



Who is running faster, the virus or the vaccine?

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Vaccinating the world population against the COVID-19 faces both classical challenges such as vaccine transport and new challenges such as public trust. Here, we detail issues and potential solutions that will require a world collaboration of public authorities, industries and scientists from both physical and social sciences.

Lab-to-job

As the global coronavirus pandemic progresses into the tenth month, vaccination, one of the most important public health interventions invented by Dr. Edward Jenner (1749-1823) and pioneered by Professor Louis Pasteur (1822-1895), is once again coming under the spotlight (Fujiwara and Quinn 2020; Hanson et al. 2017; Hasselgren 2020 https://en.wikipedia.org/wiki/Louis_Pasteur). While progress on vaccine development has been achieved at an unprecedented speed, safety, efficacy, production capacity and universal accessibility of vaccines are major challenges in the forthcoming lab-to-job process (Callaway 2020; Wang et al. 2020a) (Fig. 1). In particular, transport and storage of vaccines present a significant obstacle, especially in developing countries and remote areas (Kartoglu et al. 2020). Who is running faster—the virus or the vaccine—will not only depend on *when* the vaccines become available but *where* and *how* we vaccinate a global population in a safe and most efficient manner. Even when the vaccine becomes available, the average public acceptance to take the COVID vaccine still amounts to only

67% in the USA (Malik et al. 2020). Therefore, scientists and public health authorities ought to pursue innovative and pragmatic solutions in the early planning stage to prepare for the upcoming actions.

Fair priority

Countries all around the world have started clinical trials for COVID-19 vaccines (Mahase 2020). To date, there have been more than 200 candidates registered with the World Health Organization (WHO), including nine currently in Phase 3 clinical trials (WHO 2020a). Communities with inadequate healthcare, vulnerable population groups, and areas with community spread of COVID-19 are in most need of vaccines (Singh 2020). While researchers are racing against time, it is of paramount importance to ensure the safety of the vaccines that are about to be used by a significant portion of the global population (Makoni 2020). The WHO reiterated that after passing all safety tests, vaccines would be distributed to both high-income and low-income countries through the COVAX project, the global vaccine alliance that aims to deliver about two billion doses of COVID-19 vaccines to 156 countries by the end of 2021 (WHO 2020b). To ensure fair distribution and prevent hoarding of COVID-19 vaccines, some researchers proposed a Fair Priority Model (Emanuel et al. 2020; Liu et al. 2020). Based on an ethical framework, the model aims to achieve the most effective allocation of vaccines by transcending economic, political and ethnic barriers.

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Bumpy road

Maintaining the potency of vaccines during their transport and storage is a prerequisite. Most human vaccines require low-temperature storage, where a specific range of temperatures must be kept to avoid any impairment on vaccine potency (Hanson et al. 2017; Matthias et al. 2007). Deviations from the required storage conditions may render

