Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Perspective

COVID-19 vaccines: Global challenges and prospects forum recommendations

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ABSTRACT

The **11th KAIMRC Annual Research Forum Themed "COVID-19 Vaccine: Global Challenges and Prospects Forum"** discussed COVID19 Vaccines. The Forum was a vital event as it provided a hub for leading COVID-19 vaccine scientists, regulators, developers, and distributors to learn about COVID-19 vaccines in development, make decisions about the best vaccines to use, and develop appropriate plans for global distribution and pricing. The COVID-19: Global Efforts for Development, Clinical Trials and Distribution Symposium brought together leading scientists, clinicians, pharma, decision makers, academic institutions and businesses to present and discuss the vaccines that are being currently developed for the COVID19. This event was held to shed light on these vaccines as many are at the late stage of Phase III clinical trials and ready to be marketed. This follows the confusion that few vaccines were produced and pushed into phase III without sharing all the necessary data preventing the scientific and clinical community to judge its efficacy and safety. This event allowed a discussion into the challenges in the distribution, pricing and accessibility of the vaccines. Moreover, the symposium discussed the importance to invest in Biotech-Pharma to combat and overcome any future health crisis. The discussion focused on Saudi Arabia leading initiatives as front runner in the field among G20 members.

Perspective

On November 4 and 5, 2020 the **11th Annual KAIMRC Global Forum** was organized as a G20 related event entitled **COVID-19 Vaccines: Global Challenges and Prospects**, https://globalcovid19vaccines.com. It was a vital event that provided a hub for leading COVID-19 scientists, regulators, pharmaceutical representative, funders and charities to learn about COVID-19 vaccines in development, discuss different vaccine candidates, make recommendations, highlight lessons learned and address appropriate plans for global distribution and pricing. Over 10,000 people from 94 countries attended the forum.

The leading COVID-19 vaccines presented use different technologies including: (a) Non-replicating viral vector based vaccines, ChAdOx1 nCoV-19/AZD1222 vaccine developed by Oxford-AstraZeneca (van Doremalen et al., 2020), the Sputnik V developed by the Russian Gamaleya Institute consisting of two components, a recombinant adenovirus type 26 (rAd26) vector and a recombinant adenovirus type 5 (rAd5) vector (Logunov et al., 2020), and the Ad26.COV2.S developed by the Center for Virology and Vaccine Research at Harvard Medical School in collaboration with Janssen Vaccines and Prevention BV, Leiden (Mercado et al., 2020). (b) Nucleic Acid, DNA- or RNA- based vaccines that include the mRNA-1273 vaccine that is being developed by Moderna (Anderson et al., 2020), and a self-amplifying (saRNA) vaccine termed VGHsa111 developed by Imperial College, London as well as another co-developed by Pfizer and BioNtech. An example of a DNA based vaccine against COVID19 is INO-4800, which is being developed by Inovio Pharmaceuticals Inc. (Smith et al., 2020). (c)

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Protein based vaccines, CoV RBD219-N1 Vaccine from Baylor College of Medicine, Texas that is based on a yeast-derived (Pichia pastoris) protein (Hotez and Bottazzi, 2020) and from Anhui Zhifei Longcom Biopharmaceutical Co. Ltd (Dai et al., 2020).

Representatives from the Bill & Melinda Gates Foundation, the Bring Hope Humanitarian Foundation (BHHF), and the Coalition for Epidemic Preparedness Innovations (CEPI) presented their plans for distributing the vaccines to people in need around the world including the low-income countries. They are also developing educational programs to train health workers in immunization procedures.

The COVID-19 vaccines: global challenges and prospects forum led to sixteen recommendations

1. **Diversify types of vaccines**

Diversify the types of vaccines to increase the ability to protect different populations and races with different genetic backgrounds that might develop variable immunity or sensitivity to one vaccine compared to another. Having many vaccines in the pipeline increases the chances of providing vaccines for over 7 billion people worldwide with affordable prices. Having different types of vaccines available will be important in the event that some vaccines work better in certain populations compared to others.

