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CORONAVIRUS

How to vaccinate the world against covid-19

In the scramble for covid-19 vaccines richer countries, predictably, have secured stocks first. With the headache of distribution on top of procurement, how will the world reach the herd immunity levels needed to defeat the virus? **Chris Baraniuk** reports

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When Senjuti Saha, a scientist at the Child Health Research Foundation in Bangladesh, saw pictures of Western citizens receiving the first covid-19 vaccines last December, she felt a familiar pang. To her, it was like waiting in the economy class queue to board a plane while the first class passengers stroll on ahead. "By the time we board they're already seated, with champagne in their hand," she says.

There's a certain amount of injustice in how the initial vaccines have been rolled out, she argues: inequity, not just inequality. Millions of people have received doses in countries such as the UK, the US, Israel, and China, largely thanks to special contracts between governments and vaccine manufacturers. Meanwhile, most of the "global south"—Asia, Africa, Latin America, and the Pacific Islands—remains almost completely untouched by covid-19 vaccines. Many countries have guarantees of vaccine doses to cover only a small fraction of their population this year, far below what would be required to achieve herd immunity.

A race is now on to vaccinate as many people worldwide as possible in 2021.

Contracts and supplies

Manufacturers have already been churning out vaccine doses by the million, but there's still a long way to go before enough have been produced to cover the world's 7.7 billion population. Pfizer-BioNTech aims to make two billion doses this year¹—enough for a billion people to receive their two doses. AstraZeneca hopes this year to produce as many as three billion doses of its vaccine, developed with Oxford University.² Moderna, meanwhile, plans to deliver as many as a billion doses.³ This is before counting what manufacturers in China, India, and Russia may be able to deliver (see box, "Vaccine diplomacy").

In the initial scramble for a scarce resource, who gets their hands on the first stocks? This is where things get complicated: a complex mix of individual, country level deals, non-profit intervention, and other arrangements.

A key determining factor is pre-purchase agreements between national governments and the drug companies that produce vaccines. Analysis of these agreements published in *The BMJ* in December revealed that most vaccines had been snapped up by high income countries. ⁴ As a result the article authors estimated that, even if all 13 vaccine manufacturers

in their analysis were to achieve approval for their products, nearly a quarter of the world's population would still not have access to a vaccine until 2022.

Anthony So, lead author and professor of the practice at Johns Hopkins Bloomberg School of Public Health in Baltimore, says, "We obviously could have done a much better job in the first generation of vaccines in globally coordinating this."

Frederik Kristensen, deputy CEO at the Coalition for Epidemic Preparedness Innovations, says that the present situation is "far from ideal." The coalition—along with the World Health Organization and Gavi, the Vaccine Alliance—is part of a consortium called Covax, which aims to accelerate access to covid-19 vaccinations for low and middle income countries.

Covax has made progress in securing some key supplies. It has reserved two billion doses of various vaccine candidates for 2021,⁵ alongside manufacturing capacity at drug facilities in South Korea and Spain. Some of the manufacturing capacity reserved by the Coalition for Epidemic Preparedness Innovations will be used for producing doses of the vaccines already secured and announced by Covax (for example, SK Bioscience in South Korea is already producing AstraZeneca doses), while some further capacity will go towards additional doses, beyond the initial two billion, to be doled out by Covax. The first vaccine deliveries to some of the 92 low and middle income countries currently signed up to Covax should happen in early February, says Kristensen.

Covax may represent a significant slice of the vaccine rollout in many countries this year—but it's far from the whole pie. In Africa, for example, the consortium aims to supply 600 million doses, while the African Union has provisionally secured an additional 270 million. Given that the population of the African continent is more than 1.2 billion, this is still far from enough doses to achieve the 60-70% coverage required for herd immunity. And South Africa has revealed that, to procure stocks of the Indian version of the shot, it has had to pay more than double what the European Union paid for the Oxford-AstraZeneca vaccine. The construction of the shot, it has had to pay more than double what the European Union paid for the Oxford-AstraZeneca vaccine.

