B.1.351 (South Africa) and P1 (Brazil).

B.1.1.7 variant

There is now more information from the UK on the severity of illness caused by this variant. The New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG) recently concluded that infection with this variant is associated with a significantly increased risk of hospitalisation, ICU admission and death compared with the earlier strain[23]. This conclusion was based on a number of studies where the increased risk of death ranged from **35 per cent to 71 per cent**. This may be the result of one of the mutations in the spike protein of the variant — a mutation called "N501Y". One preprint paper, yet to be peer reviewed, found N501Y is associated with increased binding of the virus to a receptor found on the surface of human cells, called "ACE2"[24]. This could mean the variant is even more efficient at entering cells.

However, a number of vaccines have been shown to be effective in preventing symptomatic infection with the UK variant. The Novavax vaccine was 86 per cent effective against the new variant. A recent study, not yet peer-reviewed, suggests that the Pfizer vaccine induces high levels of neutralising antibodies against the B.1.1.7 variant[25]. Similar studies suggest that Moderna will have a similar effect[26]. Data from the Oxford-AstraZeneca team published in a pre-print paper suggest it protects just as well against the new UK variant[27].

B.1.351 variant

The South African variant carries a mutation, called N501Y that appears to make it more infectious. The South African variant also contains other mutations of concern, including E484K and K417N. These two mutations are thought to explain why the South African variant appears to be better able to evade neutralising antibody responses by the body. Recent results from the Novavax COVID vaccine trials support this concern: while the vaccine had 95.6 per cent efficacy against the original coronavirus and 85.6 per cent against the UK variant, it had an efficacy of only 60 per cent against the South African variant. At present, there are no indications that the South African variant results in more severe disease, or different symptoms.

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[22] https://www.health.gov.au/sites/default/files/documents/2021/02/covid-19-vaccination-covid-19-vaccination-decision-guide-for-women-who-are-pregnant-breastfeeding-or-planning-pregnancy.pdf

[23]https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/961037/NERVTAG_note_on_B.1.1.7_severity_for_SAGE_77__1_.pdf

[24] https://www.nature.com/articles/s41423-020-0458-z

[25] https://www.biorxiv.org/content/10.1101/2021.01.18.426984v1

[26] https://www.bbc.com/news/health-55797312

[2727] https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3779160

P.1 variant

The P.1 variant was first detected in samples from Manaus in the Amazonas state in northern Brazil in mid-December. The P.1 variant (also known as B.1.1.248) concerns scientists for a few reasons, starting with how it has two notable mutations that may make it more dangerous. The N501Y mutation enables the virus's spike proteins to more easily bind with human cells, which may make it more infectious.

The P.1 variant also 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. This is confirmed by reports of large numbers of reinfections in Manaus where the variant was first identified. The first confirmed reinfections involving P.1 were reported in Manaus on 18 January[28].

P.1 and the B.1.351 variant also share another mutation, K417N/T, but less is understood about how that benefits the virus. When variants of concern evolve with the same advantageous mutation(s) in separate geographically distinct locations at the same time, it suggests those mutations are significant evolutionary leaps for the virus.

While vaccines have not yet been tested against the P.1 variant, both Moderna and Pfizer-BioNTech have reported that their mRNA vaccines provide protection against the other two major variants of concern. Both said they could develop adjusted vaccines to provide equal protection against the new variants in a matter of weeks.

B.1525 variant

This variant is the subject of a report by researchers at the University of Edinburgh, who say it has been detected through genome sequencing in 10 countries including Denmark, the US and Australia (17 January), with 32 cases found in the UK so far[29]. The earliest sequences were dated to December and were identified in the UK and Nigeria. The researchers say the variant has similarities in its genome to the B117 variant and it contains a number of mutations of concern, including the E484K mutation to the spike protein. This E484K mutation is present in variants that emerged in South Africa and Brazil and is thought to help the virus evade neutralising antibodies. According to Public Health England, there is currently no evidence that this set of mutations causes more severe illness or increased transmissibility. The discovery that several variants of concern share the same mutations may mean that tweaks to the current COVID-19 vaccines would be expected to offer protection against multiple new variants.

CAL.20C/B.1.427 variant

In a study recently published in JAMA, a novel variant of SARS-CoV-2, CAL.20C/B.1.427, was identified, which emerged in Southern California contemporaneously with the local surge in cases[30]. Unlike clade 20G, currently the largest reported clade in North America, this strain is defined by three mutations in the S-protein characterising it as a subclade of 20C. The S protein L452R mutation is within a known receptor binding domain that has been found to be resistant to certain spike (S) protein monoclonal antibodies.

