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Challenges in the rollout of COVID-19 vaccines worldwide

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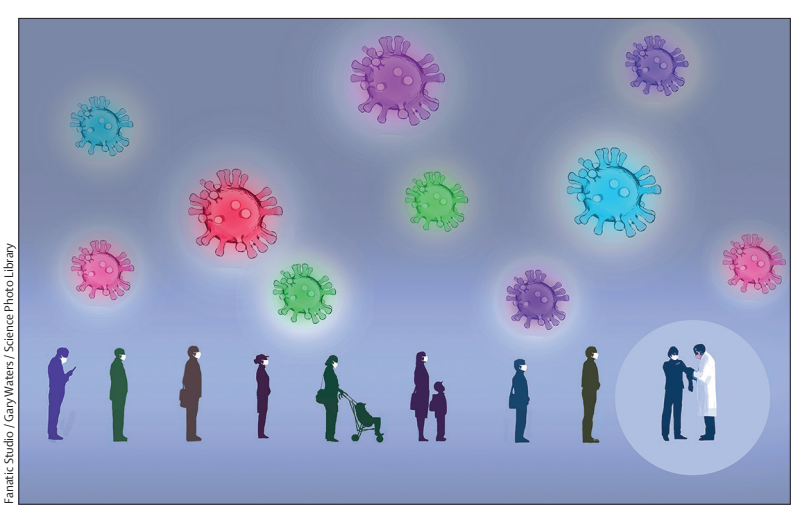
For the **Reuters' report** see https://www.reuters.com/article/health-coronavirus-eu-astrazeneca-idUSL1N2KT147

On Feb 24, 2021, 600 000 doses of the Oxford–AstraZeneca COVID-19 vaccine arrived in Ghana. 2 days later, 500 000 doses of the same vaccine landed in the Ivory Coast. The west African nations are the first countries to receive the product as part of the COVAX initiative, a joint endeavour between WHO, Gavi, and the Coalition for Epidemic Preparedness Innovations, which aims to ensure that the COVID-19 vaccines are equitably distributed around the world. Demand for the vaccines will far exceed supply this year and there are growing concerns that poorer countries will get left behind.

COVAX hopes to deliver more than 2 billion doses of the vaccines in 2021. At least 1·3 billion doses are earmarked for the 92 low-income and middle-income countries (LMICs) eligible for support under the terms of the pooled procurement mechanism that underpins the initiative. The virtual G7 meeting, held in February, 2021, saw several nations make sizeable financial commitments to COVAX. The USA has pledged US $4 billion over the next 2 years. Canada, France, Norway, and the UK have agreed to donate vaccines left over from their national campaigns.

All of which is highly encouraging. But even if everything goes according to plan, countries relying on COVAX alone cannot expect to vaccinate more than 20% of their population. As long as the supply of vaccines remains constrained, it is hard to see how the majority of LMICs will be able to start the kind of mass vaccination programmes that are gathering pace in the developed world. "There are seven billion people on the planet; the total manufacturing capacity for all the producers of the COVID-19 vaccines cannot come near to covering this number of people over the next few months", said Andrew Pollard, director of the Oxford Vaccine Group and chief investigator on the global trials of the Oxford-AstraZeneca COVID-19 vaccine.

Ashish Jha, Dean of the Brown University School of Public Health, reckons that most high-income countries will have completed their vaccination drives by the end of 2021. As of March 1, 2021, over 244 million people worldwide have been injected with at least one dose of a COVID-19 vaccine. The UK is preparing to start vaccination of 40–49 year olds; more than half of Israelis have received the first dose of the Pfizer–BioNTech vaccine; and 25 million Americans have had both doses of either the Pfizer–BioNTech or the Moderna vaccine. But these countries are not typical of the global situation.



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On Feb 10, 2021, WHO and UNICEF issued a joint statement pointing out that 10 nations accounted for more than three-quarters of the administered vaccines, while well over 100 countries, home to 2·5 billion people, had not administered a single dose. "This self-defeating strategy will cost lives and livelihoods, give the virus further opportunity to mutate and evade vaccines, and will undermine a global economic recovery", warned WHO and UNICEF.

"A lot of high-income countries are giving plenty of money to COVAX, but at the same time they are buying up much more vaccine than they can possibly use", adds Jha. Canada, for example, has secured 11 doses of vaccine per adult. If the European Union receives all the COVID-19 vaccines it has ordered, it will be able to cover a population twice its size. The same applies to the USA. A *Lancet* Health Policy report, on global access to COVID-19 vaccines, outlined how high-income countries comprising 16% of the world's population have placed orders amounting to more than 70% of the available doses in 2021 of five leading COVID-19 vaccine candidates. "New vaccines will mean little to individuals around the world if they are unable to get vaccinated in a timely manner", concluded the authors.

