CHRIS MCGRATH/GETTY

A mobile vaccination team at work during a house call in a remote region of Turkey.

HOW COVID VACCINES SHAPED 2021 — IN EIGHT POWERFUL CHARTS

The extraordinary vaccination of more than four billion people, and lack of access for others, were major forces this year — while Omicron's arrival complicated things.

By Smriti Mallapaty, Ewen Callaway, Max Kozlov, Heidi Ledford, John Pickrell & Richard Van Noorden

A year ago, vaccine drives against COVID-19 were just beginning. Now, more than 4.4 billion people have had one or more dose — about 56% of the world population. The vaccination of so many in such a short space of time, so soon after the unparalleled rapid development of the vaccines, has saved huge numbers of lives and is a triumph for science and research.

Sadly, the vaccines have not been shared or taken up equitably across the world, nor even, sometimes, within nations. But the extraordinary roll-out of a plethora of COVID-19 vaccines — or the lack thereof — has been a major force shaping politics, science and everyday life in 2021. In this graphics-led story, *Nature* offers a guide to the successes, failures and impact of COVID-19 vaccines in 2021.

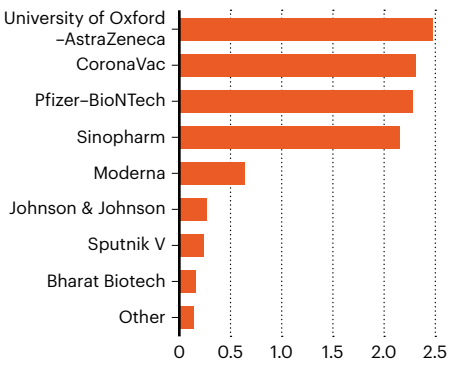
Winning the race

More than eight billion doses, mostly of eight front-runner vaccines, have now been administered around the world, the vast majority in 2021 (see 'The race to vaccinate'). "Just making that much vaccine has been the standout success," says Gagandeep Kang, a virologist at the Christian Medical College in Vellore, India.

"The vaccines have had a huge impact on averting deaths and helping countries' economies return to normal," says Soumya Swaminathan, chief scientist at the World Health Organization (WHO) in Geneva,

THE RACE TO VACCINATE

Nearly 10 billion doses of COVID-19 vaccine have been delivered around the world since mid-2020, 8.5 billion of which had been administered by late 2021. Eight different vaccines make up the vast majority of doses*.

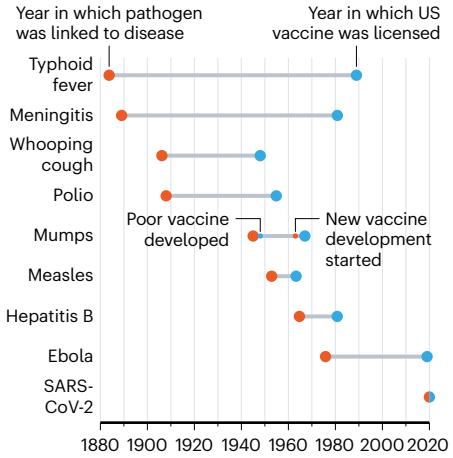


*Data as of 14 December 2021.

SOURCE: DATA FROM AIRFINITY

VACCINE INNOVATION

Most vaccines take years to develop, but scientists created multiple vaccines for SARS-CoV-2 within a year.



SOURCE: OUR WORLD IN DATA: *NATURE* ANALYSIS

Switzerland. "In countries with high coverage, infections have been uncoupled from deaths, so that even with new surges of infection, deaths have stayed low."

Also noteworthy is the speed of vaccine development (see 'Vaccine innovation'). No vaccines in history have been developed so fast, yet 23 vaccines against SARS-CoV-2 have already been approved for use around the world – and hundreds more are in development.

It is estimated that this astonishingly rapid development and deployment has saved at least 750,000 lives in the United States and Europe alone – and probably many more globally, although researchers are as yet unwilling to commit to a number. A study by the WHO and the European Centre for Disease Prevention and Control in Solna, Sweden, published last month[1], estimated that 470,000 deaths had been averted across 33 European countries in those aged 60 and over alone. Another modelling study, which is yet to be peer reviewed, by epidemiologists at Yale University in New Haven, Connecticut, estimated that 279,000 lives had been saved by late June by the vaccination drive in the United States (see go.nature.com/3gs7kgy).

