



# Vaccine development in the SARS-CoV-2 pandemic: a balancing act on accuracy and speed

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Developing a safe and effective vaccine against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is crucial to ending the COVID-19 pandemic. But even during a global public health crisis, precautions and careful measures are necessary to ensure that new vaccines are safe for the population (Hotez et al. 2020).

Accelerated vaccine development is being guided and supported by regulatory agencies like the EMA and the FDA. The WHO has also released the target product profile (TPP) to guide the development of future vaccines. If the necessary safety and efficacy endpoints are met, the first licensed vaccine candidate should be available at the beginning of 2021. More than 320 different SARS-CoV-2 vaccine candidates are in development on a variety of vaccination platforms (Le et al. 2020; LSHTM 2020). Ten of these are currently being tested for efficacy trials in several thousands of people in high incidence countries.

Vaccine design has been hampered by the limited quality and quantity of immunological data on SARS-CoV-2 (Vabret et al. 2020). Researchers must identify the

immune correlates of protection and the durability of immune responses to create an effective vaccine. They need to determine also the risk–benefit ratio of vaccination in different populations (e.g., elderly immunocompromised person, recovered cases, and those as yet unexposed).

Researchers working to accelerate SARS-CoV-2 vaccination development have inferred answers to many of these questions based on data from past coronavirus epidemics (SARS-CoV and MERS-CoV) that caused severe respiratory syndromes (Ahmed et al. 2020; Vabret et al. 2020). But it is tricky to determine the portion of the virus that should be included in vaccine formulations to balance efficacy and safety. The SARS-CoV spike protein, for example, is highly immunogenic, but it may increase antibody-dependent enhancement that might exacerbate lung disease in people re-exposed to the virus (Hotez et al. 2020; Iwasaki and Yang 2020). Researchers do not know if the primary immune response against SARS-CoV-2 or its vaccine will exacerbate secondary immune response, so this question must be answered by clinical studies.

Efficacy and safety are not the only important criteria. Vaccine candidate production must also be scalable. Production of authorized vaccines from raw materials can take 6–36 months to come to market (Plotkin et al. 2017), and a delay can drastically increase the number of infected people and the toll that preventive measures take on a country's economy. Vaccine development and production must thus be expedited. Therefore, it is important to select the adequate vaccine platform to accelerate vaccine development.

Although traditional vaccines (inactivated, life attenuated, and subunit vaccines) are now safe and effective at a low cost per dose, they have several disadvantages during development: it is hard to scale up production processes, and setting up new manufacturing facilities takes several years to build. Thus, satisfying the global vaccine demand using traditional vaccine technologies could take two to three years. Newer versatile vaccination technologies (like vector-based vaccines and nucleic acids vaccines) may be

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faster and cost-efficient. For example, nucleic acids vaccination technologies may dramatically decrease development costs and production, making it easier to scale up during a pandemic (Kis et al. 2018). Validated manufacturing facilities stand ready to produce nucleic acid vaccines. However, we must be cautious about these technologies because no nucleic acid vaccines for humans are yet on the market.

Furthermore, there is a multitude of challenges facing routine vaccination. Who will get the vaccine, and how will the vaccination program be implemented? The disease has rapidly spread across the globe, with more than 37 million affected (Dong et al. 2020). The pandemic has resulted in substantial direct and indirect economic losses. Pharmaceutical companies have made enormous investments for vaccine development. With the tremendous demand and the limited supply for the first batch of vaccines, the basic principles of the market economy would be unethical to follow. High-income countries, which have high purchasing capacities, may gain better access to the vaccines, just as the current access to medical supplies and drugs for COVID-19. Similarly, within a country, a disparity in access might occur. The elderly population, who are considered mainly as economic dependents but face a higher risk of dying, would benefit more from the vaccines compared to the income earners who consist mostly of the middle-age group. Ideally, vaccination strategies should be focused first on the more vulnerable populations and those working on the frontlines of the healthcare system to lower the burden of the disease.

In the race for a vaccine, multiple products are needed to meet the enormous global demand. Speeding up the development of new vaccines against SARS-CoV-2 is important, but ensuring safety and efficacy in clinical trials. Future vaccines must ensure the scalability, an adequate price for sustainable investment, and equitable distribution of life-saving vaccines.

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