

# **In-Depth Science Review**

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The glut of COVID-19 vaccines is a myth: How we can — and must remove barriers to vaccinating the world against COVID-19

This science review is a snapshot of the new and emerging scientific evidence related to COVID-19 during the period specified. It is a review of important topics and articles, not a guide for policy or program implementation. The findings captured are subject to change as new information is made available. We welcome comments and feedback at covid19eiu@vitalstrategies.org.

### The glut of COVID-19 vaccines is a myth: How we can — and must remove barriers to vaccinating the world against COVID-19

#### Main message:

Despite the speed with which highly effective and safe COVID-19 vaccines have been developed, people in many countries continue to have extremely limited access to vaccines. COVID-19 cases and deaths continue to come in waves, health systems are stretched to capacity or beyond, economies continue to struggle, trade and travel are disrupted and the secondary impacts of the pandemic and consequent mitigation efforts continue to affect many. Increasing immunity globally will protect people everywhere from disease and death, reduce the global risk of new variants and allow health systems, governments and economies to function fully. Unfortunately, time and time again, vaccination coverage targets set by governments and public health authorities have not been met. Thus far, vaccine distribution has been largely dependent on country wealth. Most people in high-income countries have been fully vaccinated and tens of millions have gotten boosters, while most of the world's population has yet to receive a single shot. Why has this happened? There are many factors, but the biggest barrier to greater global vaccination coverage has been – and will continue for many months, if not years, to be – vaccine supply.

#### Progress towards vaccinating the world

As of Oct. 25, 2021, 7.8 billion vaccine doses had been delivered to 208 countries and territories. If doses had been distributed evenly, more than 50% of each country's population including every high-risk person in the world! could have been vaccinated. However, distribution has been highly uneven. In May 2021, the World Health Organization (WHO) set a target of 10% COVID-19 vaccination coverage in all countries by the end of September 2021 and 40% coverage by the end of the year. On October 1, the 10% coverage target had not been met by 56 countries comprising 20% of the global population. According to WHO, as of early September, 75% of COVID-19 vaccines had gone to just 10 countries. Distribution has largely been dictated by country wealth. Human Rights Watch estimated that the world's richest countries have administered 100 times as many doses as the poorest.



Source: Schellekens (2021); OWID; WDI; WHO; WPP. Updated: 2021-10-28. Latest: pandem-ic.com. Note: Acronyms: high (HIC), upper-middle (UMIC), lower-middle (LMIC) & low income (LIC) countries. Doses exclusive of boosters. Doses of single-dose vaccines converted into double-dose equivalents (counted twice) to achieve full vaccination threshold of 200.

#### Source: pandem-ic



#### Source: UNDP

In Africa, as of the end of October, less than 4% of the population had been fully vaccinated. Only three countries had met the WHO target of 40% (Seychelles, Mauritius and Morocco). Several countries including Chad, Democratic Republic of the Congo, Guinea-Bissau and South Sudan had vaccinated less than 1% of their populations; one country (Eritrea) had received no vaccine doses at all.

#### How do different countries get vaccines?

Even before COVID-19 vaccines were tested and approved, governments and multinational organizations began pre-ordering and securing doses for their own future use. This process is quite different for countries that have bargaining power and can afford large numbers of doses. For example, Canada, the European Commission and the United States government each paid billions of dollars to secure millions of doses. For countries without the financial resources to compete for vaccine supplies, there are different sources of vaccines, including COVAX, direct sales and donations.

<u>COVAX</u> is the vaccines pillar of the Access to COVID-19 Tools Accelerator (ACT-A). ACT-A is a voluntary global initiative to accelerate the development, production and rollout of COVID- 19 tests, treatments and vaccines. With the aim of increasing vaccine access, COVAX pools the purchasing power of wealthier countries to negotiate COVID-19 vaccine prices and prepurchase doses that are distributed to participating countries. Both <u>"self-financing"</u> countries that can afford vaccines and <u>"funded" countries that cannot afford vaccines</u> participate in COVAX. The COVAX initial scheme – currently under revision – was to give selffinancing countries doses in proportion to how much each country bought into COVAX, and to give <u>92 participating funded countries</u> enough doses to vaccinate at least 20% of their populations.

