COVID-19 vaccines: the pandemic will not end overnight

"This is the weapon that is going to win the war", declared New York Governor Andrew Cuomo about severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine BNT162b2 (Pfizer/BioNTech), as its tentative rollout begins in the UK, the USA, and Canada. A great achievement for sure, but this first step in what will need to be a global mass immunisation programme will not immediately end the COVID-19 pandemic. Although control over the infection's most harmful effects is expected and limiting its spread can be hoped for, it will likely be a few years before the virus can be brought under control worldwide.

Ideally, multiple vaccines will be approved in most countries and we will have a detailed understanding of their efficacy, the duration of the immunity they induce, and their effect on viral transmission. At the time of writing, there have been efficacy reports from phase 3 trials of five vaccines (BNT162b2, mRNA-1273 [Moderna], ChAdOx1 nCoV-19 [University of Oxford and AstraZeneca], Sputnik V [Gamaleya Research Institute], and BBIBP-CorV [Sinopharm]), but the data to support these reports have only been published in peer-reviewed journals for BNT162b2 and ChAdOx1 nCoV-19, and only the former has been evaluated by drug regulatory authorities and approved for emergency or limited use in some countries. Despite the lack of official assessments, Russia has started distributing Sputnik V and the United Arab Emirates and Barhain have fully approved BBIBP-CorV, already widely distributed in China, despite uncertainties surrounding its efficacy and safety.

Even for the vaccines for which data are publicly available, many unknowns with a bearing on the effectiveness of immunisation programmes remain. How long does immunity last? By necessity, trials have collected data for just a few months, but only long-term, post-immunisation monitoring will clarify whether the initial vaccine doses are sufficient or further boosts are needed. Do any of the vaccines prevent viral transmission? Such data are only available from the ChAdOx1 nCoV-19 vaccine trial, but it was underpowered to generate firm conclusions. Still, data from participants who received a first half dose and a second full booster dose indicate fewer asymptomatic SARS-CoV-2 infections than in the control group, suggesting reduced transmission. Are the vaccines safe and efficacious in populations that have

not been included in trials and might be at increased risk of severe disesase, such as pregnant women? Only their inclusion in trials will answer this question. But in the meantime, should they be vaccinated (by weighing the risks of possible adverse reactions) or protected through shielding or herd immunity? The unknowns of how the vaccine affects transmission makes the possibility of achieving herd immunity through vaccination uncertain.

In addition to these unknowns, the world has never before needed to implement mass immunisation of its entire adult population. The challenges it entails range from financial, to logistic, to social and will affect how quickly and successfully the countries that have already started distributing a vaccine—all upper-middle-income or high-income countries—will be able to start controlling the disease. However, these countries should remember that the pandemic will really only be over when it is under control globally. International initiatives, most notably the COVAX Facility, are in place to support low-income and middle-income countries (LMICs) in establishing vaccination programmes and ensuring equitable access to vaccine doses. However, by Dec 16, 2020, COVAX had only secured about 400 million of the 2 billion doses needed to guarantee that 20% of the population of participating LMICs has access to a vaccine in 2021, while the EU, the UK, the USA, and Canada have already made deals with manufacturers to buy more than 50% of the doses expected to be available in 2021, despite these countries representing only 14% of the global population. AstraZeneca is the only manufacturer of those whose efficacy reports have been confirmed that has pledged to sell vaccine doses to LMICs at cost. There is hope that if the efficacies of Sputnik V and BBIBP-CorV are confirmed and these vaccines are approved, they will provide a new pool of doses for LMICs.

Vaccines will be instrumental in the control of COVID-19, but their global distribution will be challenging and their effect won't be immediate. As cases and deaths continue to rise across the world, the non-pharmaceutical interventions to constrain the spread of SARS-CoV-2 that the global population has by now become accustomed to will need to remain in place for a while longer.

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For more on the **COVAX Facility** see https://www.gavi.org/vaccineswork/covax-explained

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