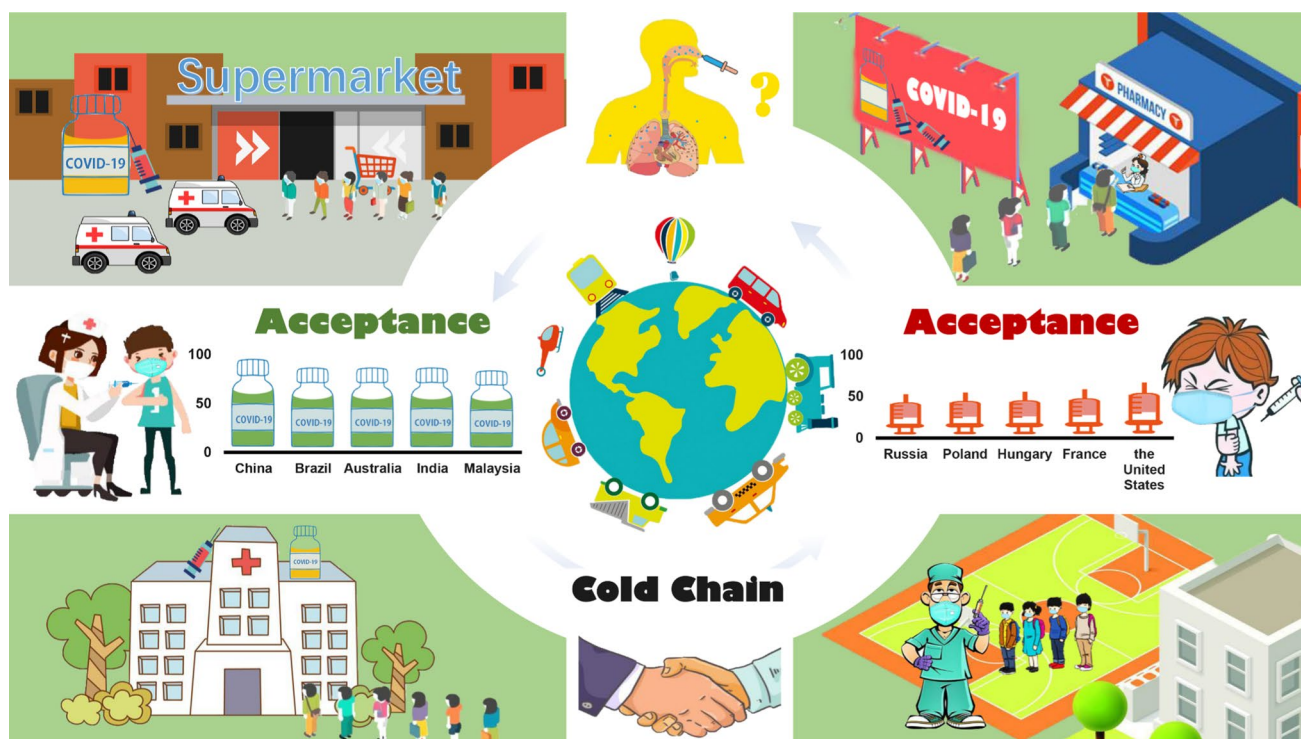


Fig. 1 Major challenges for vaccinating a global population for COVID-19, e.g., cold-chain logistics, vaccination sites, on-site staffing of medical staff and public acceptance after the successful development and production of safe and effective vaccines in sufficient quantities. Facing an ongoing pandemic, these challenges call for

innovative approaches, including the development of thermostable and self-administered nasal vaccines, and collaborative efforts from public health authorities, industries and researchers from the global scientific community

vaccines unusable, potentially putting users at greater risks of contracting illnesses (Kartoglu and Milstien 2014). Important lessons come from the mass vaccination of polio (Billah et al. 2017), Ebola (Chisholm et al. 2019; Davis et al. 2020) and influenza (Dubrovina et al. 2018). For instance, manufacturers firstly need to test the effectiveness of vaccines in the widest possible temperature ranges (Zipursky et al. 2011), and make their data accessible to allow enough time of preparation for the upcoming logistics. Thermostable vaccines, albeit difficult to develop, is one way to circumvent these issues (Kartoglu et al. 2020).

Heat-sensitive labels

Adjustments need to be made throughout the existing cold chain to accommodate the needs for distributing COVID-19 vaccines. Facilities along the cold chain should be coordinated, regardless of political boundaries, based on the storage requirements, quantities, and destinations of delivery, following the priority settings for vaccine allocation. Meanwhile, the WHO and local public health authorities should be authorized to inspect the facilities throughout the cold chain prior to and during vaccine deployment. The storage

conditions of vaccines should be kept as consistent as possible throughout the transport to avoid weak or broken links along the steps before vaccines reach the end users. Heat-sensitive thermochromic labels affixed on vaccine vials, also known as Vaccine Vial Monitors, can help reduce the likelihood of using vaccines that have been exposed to excessive heat (WHO 2011). By providing visual indication on the preservation of potency, these can be particularly useful for delivering vaccines to remote areas or places without intact cold chains.