In theory, COVAX investments support worldwide manufacturing potential and ensure rapid access to safe and effective vaccines that receive regulatory approval. Unfortunately, COVAX has repeatedly faltered in its delivery. To date, it has supplied fewer vaccine doses to low- and middle-income countries than other mechanisms. In Africa, more doses have come from bilateral agreements between countries and vaccine manufacturers than from COVAX. Donations have also been a major source of vaccine supply. Billions of doses have been pledged for donation by high-income countries, including over 1 billion doses from the United States, the vast majority of which remain to be delivered. A significant proportion of sold and donated doses have come from China, which

has raised questions about vaccine efficacy, as reviewed below. There are also other multinational efforts to secure doses, such as the <u>African Vaccine Acquisition Trust</u>.

The Sinovac and Sinopharm vaccines, developed in China, account for approximately half of the vaccines produced thus far. These vaccines were granted Emergency Use Listing (EUL) status by WHO after satisfying the criterion of at least 50% efficacy against COVID-19. However, limited data gathered after rollout suggest that the protection offered is lower than what is offered by other vaccines. For example, a study in Brazil found that Sinovac was as little as 44% protective against death in people over age 80 years. A study in Thailand found that 10 weeks after a second dose of Sinovac, only two of 207 health care workers had antibodies that could neutralize the Delta variant. There are no real-world data on Sinovac or Sinopharm vaccine effectiveness against the Delta variant. Because of high numbers of cases and deaths among people fully vaccinated with these vaccines, China, Indonesia, Brazil and other countries are offering or planning to offer boosters to all Sinovac/Sinopharm recipients, and some are recommending booster doses of other vaccines. WHO's expert committee on immunizations has recommended boosters for all Sinovac and Sinopharm recipients aged 60 years of age or older. These vaccines comprise a significant proportion of the doses available through COVAX, and many of the countries to which these vaccines have been allocated are in Africa. Several countries' public health authorities have rejected these vaccines or accepted them reluctantly given no other options.

#### Barriers to vaccinating the world

#### 1. Vaccine technology sharing

Failure to transfer vaccine technology is a major factor in the world's failure to meet global vaccination targets. Sharing vaccine production know-how, as well as working collaboratively to address supply chain weaknesses, would allow other manufacturers to produce vaccine doses that have already been tested and authorized. mRNA vaccines are ideal candidates for technology transfer and rapid scale-up of mass production. However, neither Pfizer nor Moderna has agreed to transfer their vaccine technology, despite international pressure to do so, an offer from WHO to contribute to the establishment of a vaccine production hub site, and options to fairly compensate the original manufacturers for all doses produced. Failure to transfer technology has left the vaccine manufacturing and distribution process more vulnerable to other issues. Existing manufacturing plants for nearly all vaccines have experienced production failures and delays. The supply chains needed to support vaccine production are complex, and various obstacles could have been partially mitigated through local or regional vaccine production hubs, commercial coordination and government action. There are examples of pharmaceutical companies transferring technology in order to increase global access to their products. One current example is the pharmaceutical company Merck Sharp & Dohme (MSD) agreeing to a license and technology transfer through the Medicines Patent Pool for its new drug molnupiravir, an oral antiviral medication that has been shown to prevent severe disease and death among patients with COVID-19. This agreement is an important step, as it will allow manufacturers to make the product and supply available cheaply and widely in 105 countries.

#### 2. Dose delivery

Over one billion doses have been pledged for donation by G7 countries and the European Union. However, doses promised and produced does not equal doses delivered. As of August 2021, less than 15% of promised doses had been delivered via any mechanism, including direct donation and COVAX. The European Union is likely to fall particularly short, potentially delivering less than a quarter of the doses it had promised. COVAX's target was to provide 2 billion vaccine doses in 2021; as of October 13, COVAX had delivered approximately 360 million vaccine doses – less than one fifth of its target.