AstraZeneca has faced manufacturing problems. The company stipulated that it will be able to provide 3 billion doses of its vaccine this year. But according to a report by Reuters, it was only able to deliver 40 million of the 90 million doses it had committed to provide the European Union for the first quarter of 2021, and is likely to deliver less than half of the 180 million doses it has committed for the second quarter of the year.

The prospects are good for a few middle-income countries.

For more on the **efficacy of the Pfizer—BioNTech vaccine** see *N Engl J Med* 2021; published online February 17. DOI:10.1056/NEJMc2036242

For the **study by Pollard et al** see **Articles** *Lancet* 2021; published online Feb 19. https://doi.org/10.1016/S0140-6736(21)00432-3

Russia and China have their own COVID-19 vaccines, along with the manufacturing capacity to cover their populations. Cuba will start phase 3 trials of its vaccine in March. If successful, the Caribbean nation will be well-placed to vaccinate its 11 million citizens. The Serum Institute in Pune, India, has been licensed to produce the Oxford–AstraZeneca vaccine, though the domestic rollout is progressing slowly.

On Feb 27, 2021, the US Food and Drug Administration issued emergency authorisation for the Johnson & Johnson vaccine. The Novavax vaccine is expected to obtain regulatory approval soon; the Serum Institute has a licence to produce it. Researchers in Canada have calculated that a single dose of the Pfizer–BioNTech vaccine has an efficacy of 92·6%, which is roughly the same as that of a single dose of the Moderna vaccine. A single dose of the Oxford–AstraZeneca vaccine has an efficacy of 76% for up to 3 months after administration, according to a study co-authored by Pollard. In which case, countries with limited supplies of vaccines could reasonably choose to prioritise covering as many people as possible with a single dose, before starting to administer the second dose.

Olivier Wouters, Assistant Professor of Health Policy at the London School of Economics and Political Science, was lead author on *The Lancet* Health Policy paper on global access to COVID-19 vaccines. "The rate-determining step is the production of these vaccines", said Wouters. He thinks governments could do more to get companies to license more widely and accelerate production. Vaccine developers, for example, could partner with manufacturers in different parts of the world to produce the vaccines. For this to happen, there would have to be a transfer of not only intellectual property, but also expertise and data. "Governments and non-profits have invested heavily in the development and production of leading COVID-19 vaccines, in some cases billions of dollars, so they certainly have the leverage to encourage companies to share vaccine know-how", said Wouters. "There is untapped manufacturing capacity out there."

Jha notes that mRNA vaccines, such as the Pfizer–BioNTech and Moderna products, are extremely difficult to produce and require specific types of raw material that are currently in short supply. "Intellectual property is not the constraint here", he told *The Lancet Respiratory Medicine*.

Even if the vaccines were made available, building the capacity for mass campaigns is a huge task. The measles and polio campaigns of the past few decades will have provided valuable experience in some places. Nonetheless, dozens of countries, particularly in sub-Saharan Africa, do not conduct any adult immunisation campaigns. They would have to establish the infrastructure to call patients by priority group for the first dose of the COVID-19 vaccine and have them return at the right time for the second dose. The Johnson & Johnson vaccine would simplify matters since it only requires a single dose.

"We need sustainable funding mechanisms for governments to set up the COVID-19 vaccination programmes", stresses Wouters. "It is important that governments do not divert money from other essential health-care services; they have to continue the routine immunisation work and efforts towards establishing universal health care, otherwise the negative long-term effects on health and economic development may be severe."

The final major obstacle is likely to be vaccine hesitancy. On Feb 25, 2021, *The Guardian* reported that four in five doses of the Oxford–AstraZeneca vaccine that had been delivered to the European Union had not been administered. German Chancellor Angela Merkel has talked of the vaccine having an "acceptance problem". French President Emmanuel Macron hardly helped matters when he described the product as being "quasi-ineffective" in people older than 65 years. "We really do need clear and consistent messaging that these vaccines are highly protective and safe", said Pollard.

Heidi Larson is director of the Vaccine Confidence Project at the London School of Hygiene and Tropical Medicine. She points out that confidence levels fell in the summer of 2020, before starting to rise again towards the end of the year. The most recent data indicates worrying levels of scepticism in France, Lebanon, and Serbia, while the Vietnamese, Indians, and Chinese tend to be more trusting. Larson emphasises the importance of keeping lines of communication open. "You may think there is an ideological reason people are refusing a vaccine, and then it turns out to be something practical that can be fixed", she said.

The newness of the mRNA vaccines and the speed at which the COVID-19 vaccines were produced has caused anxiety in some quarters. "We still have not resolved the issues with Black and minority ethnic groups, who often have good historical reasons to be suspicious of the government and medical authorities", adds Larson. "There have been some successful trust-building efforts from within these communities, as well as religious and other community leaders getting themselves vaccinated and motivating others." Similar efforts will be needed in Africa to prepare for the mass vaccination campaigns. There is good news on that front. As *The Lancet Respiratory Medicine* went to press, the rollout of the COVID-19 vaccines had begun in Ghana and the Ivory Coast.

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