Access to COVID-19 vaccines: Global approaches in a global crisis

18 March 2021

Following the extraordinarily rapid development of COVID-19 vaccines, immunisation is underway in many OECD countries. However, demand will continue to outstrip supply for some time and currently, distribution is strongly skewed in favour of high-income countries. This both inequitable and inefficient. Directing vaccine to where need is greatest would maximise the number of lives saved and speed bringing the pandemic under control, by slowing transmission and reducing the likelihood of the emergence of viral variants of concern. Governments should therefore act now to accelerate vaccination globally, regardless of international borders, by reallocating supplies to areas of greatest need; continuing the scaling-up of production; ensuring that necessary logistics and health care infrastructure are in place; providing further financial and in-kind support to COVAX; and developing long-term strategies that include commitments to making vaccines available where they are needed most, including through sharing intellectual property and facilitating technology transfer.

Key findings

- **The rapid development of effective COVID-19 vaccines is an extraordinary achievement**. By early March 2021 stringent regulatory agencies around the world had authorised several highly effective vaccines, and authorisations for additional products were imminent.
- **Although immunisation is now underway in many OECD countries, demand will continue to outstrip supply for some time**. Despite production and distribution being strongly skewed in favour of high-income countries, some OECD and EU countries are still struggling to vaccinate their priority populations. Meanwhile, low- and middle-income countries are only now receiving their first shipments, including under the COVAX scheme; without prompt action it may be years before their populations can be immunised.
- **Governments should act collectively now to accelerate vaccination in *all* countries.** The currently skewed distribution of vaccine is both inequitable and inefficient. Directing vaccines to where the need is greatest would not only maximise the number of lives saved, but is also the fastest way to bring the pandemic under control by slowing transmission and reducing the likelihood of the emergence of viral variants of concern.
- **In a few months, the projected expansion of production will likely see the bottleneck move from securing supply to vaccinating people.** By the end of 2021, high-income countries are expected to have large quantities of doses in excess of those needed to vaccinate their priority populations, and should
  - **allocate supplies to areas of high need in other countries**, before vaccinating their entire populations;
  - **continue building production capacity and increasing supply**, not only for the approved vaccines and late-stage candidates, but also for ancillary products;
  - **anticipate the surge in supply and ensure that logistics and infrastructure** are in place for vaccinating populations;
  - **provide further support to the ACT-Accelerator, including financial support to COVAX**, to enable the facility reaching its funding targets, and donate any surplus vaccine;
  - **develop long-term strategies that include binding commitments to making vaccines available** where they are needed most, such as expanding licencing arrangements to accelerate production, as well as co-ordinated approaches to sharing of intellectual property and technology transfer, for example, through participation in the WHO COVID-19 Technology Access Pool (C-TAP), or through multilateral approaches in the World Trade Organization;
  - **ensure future contracts for publicly-funded development of products addressing health emergencies include provisions for sharing of IP and facilitating technology transfer.**

The development of vaccines against COVID-19 has been extraordinarily rapid, with less than one year elapsing between the sequencing of the novel viral genome and the commencement of major vaccination campaigns in different parts of the globe. Nevertheless, the advent of effective COVID-19 vaccines is merely the beginning of the next chapter in this global crisis. Immense challenges remain, not only in vaccine production, supply, and distribution, but also in creating the infrastructure and managing the logistics needed to get vaccines into arms. This brief reviews developments to date, and discusses policy approaches to the issues that will determine the pace of progress toward herd immunity, and the global goals of health and economic recovery.

The development of COVID-19 vaccines is unquestionably a success story

The rapid development of COVID-19 vaccines is the result not only of unprecedented levels of international collaboration, but also of massive public investment in R&D and manufacturing capacity (see Box 1). It is particularly significant when framed against previous estimates of the probability of approval of a vaccine entering clinical trials of as little as 12 to 33%, after some 7 to 9 years of development (OECD, 2020[1]).

As of the beginning of March 2021, stringent regulatory authorities[1] around the world had authorised one or more of several highly effective vaccines,[2] albeit under a variety of emergency or conditional protocols.[3] Authorisations for other COVID-19 vaccines are anticipated in the very short term; at least three products[4] are currently under evaluation or rolling review by the European Medicines Agency (EMA), and a substantial number of additional vaccine candidates are in late-stage development. In addition, four vaccines developed in China and Russia have been authorised and are in use in several countries (see Annex 1.A for details of the products approved or in late development stage as of early March 2021, and Annex 1.B for details of the different vaccine platforms).

[1] The concept of a stringent regulatory authority was developed by the WHO Secretariat and the Global Fund to Fight AIDS, Tuberculosis and Malaria to guide medicine procurement decisions, and is now widely recognised by the international regulatory and procurement community as a regulatory authority that is:

- a member of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), being the European Commission, the US Food and Drug Administration and the Ministry of Health, Labour and Welfare of Japan also represented by the Pharmaceuticals and Medical Devices Agency; or
- an ICH observer, being the European Free Trade Association, as represented by Swissmedic, and Health Canada; or
- a regulatory authority associated with an ICH member through a legally-binding, mutual recognition agreement, including Australia, Iceland, Liechtenstein and Norway."

See: WHO Expert Committee on Specifications for Pharmaceutical Preparations Fifty-first report (Technical Report Series, No. 1003, 2017)

[2] These are the vaccines produced by Pfizer/BioNTech, Moderna, Oxford/AstraZeneca, and Johnson & Johnson.

[3] These include general, as well as conditional, emergency and temporary authorisation protocols.

[4] These are the vaccines produced by Novavax, CureVac, and the Gameleya Institute.

Box 1. Factors contributing to the rapid development of COVID-19 vaccines

In more usual circumstances, developing new vaccines can be a lengthy process, with the different phases of development undertaken sequentially. In the case of COVID-19, a number of factors contributed to significantly speeding successful development, as well as rapid regulatory assessment and authorisation:

- Development was facilitated by extensive knowledge gained with previous vaccines, coupled with unprecedented levels of engagement and collaboration among researchers internationally;
- A large number of vaccine candidates have been, and are continuing to be developed and tested in parallel, using a variety of different platforms, increasing the chances that one or more will prove successful.
- Some vaccine candidates, and two of the products already authorised, rely on a novel messenger ribonucleic acid (mRNA) platform, which allows them be developed, modified and manufactured more rapidly than vaccines using traditional platforms.
- Governments invested heavily both in R&D and in manufacturing capacity, the latter to enable the production of large quantities of vaccine before the results of the phase III trials were available, and in many cases potentially absorbing the full financial risks of R&D failure.
- The combination of the high prevalence of COVID-19 in many locations and rapid clinical trial recruitment accelerated the demonstration of efficacy in preventing symptomatic infection.
- Approval processes have also been accelerated, in part through the use of emergency procedures that allow the acceptance of more preliminary evidence in circumstances of significant unmet need or public emergency.

Source: OECD (forthcoming[2]), "Enhancing public trust in COVID-19 vaccination".

The immunisation effort is underway, and already showing promising results

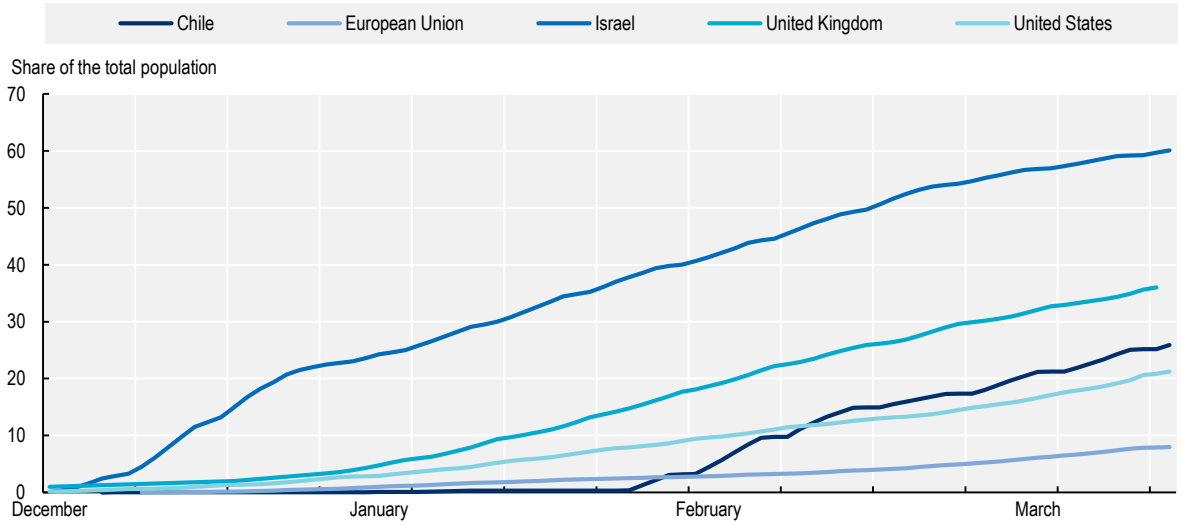
In the United Kingdom, the United States and the European Union, the first vaccinations began immediately after authorisations were granted, with priority given to high-risk older adults, such as long-term care facility residents, as well as frontline health care workers.

As of mid-March 2021, 380 million doses of COVID-19 vaccine had been administered globally; 29% of which in the United States, 13% in the European Union, and 7% in the United Kingdom. By contrast, South America accounted for less than 6% of doses administered globally. The proportion of the population who had received at least one dose was 60% in Israel, (see Figure 1), followed by the United Kingdom (36%), the United Arab Emirates (35%) and Chile (26%).[5] Rapidly emerging evidence of the effectiveness of vaccination in Israel and the United Kingdom – not only in terms of preventing severe illness, hospitalisation and death, but also in reducing infections – is encouraging (see Box 2).