Source: Launch and Scale

On Oct. 7, WHO launched the <u>Strategy to</u> <u>Achieve Global Covid-19 Vaccination by mid-</u> <u>2022</u>, which outlines the actions required by the global community to vaccinate 70% of the world's population against COVID-19 by mid-2022. The strategy also identifies key barriers to achieving vaccination targets, including export restrictions and regulatory issues.

• Export restrictions: One important export restriction has been the suspension of vaccine exports from India. After establishing manufacturing of the Covishield vaccine, which uses the AstraZeneca vaccine formulation, the Serum Institute of India became a major supplier of global COVID-19 vaccines. However, in the face of a COVID-19 surge caused by the Delta variant in March 2021, the Indian government halted vaccine exports. Although vaccination drives within India increased domestic vaccination coverage rates, cessation of vaccine exports from India reduced supply in other countries, particularly low-income countries. India's health ministry announced that the country would resume vaccine exports in October 2021; as of Oct. 20 it had resumed exports to neighboring

## countries while further delaying delivering vaccines to COVAX.

• Regulatory issues: After a company has developed and tested a vaccine, it usually must receive regulatory approval by a recognized authority before the vaccine can be administered outside a clinical trial. Thorough review of safety and efficacy data as part of the regulatory process is important, but the time required for this can reduce expected vaccine supply. Approval sometimes comes from a country's government agency (for example, the Food and Drug Administration in the U.S., or the South African Health Products Regulatory Authority in South Africa). Many countries look to regional authorities (e.g., the European Medicines Agency or the African Regulatory Taskforce) and others look to WHO. For countries that rely on funds from multilateral development banks (e.g., the World Bank or the African Development Bank) to purchase vaccines, the question of which regulatory authorities are recognized by the banks has also contributed to delays. As of this writing, 23 COVID-19 vaccines have been approved for use by at least one country, and seven

<u>COVID-19 vaccines</u> have been granted EUL from WHO.

In part because of these delivery issues, failure to expand vaccine manufacturing through technology sharing has impacted not only supply but also access. Countries that produce vaccines have more access than those that do not. As one example, the global distribution of Moderna vaccine manufacturing and purchasing is shown below.



#### **Manufacturing and Purchases for Moderna**

Source: Launch and Scale

#### 3. Purchasing agreements

High-income countries have established purchasing agreements with manufacturers that are detrimental to expanding global vaccine coverage. It is likely the disproportionate share of doses delivered to high-income countries will continue with future doses and that ongoing lack of transparency about pre-purchased doses will continue to compound the problem. According to the UNICEF COVID-19 Vaccine Market Dashboard, as of the end of October 2021, nearly 20 billion vaccine doses had been purchased. Many high-income countries have purchased more than 5 doses per person (and some have purchased more than 10), while many low-income countries have purchased fewer than 0.1 doses per person.



Source: Launch and Scale

#### 4. Budgetary shortfalls

Not only have low- and middle-income countries been unable to compete with highincome countries to purchase vaccine doses, but also the Access to COVID-19 Tools Accelerator (ACT-A), under which COVAX falls, has been chronically underfunded. In early 2021, COVAX had a funding gap of over 7 billion dollars. Mobilization of funds from various sources has helped close the gap, resulting in an estimated budgetary shortfall of 0.4 billion dollars for 2021. However, a new ACT-A draft budget has estimated that nearly 15 billion additional dollars will be needed to ensure equitable access to vaccines to end the acute phase of the pandemic.

5. Vaccine dose expiration

There are many reports of vaccines expiring before they can be used. In the U.S., an estimated 15 million vaccine doses were discarded between April and September 2021. Some excess doses that have been donated by high-income countries have been delivered too close to their expiration dates, which has forced countries that desperately need more vaccine doses to discard them. For example, in March 2021, officials in Malawi – a country with one of the lowest vaccination rates in the world – destroyed 20,000 doses of AstraZeneca because the expiration date would not have allowed anyone who got a first dose to get a second.