Analysis of 10,431 samples from California, including 4,829 from Southern California, revealed that CAL.20C/B.1.427 was first observed in July 2020 in one of 1247 samples from Los Angeles County and not detected in Southern California again until October. Since then, this variant's prevalence has increased in California state and Southern California, where on January 22, 2021, it accounted for 35% (86 of 247) and 44% (37 of 85) of all samples collected in January, respectively.

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[28] https://virological.org/t/sars-cov-2-reinfection-by-the-new-variant-of-concern-voc-p-1-in-amazonas-brazil/596

[29] https://cov-lineages.org/global_report_B.1.525.html

[30] https://jamanetwork.com/journals/jama/fullarticle/2776543

SNAPSHOTS | DIAGNOSIS, EPIDEMIOLOGY AND OUTCOMES

COVID-19 Linked Syndrome in Children is Growing

Physicians across the US, UK and some other countries have been seeing a significant increase in the number of young people with a condition called **Multisystem Inflammatory Syndrome in Children** or MIS-C[31]. Even more worrisome, they say, is that more patients are now very sick than during the first wave of cases, which alarmed doctors and parents around the world last spring. The US CDC has been conducting a surveillance system for MIS-C and uses a case definition as follows[32]:

- An individual aged ‹21 years presenting with fever (›38C for ›24 hours), laboratory evidence of inflammation, and evidence of clinically severe illness requiring hospitalisation, with multisystem (›2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); **AND**
- No alternative plausible diagnoses; **AND**
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms.

According to the CDC, as of 1 October 2020, the number of cases meeting the case definition for MIS-C in the United States surpassed 1,000. As of 1 February 2021, this number surpassed 2,000[33]. This increase may reflect the surge in overall COVID-19 cases during this period. CDC has reported a total of 30 deaths from the syndrome. Most cases were in children and adolescents between the ages of 1 and 14 years, with a median age of 9 years. Cases have occurred in children and adolescents from ‹1 year old to 20 years old. 69 per cent of reported cases have occurred in children who are Hispanic or Latino (690 cases) or Black, Non-Hispanic (600 cases).

So far, there's no evidence that recent coronavirus variants are responsible, and experts say it is too early to speculate about any impact of variants on the syndrome. US paediatricians say most patients test positive for COVID antibodies that indicate previous infection, but some patients also test positive for active coronavirus infection[34]. Many children were previously healthy and had few or no symptoms from their initial COVID infection. Doctors are uncertain which factors predispose children to the syndrome. Doctors say they've learned effective treatment approaches, which, besides steroids, immunoglobulin and anticoagulants, can include blood pressure medications, an immunomodulator called anakinra and supplemental oxygen.

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[31] https://www.nytimes.com/2021/02/16/health/covid-children-inflammatory-syndrome.html

[32] https://emergency.cdc.gov/han/2020/han00432.asp

[33] https://www.cdc.gov/mis-c/cases/index.html

[34] https://www.nytimes.com/2021/02/16/health/covid-children-inflammatory-syndrome.html

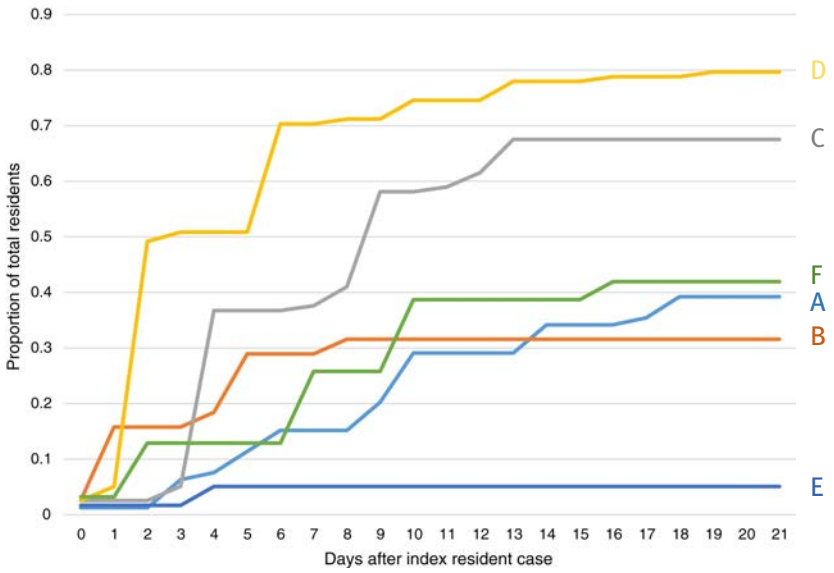
Melbourne study finds that children are protected by a robust immune response