[5] https://ourworldindata.org/covid-vaccinations.

Figure 1. Percentage of the population having received at least one dose of vaccine in selected countries

As of 15 March 2021



Source: Our World in Data, 15 March 2021.

The European Union plans to vaccinate 70% of its adult population by the end of August 2021. As of 15 March 2021, more than 51 million doses of vaccine had been administered in the EU, with Denmark and Spain reporting the highest levels of vaccination per capita (respectively 10.1% and 8.4% of their population had received at least one dose).[6]

As of 15 March 2021, in the United States 71 million people (22% of the population) had received at least one dose of vaccine and almost 40 million were fully vaccinated. A total of 110 million doses had been administered, more or less equally divided between the Pfizer/BioNTech and Moderna products.[7]

Russia began public vaccination in Moscow on 5 December 2020, using the non-replicating viral vector vaccine developed by Gameleya Institute. By 10 February 2021, 2.2 million Russians, or just under 2% of the population, had received their first dose of the two-dose vaccine, and more than 1.7 million had received both doses. The Ministry of Health has announced plans to vaccinate 60% of the population by the end of June.[8]

In China, authorities have already approved four COVID-19 vaccines (developed by three Chinese manufacturers) for emergency use (see Annex 1.A). As of 28 February 2021, China had administered 52 million COVID-19 vaccine doses, or roughly 3.6% of its population.[9] In early March, China's most senior COVID-19 health official announced plans to vaccinate 40% of China's 1.4 billion people by the end of June 2021.

[6] https://ourworldindata.org/covid-vaccinations.

[7] https://ourworldindata.org/covid-vaccinations.

[8] https://apnews.com/article/russia-COVID-19-vaccination-increase-39d1a56a6e533981d56dfc32f7d6585c.

[9] https://fortune.com/2021/03/02/china-covid-vaccine-goal-billion-people/.

Box 2. Israel and the United Kingdom are already observing the effects of vaccination on health outcomes

Israel's vaccination campaign began on 20 December 2020, and by the end of February 2021, 55% of the adult Israeli population (and more than 90% of those aged 60 and over) had received at least one dose of vaccine and almost 40% were fully vaccinated. Around 150 000 Israelis are being vaccinated every day.

Israel's highly digitised, health maintenance organisation (HMO)-based health system and its centralised government have certainly contributed to its ability to design and deliver a massive vaccination campaign rapidly. The government also engaged in early negotiations and was willing to pay higher prices than other countries to vaccine manufacturers, many of which were interested in supplying Israel because of its ability to gather reliable data. In fact, Israel is providing Pfizer/BioNTech with weekly updates on the progress of its immunisation programme, sharing epidemiological data such as the number of confirmed COVID-19 cases, hospitalisations, ventilated patients, and deaths, as well as age and other demographic data.

Data collected by Israel's Ministry of Health showed a 41% drop in confirmed COVID-19 infections in the over 60 age group, and a 31% drop in hospitalisations from mid-January to early February. In comparison, among people under 60 – of whom just over 30% had received at least one dose of vaccine – case numbers declined by only 12% and hospitalisations by 5% over the same period. A large case-control study conducted by Clalit, Israel's largest HMO, confirmed that the vaccine appeared to be effective in preventing not only symptomatic COVID-19 cases, but also incident infections, across all age groups vaccinated. This is one of the strongest indicators thus far that vaccination reduces disease transmission, though this is yet to be conclusively demonstrated.[10]

In the United Kingdom, a study by Public Health England found that the risk of COVID-19 among health care workers decreased by 65-72% after the first dose of the Pfizer/BioNTech vaccine, and more than 85% after the second dose. Additionally, the risk of infection decreased by 70% in those who received one dose and 85% in those who received both doses. Also, data from Public Health Scotland indicates that hospitalisation risk decreased by 94% for individuals vaccinated with the Oxford/AstraZeneca vaccine and 85% for the Pfizer/BioNTech vaccine.

Source: Mallapaty (2021[3]), "Vaccines are curbing COVID: Data from Israel show drop in infections", https://doi.org/10.1038/d41586-021-00316-4; Israel Ministry of Health (2021[4]), *Coronavirus in Israel – General situation*, https://datadashboard.health.gov.il/COVID-19/general; Dagan et al. (2021[5]), "BNT162b2 mRNA COVID-19 Vaccine in a Nationwide Mass Vaccination Setting", https://doi.org/10.1056/nejmoa2101765; GOV.UK (2021[6]), "First real-world UK data shows Pfizer-BioNTech vaccine provides high levels of protection from the first dose", https://www.gov.uk/government/news/first-real-world-uk-data-shows-pfizer-biontech-vaccine-provides-high-levels-of-protection-from-the-first-dose; Politico (2021[7]), "UK: Coronavirus vaccines cutting hospitalisation after first dose", https://www.politico.eu/article/uk-coronavirus-vaccines-cutting-hospitalisation-and-death-rates/.

In light of their relative success in limiting transmission through non-pharmaceutical interventions, some countries in Asia and Oceania reportedly delayed the initiation of their vaccination campaigns. In Australia, the government announced plans to administer the Pfizer/BioNTech vaccine to the highest priority groups,

[10] The phase III clinical trials of the vaccines authorised to date were not designed to measure effects of vaccine on disease transmission, but on the occurrence and severity of symptomatic disease. Promising data, such as the results seen in Israel, are gradually emerging, but are not yet considered by WHO to be conclusive evidence.

but to use mainly locally-manufactured Oxford/AstraZeneca vaccine in the broader population.[11] In New Zealand, the government announced plans to vaccinate the entire population (5 million), largely in the second half of 2021.[12] South Korea announced that it began COVID-19 vaccination in February 2021 in line with the delivery of its initial batches of vaccine, while Japan also commenced its vaccination campaign in mid-February, focusing initially on health care workers and older adults.[13]

Limited supplies are slowing vaccination campaigns in many countries

Most OECD countries are yet to receive supplies sufficient to vaccinate all their priority populations. As a result, some countries, such as the United Kingdom, have decided to delay administration of the second dose in order to provide more people with the initial dose (see Box 3).

Box 3. Dosing interval adjustment to expand coverage

Dosing intervals are based on clinical trial data submitted to regulatory agencies and WHO. The currently recommended intervals for those vaccines requiring two doses are summarised in Annex 1.A.

In the context of limited supply, however, some countries (e.g. the United Kingdom, some Canadian provinces) have imposed delays in the administration of the second dose of vaccine in order to provide more rapid first-dose coverage to a broader cross-section of the population. This raises questions as to whether the gain in coverage of the population might be offset by a theoretical increased risk of viral mutation, a risk which is generally greatest when vaccination coverage is expanded in the presence of high levels of active transmission (See Box 4). However, early data suggest that current COVID-19 vaccines might already achieve very high levels of efficacy after a single dose; lending support to this approach.

In addition, in the case of the Oxford/Astra-Zeneca vaccine there may be some potential for increasing the effectiveness of the vaccine with a longer than recommended interval between the first and second doses. Recently, data from Phase III clinical trials evaluating alternative timing of the second dose showed that the efficacy of the first dose did not wane in the first 12 weeks, and was 82.4% among participants who received their second dose 12 weeks or longer after the first dose, compared with 54.9% in those receiving their both doses less than 6 weeks apart. These results provide support for vaccination programmes that delay the second dose of the Oxford/AstraZeneca vaccine beyond the recommended 4 weeks, a finding that has since been endorsed by the WHO Strategic Advisory Group of Experts on Immunization (SAGE) Committee. While this finding cannot be extrapolated to other vaccines, it may prompt further research on optimising dosing intervals.

There is also emerging evidence that while people who have previously had a COVID-19 infection should be vaccinated, they may be adequately protected with only a single dose. This could prompt an approach that includes serology testing at or prior to first vaccination in order to prioritise the use of booster doses in individuals without previous infection.

Source: WHO (2021[8]), "Interim recommendations for use of the AZD1222 (ChAdOx1-S (recombinant)) vaccine against COVID-19 developed by Oxford University and AstraZeneca", https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-AZD1222-2021.1; Manisty et al. (2021[9]), "Antibody response to first BNT162b2 dose in previously SARS-CoV-2-infected individuals", https://doi.org/10.1016/s0140-6736(21)00501-8; Prendecki et al. (2021[10]), "Effect of previous SARS-CoV-2 infection on humoral and T-cell responses to single-dose BNT162b2 vaccine", https://doi.org/10.1016/s0140-6736(21)00502-x.

[11] https://www.abc.net.au/news/2021-01-12/astrazeneca-pfizer-what-is-the-difference-in-COVID-19-vaccines/13048284.

[12] https://www.reuters.com/article/us-health-coronavirus-newzealand/new-zealand-plans-vaccine-roll-out-in-second-half-of-2021-idUSKBN28R010.

[13] https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/vaccine_sesshujisseki.html.