2. **Consider using boosters and adjuvants**

Some vaccines may create a strong immunity to COVID-19 that could last for months or years, while others may need a booster vaccine. A few vaccines such as protein based vaccines are developed using adjuvants to increase efficacy and reduce the amount of antigen used to decrease the cost (Forni and Mantovani, 2021; Cheryl Keech et al., 2020). The new generation of COVID-19 vaccines, such as those from Pfizer and Moderna, also use encapsulated LNPs. Even a short length of immunity might be long enough to break the chain of transmission since SARS-CoV-2 does not mutate or switch strain as fast as other viruses such as influenza and HIV. A typical SARS-CoV-2 virus accumulates only two single-letter mutations per month in its genome—a rate of change about half that of influenza and one-quarter that of HIV (Callaway, 2020). In this regard, the COVID-19 vaccines may be efficacious for a longer period and boosters may not be needed for the same virus strain. However, several important mutated SARS-CoV-2 strains have emerged (e.g., (a) B.1.177 with mutation A222V, (b) B.1.1.7 with mutation N501Y, (c) B.1.351 with mutation E484K, N501Y, K417N, (d) B.1.1.28, with either mutations: E484K, K417N/T, N501Y or only E484K and others that may arise) that are showing a higher rate of spreading and also escaping the antibodies raised against the original strain. This will require re-engineering of the vaccines to enable protection from these strains (Reardon, 2021). Depending on the results during the first year, scientists may recommend a booster vaccine. Evidence is also emerging from animal studies that combining antibodies with vaccines leads to improved immunity.

3. **Continue to study the immune response**

Continue to dissect the immune system response to SARS-CoV-2, and other viruses, to inform the discovery of new immunogenic or therapeutic targets for future vaccine and drug discovery and development. Much is still unknown about COVID-19 immunity: Would people who had previously been infected by other coronaviruses develop a better immunity and antibodies? Recently, studies have shown that those people who were infected with a certain virus would develop neutralizing antibodies and T cells that recognize the virus. Interestingly, scientists found that a number of individuals who have never tested positive for SARS-CoV-2 have antibodies that recognize the virus (Ju et al., 2020; Grifoni et al., 2020). Since the immune response to SARS-CoV-2 is still not fully understood, more systems immunology-based approaches are needed to define signatures that can be used to predict vaccine immunogenicity and efficacy, and delineate the molecular mechanisms driving protective immunity that are now being used in clinical trials. The immune responses in exposed or recovered people may also guide a better vaccination strategy as some reports showed that previously seropositive individuals may only require a single dose of a vaccine to mount strong immune responses that are similar to two doses in seronegative individuals (Krammer et al., 2021).

4. **Standardize immunoassays**

Although almost all of the vaccines that are being developed use the same antigen, the immunoassays employed to detect antibodies are different. Hence, we cannot compare data from different studies and vaccine efficacies. Therefore, standardization of immunoassays is a necessity and we commend the ongoing efforts by WHO, CEPI, and NIBSIC in this regard.

5. **Continue social distancing, using masks and sanitizers**

Scientists recommend that people continue to follow safety measures such as social distancing, wearing masks, and using sanitizers. These measures have proven to be efficacious in lowering the rate of disease transmission before a safe vaccine can be developed and distributed. Infected people are not necessarily protected from being infected a second time. Although less than 1% of patients who have recovered from COVID-19 get re-infected, those who do become re-infected can carry high levels of the virus in their nose and throat, even when they do not show symptoms (Hall et al., 2021).

6. **Set up global consortium equipped with Artificial Intelligence platform to follow and assess the short and long term safety and efficacy COVID19 vaccine profiles**

It is of high importance to strictly adhere to WHO recommendations to follow up on the short and long term safety and efficacy profiles of these vaccines because more than 200 vaccines are in development, several of them were approved in one year's time, and there are new technologies employed in a number of these vaccines (World Health Organization, 2021). Moreover, as the world population must all be vaccinated, the data generated on the safety and efficacy of these vaccines will be immense. Hence, it is highly recommended to set up a global consortium of leading vaccine experts equipped with Artificial Intelligence platforms to enable the analysis of the data to draw conclusions and give recommendations. The consortium must have working groups across the globe and especially in the developing world where vulnerable populations must be monitored closely after vaccination to protect them from any side effects.

7. **Improve alignment between regulators and vaccine developers**

Improving alignment between regulatory authorities and vaccine developers would accelerate vaccine development and subsequently the approval process. Regulators around the world have different criteria that they use to approve or reject a vaccine. Each regulator is sovereign and they may apply different rules to clinical trials and to assess safety and efficacy of the developed drug. These regulations are not internationally standardized, and there is no global organization to assist regulators in developing a universal standard. Some regulators are faster than others to develop familiarity with innovations and novel technologies such as mRNA vaccines. Worldwide, there is a disparity between regulators, with some authorities approving large scale conditional use of vaccines tested only in some hundreds of individuals while others require tens of thousands of subjects to have been dosed for emergency use authorization. Requirements for emergency use authorization should also be discussed with a view to greater harmonization. We recommend a global organization be established to help regulators align their processes, especially during pandemics.

