Equitable distribution of COVID-19 vaccines

The announcement of the first results of Phase 3 trials for vaccine candidates for COVID-19 opens questions on future global access to licensed vaccines. Talha Burki reports.

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If everything goes according to plan, November 2020 will be remembered as the beginning of the end of the COVID-19 pandemic. The past few weeks have seen a remarkable run of developments. Four manufacturers reported efficacy rates in excess of 90% for each of their candidate COVID-19 vaccines. As *The Lancet Infectious Diseases* went to press, the UK had started vaccinating priority groups. The US Food and Drug Administration (FDA) is expected to approve two COVID-19 vaccines in mid-December; the USA will probably start vaccinating healthcare workers before Christmas.

On Nov 9, Pfizer became the first pharmaceutical company to announce results of a phase 3 trial for a vaccine candidate. Their mRNA vaccine candidate, BNT162b2, that it has developed in partnership with BioNtech, has been studied in a phase 3 trial involving more than 43 000 participants. 170 cases of COVID-19 have been confirmed, 162 of which were in the placebo group. There were ten cases of severe disease, only one of which occurred in the intervention group. The vaccine showed an efficacy of 95%. The results were enough to convince the UK regulator to issue an emergency authorisation for the vaccine. But matters are complicated by the fact that BNT162b2 has to be maintained at –70°C, though once thawed it can be stored for up to 5 days in a conventional refrigerator.

The UK has ordered 40 million doses of the Pfizer-BioNtech vaccine, starting with 800 000 doses to kick off its vaccination programme. The FDA was due to discuss emergency authorisation on Dec 10. The USA has reserved 100 million doses of BNT162b2, with the option of purchasing a further 500 million doses. Pfizer says it will be able to produce up to 1·3 billion doses in 2021.

"The logistical requirements of the Pfizer-BioNtech vaccine are pretty challenging", commented Zoltán Kis, research associate in the Future Vaccine Manufacturing Hub at Imperial College London. "On its own, it is not a vaccine that can end the pandemic, because it will not be possible to establish an ultra-cold chain all over the world." In the context of developed countries, Kis reckons the product is best suited to large cities which have the capacity for storage and can deliver large numbers of people for vaccination within a few days. Cost could also prove problematic. COVAX, a joint initiative between Gavi, the Coalition for Epidemic Preparedness Innovations, and WHO, is tasked with ensuring the COVID-19 vaccines are distributed fairly and equitably. BNT162b2 is not part of the COVAX portfolio. Its initial price has been set at US $20 per dose.

Interim results for Sputnik V, the adenovirus vector vaccine developed by Russia's Gamaleya National Center of Epidemiology and Microbiology, indicated an efficacy rate of 92%. The findings, released on Nov 11, were based on 20 infections in the ongoing phase 3 study. On Dec 5, Russia began vaccinating essential workers with Sputnik V, which was approved by the Russian authorities in August, before the late stage trial had begun.

Moderna announced interim results for its vaccine candidate, mRNA-1273, on Nov 16. The product is being studied in a phase 3 trial of more than 30 000 volunteers. Of the first 95 cases of COVID-19, 90 were in the placebo group, meaning the vaccine had an efficacy rate of 94.5%. There were no severe cases of the disease among those who had received the vaccine. The FDA will look at mRNA-1273 on Dec 17. The USA has made an advanced purchase of 100 million doses. Moderna expects to have the capacity to produce somewhere between 500 million and 1 billion doses in 2021. mRNA-1273 requires a temperature of –20°C, which is far more manageable than BNT162b2. Moderna is not participating in COVAX, and the price of the vaccine is unclear.

Finally, on Nov 23, AstraZeneca released results for AZD1222, its viral vector vaccine. At the time of analysis, 11 636 people had received the vaccine as part of two late stage trials in Brazil and the UK. The overall efficacy was 70%. As with the other three candidates, AZD1222 is given in two doses. But an error meant that a subset of 2741 people actually received half a dose in their first shot of the vaccine. For these individuals, who ended up with 1·5 doses rather than the intended two, AZD1222 showed an efficacy of 90%, perhaps because the full schedule prompted the body to generate a stronger immune response to the viral vector.

AstraZeneca has joined COVAX so its vaccine is available at $4 per dose, and has pledged to permanently keep the price low for developing countries. The product can be stored at temperatures of 2–8°C; AstraZeneca reckons it will be able to produce up to 3 billion doses in 2021.