Manufacturers frequently cite production problems in explaining delays in supply. Pfizer undertook to deliver 350 million doses to the European Union by the end of September 2021 but announced in January 2021 a temporary halt to supply in order to increase production in the future. The company has said it will make up for the shortfall and honour the total first-quarter deliveries to which it has committed. Nevertheless, the disruption has slowed immunisation efforts. Romania received only 50% of its planned volume in February (the other half to be allocated gradually by the end of March); Poland also received 50% less than expected.[14]

AstraZeneca has also faced production issues in the European market. In late January 2021, the company announced that it would reduce EU supplies of its COVID-19 vaccine in the first quarter due to low cell culture yields.[15] This led to concern within the European Commission and among Member States that the manufacturer appeared to be prioritising markets outside the EU with products manufactured in its territory.[16] More recently, AstraZeneca said it would be able to deliver only half the vaccine it was contracted to supply to the EU in the second quarter of 2021, an estimated reduction of 90 million doses.[17]

Many vaccine manufacturers have significantly scaled-up production capacity, and have sub-contracted manufacturing to other major (at times, rival) bio-pharmaceutical manufacturers lacking vaccine candidates of their own. For example, Johnson & Johnson (J&J) and Merck & Co. recently announced they will work together to manufacture the Johnson & Johnson vaccine. Merck will convert two of its manufacturing facilities to produce the new vaccine.[18] Despite this, demand will continue to outstrip supply for some time yet and recent pharmacovigilance issues might also contribute to delaying the immunisation effort in some countries.[19]

Deploying vaccines globally to save lives – and end the pandemic

While the immunisation effort is gaining momentum in many advanced economies, large gaps remain in vaccine access globally. Some 130 countries are yet to administer a single dose. In Africa, for example, by the end of February 2021, reports indicate that only 11 countries had administered *any* vaccinations, and less than 4 million doses in total, the vast majority of which (97%) were in Morocco.[20]

There are two primary approaches to saving lives using vaccines: first, vaccinating vulnerable populations (e.g. the elderly, front line health workers) to reduce morbidity and mortality *directly,* by reducing the incidence of severe COVID-19; and second, assuming vaccination is effective at limiting transmission, vaccinating those sections of the population most susceptible to transmitting the virus, in order to protect

[14] https://www.reuters.com/article/us-health-coronavirus-pfizer-europe-idUSKBN29Q2BX.

[15] https://www.dw.com/en/astrazeneca-covid-vaccine-oxford/a-56427963.

[16] https://www.nytimes.com/2021/01/29/world/europe/EU-AstraZeneca-vaccine-export.html.

[17] https://www.reuters.com/article/us-health-coronavirus-eu-astrazeneca-exc-idUSKBN2AN1ZY.

[18] https://www.nbcnews.com/politics/white-house/biden-announce-merck-will-help-manufacture-johnson-johnson-s-coronavirus-n1259262.

[19] In early March 2021, several European countries partially or fully suspended the use of the Oxford/ AstraZeneca vaccine following reports of a small number of severe thromboembolic adverse events. By 15 March 2021, Austria, Bulgaria, Estonia, France, Germany, Ireland, Italy, Lithuania, Luxembourg, Latvia, the Netherlands, and Sweden had temporarily suspended the use of at least some batches of the vaccine, although a causal relationship had not yet been confirmed by the European Medicines Agency or any other regulatory authority. See https://www.bmj.com/content/372/bmj.n699.

[20] Algeria, Cote d'Ivoire, Egypt, Ghana, Mauritius, Morocco, Nigeria, Senegal, the Seychelles, South Africa, and Zimbabwe.

vulnerable populations *indirectly*, and at the same time, slowing the emergence of new variants against which existing vaccines may be less effective. The choice of approach will be influenced by a number of factors, including the efficacy of the COVID-19 vaccine(s) in reducing severe disease in different population groups, and in limiting transmission; the extent of vaccine supply, and the level of transmission in the population.

In September 2020, the WHO published a 'values' framework (WHO, 2020[11]), followed by a 'roadmap' in November (WHO, 2020[12]) to support countries in prioritising population groups for vaccination, across three broad epidemiologic scenarios: (i) community transmission, (ii) sporadic cases or clusters, and (iii) no cases. The roadmap also considers the extent of vaccine supply. In a scenario of high community transmission and constrained supply, the WHO roadmap suggests an initial focus on direct reduction of morbidity and mortality in high-risk population groups, and maintenance of most critical essential services. Once these groups are vaccinated, the roadmap recommends targeting those population groups susceptible to spreading the virus, to focus on indirect protection. The approach is similar in a scenario of sporadic cases or clusters, however, with a focus on the locations of local outbreaks or clusters only. In a scenario where there are no, or only a very small number of cases, prioritisation shifts towards the strategy of vaccinating potential spreaders first.

However, regardless of which strategy is chosen, the allocation of limited vaccine volumes is efficient and equitable on a global level only if priority is given to where the need is greatest (e.g. where there are large vulnerable population groups such as the elderly, people with pre-existing or chronic conditions, health professionals) and where the risk of development of variants of concern is highest, i.e. where community transmission and/or prevalence are greatest.

Protecting the most vulnerable

The most direct way to protect populations from COVID-19 and reduce morbidity and mortality is to prioritise vulnerable populations for vaccination, including the elderly, people with pre-existing conditions and those particularly exposed to SARS-CoV-2, such as health care workers. In their phase III clinical trials, all of the vaccines authorised thus far have been shown to reduce both mortality and the incidence of severe COVID-19 (see Annex 1.A).

Most countries are currently pursuing this approach. As vaccines began receiving authorisation in December 2020, many OECD countries were experiencing community transmission and supply was initially heavily constrained. Most national vaccination campaigns have initially been focussed on those for whom COVID-19 poses the greatest health threat.

In Denmark and Poland, for example, 59% and 42% of the respective populations over 80 years of age had been vaccinated with one dose by 15 March 2021, in contrast to 13% and 26% of people aged 70 to 79, and less than 10% in all other age groups (ECDC, 2021[13]). In the United Kingdom, more than 90% of the population aged 65 years and over were reported to have received at least one dose by 11 March 2021 (NHS England, 2021[14]). In the United States, 26% of the population aged over 65 years was reported to have been fully vaccinated by 15 March 2021, compared with 8% to 19% in all other adult age groups (CDC, 2021[15]). Several EU member states also report having vaccinated more than 50% of their health care workers.

Indonesia is one of only a few countries that is prioritising working-age over elderly adults for vaccination, reportedly because of insufficient data on efficacy in older people of the Chinese vaccine being used.[21] Maintaining productivity in the population has also been reported as a motivation for this approach (Lloyd-Sherlock, Muljono and Ebrahim, 2021[16]).

[21] See https://www.reuters.com/article/us-health-coronavirus-indonesia-idUSKBN29I09U.

Slowing the emergence of new variants

Another strategy is to prioritise the use of vaccine to reduce transmission of SARS-CoV-2. This is an advantageous strategy for two reasons. First, containing the spread of the virus reduces the number of incident infections and the occurrence of symptomatic disease, and this confers protection on high-risk populations indirectly. Second, and perhaps more importantly, reducing transmission reduces viral replication, thereby also reducing the frequency of mutation and the potential emergence of new variants (see Boxes 4 and 5). If existing vaccines prove to be inadequately effective against the dominant emergent strains, high rates of (re)-infection could occur, leading to third and fourth waves of the pandemic as vaccine manufacturers strive to catch up, particularly if new variants are associated with higher rates of transmission, or more severe disease. Thus, in a context of high community transmission, strategies that prioritise interrupting the spread of the virus, and thus the potential for emergence of new variants, should be considered a priority.

Although the effects of vaccination on transmission were not a primary endpoint of the phase III clinical trials, evidence is now beginning to emerge that some COVID-19 vaccines, in particular the Pfizer/BioNTech product studied in Israel (see Box 2) and the United Kingdom (Weekes et al., 2021[17]), are also effective in averting new infections, including asymptomatic cases. A number of studies are still underway to determine how effective the various vaccines are in terms of blocking transmission (Mallapaty, 2021[18]). At this stage, available evidence suggests that protection from symptomatic COVID-19 is associated with lower viral load and thus a lower propensity for viral shedding, thereby reducing transmission to some degree. According to the World Health Organization, the evidence about the performance of the COVID-19 vaccines to prevent infection or transmission remains limited, but it appears at this stage "reasonable to assume there will be some level of protection against transmission".[22]

Box 4. Reducing viral replication is necessary in order to limit the emergence of viral mutations

The risk of viral mutation is generally greatest when vaccination is expanded in the presence of high levels of active transmission. In the initial stages of an infectious viral illness outbreak, no effective adaptive immune response has yet developed, so there is little selective pressure on viral variants, and the most rapidly replicating variant will dominate the virus population.

As infection spreads, the virus will develop a degree of adaptive mutation to an as-yet, weak immune response, leading to an intermediate rate of adaptation. However, as immune selection increases, this creates a competitive advantage for new variants, which persists until stronger immune responses – as engendered by the introduction of vaccination – significantly reduce the virus population size, which will in turn limit the occurrence of mutations and the emergence of variants.

Clinically significant mutations of the SARS-CoV-2 virus have recently emerged at a concerning pace. This not unexpected and will likely continue while the pandemic persists. A larger pool of infected people in countries where the pandemic remains uncontrolled provides a larger "laboratory" for viral variants vying for genetic dominance.

Source: Grenfell et al. (2004[19]), "Unifying the Epidemiological and Evolutionary Dynamics of Pathogens", https://doi.org/10.1126/science.1090727.

[22] https://globalnews.ca/news/7686306/coronavirus-vaccines-transmission-COVID-19/.

Accelerating vaccination is essential to recovery

The fact that all countries are giving priority to vaccinating their own populations reflects legitimate concerns by politicians whose primary accountability is to their own citizens. However, in the context of a pandemic, the skewed distribution of limited vaccine volumes between rich and poor countries is inequitable and inefficient. Allocating scarce resources for health care according to need – equitable access according to need – is a basic principle of equity supported by health policy in most OECD countries. Such an allocation is also efficient because it maximises the overall health benefits that can be generated from available resources.