According to a new study by the Murdoch Children's Research Institute, children are protected from severe COVID-19 because their innate immune system is quick to attack the virus[35]. The research, published in Nature Communications, found that specialised cells in a child's immune system rapidly target SARS-CoV-2. The study involved an analysis of blood samples from 48 children and 70 adults across 28 Melbourne households infected with, or exposed to, the new coronavirus. Immune responses were monitored during the acute phase of infection and up to two months afterwards. One of the researchers said that coronavirus infection in children was characterised by activation of neutrophils, the specialised white blood cells that help heal damaged tissues and resolve infections, and a reduction in first-responder immune cells such as monocytes, dendritic cells and natural killer cells from the blood. This suggests that these infection-fighting immune cells are migrating to infection sites, quickly clearing the virus before it has a chance to really take hold. "This shows that the innate immune system, our first line of defence against pathogens, is crucial to prevent severe COVID-19 in children. Importantly, this immune reaction was not replicated among adults in the study" she said[36].

The contrast between this study and the reports of MIS-C in the US and UK probably reflects the small sample size in the Melbourne study.

Factors Influencing Infection Rates in Victorian Residential Aged Care Facilities

This study, recently published in *Internal Medicine Journal*, describes experiences in 2020 with six separate Victorian outbreaks in residential aged care facilities (RACF) that the authors' Residential In-Reach (RiR) service was involved with[37]. The RiR team members visited facilities daily during the outbreaks to review goals of care, provide medical treatment, liaise with medical treatment decision-makers and general practitioners, and to arrange transfers to a hospital where clinically indicated or when basic care needs could not be met due to staff furloughing. The team monitored daily cases in each facility, labelled A to F. After 21 days, 80 per cent of residents were infected in Facility D, 68 per cent were infected in Facility C, while in Facility E only 5 per cent were infected.



[35] https://www.scimex.org/newsfeed/immune-system-protects-children-from-severe-covid-19

[36] https://about.unimelb.edu.au/newsroom/news/2021/february/immune-system-protects-children-from-severe-covid-19

[37] https://onlinelibrary.wiley.com/doi/full/10.1111/imj.15143

The authors looked at seven variables that were assessed by the RiR teams and ranked each facility.

1. Age of the facility and associated infrastructure.
2. Whether or not the index case was extricated to hospital.
3. Personal protective equipment availability and adequacy in the context of working guidelines at the time.
4. Whether PPE use included aerosol protection (N95).
5. The presence of embedded infection prevention control staff as noted by local management.
6. Whether or not local management had an outbreak contingency plan they were confident in enacting as perceived by RIR staff.
7. The rapidity of cohorting as observed by RIR staff.

Facility E was the only RACF to rank highly in all seven criteria. Facilities C and D ranked poorly in all criteria. The facilities with an established COVID-19 outbreak plan that was confidently and promptly enacted were observed to have the lowest magnitude of spread (A, B and E). The authors noted that given the multifactorial nature of a COVID-19 RACF outbreak it is unlikely that removing an index case as a sole strategy would be successful in containing and minimising spread. The question of whether or not all residents should be transferred to a hospital remains contentious. While acknowledging the limitations of this study, the authors found it evident that a prompt and well-coordinated multifactorial approach is necessary for optimal management of a RACF COVID-19 outbreak. It is clear that relying on index case removal as a sole strategy is likely to fail, but when combined with other measures, may attenuate the magnitude of COVID-19 spread.

Prevalence and Outcomes of SARS-CoV-2 Infection among Migrant Workers in Singapore

The COVID-19 outbreak among Singapore's migrant workers was characterised by a high prevalence of infection, low morbidity with few ICU admissions, and low mortality. Active surveillance was conducted in the crowded dormitories where migrant workers were housed, including asymptomatic exposed residents, those with medical conditions, and those living in close contact with clustered outbreaks. Toward the end of the outbreak, beginning 23 May, testing was performed to determine the status of all residents not previously known to be infected, using a combination of serology and/or PCR, with serology performed in heavily infected dormitories and PCR in less-infected dormitories. Summary data were published recently in *JAMA*[38].

Migrant workers residing in all purpose-built dormitories in Singapore between 25 March and 25 July 2020, were included in the review. There were 43 dormitories housing 198,320 migrant workers with a median occupancy of 3,578; 99.8 per cent of residents were male, with a median age of 33 years. As of 25 July, 95.1 per cent of all residents had at least one SARS-CoV-2 test, including 63.6 per cent with PCR and 68.4 per cent with serology. There were 111,280 residents with a positive PCR or serology result, for an **overall infection prevalence of 56.1 per cent** (range per dormitory, 0%-74.7%; median, 52.9%). There were 24,197 clinical cases (12.2% of all residents; 21.7% of infected) and 87,083 subclinical cases (43.9% of all residents; 78.3% of all infected). Of all clinical cases, 20 cases required ICU admission (0.08%), with one COVID-19–attributable death.