Estimates of the number of doses that are within two months of expiration and/or will expire in the last four months of 2021 are pictured below, along with the shelf-life of some vaccines.



Source: airfinity

**6.** Barriers to vaccine administration: rollout and hesitancy

In every country, mass COVID-19 vaccine rollout has required immense resources and infrastructure, including vaccinators, administrators, data management systems, transport and supplies for cold-chain storage and vaccine administration. Problems have been reported at many points in the rollout process. For example, after Kenya received a donation of Pfizer vaccines from the U.S., the doses could not be administered because of a lack of special syringes. Delivery of vaccines without warning, especially if doses are soon to expire, can make rollout difficult if not impossible. However, many low- and middleincome countries have extensive experience rolling out vaccines - including mass vaccination of adults, in emergency situations, among hard-to-reach populations and with ultra-cold vaccine storage - and organizations such as UNICEF and Gavi have extensive experience supporting vaccine campaigns. The first and most critical step in getting shots into arms is to ensure sufficient supply. In many countries where supply has increased, there has been rapid concurrent increase in vaccine administration.

Some have postulated that vaccine hesitancy in low- and middle-income countries will reduce the need for vaccines. However, this is not supported by available data. Evidence suggests that demand for vaccines in Africa is high, and vaccine acceptance rates are higher than in the U.S. and other high-income countries. A study conducted by Africa CDC at the beginning of vaccine rollout suggested that nearly 80% of Africans would accept a COVID-19 vaccine, though acceptance rates varied by region and other factors. Recent survey data from the Partnership for Evidence-Based Response to COVID-19 show that vaccine acceptance rates in Africa continue to be high. More than three in four survey respondents in 19 African countries reported they had either already received a COVID-19 vaccine or were likely to get vaccinated.

#### How many doses do we need?

As new, highly transmissible SARS-CoV-2 variants have emerged, vaccination coverage targets have shifted. The <u>oft-cited coverage</u> target of 70% has been revised upwards to 90% by some experts. Assuming a two-dose vaccination series, the world would need 12.6 billion doses to cover 80% of the world's 7.9 billion people (or 14.2 billion doses to cover 90%). As of this writing, 7.8 billion doses had been delivered, suggesting a global vaccine deficit of approximately 5 billion doses. However, at least three variables may change the number of doses needed:

- Booster doses The Director-General of WHO has repeatedly urged wealthier nations to delay administration of booster doses until global vaccination targets have been achieved. Although some high-income countries have claimed that they can provide boosters to their own populations while also increasing global vaccine access, all vaccine doses come out of the same global supply. In late October 2021, highincome countries were administering about one million booster doses per day, which was approximately three times the number of daily doses being administered in lowincome countries. If all high- and uppermiddle-income countries recommend boosters for ages 50+, nearly one billion vaccine doses would be needed - an amount that could fully vaccinate nearly 40% of Africa's population with a two-dose series.
- Variants If variant-specific boosters or new two-dose series are needed, that would require an additional 8-16 billion doses globally.

 Children - Some countries may not recommend COVID-19 vaccination for people below a certain age, and some may recommend single doses for some age groups. This could reduce the number of doses needed. Globally, approximately 30% of the world's population is under 18, including approximately 330 million children under age 5.

The pace of vaccination is also important. Per WHO, the most effective strategy for reducing the risk posed by new variants is to get population immunity as high as possible as rapidly as possible. Quickly achieving high vaccine coverage rates will also prevent as many illnesses and deaths as possible. As of Oct. 28, 2021, the latest seven-day rolling average of daily vaccinations administered worldwide, including primary and booster doses, was approximately 23 million. If that daily rate were maintained, it could take 260 days – more than eight months – to give 80% of the world's population two vaccine doses. But these numbers hide large regional variation. In Africa, where the pace of vaccination is slower largely because of inadequate supply, it could take several years to vaccinate 80% of Africa's 1.3 billion people. The map below shows the number of days it will take world regions to vaccinate 80% of their populations if current regional vaccination rates are maintained.