Beyond the ethical imperatives, the efficiency arguments are compelling. First, prioritising the administration of vaccine according to need will minimise the number of deaths due to COVID-19 on a global scale. Second, prioritising the administration of vaccine where community transmission is the greatest is also essential to gaining control of the pandemic. It is thus in the interest of high-income countries who have vaccinated their priority populations to allocate some proportion of their existing supplies to areas of high need in other countries, rather than attempting to immunise their entire populations first. International supply chains and movements of people and goods will inevitably lead to the transmission of emerging variants across borders, potentially inflicting further damage on populations (and economies), even those fully vaccinated. The economic costs in high-income countries could well exceed the costs of helping poorer countries become fully vaccinated by as much as 10 to 100 fold (Bown, de Bolle and Obstfeld, 2021[20]), although even these estimates may be conservative.

Recent models estimate that faster progress on ending the pandemic will raise global income cumulatively by USD 9 trillion over between 2020 and 2025, with benefits for all countries, including around USD 4 trillion for advanced economies (Cakmakli et al., 2021[21]). The latest OECD Economic Outlook further emphasises that everything necessary should be done to enhance the capacity for a faster pace of vaccinations and that failure to do so would raise the long-lasting economic and social costs from the pandemic (OECD, 2021[22]).

Unlike the scientific collaboration seen during their development, recent actions taken by governments have not shown commensurate levels of international co-operation and solidarity with respect to the production and distribution of vaccines. Some countries continue to threaten restrictions on vaccine exports, similar to those seen in 2020 in relation to personal protective equipment and other medical supplies. In a more promising development, in February 2021, G7 leaders issued a joint statement pledging improved international collaboration and support for the global COVID-19 response, including additional funding for the COVAX facility, offering some signs of greater emphasis on collaboration.[23]

[23] See https://www.consilium.europa.eu/en/press/press-releases/2021/02/19/g7-february-leaders-statement/.

Box 5. Vaccine efficacy and the emergence of viral variants of concern

Vaccine efficacy against emerging SARS-CoV-2 variants is a growing issue. Several notable variants of SARS-CoV-2 have emerged in recent months, including the B.1.1.7, B1.351 (also known as 501Y.V2) and P.1 variants, first identified in the United Kingdom, South Africa and Brazil, respectively. Each of these variants involves changes to the spike protein, which create the potential for immune escape. There is also early evidence from two vaccine clinical trials suggesting reduced efficacy in preventing mild to moderate COVID-19 in individuals infected with the B.1.351 variant.

Over time, uncontained spread and accelerated evolution in immunocompromised hosts could drive enough mutation to reduce the efficacy of current vaccines considerably, or even entirely. The best and most immediate way to combat the threat of emerging variants is therefore to vaccinate as many people as possible quickly with the existing vaccines.

Vaccine producers are already working to modify their products to tackle the emerging viral variants. One option is to modify the spike protein to include the specific amino-acid sequences that hinder antibody responses. For example, Moderna has started work on updating its mRNA vaccine to match spike mutations in 501Y.V2. Researchers will need to determine whether any such changes have flow-on effects that alter the way in which the immune system reacts to the vaccine. Another option is to include both new and old forms of the spike protein in a single product (a multivalent vaccine).

In anticipation of vaccines adapted for emerging variants, the US FDA released guidance in early March 2021 concerning the way applications for Emergency Use Authorizations (EUAs) will be evaluated for COVID-19 vaccines that target emerging variants. Most notably, the FDA indicated that it could accept data from smaller clinical trials, similar to those conducted for seasonal influenza vaccines. This could accelerate the review process for modified versions of vaccines that have already demonstrated acceptable safety and efficacy profiles. Similar guidance has also been released by a consortium of regulatory agencies from Australia, Canada, Singapore, Switzerland and the United Kingdom.

If SARS-COV-2 becomes endemic, COVID-19 vaccine updates could also follow a process similar to that of seasonal flu vaccines. Researchers use studies in ferret models to determine whether a new influenza strain is likely to evade the previous season's vaccine, and which would therefore necessitate an update to the vaccine. This is undertaken annually for each hemisphere's flu season, and changes are made only when a vaccine-evading strain is widespread. Generally, the threshold for updating flu vaccines is similar in magnitude to the threshold for changes in neutralising-antibody responses that researchers have linked to the 501Y.V2 variant.

Source: Callaway and Ledford (2021[23]), "How to redesign COVID vaccines so they protect against variants", https://doi.org/10.1038/d41586-021-00241-6; Burton and Topol (2021[24]), "Variant-proof vaccines – invest now for the next pandemic", https://doi.org10.1038/d41586-021-00340-4; FDA (2021[25]), "Coronavirus (COVID-19) Update: FDA Issues Policies to Guide Medical Product Developers Addressing Virus Variants", https://www.fda.gov/news-events/press-announcements/coronavirus-COVID-19-update-fda-issues-policies-guide-medical-product-developers-addressing-virus; TGA (2021[26]), "TGA adopts Access Consortium guidance for fast-tracking authorisations of modified COVID-19 vaccines for variants", https://www.tga.gov.au/tga-adopts-access-consortium-guidance-fast-tracking-authorisations-modified-COVID-19-vaccines-variants.

Rebalancing supply arrangements and preparing for an unprecedented immunisation effort

In light of the latest developments, and in particular the emergence of several new and concerning variants of SARS-CoV-2, governments must act now to rebalance supply arrangements. Needs-based global allocation, reflecting greater equity and efficiency, should replace the current "our country first" approaches. Meanwhile, governments should continue efforts to expand supply sufficiently to vaccinate the entire global population and organise massive vaccination programmes. This should involve:

- allocating supplies to areas of high need in other countries, before vaccinating their own entire populations;
- boosting production capacity and increasing supply, not only for the approved vaccines and late-stage candidates, but also for ancillary products. This also includes facilitating the sharing of IP and knowledge transfer so that supply can be increased in countries in addition to those where production is currently taken place;
- supporting COVAX further, financially to help the facility reaching its funding targets and through donating surplus vaccine;
- anticipating the surge in supply and ensure that logistics and infrastructure are in place for vaccinating populations;
- developing long-term strategies that include binding commitments to making vaccines available where they are needed most. This includes expanding licencing arrangements to accelerate production of vaccines, as well as co-ordinated approaches to sharing intellectual property and technology transfer, for example, through participation in the WHO COVID-19 Technology Access Pool (C-TAP), or through multilateral approaches in the World Trade Organization; and
- ensuring future contracts for publicly-funded development of products addressing health emergencies include provisions for sharing of IP and facilitating technology transfer.

Most high-income countries placed large advance orders to ensure priority access

Several OECD countries with domestic vaccine R&D and manufacturing capacity invested in both, the development of COVID-19 vaccine candidates and the building of manufacturing capacity, in return for supply commitments and/or guaranteed purchase of specified vaccine volumes. Backed by this public funding, several manufacturers built production capacity in parallel with vaccine development, thus allowing significant quantities of vaccines to be available immediately on regulatory approval. This has led to a scenario in which several OECD countries have secured quantities of vaccine that would enable them to vaccinate their populations many times over.

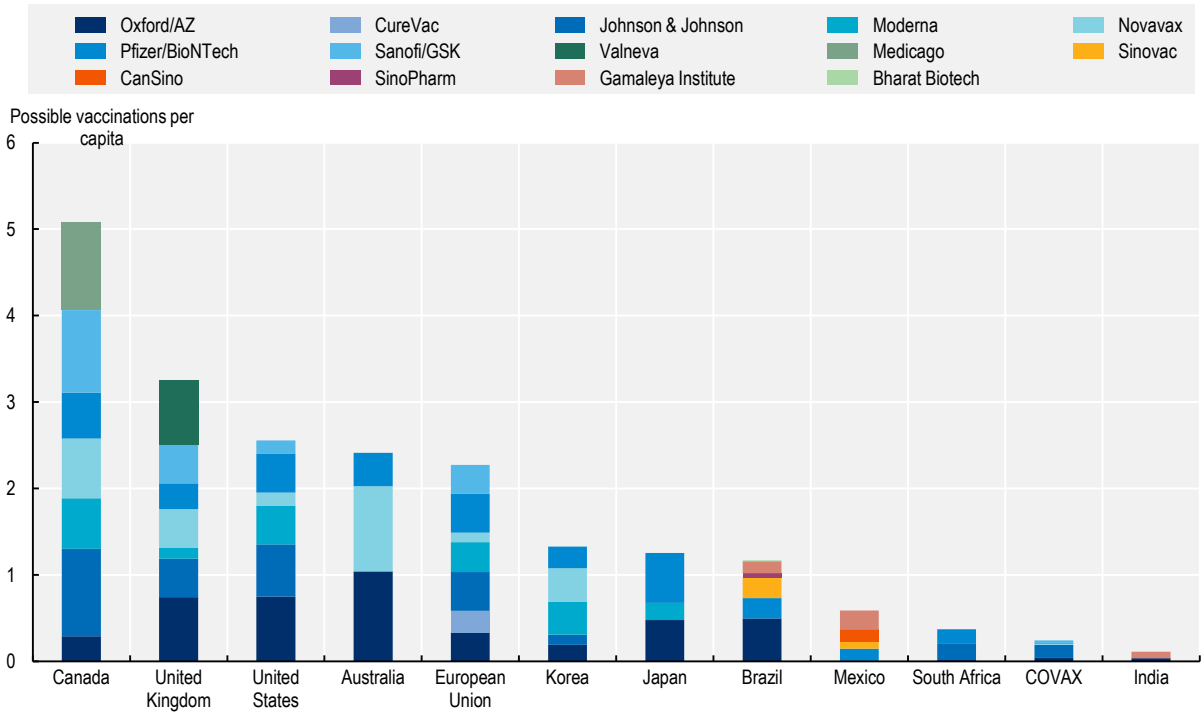
Figure 2 shows the number of doses secured by some OECD countries relative to their populations, based on publicly available information on supply agreements. As of mid-March 2021, high-income countries (16% of the global population) had negotiated supply agreements amounting to approximately half of the world's vaccine supply,[24] leading to allegations of 'vaccine nationalism'. The limited data available on prices suggest that high-income countries also pay higher average prices per dose than low- and middle-income countries, which may be another reason for being supplied first (see Annex 1.C). Some countries, such as Argentina, Brazil and India, gained priority access through hosting clinical trials and "licensing-in" of technology for local manufacturing.[25]

[24] www.knowledgeportalia.org/COVID-19-vaccine-arrangements.