8. **Increase transparency in vaccine development strategies**

Maintain and seek to improve transparency in vaccine development strategies and share data better to enhance public confidence. It took thousands of global vaccine researchers using different vaccine technologies for just one antigen, the spike protein, to design these vaccines. Since the outbreak of COVID-19, vaccine developers have successfully reduced vaccine development time from an average of almost a decade to less than one year without clear evidence that this has jeopardized safety.

This emphasizes the potential for funders and regulators to help speed up the vaccine development process as highlighted above in recommendations 7 and 14.

9. **Increase collaboration between industry and academia**

We must increase industry-academia collaborative efforts during pandemics to increase our chances of developing efficacious and safe vaccines and therapies more quickly. Of the current 47 vaccines in the pipeline, only 5 came from academia (Japan, China, Australia, and UK). Vaccine development is a diverse specialty, and as such, requires collaboration between multiple specialties, and academia is the natural base for multi-disciplinary research and development. We must encourage basic research and collaboration between multiple disciplines, and create a strategic fund to support collaborative research in vaccine development.

10. **Offer education and awareness to enhance public confidence in vaccines**

Develop educational programs in vaccination science to increase trust and decrease skepticism towards vaccination. Education in vaccine science and science-based therapies could increase engagement between the scientific community and the public and, consequently, build greater trust. We must improve engagement between scientists and governments so that scientists can support governments to be prepared and to avoid pandemics like COVID-19 in the future.

Anti-vaccination campaigns around the world continue to impede vaccination efforts. The anti-vaccination movement is based on unscientific ideas that vaccination can harm the body in diverse ways, including generating long lasting genetic changes in humans, and weakening the body's own defenses.

11. **Better not to label the vaccines based on the country of origin**

Humanity is looking for efficacious vaccines and therapies regardless of country of origin. During pandemics we must stop labeling vaccines and therapies based on country of origin. Since the emergence of COVID-19, scientists have raced against time in a collaborative manner to quickly disseminate their discoveries to find an efficacious cure and a vaccine against COVID-19. Drug development, manufacturing and access provision during a pandemic such as COVID-19 should be conducted regardless of race and religious belief and political affiliation, and scientific efforts should be led by those who are best able to deliver vaccines and provide solutions to save lives.

12. **Increase measures for fair vaccine accessibility and affordability**

Increase measures for fair vaccine accessibility and affordability to be able to vaccinate vulnerable populations in low-income countries. Vaccination of people in low income countries can be facilitated by developing vaccines that do not require cold chains. The companies and institutions producing these vaccines need to set up production sites in the developing world countries to enable easy access with affordable prices.

13. **Work with local leaders to increase trust in vaccines**

Work with local leaders to increase trust in vaccines that will be distributed in their communities. Another crucial issue is cultural perception, where critical attitudes of local landlords, warlords, and religious and tribal leaders towards vaccination must be taken into consideration. In the case of COVID-19, the skepticism and lack of trust towards a possible vaccine has been increased worldwide, especially in developing countries. It is also critical that there should be collaboration between vaccine developers, regulators, governments, manufacturers, vaccination financiers, and public private sector deliverers, on one side, and government departments and local leaders, as well as local logistical partners to build the trust required to optimize the complex vaccination system and achieve self-sufficiency.

14. **Increase investment in basic research in infectious diseases and vaccine development technologies**

Increase investment in basic research with a focus on infectious diseases to avoid another pandemic like COVID-19. The basic research that was performed for MERS and SARS has facilitated the rapid development of the vaccine candidates for COVID-19. Prior to the current pandemic, many scientists warned decision makers that a similar COVID-19 like pandemic might occur and the world should be prepared (Hughes, 2004). When COVID-19 emerged in December 2019 in China, the debate started about whether it was man-made. Virologists subsequently sequenced the SARS-CoV-2 genome and have rejected that theory, and concluded that the virus evolved naturally in wildlife (Paraskevis et al., 2020). As soon as the COVID-19 cases emerged, scientists worked tirelessly to discover if SARS-CoV-2 had similar symptoms to Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) and Middle East Respiratory Syndrome coronavirus (MERS-CoV). During the SARS and Zika outbreaks, scientists were given funding, but the funding abruptly stopped. Funding to study COVID-19 should continue even after a vaccine is developed.

In addition to prioritizing investment, it is crucial to fund innovative medical research in general and vaccine development, production and distribution in particular. During pandemics, we need to focus on vaccine technology that prioritizes safety, immunogenicity, efficacy and scalability.