A different headache for every country

Countries will generally follow through with orders for vaccines only when a particular candidate has received regulatory approval or emergency use pre-approval. The timing of these approvals varies greatly among nations, and some countries may need to wait for WHO prequalification before Covax can deliver.

Unicef, which will distribute hundreds of tonnes of vaccines on behalf of Covax, can generally procure vaccines only once prequalification is achieved, says Benjamin Schreiber, deputy chief of Unicef's global immunisation programme. In the meantime, the charity has reserved half a billion syringes and put in place logistical arrangements so that it is ready to ship vaccines when required.

Elsewhere, a lack of transparency on clinical trial data for some vaccines may hold up distribution. Some countries may be offered vaccines that have never been trialled among their citizens, requiring a decision as to whether to insist on local trials but delay rollout—as India has done with Pfizer⁸—or to accept the risk.

Local considerations are also key to vaccine acceptance. Indonesia, which began a vaccine drive on 16 January using a vaccine produced by China's Sinovac, is dealing with citizens' doubts about whether foreign developed vaccines qualify as halal, as the vast majority of Indonesia's population is Muslim. The vaccine was declared halal by the country's top Muslim organisation on 8 January.

But supply, to some extent, determines "who" gets a jab. South Africa has yet to vaccinate any of its 58 million people but has 20 million doses on order. One and a half million of these, the Oxford-AstraZeneca vaccine, will be manufactured by the Serum Institute in India.

"We'll get small quantities rather than the quantities that we need, which means we'll have to prioritise who gets it in a rather focused and targeted way," says Yogan Pillay, deputy director general at South Africa's National Department of Health. Healthcare workers will be at the front of the queue. However, Pillay hopes that South Africa's reasonably well maintained road infrastructure will ensure smooth delivery of doses to vaccination centres.

Distribution dilemmas

Cesar Ugarte-Gil, an epidemiologist at Cayetano Heredia University in Lima, says that he's hopeful about the prospect of mass vaccination in Peru because of its strong history of administering vaccines. This includes dispatching doses to areas that are incredibly hard to reach, such as settlements accessible only by boat along the Amazon. A string of such villages can be reached via Iquitos, the largest city in the world without road access, although it does have an airstrip.

But many countries around the world lack the infrastructure or security to facilitate a mass vaccination programme without hiccups along the way. Some don't have the freezers required for storing the Pfizer-BioNTech and Moderna vaccines, which must be kept at -70°C or below. This has led countries such as India and Indonesia to consider vaccine candidates including Russia's Sputnik V, which when freeze dried, can be stored at temperatures more easily achievable in their tropical climates.

Bangladesh "has a vaccine coverage of more than 90%—it has the highest coverage in the world," says Saha, noting that South Asia has a track record of distributing (less temperamental) vaccines across a wide variety of terrains, from deserts to mountains. But she's sceptical about whether transport and storage requirements could be met for the Pfizer and Moderna vaccines.

In remote areas, vaccines that can be kept in regular fridges, or that don't require cold storage at all, are preferable. But some places have yet other barriers, notes Schreiber: conflict zones in countries such as Syria or Yemen may be hard to enter safely, and in some countries comprehensively vaccinating the residents of urban slums

can be particularly difficult. He adds, "These are often areas that are not recognised or not served by official systems in place."

That said, Unicef is working with countries to plan for vaccine distribution. This includes assisting several nations in their first adoption of electronic systems that track the locations of vaccine batches. Countries will use QR codes and barcode scanners linked to such systems to record when vaccines arrive in warehouses or are shipped to vaccination centres, Schreiber explains. Once established, the technology could help in future rollouts of vaccine or medicine.

Practice may make perfect. India has held a series of "dry run" drills—trial vaccine rollouts—to prepare hospitals and clinics for when the first doses arrive. And the country's experience of running the world's largest elections may help, suggests Anant Bhan, adjunct professor in the department of community medicine at Yenepoya University.

Altruism

Ultimately, the world has a fight on its hands in terms of bringing vaccines to more than seven billion people within the next 12 months, particularly as each country is desperate to get its own economy moving again.