Vaccination in parking lots and shopping malls

Since there is no experience to follow on vaccinating a global population in the midst of an ongoing pandemic, plenty of planning work will be needed with innovative approaches to avoid chaos or mis-management. Appropriate sites must be first selected for community-wide vaccination. The designated sites need to accommodate a large number of visitors, while preventing virus spread from crowd gathering (He and Han 2020) and reducing the pressure on transportation to control the cost of vaccination (Wang et al. 2020a).

Medical institutions such as hospitals, clinics and pharmacies are often considered first choices, given that medical professionals and cold-storage facilities are available on-site. However, healthcare facilities are already under tremendous pressure for diagnosing and treating COVID-19 patients. Alternatively, large grocery shops, community survival centers, shopping malls and airports may be used as alternative sites owing to their high foot traffic and large open spaces, e.g., parking lots. Using these sites can also reduce the need of commuting for people to receive vaccination, that is no need to make separate trips. All these facilities require mobilized medical staff and storage facilities, with the exception of grocery shops which often have ample cold-storage facilities on-site that may be adapted for the temporary storage of COVID-19 vaccines.

Where possible, centralized vaccination can achieve highly efficient vaccination within a short timeframe. Kindergarten, schools and colleges, including their students and employees, should be vaccinated in this manner given their regular and large number of daily attendees. When not in use, these facilities can also be used for community vaccination given the large open grounds often available at these facilities, e.g., sports fields and parking lots, and given their convenience of access for people living in the community. Other institutions may also receive centralized vaccination from mobile medical teams, such as nursing homes, retirement villages, prisons and correctional facilities. People who are at elevated risks or more vulnerable to COVID-19 infections, including healthcare workers, medical first responders, the elderly, pregnant women, children (Wang et al. 2020b), and those with chronic respiratory diseases or having frequent contact with people, could be given priority for receiving COVID-19 vaccinations. It is also important to include people living in remote locations, the elderly living alone, and those who are physically challenged or have limited mobility in future vaccination programs for COVID-19. Authorities may need to formulate intervention measures for these groups to ensure their vaccinations (Williams et al. 2020).

Mail-in vaccines

The immense scale of the COVID-19 vaccination program also calls for innovations on the administration route of the vaccines. Most human vaccines, including vaccines currently in the developmental stage for COVID-19, are administered subcutaneously. Such practices require the presence of trained medical staff to safely conduct the procedures for each person to be vaccinated. Under this scenario, the availability of trained staff on-site and the time required for completing the procedures for each person become the limiting factors when vaccinating a large group of people.

Alternatively, given that most COVID-19 vaccines currently in clinical trials require two separate doses (Weintraub 2020), self-administered vaccines would be highly desirable to reduce a lot of the need for medical staff and vaccination sites. For instance, intranasal administration has long been exploited for delivering drugs to the human respiratory tract, for both therapeutic and recreational purposes (Parhi 2020). Intranasal administration can provide both systemic and localized treatment for respiratory diseases, which can be easily administered by the users themselves (Mato 2019). Recent studies show potent immune response throughout the body with particularly high immunity in the nose and respiratory tract against SARS-CoV-2 via intranasal administration of spike proteins carried by harmless adenovirus (Feng et al. 2020; Hassan et al. 2020). On September 9, 2020, China approved the first Phase I human testing for a nasal spray vaccine, which became the first COVID-19 trial vaccine that does not require a needle injection (Deese 2020). Should thermostable COVID-19 vaccines also become a reality, it may even be possible to have “mail-in vaccines” designed for users’ self-administration, which can circumvent the logistic challenges as well as site constraints and on-site staffing for vaccinating the global population.