[25] For example, Argentina and Brazil hosted phase III clinical trials of the vaccine candidates developed by Johnson & Johnson, Oxford/AstraZeneca and Pfizer/BioNTech (LSHTM Vaccine Centre, 2021[40]). India hosted trials of the

Figure 2. Number of possible vaccinations per capita (based on volumes secured through supply agreements)

As of 15 March 2021



Note: The numbers of doses per country are based on publicly available information; data are likely to be incomplete and more supply agreements may exist than are publicly disclosed. The number of doses secured does not include purchase options and may therefore underestimate the number of doses secured by countries. The number of doses for COVAX only includes confirmed supply agreements, but not 1 billion doses that COVAX has a first right of refusal access as a result of R&D funding by CEPI. The number of doses for the European Union includes supply agreements with the European Commission but not bilateral contracts between EU member states and manufacturers.
Assumes that 2 doses of any given vaccine are necessary for full initial immunisation, except the single-dose vaccine produced by Johnson & Johnson. The populations of the COVAX-eligible countries represent the global population minus OECD countries and non-OECD countries with national production capability (Brazil, China, India, Russia).
Source: OECD analysis based on data on vaccine doses published by UNICEF, https://www.unicef.org/supply/COVID-19-vaccine-market-dashboard, 5 March 2021, and OECD population estimates.

COVAX remains underfunded

The Gavi COVAX facility is currently the only mechanism that aims to secure access to successful vaccine candidates multilaterally and proposes a rational allocation sequence between governments. It is essentially a joint procurement scheme that negotiates supply contracts with manufacturers on behalf of participating countries.[26] Self-funding countries (middle- and high-income countries) will be allocated

Oxford/AstraZeneca vaccine and, as early as mid-2020, the Serum Institute of India became a licensee to produce and supply the vaccine to the domestic market and to some low- and middle- income countries. See https://www.seruminstitute.com/news_gavip_partnership_annoucement.php. It is also being manufactured under licence in several high income countries.

[26] Nine vaccines developed with CEPI support were intended to become part of COVAX. CEPI is a public-private partnership that finances and co-ordinate the development of new vaccines to prevent and contain infectious disease epidemics. Of the nine, one developed by the University of Hong Kong is not yet in clinical trials, and the development

vaccines for 10-50% of their populations depending on their financial contributions to the mechanism. Vaccine will also be supplied for 20% of the populations of 92 low- and middle-income countries (LMICs) eligible for donor funding.

To date, however, COVAX remains underfunded, and continues to compete for supply against bilateral supply agreements between governments and manufacturers. In 2020, the goal was to raise initial funding of USD 2 billion for LMICs, and this was reached by December 2020. However it is estimated that a further USD 5 billion will be needed for LMICs in 2021, excluding funds for self-financing countries. Although the G7 Leaders' Summit in February 2021 resulted in additional pledges,[27] COVAX is still USD 800 million short of its funding needs for the year. Despite this progress, doubt persists as to the ability of COVAX to attain its goal of delivering 1.8 billion vaccine doses in 2021.

On 2 March 2021, Gavi published an updated information regarding the first round of COVAX allocations (Gavi, 2021[27]). The first allocation includes 237 million doses of the Oxford/AstraZeneca vaccine to 142 countries, with projected deliveries through May 2021. Additionally, there is an "exceptional distribution" of 1.2 million doses of the Pfizer/BioNTech vaccine to countries that requested it and demonstrated the ability to manage the logistical requirements. Deliveries for the first round of allocations has already begun, with India, Ghana and Cote d'Ivoire receiving doses of the Oxford/AstraZeneca vaccine. Both Ghana and Cote d'Ivoire began vaccination campaigns utilising these doses on the 1 March 2021.

Yet, even with the acceleration in vaccine distribution through COVAX, questions remain over how low- and middle-income countries will be able to achieve extensive levels of coverage in the medium term. A recent report by The Economist Intelligence Unit (2021[28]) estimates that some parts of South America, Africa, and Asia will not achieve widespread vaccination coverage until 2023.

Countries must continue to increase supply and act now to build capacity for vaccination campaigns

In the first quarter of 2021, production capacity and supply remain a key constraint for the pace of national vaccination campaigns. Little information is available about the delivery sequences specified in supply contracts or the stipulations of licensing contracts around the destinations of vaccine doses produced locally. Some producers with licenses for local production are only supplying national markets first. The Serum Institute of India, for example, will initially supply India only with the Oxford/AstraZeneca vaccine, which was approved in India for emergency use on 3 January 2020, before distributing it to other countries.[28] The Serum Institute is the world's largest vaccine manufacturer by volume, and has been licensed to produce 1 billion doses. The Oxford/AstraZeneca vaccine is also being manufactured under license in Australia, the Netherlands, Germany, Brazil, Argentina and the United States.

Efforts in the near term need to continue to focus on building production capacity and increasing supply. This includes not only a massive scale-up of manufacturing capacity for the approved vaccines and late-stage candidates, but also the building of additional capacity to produce ancillary products (e.g. vials,

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of two others, developed by Institut Pasteur/Merck/Themis and by University of Queensland/CSL has been terminated. Of the remaining six vaccines, developed by Inovio, Moderna, CureVac, Oxford/AstraZeneca, Novavax, Clover, only the Oxford/AstraZeneca vaccine is already being supplied. Additional supply agreements with Pfizer/BioNTech, Johnson & Johnson and Sanofi/GSK have also been announced.

[27] See https://www.who.int/news/item/19-02-2021-g7-leaders-commit-us-4.3-billion-to-finance-global-equitable-access-to-tests-treatments-and-vaccines-in-2021.

[28] https://www.nytimes.com/2021/02/21/world/serum-institute-india-covid-vaccine.html.

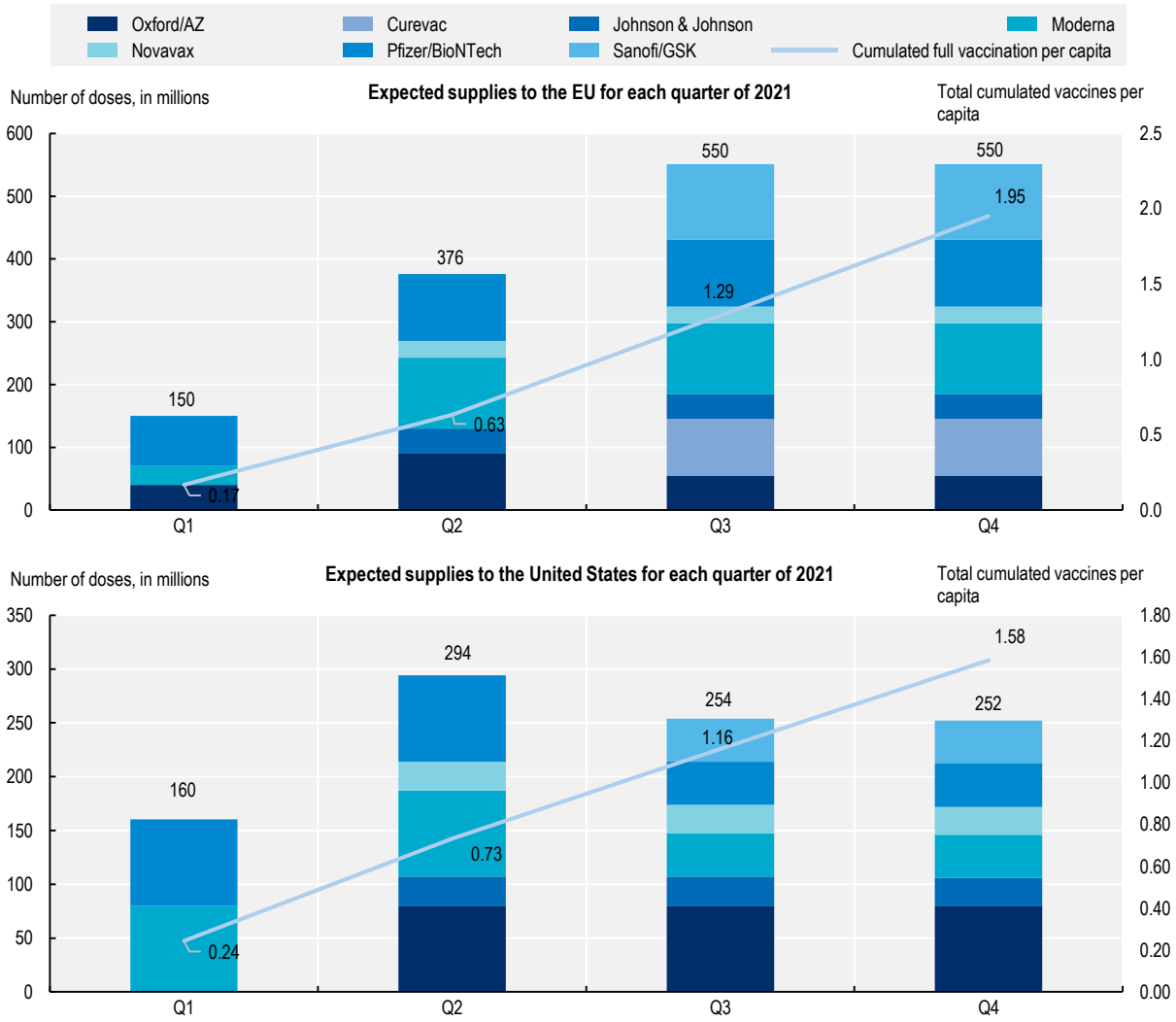
syringes, refrigeration equipment). This requires more extensive sharing of intellectual property at low or no cost, but also, and as importantly, technology transfer to enable local production.