Source: GCPPP

#### How many doses will we have?

The 2021 production targets from COVID-19 vaccine manufacturers totaled 20.8 billion doses - enough to vaccinate the entire global population with a two-dose vaccine series and still have billions of surplus doses. However, low monthly production numbers in the first half of 2021 suggested that supply would fall far short of this target. In September, 1.58 billion doses were manufactured, an increase of 25% over August. If this production pace continues without any major disruptions, approximately 12 billion doses could be produced in 2021. Although 12 billion doses is nearly 50% less than the stated target, this is an improvement from 2020, when production fell short of the global target by 96%.

Most vaccines produced to date are Sinovac (1.99 billion doses) and Sinopharm (over 1.53 billion), followed closely by Pfizer (1.48 billion) and AstraZeneca (1.43 billion), with Moderna as a distant fifth (0.41 billion). With just three months until the end of 2021, most leading manufacturers' 2021 targets are likely to prove unattainable. Sinovac is the only manufacturer likely to meet or beat its target of 2 billion doses. Pfizer is approximately halfway to its target of 3 billion doses. Both AstraZeneca (3.2 billion) and Moderna (1 billion) are less than halfway to their targets, and Sinopharm is less than one-third of the way to its target (5 billion doses). Together, these data show that production targets are being dramatically missed and there is continued global reliance on the Sinovac and Sinopharm vaccines.

#### Total vaccine production by manufacturer, to September 2021



#### Source: GCPPP

#### Conclusion

The idea that we have enough vaccine doses to sufficiently vaccinate the world's population against COVID-19 is a myth. We don't have enough, and we won't have enough soon enough, unless vaccine production and distribution patterns change. Increasing the global vaccine supply is not only an epidemiologic imperative, but also an ethical one. If we have learned one thing during the pandemic, it is that the world is inextricably interconnected. None of us are safe until all of us are safe.

We must quickly increase production of all safe and effective vaccines, including through technology transfer to manufacturers with untapped production potential and regional transfer hubs. The projected 2021 vaccine supply of 12 billion doses could be enough to give two vaccine doses to every adult in the world. However, there is no guarantee that these doses will be produced. Historically, vaccine manufacturers have fallen woefully short of their production targets, in part due to failure to sufficiently expand production and transfer technology, which has also increased vulnerability to other factors that hinder production.

We must increase distribution equity. Even if 12 billion doses are produced in 2021, this is unlikely to achieve global vaccination targets. Millions of extra doses may be necessary to counter vast inequities in vaccine access and distribution. We have already produced enough vaccine doses to cover 50% of the world's population, yet in some countries fewer than 1% of people have been vaccinated. Compensatory global mechanisms that distribute doses to low- and middle-income countries have fallen well short of their targets. Countries with high vaccination coverage must allow countries with low coverage to access existing vaccine supplies.

We must do a better job of planning and supporting rapid vaccine rollout. Countries must start fully honoring their promises of vaccine exports and donations. There must be transparency about forthcoming supply source and volume so that advanced planning for the timely delivery and rapid administration of promised doses is possible. We must shorten projected vaccination timelines; current estimates suggest it will take years to achieve sufficient COVID-19 vaccine coverage in Africa.

Global vaccine needs are increasing because of boosters. The potential emergence of vaccineresistant variants – which is more likely if we are slow to achieve vaccination coverage targets – could further increase vaccine needs by billions of doses. It has been nearly one year since the first COVID-19 vaccines were authorized for use. During this time, more people have died from COVID-19 than in the time before COVID-19 vaccines were available. Yet we have repeatedly squandered opportunities to better address supply shortages through technology transfer and the creation of additional production hubs. We must do better.

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