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SARS-CoV-2 vaccines: fast track versus efficacy

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For **WHO's COVID-19 dashboard** see https://covid19.who.int

For more on **SARS-CoV-2 vaccines** see https://ourworldindata.org/covid-vaccinations

According to WHO, as of Feb 2, 2021, global cases of COVID-19 have surpassed 103 million, and deaths exceed 2·2 million. The word vaccine has become synonymous to the word solution, and vaccines against SARS-CoV-2—the virus that causes COVID-19—are the only solution to this pandemic, to avoid further mass casualties. Several frontrunner SARS-CoV-2 vaccines are already approved in 64 countries, surpassing the average pace of licensure and approval fivefold.[1] More than 100 million doses of a SARS-CoV-2 vaccine have now been administered, and although the effect of the global COVID-19 pandemic has been vast, there is still hesitation about vaccine safety. These concerns are irrevocably associated with the rapid pace of development, production, and approvals.

Approved SARS-CoV-2 vaccines are based on novel vaccine technologies. Nucleic acid vaccines (either RNA or DNA) rely on host cells to produce the desired protein vaccine antigen, instead of the antigen being purified and delivered directly, as in a traditional vaccine. Nucleic acid vaccine components are much easier to generate than are purified antigens, which has been an important element to fast-tracking SARS-CoV-2 vaccines. For example, a live-attenuated rotavirus vaccine took 16 years to be licensed,[2] and a recombinant protein meningococcal group B vaccine took 7 years to reach licensure.[3] Before the SARS-CoV-2 vaccines, no nucleic acid platforms were licensed for infectious diseases, and rapid progression of the SARS-CoV-2 vaccines was assisted by the successful use of this platform in personalised oncology vaccines.[4] With mRNA-based vaccines showing high neutralising titres,[5] similar to titres of vaccines developed using traditional vaccine technologies, it is clear that we are entering a new era of vaccine design.

Because of the devastating effects of the COVID-19 pandemic and the urgency to alleviate its impact, key vaccine development processes are still ongoing. Phase 4 trials (although not needed for licensure) have not been prioritised by the leading pharmaceutical companies: data for long-term safety and rare adverse reactions are, in effect, being gathered within the vaccinated population. The importance of phase 4 trials has been underlined by the potential link between vaccination and deaths of elderly individuals in Germany and Norway.[6] Additionally, vaccine-enhanced disease (induced by immunisation) could cause an aggravated form of COVID-19 and should be investigated. Vaccine-enhanced disease has been reported in vitro and in animal models of severe acute respiratory syndrome,[5] and it is important to investigate if COVID-19 could occur after SARS-CoV-2 vaccination in humans. To date, no cases of vaccine-enhanced disease have been reported in people who have received a SARS-CoV-2 vaccine.

An indirect effect on vaccine efficacy is the cost of production. The expense from advancing one successful vaccine candidate to phase 2 clinical trials could range from £1 billion to £6 billion.[7] For vaccines to have an impact on diminishing the COVID-19 pandemic, vaccinations need to be expedited without the high price tag. A no-cost or low-cost SARS-CoV-2 vaccine should be in place for low-income countries. Additional costs surface when suitable transportation and storage is necessary to guarantee vaccine stability. Some SARS-CoV-2 vaccines must be kept at temperatures of –20°C or –70°C, creating difficulties for low-income countries with no cold-chain distribution network. However, different SARS-CoV-2 vaccines that do not require sub-zero temperatures for storage could be offered as an alternative.

WHO listed vaccine hesitancy as one of the ten threats to global health in 2019.[8] As a result of this hesitation, the prevalence of some vaccine-preventable diseases (eg, measles) is rising.[9] The herd immunity threshold for SARS-CoV-2 is estimated at 60–83%.[10] Education of the general public by frequent communication with the scientific community is key to regain and retain trust and to ensure high vaccine uptake and herd immunity in the population.

Even the most technologically advanced and economically flourishing nations can succumb to an infectious disease pandemic. Time is always important. New manufacturing capabilities, reliable cold-chain distribution networks, and continuous research need to be in place to streamline development and maintain safety and efficacy of future vaccines. Unprecedented as the COVID-19 pandemic might have been, more variants of SARS-CoV-2 will enter circulation and zoonotic pathogens will arise. Fast-tracking vaccines could become the new norm.

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