"We will certainly need more than one vaccine, and it would be really good if we could get some products which only require one dose", points out Anna Mouser, Vaccines Policy and Advocacy Lead at the Wellcome Trust. A range of vaccines will be especially important if it turns out that

immunity to SARS-CoV-2 is short-lived.

Countries will have to ensure that they have the infrastructure for mass immunisation campaigns. Those without experience in distributing the influenza vaccines must learn how to establish platforms for adult vaccination. Vaccine hesitancy will have to be overcome.

COVAX estimates that it will require $5 billion to fund its activities for 2021. 92 low and middle income countries are eligible for support from the organisation. "It would be a complete calamity if high-income countries were protected against this virus and low-income countries were not", said Liam Smeeth, professor of clinical epidemiology at the London School of Hygiene and Tropical Medicine. But he believes that there are promising early signs of a concerted international effort to ensure the vaccines get to those most in need, wherever they may be.

"The onus is on companies to do the right thing and make their vaccines available to COVAX and low-income nations at affordable prices", adds Mouser. She noted that high-income countries have made a succession of bilateral deals with vaccine manufacturers, creating a genuine risk that supplies for poorer nations could run short. "We really need to get behind multilateral efforts, and make sure that countries do not acquire more vaccines than they need", Mouser said. There is also the question of the order in which vaccines are despatched after they become available. "We still do not know which countries or organisations are at the front of the queue", explains Mouser. "If a company has promised doses to COVAX as well as to several individual nations, which deals will it service first? It could be a very difficult issue to navigate".

With global demand for COVID-19 vaccines almost certain to exceed supply for most of 2021, there is a long way to go before victory can be declared. Still, the recent reports are extremely encouraging, especially considering that the FDA had initially suggested 50% was a reasonable benchmark efficacy rate for a COVID-19 vaccine. "If you had asked me in February 2020, I would have said it would take a year or two before the vaccine arrived, and I would never have predicted 90% efficacy", said Smeeth.

Moreover, successful mRNA vaccines could have implications stretching far beyond COVID-19. "mRNA vaccine platforms are very powerful technologies and they can produce candidates against virtually any viral disease", said Kis. "Once you know the virus, you can very quickly design a vaccine, and you can use the same production process to make a very wide range of products". In which case, 2020 may not turn out to be such a loss after all.

Talha Burki

Infectious disease surveillance update

For more on **measles in Bolivia** see https://promedmail.org/promed-post/?id=7983214

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Measles in Bolivia

On Nov 27, Bolivia health officials confirmed the third case of measles virus occurring this year in the Santa Cruz region; measles cases were reported this year for the first time after 20 years. The most recent case was a 16-month-old who had attended a regional health centre with symptoms of fever and dehydration; after differential testing, the diagnosis of measles was confirmed. Three further suspected cases of measles have been identified following investigations. The first two cases of measles had been reported in April 2020, the first case was a pregnant woman who was a doctor in the Santa Cruz region and the second case was a child believed to have infected the doctor. Case finding activities are ongoing to identify possible cases and children who may not be fully vaccinated.

Rabies in Malaysia

On Dec 3, two cases of human rabies have been reported in Malaysia including one death bringing the reported total numbers of cases so far this year to eight. The first case was a 58-year-old man who was admitted into Sarawak General Hospital on Nov 19 and later died after his condition deteriorated on Nov 25. The second case was a 3-year-old boy who received post-exposure treatment immediately after exposure on Nov 2 and was discharged. The cases were reported from Sarawak where a rabies outbreak was declared. Since July 1, 2017, 30 cases have been reported including 28 deaths.

Salmonella in France

31 cases of salmonellosis including seven hospitalisations have been reported in France, having been identified by the National Reference Centre for Salmonella at the Institute Pasteur. The infection was caused by *Salmonella enterica* serotype Bovismorbificans, which affected young people as at least 17 children fell ill. The strain of salmonella was isolated between Sep 22 and Nov 14 from patients who live in seven different regions of the country. The patients all reported having eaten pork sausage from the same brand before their illness, bought from the same supermarket chain in several locations. The Directorate General for Food in France had previously made a link between eating cold dry meats from a company based in the Rhone region and falling ill. Food recalls have also been made for batches of this potentially contaminated meat in Belgium, Luxemburg, Poland, Slovenia and Portugal.

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