SOURCE: DATA FROM AIRFINITY

Vaccine haves and have-nots

But despite the astonishing success of the vaccines, it's a story of haves and have-nots, and the roll-out has been anything but equitable. "We were so together and so divided," says Kang. "Very together on the science, very divided on the access."

In the world's most-vaccinated nations, such as the United Arab Emirates, Chile and Cuba, more than 200 doses have been administered per 100 people – but at the opposite end of the scale, in places such as Tanzania, Afghanistan and Papua New Guinea, fewer than 20 people per 100 have received at least one dose (see 'Global doses').

"Vaccine inequity has been one of the most painful experiences of the pandemic," says Swaminathan, who notes that there now exist two parallel worlds. In some regions, infections have been uncoupled from deaths and life is normalizing. But in others, there is "fear in opening up, schools remain shut, long-term plans cannot be made, and surges in infections translate soon into higher deaths," she says.

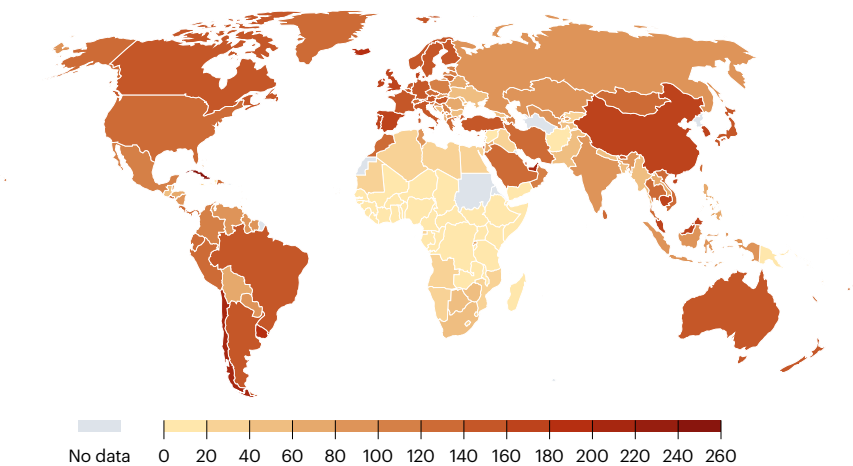
On average, in high-income countries, 83% of the eligible populations have had at least one shot, but in low-income countries that number falls to 21%. These figures "never cease to amaze", says Andrew Azman, an infectious-disease epidemiologist at Johns Hopkins University in Baltimore, Maryland, who co-authored an analysis on the inequities in doses, posted as a preprint[2] in October.

It was expected that poorer nations would get increased supplies once demand fell in wealthy nations, but most rich countries are now administering boosters. This, combined with the fact that many countries are stockpiling doses, could be contributing to a lack of access for those who really need them, says Kang.

Disparities exist not just between countries, but also within them. One study in the United States found lower vaccination coverage in areas that had larger numbers of people on low incomes, or who were single parents, or who had disabilities[3]. Other studies show disparities in vaccination coverage along racial or ethnic lines[4].

GLOBAL DOSES

Vaccines have been rolled out unevenly across the world, as shown by the number of COVID-19 vaccine doses administered per 100 people in the total population*.

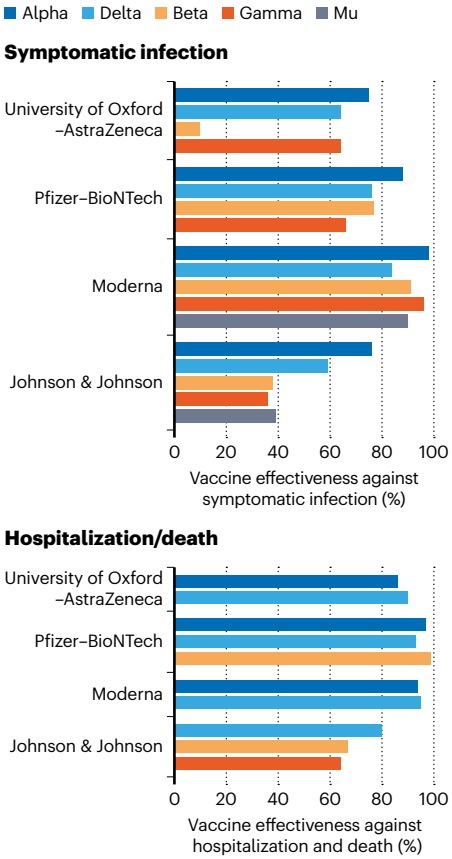


SOURCE: OUR WORLD IN DATA

*Data as of 29 November 2021. Data don't reflect the number of people who have been vaccinated because some people have received two doses of a vaccine. Nature publications remain neutral with regard to contested jurisdictional claims in published maps.