Madhukar Pai, Canada research chair in translational epidemiology and global health at McGill University in Montreal, suggests that the inequity of covid-19 vaccine access has revealed a need to establish greater drug manufacturing capacity around the world. Anthony So adds that, going forward, wealthy countries should focus on bolstering the Covax consortium and working together with low and middle income countries to ensure that vaccines reach them as quickly as possible. The existing web of bilateral agreements has slowed this process down, he argues.

But there are already signs of altruism. As this year progresses, poorer countries may find themselves becoming the beneficiaries of richer nations' vaccine spending sprees. Canada, which has secured enough doses to vaccinate its population five times over, has expressed an interest in donating surplus supplies. And New Zealand, which has reserved enough doses for three times its own population, has already committed to giving some away to neighbouring Pacific islands. 10

Saha is cautiously optimistic that the global response to covid-19 will end up being fairer and more equitable. She says, "This is a time when we can set an example and show that it doesn't have to be this way."

Vaccine diplomacy

On Christmas Eve morning, at about 10:30 am local time, a plane with 300 000 doses of Russia's Sputnik V vaccine touched down in Buenos Aires after an 18 hour trip from Moscow. Nicknamed the "Flight of Hope," this delivery represented the first vaccines to arrive in Argentina. But the country is also hoping for access to the Oxford-AstraZeneca vaccine; it just hasn't been able to acquire it yet.

With the US and Europe focusing on securing enough stocks for their own populace, a gap has appeared. The scramble for vaccine stocks is the latest manifestation of international competition, with economic recovery, global leadership, and public health on the line. Russian authorities have even faced criticism at home after the Argentinian stock matched the same number that were earmarked for St Petersburg but were yet to be delivered.

Some nations around the world have found it easier to obtain orders for doses of Russia's Sputnik V or the vaccines produced by China's Sinovac and Sinopharm. Crucially, none has yet completed phase III trials—and the data that are available remain unpublished and sparse. Russia says

that its vaccine is 91% effective. Interim data show various efficacies among the Chinese vaccines: Sinovac's, for instance, achieved just 50.4% efficacy in a trial in Brazil. 11

That disappointing result led to the Brazilian government reaching out to India for stocks of its domestically developed Covaxin vaccine—also controversially approved for domestic use despite not completing phase III trials—as well as Covishield, the Indian version of the

Oxford-AstraZeneca vaccine produced under licence. ¹² India is also donating Covaxin shots to Bangladesh, Mauritius, the Philippines, and Myanmar, among others, as a gesture of good will.

Other governments have decided to approve some of these vaccines anyway and have even begun administering doses to the public. Indonesia has received three million doses of Sinovac from a total order of more than 125 million, ¹³ and vaccinations began on 16 January. Malaysia has booked 14 million doses of the same vaccine, ¹⁴ while the Philippines has ordered 25 million.

Other countries that have secured access to Chinese vaccines include Algeria, Cambodia, Serbia, and Turkey. Hungary approved Russia's vaccine for emergency use on 21 January, while Bosnia, fearing delays in EU deliveries, has reportedly ordered vaccines from both Russia and China.

Prioritisation

The World Health Organization recommends that countries begin by vaccinating the following three priority groups: frontline health and social care workers; people over 65; and people under 65 with underlying health conditions that put them at additional risk of death from covid-19. 15

Most countries are following this advice, although the Pacific archipelago of Palau, for example, is including key officials and decision makers in its early priority groups.

Indonesia reportedly intended to vaccinate 18-59 year olds after health workers, but it has now seemingly started with elderly people instead—although social media influencers are also being targeted in a bid to overcome vaccine hesitancy among the population. The president received his first dose live on national television, alongside the TV personality Raffi Ahmad, who has nearly 50 million Instagram followers.

Addendum: On 9 February 2021 we amended paragraph 3 of the "Distribution dilemmas" section to make clear that this refers to distribution in South Asia. not just Bangladesh.

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