15. **Enhance cold-chain capabilities in developing countries**

Enhance manufacturing and cold-chain supply capabilities in developing and low-income countries. Although there has been innovation in vaccine technologies such as RNA, innovation in manufacturing capacity has been more limited. Manufacturers should invest in scalable GMP facilities to facilitate the fast-track production of billions of doses when needed. More importantly there is an urgent need to address work force and infrastructural deficits through proper funding and training in routine immunization services in the developing world.

16. **Continue to host annual global forums**

Continue to host Annual Global Forums for top vaccine scientists from around the world to encourage good will, transparency, collaboration and sharing recommendations and ideas. For this conference, all lectures and presentations from this conference have been made public on YouTube: day1: https://www.youtube.com/watch?v=OawdEU0NZm0&feature=youtu.be, Day2: https://www.youtube.com/watch?v=EC5w_49J1rs

Conflict of interest

None declare.

Ethical approval

We declare we obtained all the ethical approval prior submitting this paper

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Declaration of Competing Interest

The authors report no declarations of interest.

References

Anderson EJ, Rouphael NG, Widge AT, et al. Safety and immunogenicity of SARS-CoV-2 mRNA-1273 vaccine in older adults. N Engl J Med 2020;1–12 NEJMoa2028436.

Callaway E. The coronavirus is mutating — does it matter?. Nature 2020;585:174–7.

Cheryl Keech C, Albert G, Cho I, et al. Phase 1-2 trial of a SARS-CoV-2 recombinant spike protein nanoparticle vaccine. Clin Trial N Engl J Med 2020;383:2320–32.

Dai L, Zheng T, Xu K, et al. A universal design of betacoronavirus vaccines against COVID-19, MERS, and SARS. Cell 2020;182:722–33.

Forni G, Mantovani A. COVID-19 vaccines: where we stand and challenges ahead. Cell Death Differ 2021;28:626–39.

Grifoni A, Weiskopf D, Ramirez SI, et al. Targets of T cell responses to SARS-CoV-2 coronavirus in humans with COVID-19 disease and unexposed individuals. Cell 2020;181:1489–501.

Hall V, Foulkes S, Charlett A, et al. Do antibody positive healthcare workers have lower SARS-CoV-2 infection rates than antibody negative healthcare workers? Large multi-centre prospective cohort study (the SIREN study), England: june to november 2020. medRxiv 2021;, doi:http://dx.doi.org/10.1101/2021.01.13.21249642 preprint.

Hotez PJ, Bottazzi ME. Developing a low-cost and accessible COVID-19 vaccine for global health. PLoS Negl Trop Dis 2020;14:e0008548.

Hughes JM. SARS: an emerging global microbial threat. Trans Am Clin Climatol Assoc 2004;115:361–72.

Ju B, Zhang Q, Ge J, et al. Human neutralizing antibodies elicited by SARS-CoV-2 infection. Nature 2020;584:115–9.

Krammer F, Srivastava K, the PARIS team, Simon V. Robust spike antibody responses and increased reactogenicity in seropositive individuals after a single dose of SARS-CoV-2 mRNA vaccine. medRxiv 2021;, doi:http://dx.doi.org/10.1101/2021.01.29.21250653 preprint.

Logunov DY, Dolzhikova IV, Zubkova OV, et al. Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia. Lancet 2020;396:887–97.

Mercado NB, Zahn R, Wegmann F, et al. Single-shot Ad26 vaccine protects against SARS-CoV-2 in rhesus macaques. Nature 2020;586:583–8.

Paraskevis D, Kostaki EG, Magiorkinis G, et al. Full-genome evolutionary analysis of the novel corona virus (2019-nCoV) rejects the hypothesis of emergence as a result of a recent recombination event. Infect Genet Evol 2020;79:104212.

Reardon S. The most worrying mutations in five emerging coronavirus variants. Sci Am 2021;29(January). https://www.scientificamerican.com/article/the-most-worrying-mutations-in-five-emerging-coronavirus-variants/.

Smith TRF, Patel A, Ramos S, et al. Immunogenicity of a DNA vaccine candidate for COVID-19. Nat Commun 2020;1:2601–13.

van Doremalen N, Lambe T, Spencer A, et al. ChAdOx1 nCoV-19 vaccine prevents SARS-CoV-2 pneumonia in rhesus macaques. Nature 2020;586:578–82.

World Health Organization. COVID-19 vaccines: safety surveillance manual, module: establishing surveillance systems in countries using COVID-19 vaccines. 2021. https://www.who.int/vaccine_safety/committee/Module_Establishing_surveillance_systems.pdf.