VARIANTS AND VACCINES

Over the course of the past year, the emergence of SARS-CoV-2 variants Alpha, Beta, Gamma, Delta and Mu has challenged the effectiveness of vaccines, although most have held their ground. How vaccines will fare in the face of highly mutated Omicron is yet to be determined*.



*Data as of 25 November. Estimates of vaccine effectiveness modelled by Airfinity, based on available data. Figures on effectiveness against hospitalization and death not available for all variants.

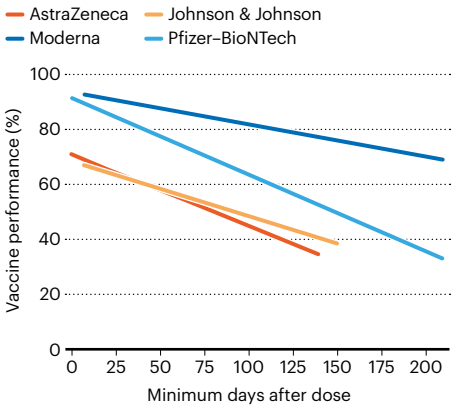
Waning immunity and variants

2021 was the year of COVID-19 vaccines, but it was also the year of variants. Researchers identified a trio of SARS-CoV-2 'variants of concern' in late 2020 and early 2021, now called Alpha, Beta and Gamma (see 'Variants and vaccines'). These seemed to spread faster than viral lineages in circulation earlier, and scientists worried that these variants might also blunt the effectiveness of vaccines.

Laboratory studies and real-world epidemiology confirmed that vaccines remained highly effective against the most widespread of the three, Alpha, which was identified in the United Kingdom. But Beta and Gamma – first

WANING IMMUNITY

The immunity conferred by COVID-19 vaccines, particularly to prevent infections, falls over time — as shown in these estimates of vaccine efficacy against Delta in the months following a second dose*



*Data as of 25 November 2021. Estimates of vaccine effectiveness modelled by Airfinity, based on available data.

SOURCE: DATA FROM AIRFINITY

spotted in South Africa and Brazil, respectively — were linked to reduced effectiveness of some vaccines, particularly those based on viral vectors, such as the Oxford–AstraZeneca vaccine, or on inactivated viruses, such as those developed in China and India.

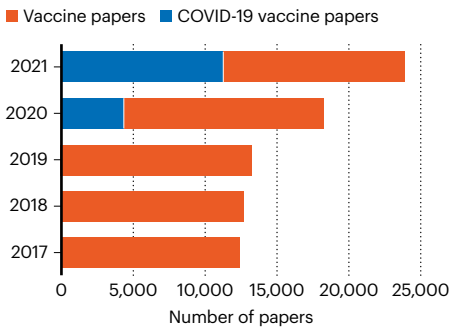
Delta, designated by the WHO as a variant of concern in May, is currently responsible for most new infections globally and has further challenged vaccines. Countries such as Israel, the United States and the United Kingdom that began their vaccination campaigns early are now seeing signs that vaccines lose their potency over time (see 'Waning immunity').

Despite these challenges, the vaccines are still doing a good job at protecting against the most severe forms of COVID-19, says Laith Jamal Abu-Raddad, an infectious-disease epidemiologist at Weill Cornell Medicine–Qatar in Doha. "We now have lots of data and we see a very clear pattern that the vaccines are working very well against severity."

However, researchers are racing to determine how different vaccines will hold up against the fast-spreading Omicron, designated a variant of concern in late November. A preliminary study from the United Kingdom found that two vaccine doses offer little protection against becoming infected with Omicron (a third booster dose restored vaccine effectiveness to above 70%). Researchers expect that vaccines will continue to prevent severe disease caused by the variant — but to what extent is not yet clear.

EXPLOSION OF KNOWLEDGE

More than 15,000 vaccine-related papers that mention COVID-19 or SARS-CoV-2 have been published since early last year; 11,000 were published in 2021 alone, making up an astonishing 47% of all vaccine-related publications this year*.