Public trust

Vaccinating a large and culturally diverse global population means that challenges are not only technical but arise also from the attitude of vaccine users. Researchers have indeed warned that vaccine hesitancy and crowd boycott could be the ultimate challenge in the fight against COVID-19 (Peretti-Watel et al. 2020). Moreover, a global survey on COVID-19 vaccine acceptance showed that in many countries, including those with very active COVID-19 infections, a significant portion of the population refused to vaccinate for COVID-19, including Russia (47%), Poland (45%), Hungary (44%), France (41%), and the USA (33%) (Ipsos 2020). Such a resistance appears to be due to skepticism on science and a lack of public trust in government authorities (Dror et al. 2020; Peretti-Watel et al. 2020). Other resistance factors include conspiracy theories, misinformation and the long-disproven link on vaccine and autism, which are still widely circulating in communities (Stefanelli and Rezza 2014; Zuk et al. 2019). In Europe, the anti-vaccine movement has a long history tracking back to the eighteenth’s century, which now owes much to the social-culture and political context. The current pandemic may have exacerbated this feeling due to the emotional distress and impaired access to normal healthcare (Dror et al. 2020). It is thus essential to promote the transparency of vaccine research and data in the course of development of COVID-19 vaccines, and

to maintain good communication with the public to avoid fear and mistrust.

Vaccine hesitancy may also derive from the public perception that there is a low risk following COVID-19 infection, particularly in countries with advanced universal healthcare. This trend is in agreement with the fact that countries with limited healthcare generally show high acceptance for the vaccine (Ipsos 2020), such as China (97%), Brazil (88%), and India (88%) where preventive treatment plays a pivotal role in their healthcare systems (Makoni 2020; Singh 2020). To encourage acceptance, public health authorities and members of the scientific community need to actively engage in communications with the public to ensure recognition of the risks associated with COVID-19 infections and the benefits of protection provided by the vaccine (Stefanelli and Rezza 2014; Wang et al. 2020c). For low-income groups, the cost of COVID-19 vaccination may be borne or subsidized to encourage acceptance.

Overall, the very act of vaccination does not bring an end to our fight against COVID-19, as several foreseeable challenges may persist in the post-vaccination era. For instance, given that most vaccines currently in development require two separate doses at least 3–4 weeks apart, there is still a risk of transmission during the interim period. Even after receiving the second dose, it may still take few days to few weeks for immunity to fully build up. Just-vaccinated and partially vaccinated individuals must therefore continue to follow the protocols on preventing the spread of COVID-19, including maintaining social distancing, wearing face coverings, minimizing exposure to enclosed public spaces or frequently touched surfaces in community environments. In addition, receiving one dose of the vaccine may give some individuals the perception of instant immunity against COVID-19 infection: these individuals may thus subsequently engage in high-transmission risk activities. Therefore, public health authorities and medical professionals should give clear instructions to raise awareness of such risks of non immunization immediately after receiving the vaccination or during the interim period of a multi-dose vaccination.

Mutations

We should also bear in mind that the novel coronavirus is an evolving organism with ongoing mutations (CDC 2020; Korber et al. 2020). Since August 24, 2020, there has been at least four confirmed cases of COVID-19 reinfections by different, possibly mutated SARS-CoV-2 strains in Hong Kong, the Netherlands, Belgium, and most recently, in the USA (Bowen 2020; To et al. 2020; Deutsch and Blenkinsop 2020). In the most recent case, the reinfection was confirmed only 48 days after the initial infection, and the

patient showed more severe symptoms after being infected with a different SARS-CoV-2 strain (Mole 2020). These newly emerged cases not only raised questions on the earlier hypothesis of acquired immunity to COVID-19, named “herd immunity”, but signals the need of possible re-design and continual development of COVID-19 vaccines as the pandemic continues in our communities.

Before scientists find a perfect cure for treating infections by the novel coronavirus, vaccinating the global population will be the keystone in the current battle against COVID-19 (Stern 2020; Williams et al. 2020). The numerous challenges in the lab-to-jab process not only present a daunting task, but also provide an unprecedented opportunity to collaborating and finding innovative solutions, on a global scale and across different disciplines to increase the preparedness of our communities for future pandemics (Paital and Agrawal 2020; Roviello and Roviello 2020; Sharma et al. 2020; Wang et al. 2020d). Since epidemics and pandemics may emerge in a not too distant future, these experiences will become an important part of the legacy of the COVID-19 era.

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