In summary, this was a major outbreak in a young population living in crowded dormitories in a high-income country with world class medical facilities. Authorities were slow to recognise the outbreak, which came after a mild first wave was controlled in Singapore. The eventual infection attack rate was very high at 56 per cent; however, the clinical outcomes were excellent with **only one death** recorded among more than 24,000 clinical cases.

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[38]https://jamanetwork.com/journals/jama/fullarticle/2776190?utm_source=silverchair&utm_campaign=jama_network&utm_content=covid_weekly_highlights&utm_medium=email

COVID-19 linked with wider set of symptoms than previously thought

A study of over a million people in England has revealed additional symptoms that are linked with having the coronavirus. In addition to the classic symptoms – loss of sense of smell and taste, fever and acute persistent cough – a wide range of other symptoms were associated with COVID-19 according to a study by Imperial College, not yet peer-reviewed[39]. However, around 60 per cent of infected people did not report any symptoms in the week leading up to their test.

Swab tests and questionnaires collected between June 2020 and January 2021 as part of the REal-time Assessment of Community Transmission (REACT) study showed that among these other symptoms, chills, loss of appetite, headache and muscle aches were together most strongly linked with being infected, alongside the four classic symptoms. Having any of these other symptoms or the classic ones, either alone or in combination, was associated with infection with the coronavirus and the more symptoms people showed the more likely they were to test positive.

The study also found that there was variation in symptoms with age. While chills were linked with testing positive across all ages, headaches were reported in young people aged 5-17, appetite loss in 18-54 and 55+, and muscle aches in people aged 18-54. Infected 5–17-year-olds were also less likely to report fever, persistent cough and appetite loss compared with adults.

People in England are currently encouraged to take a COVID-19 test if they have at least one of the four classic symptoms: loss of sense of taste, loss of sense of smell, fever, new persistent cough. This is called 'Pillar 2 testing'. Based on these new findings, the researchers estimate that current Pillar 2 testing would pick up around half of all symptomatic infections if everyone eligible were tested. But if the additional symptoms were included, this could be improved to three-quarters of symptomatic infections.

Oxygen supplies and COVID-19 mortality in Africa

Medical oxygen is becoming a critical need as the second wave of COVID-19 unfolds in Africa and health-care systems become overwhelmed with patients, the Africa Centre for Disease Control and Prevention said in a commentary in The Lancet this week[40].

WHO Africa attributes the need for more oxygen on the continent to an almost 39 per cent increase in cases over the past month, mainly in Southern and West Africa, making the demand for treatment higher than it was in the first wave. However, the regional body admits that there is much higher oxygen production and an increased supply of oxygen concentrators than at the beginning of the pandemic—but the rapid increase in cases has caused a widening gap between oxygen supply and demand.

The issue with oxygen supply in Africa is more to do with delayed delivery and limited storage capabilities (mostly stored in cylinders) rather than issues with manufacturing. Almost all African countries have oxygen manufacturing plants or can source it from private sector providers. At the beginning of the pandemic, there were 68 oxygen generating plants, which increased to 119 now across the continent. There were also 2,600 oxygen concentrators and now there are 6,100, according to WHO Africa. The problem is financing the purchase of oxygen in the public health sector, and the delivery and storage system, according to Amref Health Africa.

To address the problems with oxygen distribution, WHO Africa has procured 2,500 additional oxygen concentrators for countries in the region. While some countries or health facilities have tried to invest in their own manufacturing plants or

[39] https://www.imperial.ac.uk/medicine/research-and-impact/groups/react-study/

[40] https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00087-4/fulltext

bulk tanks, maintenance costs remain very high and remain a big problem. Poor plant or bulk tank maintenance means the production capacity of plants to produce medical grade oxygen (90% oxygen) decreases, and in some cases oxygen quality is less than 70 per cent oxygen.

WHO, UNICEF, and other UN agencies have partnered to provide financial support to countries that require more oxygen, such as Guinea Bissau, Chad, Niger, Nigeria, Uganda, Eswatini, Ghana, and Mozambique. As of 11 November 2020, UNICEF had delivered 15,188 oxygen concentrators to 93 countries. Bulk tanks have also been built at referral hospitals — a benefit for patients with COVID-19 and also other patients who might require oxygen.

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