Increased capacity is likely to lead to very different scenario in a few months' time, when the bottleneck will move from securing the supply of vaccine doses to vaccinating people. Figure 3 shows an illustrative projection of supply increases through 2021 in selected OECD countries. By Q3 2021, the United States and EU Member States are likely to have received more than one full vaccine regimen for each individual. Governments therefore need to anticipate the surge in supply now and act decisively to ensure that the logistics and infrastructure are in place to support future warehousing and distribution in order administer available vaccine doses swiftly and avoid waste.[29] Sufficient human resources must also be made available, and governments should engage actively with their populations to ensure that people receive their vaccinations as planned.

In addition to logistics and distribution, the success of vaccination campaigns will be strongly influenced by the extent to which people trust the effectiveness and safety of the vaccines, the competence and reliability of the system that delivers them, and the principles that guide the underlying government decisions and actions (OECD, forthcoming[2]).

[29] Problems are already evident in France, where only 273 000 doses of Oxford/AstraZeneca vaccine have been administered out of 1.7 million received as of the end of February. At the same time, in Germany 1.45 million doses had been delivered, but only 240 000 had been administered. This highlights the importance of adequate advance planning of immunisation campaigns. See https://www.euractiv.com/section/coronavirus/news/unused-stocks-of-astrazeneca-vaccine-pile-up-in-france-germany/.

Figure 3. Vaccine supply is poised to increase in the coming months in Europe and the United States



Note: Data are intended as illustrative only. The following assumptions have been made: all expected deliveries have been cut by 20% to account for unforeseen production issues; deliveries of J&J vaccine starts in April, June for Novavax and September for Sanofi and Curevac.
Source: Based on Knowledge Network on Innovation and Access to Medicines (2021[29]), "COVID-19 Vaccine Purchases and Manufacturing Agreements", www.knowledgeportalia.org/COVID-19-vaccine-arrangements, accessed 15 March 2021.

Governments must share surplus vaccine

By the end of 2021, high-income countries will likely have large quantities of vaccine doses in excess of that needed to vaccinate their priority populations. These should be transferred rapidly to areas of greatest need around the globe, to protect vulnerable populations and slow the emergence of new variants, as discussed in the section "Deploying vaccines globally to save lives – and end the pandemic". As explained above, this is not only an ethical imperative but also the only way to end the pandemic as quickly as possible and in all countries' best interests.

Some governments have already announced that they would share surpluses they have purchased with their neighbouring or other countries. For instance, government officials in Australia and New Zealand

announced that they would provide vaccines and logistical assistance to neighbouring islands.[30] According to news reports, Canada and the European Union are making plans to donate excess quantities;[31] India has launched a 49-nation "friendship programme;" and China is shipping vaccine to several African countries, Turkey, and Afghanistan. While Canada is reported to be planning to donate to COVAX, the European Commission has announced that some vaccine would be shared directly with selected countries and with COVAX. It remains unclear as to how 'surplus' will be defined and at which stage of their national vaccination campaigns countries will begin sharing.[32] Also, at least one advance purchase agreement that has been made public includes provisions that preclude resale and donation of doses to other countries without prior consent of the pharmaceutical firm.[33] Meanwhile, government officials in the United Kingdom have suggested that supplies will only be shared once the entire UK population has been vaccinated.[34]

Gavi has encouraged countries with bilateral supply agreements to share vaccine through COVAX to complement the supplies secured through the contracts negotiated by COVAX itself. The principles laid down by COVAX for this purpose (Gavi, 2020[30]) could contribute to more equitable and efficient global allocation. While donations are to be welcomed, they should not be the principal avenue for sharing vaccine. WHO has repeatedly warned against a focus on bilateral or selective vaccine donations, arguing that they could result in further inequities among lower-income countries.[35] Also, various issues may need to be addressed to ensure that donations can be made and used effectively in their destination countries. These include potential contract limitations between manufacturers and governments, the need for regulatory authorisation in the destination countries, and indemnification and liability provisions (Cohen, 2021[31]). A co-ordinated effort is therefore key.

Sustained global access to vaccines cannot hinge on philanthropy

Although some progress is being made through COVAX and direct sharing of surplus vaccine doses between countries, globally efficient and equitable distribution of vaccines cannot solely rely on the goodwill of donors and ad-hoc solutions. Governments urgently need to commit themselves to structured approaches that are sustainable in the longer term and provide binding safeguards that ensure that vaccines are available where needed most. This will be particularly important if COVID-19 becomes endemic, similar to seasonal influenza, requiring vaccines to be adapted periodically and populations to be vaccinated repeatedly.

In the current stage of the pandemic, availability could be improved by making further efforts to expand production capacity and supply**.** There are a number of approaches to this. Several of the principal vaccine developers have established voluntary licensing arrangements with other bio-pharmaceutical companies – in some cases, their competitors. For example, Merck will also manufacture the Johnson & Johnson

[30] See https://www.sbs.com.au/news/how-australia-will-help-its-neighbours-to-vaccinate-people-against-coronavirus and https://www.rnz.co.nz/international/programmes/datelinepacific/audio/2018777662/COVID-19-vaccine-roll-out-starts-in-parts-of-the-pacific.

[31] See https://www.theglobeandmail.com/world/article-canada-rejects-who-request-for-immediate-vaccine-donations-to-lower/ and https://ec.europa.eu/info/sites/info/files/communication-united-front-beat-COVID-19_en.pdf.

[32] Also see note 31. For vaccine allocation to be equitable and efficient, supplies should be donated once priority population groups are vaccinated domestically. However, governments may also opt to vaccinate their entire populations before making vaccine available to other countries.

[33] See Advance Purchase Agreement between the European Commission and CureVac, at https://ec.europa.eu/info/sites/info/files/curevac_-_redacted_advance_purchase_agreement_0.pdf.

[34] See https://www.devex.com/news/inoculating-uk-population-before-donating-vaccines-undermines-country-s-claim-to-pandemic-leadership-experts-say-99213.

[35] https://www.nytimes.com/2021/02/28/opinion/covid-vaccine-global.html.

vaccine; Sanofi and Novartis, have been licensed to produce the Pfizer/BioNTech product; and AstraZeneca has granted licenses for the manufacturing of its vaccine in several countries, including for 1 billion doses to be manufactured by the Serum Institute of India. As a result, production is now actually being scaled-up quite rapidly, and a major increase in the supply of vaccines can be expected at the global level in the coming months, at which time the current bottleneck will likely shift from supply to the actual delivery at patient level.

But similar to donations by governments, voluntary licensing relies on the willingness of individual intellectual property rights holders, who have strong commercial incentives to constrain supply, to license their assets. Capacity could have arguably been scaled up even more rapidly, had governments made the massive R&D funding mobilised in 2020 conditional on subsequent licensing of intellectual property and technology transfer. This opportunity was largely missed but should serve as an important lesson for future policy.

While compulsory licensing remains a legitimate option for governments to enable additional manufacturers to produce existing vaccines, it does not on its own address the equally important issue of the technology transfer needed to do this. It might therefore only be beneficial for countries that already have the know-how and excess capacity to manufacture vaccines. To the extent that excess manufacturing facilities exist, these could instead be used to expand fill-and-finish capacity and bring the final stages of production closer to the end of the distribution chain. In addition, the unilateral and unco-ordinated use of compulsory licensing by some countries could lead to tit-for-tat trade disputes, with uncertain effects on international co-operation and the system of incentives for private investment in R&D that intellectual property protections are intended to create. Unilateral action could also potentially undermine the development of rapid and innovative responses to future health emergencies.

A co-ordinated and multilateral approach to intellectual property and technology transfer would therefore be preferable. While the large amounts of public funding for R&D of COVID-19 vaccines provide a strong justification for imposing limitations to private intellectual property rights, greater access could, for example, be achieved through broader use of the WHO COVID-19 Technology Access Pool (C-TAP). This mechanism aims to compile, in a single and centralised repository, pledges to voluntarily share knowledge on COVID-19 health technology, intellectual property and data. However, thus far only a small number of countries have endorsed C-TAP, among them none of the countries that host major R&D and production capacity, nor have any of the principal vaccine manufacturers agreed to participate.[36] Another proposal, currently being debated at the World Trade Organization, involves temporarily suspending intellectual property rights for the duration of the pandemic. Whatever the outcome, multilateral approaches can broaden access to COVID-19 vaccines and will be important in shaping approaches to sharing intellectual property and facilitating technology transfer in future public health crises.

[36] See https://www.who.int/initiatives/COVID-19-technology-access-pool/endorsements-of-the-solidarity-call-to-action.

