

Young Researcher Editorials (International Journal of Public Health)

Title

Vaccine Development in the SARS-CoV-2 Pandemic - A balancing act on accuracy and speed

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

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

12 Vaccine design has been hampered by the limited quality and quantity of immunological data on SARS-
13 CoV-2 (Vabret et al. 2020). Researchers must identify the immune correlates of protection and the
14 durability of immune responses to create an effective vaccine. They need to determine also the risk-benefit
15 ratio of vaccination in different populations (e.g., elderly immunocompromised person, recovered cases,
16 and those as yet unexposed).

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

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

30 Although traditional vaccines (inactivated, live attenuated and subunit vaccines) are now safe and effective
31 at a low cost per dose, they have several disadvantages during development: it is hard to scale up production
32 processes, and setting up new manufacturing facilities takes several years to build. Thus, satisfying the
33 global vaccine demand using traditional vaccine technologies could take two to three years. Newer versatile
34 vaccination technologies (like vector-based vaccines and nucleic acids vaccines) may be faster and cost-
35 efficient. For example, nucleic acids vaccination technologies may dramatically decrease development
36 costs and production, making it easier to scale up during a pandemic (Kis et al. 2018). Validated
37 manufacturing facilities stand ready to produce nucleic acid vaccines. However, we must be cautious about
38 these technologies because no nucleic acid vaccines for humans are yet on the market.

39 Furthermore, there is a multitude of challenges facing routine vaccination. Who will get the vaccine, and
40 how will the vaccination program be implemented? The disease has rapidly spread across the globe, with
41 more than 30 million affected (Dong et al. 2020). The pandemic has resulted in substantial direct and
42 indirect economic losses. Pharmaceutical companies have made enormous investments for vaccine
43 development. With the tremendous demand and the limited supply for the first batch of vaccines, the basic
44 principles of the market economy would be unethical to follow. High-income countries, which have high
45 purchasing capacities, may gain better access to the vaccines, just as the current access to medical supplies
46 and drugs for Covid-19. Similarly, within a country, a disparity in access might occur. The elderly
47 population, who are considered mainly as economic dependents but face a higher risk of dying, would
48 benefit more from the vaccines compared to the income earners who consist mostly of the middle-age
49 group. Ideally, vaccination strategies should be focused first on the more vulnerable populations and those
50 working on the frontlines of the healthcare system to lower the burden of the disease.

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

REFERENCES

- Ahmed SF, Quadeer AA, McKay MR (2020) Preliminary Identification of Potential Vaccine Targets for the COVID-19 Coronavirus (SARS-CoV-2) Based on SARS-CoV Immunological Studies. *Viruses* 12:254. <https://doi.org/10.3390/v12030254>
- Hotez PJ, Corry DB, Bottazzi ME (2020) COVID-19 vaccine design: the Janus face of immune enhancement. *Nat Rev Immunol* 20:347–348. <https://doi.org/10.1038/s41577-020-0323-4>
- Iwasaki A, Yang Y (2020) The potential danger of suboptimal antibody responses in COVID-19. *Nat Rev Immunol* 20:339–341. <https://doi.org/10.1038/s41577-020-0321-6>
- Kis Z, Shattock R, Shah N, Kontoravdi C (2018) Emerging Technologies for Low-Cost, Rapid Vaccine Manufacture. *Biotechnology Journal* 1800376. <https://doi.org/10.1002/biot.201800376>
- Le TT, Cramer JP, Chen R, Mayhew S (2020) Evolution of the COVID-19 vaccine development landscape. *Nat Rev Drug Discov* d41573-020-00151–8. <https://doi.org/10.1038/d41573-020-00151-8>
- LSHTM VC (2020) The London School of Hygiene & Tropical Medicine: COVID-19 vaccine development pipeline. https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/. Accessed 9 Sep 2020
- Plotkin S, Robinson JM, Cunningham G, et al (2017) The complexity and cost of vaccine manufacturing – An overview. *Vaccine* 35:4064–4071. <https://doi.org/10.1016/j.vaccine.2017.06.003>
- Vabret N, Britton GJ, Gruber C, et al (2020) Immunology of COVID-19: Current State of the Science. *Immunity* S1074761320301837. <https://doi.org/10.1016/j.immuni.2020.05.002>