*Journal articles, preprints, and clinical trial reports indexed on the PubMed database. Data as of 24 November 2021.

New vaccines on the horizon

While a little less than half the world's population still awaits a first dose of a COVID-19 vaccine, researchers are developing more than 300 fresh options. (see 'Under development').

Some of these next-generation vaccines could have key advantages over those currently available. For example, protein vaccines use SARS-CoV-2 proteins to rouse the immune system, and promise to be easier to produce and transport than some existing vaccines.

In particular, two protein vaccines made by Novavax, in Gaithersburg, Maryland, and Clover Biopharmaceuticals in Chengdu, China, will be pivotal to hitting the COVID-19 Vaccines Global Access (COVAX) initiative's goal of distributing two billion doses to low-income nations next year, says Nicholas Jackson, head of programmes and innovative technology at the Coalition for Epidemic Preparedness Innovations (CEPI) in Oslo.

Other upcoming COVID-19 vaccines are being formulated so that they can be administered by mouth or inhaled through the nose, such as nasally administered vaccines being developed by CanSino in Tianjin, China, and AstraZeneca. Because these vaccines would be administered into tissues that SARS-CoV-2 first infiltrates when it enters the body, it is hoped that oral or nasal vaccines could work well to prevent infection. They would also require fewer trained personnel to administer.

Some COVID-19 vaccines are being developed to tackle specific SARS-CoV-2 variants or even a variety of coronaviruses. Three diseases caused by novel coronaviruses have already emerged in less than 20 years, says Jackson — severe acute respiratory syndrome (SARS) in 2002, Middle East respiratory syndrome (MERS) in 2012 and COVID-19 in late 2019. "A broadly protective coronavirus vaccine could revolutionize our response to future infectious-disease outbreaks," he says.

Vaccinating children

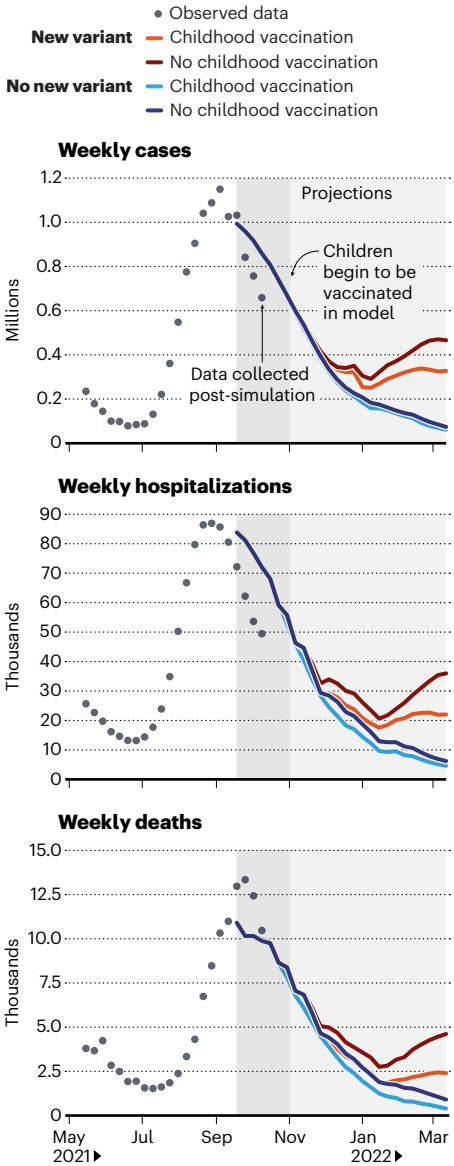
How the pandemic unfolds from now on might be driven not only by novel variants, but also by how quickly vaccines reach another large part of the global population that is yet to be vaccinated — children.

During 2021, the highly transmissible Delta variant caused a sharp rise in paediatric COVID-19 cases worldwide. Although only a relatively small proportion of kids develop severe disease, that still translates to huge numbers of severe cases globally, says Andrew Pavia, a paediatric infectious-disease researcher at the University of Utah Health in Salt Lake City. Widespread vaccination of children will limit the number of severe cases in that age group and help to control the spread of the virus, he says.