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Annex 1.A. Overview of COVID-19 vaccines currently authorised and in late-stage clinical trials

Vaccines currently authorised by stringent regulatory authorities

Annex Table 1.A.1. COVID-19 vaccines currently authorised by stringent regulatory authorities in OECD countries and the World Health Organization (WHO)

Status as of 15 March 2021

	Authorised in (date, basis of approval)*	Platform (dosing schedule), storage conditions	Summary of efficacy data
Pfizer/BioNTech, BNT162b2 (Comirnaty®)	• United Kingdom (2 Dec'20, temporary) • United States (11 Dec'20, EUA) • Mexico (11 Dec'20, emergency) • Saudi Arabia (12 Dec'20) • Singapore (14 Dec'21, interim) • Costa Rica (15 Dec'20, emergency) • Chile (16 Dec'20, emergency) • Switzerland (19 Dec'20, conditional) • European Union/EEA (21 Dec'20, conditional) • Argentina (22 Dec'20, emergency) • United Arab Emirates (22 Dec'20) • Israel (Dec'20, pandemic protection) • Canada (9 Dec' 20, conditional) • WHO (31 Dec'20, EUL) • Colombia (5 Jan'21, emergency) • Australia (25 Jan'21, provisional) • Korea (3 Feb'21) • Japan (15 Feb'21) • Brazil (23 Feb'21) • Malaysia (Feb'21) • New Zealand (2 Mar'21, with conditions)	mRNA (2 doses: days 0/21) - 80°C to -60°C, +2 to +8°C for 5 days	• Protection from symptomatic COVID-19: ≥16yrs 95% (95% CI 90-98%), ≥65yrs 95% (95% CI 67-100%) • Protection from severe COVID-19: all ages 89% (95% CI 20-100%) • No data on protection from asymptomatic infection • Mild-to-moderate, transient adverse events; serious adverse events similar in vaccine and control groups (Preliminary analysis of ongoing phase II/III trial published by Polack et al. (2020[32]) on 10 Dec'20.)
Moderna, mRNA-1273	• United States (18 Dec'20, EUA,) • Canada (23 Dec'21, conditional) • Israel (4 Jan'21, epidemic protection) • European Union/EEA (6 Jan'21, conditional) • United Kingdom (8 Jan'21, temporary) • Switzerland (12 Jan'21, conditional) • Singapore (3 Feb'21, interim)	mRNA (2 doses: days 0/28) -25°C to -15°C, +2 to +8°C for 30 days	• Protection from symptomatic COVID-19: ≥18yrs 94% (95% CI 89- 97%), ≥65yrs 86% (95% CI 61-95%) • No cases of severe COVID-19 in vaccinated group (30 cases in control) • Insufficient data on protection from asymptomatic infection • Moderate, transient adverse events; serious adverse events similar in vaccine and control groups (Preliminary analysis of ongoing phase III trial published by Baden et al. (2020[33]) on 30 Dec'20.)

	Authorised in (date, basis of approval)*	Platform (dosing schedule), storage conditions	Summary of efficacy data
Oxford/AstraZeneca ChAdOx1-S (Covidshield)	• Argentina (30 Dec'20, emergency) • United Kingdom (30 Dec'20, temporary) • India (3 Jan' 21) • Mexico (4 Jan'21, emergency) • Brazil (18 Jan'21) • Chile (27 Jan'21, emergency) • South Africa (27 Jan'21, emergency) • European Union/EEA (29 Jan'21, conditional) • Korea (10 Feb'21, emergency) • WHO (15 Feb'21, EUL) • Australia (16 Feb'21, provisional) • Saudi Arabia (18 Feb'21) • Colombia (23 Feb'21, emergency) • Canada (26 Feb'21, conditional) • Malaysia (2 Mar'21, conditional) • Indonesia (9 Mar'21, emergency) The vaccine is also reported to have been approved in a large number of low- and middle-income countries in Africa, Asia and Latin America	Non-replicating viral vector (2 doses: days 0/28) (WHO SAGE 0-84) +2 to +8°C for 6 months	• Protection from symptomatic COVID-19: ≥18yrs 70% (95% CI 55-81%); insufficient data for subgroup analysis of older participants • Insufficient data on protection from severe COVID-19 • Data from a subgroup tested for asymptomatic infection suggest no statistically significant protection • Serious adverse events similar in vaccine and control groups (Preliminary pooled analysis of ongoing phase II/III trials published by Voysey et al. (2020[34]) on 8 December 2020.)
Johnson & Johnson (Ad26.COV2-S)	• United States (27 Feb'21, EUA) • Canada (5 Mar'21, conditional) • European Union/EEA (11 Mar'21, conditional)	Non-replicating viral vector (single dose) -20°C, +2 to +8°C for 3 months	• 67% effective (95% CI 59- 73%) in preventing moderate to severe/critical symptomatic COVID-19 occurring at least 14 days after vaccination in people ≥18yrs; and 66% effective (95% CI 55-75%) in preventing moderate to severe/critical COVID-19 occurring at least 28 days after vaccination. • 77% effective (95% CI 55-89%) in preventing severe/critical COVID-19 occurring at least 14 days after vaccination in people ≥18yrs;and 85% effective (95% CI 54-97%) in preventing severe/critical COVID-19 occurring at least 28 days after vaccination. • Most adverse reactions within 1-2 days of vaccination, and of mild to moderate severity and short duration • No data on duration of protection, or prevention of transmission (Preliminary results of phase III trial released by EMA (2021[35]) and FDA (2021[36]) product information in Mar'21.)

Note: EUA: Emergency Use Authorization, EUL: Emergency Use Listing. * The list of countries may not be exhaustive; the approval protocol is provided where known.
Source: US and international clinical trials registers; websites of competent regulatory authorities and Ministries of Health; LSHTM COVID-19 vaccine tracker; news reports; sources cited in the table.

Vaccines developed in China and Russia

Convidecia developed by CanSino Biologics (China)

In August 2020, CanSino began running phase III trials in a number of countries, including Pakistan, Russia, Mexico and Chile. On 25 February, the Chinese authorities announced the approval of the CanSino vaccine for general use. The company announced that its one-shot vaccine had an efficacy rate of 65.28% in preventing symptomatic COVID-19 cases.[37]

CoronaVac developed by Sinovac (China)

Sinovac Life Sciences is a private Chinese company that focuses on research, development and manufacturing of human and animal vaccines. The company published results from the phase I/II clinical trials of its "CoronaVac" inactivated COVID-19 vaccine candidate in *Lancet: Infectious Diseases* in mid-November (Zhang et al., 2020[37]), presenting data from 743 study subjects (143 from phase I and 600 from phase II). The phase II participants were divided into 3 study groups: 2 doses administered 14 days apart (240 participants), 2 doses administered 28 days apart (240), and placebo (120), and each group was split between a low-dose (3μg) and high-dose (6μg) vaccine. Neutralizing antibodies were detectable in at least 92% of the participants in all 4 treatment groups (14- and 28-day schedules and low- and high-dose vaccines), and participants receiving the 28-day schedule exhibited slightly higher seroconversion.

CoronaVac received emergency use authorisation from the Chinese Government in August 2020,[38] and it is reported to have already been administered to several hundred thousand Chinese citizens. The vaccine has since been approved in Indonesia (11 January 2021), Turkey (14 January 2021) and Brazil (17 January 2021).

Some results of multi-country trials are being disclosed little by little, and report varying levels of efficacy. In early 2021, trials in Brazil and Turkey showed that CoronaVac could protect against COVID-19, but they delivered strikingly different results – in part because of different trial designs. In Brazil, the efficacy against COVID-19 with or without symptoms was 50%. In Turkey, the efficacy against COVID-19 with at least one symptom was 83.5%.[39]

Vaccines developed by Sinopharm (China)

Sinopharm, a Chinese state-owned company, is developing two COVID-19 vaccines. The company announced on 30 December that phase III trials of one of the vaccines showed that it was 79% effective but did not provide any further trial data. The Chinese Government approved it the following day. Outside China, the United Arab Emirates (UAE), where one of the candidates had been tested in 31 000 participants,[40] approved Sinopharm's vaccine on 9 December, and Bahrain followed several days later.

As for the other candidate from Sinopharm, the phase I/II trial showed that the vaccine produced antibodies in volunteers, some of whom experienced fevers and other side effects. Sinopharm said the vaccine's

[37] https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html.

[38] https://www.reuters.com/article/us-health-coronavirus-china-vaccines/sinovacs-coronavirus-vaccine-candidate-approved-for-emergency-use-in-china-source-idUSKBN25O0Z3.

[39] https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html.

[40] https://theconversation.com/chinas-covid-vaccines-are-already-being-distributed-but-how-do-they-work-and-where-are-they-up-to-in-trials-151589.

efficacy was 72.51% for this second candidate was approved for general use in China in February. Efficacy data from the phase III trials are yet to be published.[41]

Gam-COVID-Vac (Sputnik V) developed by Gameleya Institute (Russia)

In early February 2021, The Lancet issued a press release reporting a first round of phase III results for the Gam-COVID-Vac ("Sputnik V") non-replicating viral vector vaccine. The vaccine appears to be safe and effective in preventing symptomatic COVID-19. The clinical trials included nearly 20 000 participants, with 75% randomly assigned to receive the vaccine. The researchers identified 16 cases of COVID-19 among the treatment group (14 964 participants) and 62 cases among the placebo group (4 902), corresponding to an overall efficacy of 91.6% in terms of preventing COVID-19 disease, similar to the results for the Pfizer/BioNTech and Moderna vaccines. Notably, the vaccine also exhibited 91.8% efficacy among adults over the age of 60, and no moderate or severe cases of COVID-19 were reported among the vaccinated participants. No serious adverse events were determined to be associated with the vaccine.

It is administered in two doses, given 21 days apart. It requires the temperature to be maintained at approximately -18°C, with short-term storage at 2-8°C. Discussions are also underway with AstraZeneca to determine whether administering a combination of the two vaccines could improve efficacy. It has been reported that the initial clinical trials of the combination vaccine will be held in Russia. Since the summer, Russia has negotiated a number of deals to supply other countries with the Sputnik V vaccine, including Brazil, India, Mexico, and Venezuela. On 22 December 2021, Belarus became the first country outside Russia to authorise it. The next day, Argentina authorised the vaccine for emergency use. Algeria, Bolivia, the Palestinian Authority, Paraguay, Serbia, and Turkmenistan authorised the vaccine in January. The product is currently under evaluation by the European Medicines Agency (EMA) and has been authorised already by some EU countries.

Vaccines in late-stage clinical trials

Annex Table 1.A.2. Other vaccine candidates in phase III or combined phase II/III trials (as of 15 March 2021)

Platform	Developer	Candidate	Current trial status	Status of MA submission* / additional information
mRNA	CureVac/GSK (GER)	CVnCoV	Phase III, 37 000 participants, ongoing in GER, NLD, ESP, PER, MEX	Under rolling review by the EMA since February 2021. On 8 January 2021, CureVac announced that it had formed a partnership with Bayer, which would support the vaccine's development and production.
DNA	Inovio (USA)	INO-4800	Phase II/III, 6 600, ongoing in USA	NA. Licensing agreements announced with manufacturers in Japan.
	Osaka University/ AnGes Inc./ Japan Agency for Medical R&D (JPN)	AG0302-COVID-19	Phase II/III, 500 ongoing in JPN	NA.
	Zydus Cadila (IND)	ZyCoV-D	Phase II/III, 28 000, ongoing in IND	NA.
Subunit	Anhui Zhifei Longcom Biologic (CHN)	ZF2001	Phase III, 29 000, ongoing in CHN and UZB	NA. Phase III trials began in December 2020).
	Clover Pharmaceuticals/ GSK/ Dynavax (AUS)	AS03-adjuvanted SCB-2019	Phase III starting in March 2021	NA.

[41] https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html.

	Medicago (CAN) / GSK (GBR)	CoVLP	Phase II/III, 30 000, ongoing in Canada,USA	NA.
	Novavax (USA)	NVX-CoV2373	Phase III, 15 000 in GBR, and 30 000 in the USA and MEX	Under rolling review by the EMA. Novavax announced an interim analysis of its phase III trial on January 2021, based on 106 confirmed cases of symptomatic COVID-19, overall efficacy of 96% (95% CI 74%-100%) in preventing mild, moderate and severe COVID-19 caused by the original SARS-CoV-2 strain; no data or peer-reviewed study have been published. License agreements have been signed with manufacturers in Korea.
	Vector (RUS)	EpiVacCorona	A Phase III trial began in November in Russia, and as of 15 December 2020, 1 438 volunteers had received the vaccine.	NA. In January, Russia launched a mass vaccination campaign, using EpiVacCorona as well as Sputnik V.
Inactivated	Bahrat Biotech/ Indian Council for Medical Research/ National Institute of Virology (IND)	BBV152 (Covaxin)	Phase III, 26 000, ongoing in IND	On 3 January 2021, the Indian Government granted Covaxin emergency authorisation. In March, Bharat Biotech announced preliminary Phase III trial results, covering 25 800 participants (more than 2 400 over 60+), half of whom received the vaccine. The vaccine demonstrated overall efficacy of 81% in preventing disease (mild, moderate, or severe).
	Chinese Academy of Medical Sciences (CHN)	Vero cell	Phase III, 34 000, ongoing in BRA, MYS	NA.
	Research Institute for Biological Safety Problems (RIBSP) (KAZ)	QazCovid-in	Phase III, 3 000, ongoing in Kazakhstan	NA.

Note: Data current as of 1 March 2020.
Source: Dai and Gao (2020[38]), "Viral targets for vaccines against COVID-19", https://doi.org/10.1038/s41577-020-00480-0; LSHTM COVID-19 vaccine tracker; Novavax Inc. (2021[39]) "Novavax Confirms High Levels of Efficacy Against Original and Variant COVID-19 Strains in the United Kingdom and South Africa Trials", https://ir.novavax.com/news-releases/news-release-details/novavax-confirms-high-levels-efficacy-against-original-and-0; US, Indian and WHO international clinical trials registers; WHO COVID-19 candidate vaccine landscape and tracker; news reports.

Development of three vaccine candidates (Molecular Clamp Vaccine from CSL/University of Queensland; V590 developed by IAVI/Merck; and V591 by Institut Pasteur/Themis/Merck) are reported to have been discontinued.

Annex 1.B. Vaccine technologies (platforms)

The various vaccine platforms can be considered as two distinct groups:

- Based on traditional development platforms: these include live attenuated or inactivated vaccines, as well as recombinant protein vaccines (the latter two often require an adjuvant[42] to boost the immune reaction).
- Utilising novel development platforms: these include DNA and mRNA vaccines, as well as replicating and non-replicating viral vector-based vaccines.

Annex Table 1.B.1 describes these different vaccine platform existing and which of them are being used by COVID-19 vaccines approved or in late stages of development.

Annex Table 1.B.1. Different vaccine platforms

Platform	Description	Already approved vaccines using this platform?	COVID-19 vaccine approved [or in late development stage]
Messenger ribonucleic acid vaccine (mRNA vaccine)	Inject mRNA encoding the antigen or antigens against which an immune response is sought. The body's own cells use this genetic material to produce the antigens.	None prior to COVID-19.	• **Moderna** • **Pfizer/BioNTech** • [CureVac]
Desoxyribonucleic acid vaccine (DNA vaccine)	Inject DNA encoding the antigen or antigens against which an immune response is sought. The body's own cells use this genetic material to produce the antigens.	No	• [Inovio]
Viral vector-based vaccines	Inject only components of the pathogen, or antigens that best stimulate the immune system. Use a harmless virus or bacterium as a vector, or carrier, to introduce genetic material into cells. Viral vector vaccines may be replicating or non-replicating.	Yes, for vesicular stomatitis virus (VSV) and Ebola	• **Oxford/AstraZeneca** • **Gameleya Institute** • **Johnson & Johnson** • **CanSino**
Recombinant protein vaccines	Inject only components of the pathogen, or antigens, that best stimulate the immune system, produced in-vitro by cells into which the genetic code for the viral protein has been inserted.	Yes, for influenza, human papillomavirus (HPV) and hepatitis B (HBV)	• [Novavax] • [GSK/Sanofi] • [Medicago/GSK]
Live attenuated vaccines	Inject a weakened form of the pathogen that causes a disease, similar to the natural infection they help prevent.	Yes, for measles, mumps, rubella (MMR); rotavirus; yellow fever	
Inactivated vaccines	Inject an inactive or dead version of the pathogen that causes the disease.	Yes, for influenza	• **Sinovac** • **Sinopharm/ Beijing Institute** • **Sinopharm/ Wuhan Institute**

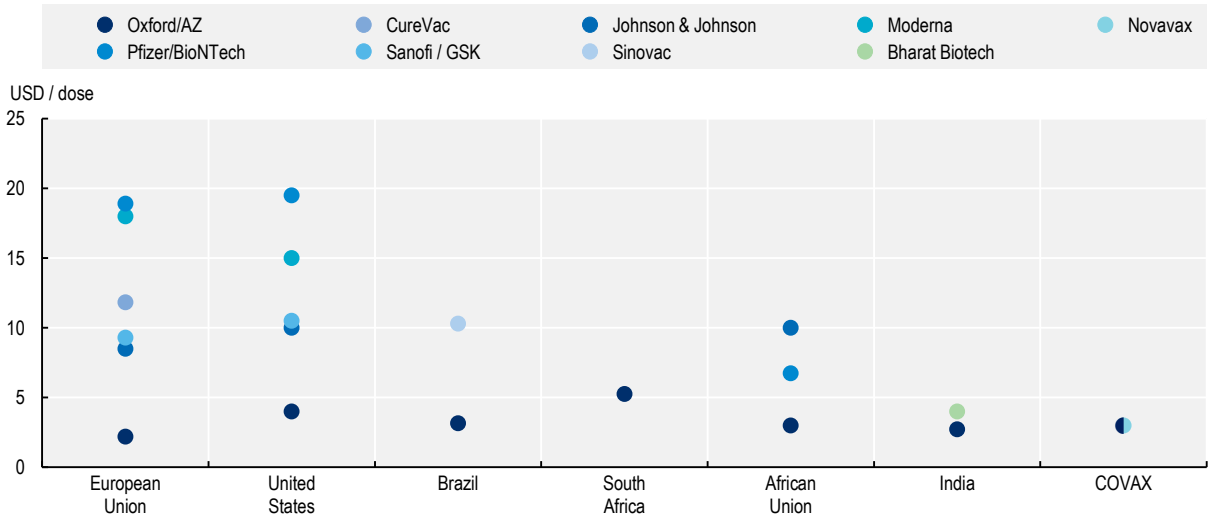
[42] An adjuvant is an ingredient used in some vaccines to help stimulate a stronger immune response in the recipient.

Annex 1.C. Vaccine prices under current supply agreements

There is only very little publicly available information regarding vaccine prices. Annex Figure 1.C.1 shows the prices of vaccines negotiated in bilateral purchase agreements and by Gavi COVAX, based on publicly available information.

Annex Figure 1.C.1. Average procurement price per vaccine dose

Status as of 15 March 2021



Note: Prices are averages per dose, calculated by dividing the financial amount committed in supply agreements by the total number of secured doses. Does not include options or resources allocated to vaccines through arrangements other than supply agreements. Average prices may therefore under- or overestimate *true* unit prices. Details of the supply agreements are not public.
Source: OECD analysis based on data on vaccine doses published by UNICEF, https://www.unicef.org/supply/COVID-19-vaccine-market-dashboard, accessed 15 March 2021.

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