In the United States — where children have accounted for the largest numbers of COVID-19 cases of any age group since late October — the Food and Drug Administration (FDA) approved Pfizer–BioNTech's vaccine for the nation's roughly 28 million kids aged 5 to 11 in early November. Since then, more than five million children there have received a dose — and modelling studies run in September that looked at the impact in scenarios where there were no new variants and where there were, show that the benefits could be significant

THE KID EFFECT

A simulation of the US pandemic, run in September and averaging multiple models, found that starting to vaccinate children aged 5 to 11 would not only lower COVID-19's toll, but would also have a large impact if a new, more transmissible coronavirus variant emerged.



SOURCE: COVID-19 SCENARIO MODELLING HUB

SOURCE: DATA FROM PUBMED; *NATURE* ANALYSIS

ELOISA LOPEZ/REUTERS

People wait to get inoculated at a mass-vaccination hub in Manila.

– particularly now, as we face the impacts of Omicron (see 'The kid effect'). The same researchers are now starting to model the possible impacts of Omicron on case numbers in the United States.

Elsewhere, vaccinations for younger children have slowly been taking off too. Regulators in Canada and Israel, and the European Medicines Agency, for example, all provisionally approved the Pfizer vaccine for children in late November, followed by Australia in early December. Colombia, Chile, Argentina and Venezuela are all now offering China's Sinopharm vaccine to children.

Vaccine papers soar

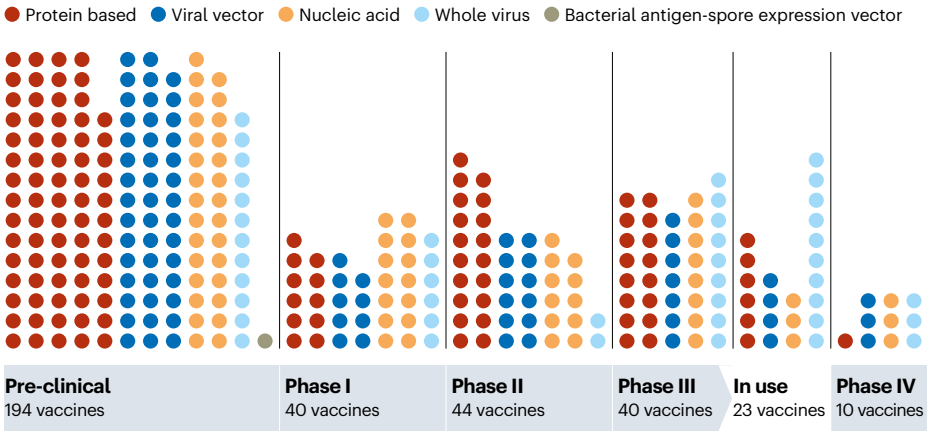
The development and deployment of COVID-19 vaccines has seen an extraordinary research effort over the past year. According to *Nature*'s calculations, at least 15,000 papers on vaccines mentioning COVID-19 or SARS-CoV-2 have been published since early last year, with more than 11,000 of those during 2021 (see 'Explosion of knowledge'). These made up more than 47% of all papers on vaccines published in 2021 – and made it a record-breaking year for vaccine-related publications.

The benefits of that research extend beyond just COVID-19 to vaccines more generally, say researchers. "Humanity coming together to develop and deploy vaccines has opened up a lot of doors for vaccines and understanding what they are, how they work and why we might want to use them in the future," says Azman.

Vaccines will continue to save lives and help some semblance of normal life to return, and energize researchers. But the extent to which the world curtails the pandemic in 2022 will depend on how quickly it provides access in low-income nations, administers boosters in populations with waning immunity, and provides doses to children – as well as the nature and extent of new variants, such as Omicron.

UNDER DEVELOPMENT

Researchers are developing more than 300 COVID-19 vaccines in addition to the 23 already in use around the world; 84 are in early-stage clinical trials and 40 are at much later stages of development*.



*Data as of 1 December 2021

SOURCE: GAVI

1. Meslé, M. M. I. *et al. Euro Surveill.* **26**, pii=2101021 (2021).
2. Chen, Z. *et al.* Preprint at medRxiv https://doi.org/10.1101/2021.10.25.21265504 (2021).
3. Barry, V. *et al. Morb. Mortal. Wkly Rep.* **70**, 818–824 (2021).
4. Wrigley-Field, E. *et al.* Preprint at medRxiv https://doi.org/10.1101/2021.11.19.21266612 (2021).