



## COMMENTARY

### The race to a COVID-19 vaccine: opportunities and challenges in development and distribution

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#### Abstract

The unprecedented toll of severe acute respiratory syndrome coronavirus 2, the virus responsible for coronavirus 2019 disease (COVID-19), jumpstarted the race towards the development and distribution of effective treatment and prevention options. With an urgent need to slow viral transmission, lessen disease severity, and reduce mortality, biopharmaceutical companies rapidly began investigating potential COVID-19 vaccinations. While typical vaccine development can take upwards of 10–15 years, COVID-19 vaccines were developed in less than a year after the identification of COVID-19. To accomplish this feat, clinical development, manufacturing scale-up and distribution are occurring in parallel for the four COVID-19 vaccine front-runners. This remarkable opportunity will forever change the drug development process and would not be possible without tremendous dedication from the public and private sectors, researchers, and clinical trial volunteers. However, many challenges still lie ahead. Comprehensive plans for equitable vaccine education, distribution, administration and

post-marketing surveillance must be implemented successfully to overcome vaccine hesitancy, supply-chain obstacles and healthcare provider shortages in an already overburdened healthcare system. We are moving forward at a remarkable pace but worldwide immunity through vaccination will take time to achieve. Thus, current prevention efforts of masking, hand hygiene and social distancing must remain in effect for the foreseeable future. We must remain diligent and not fatigue in our efforts. Ending the COVID-19 pandemic cannot rest on the promise of vaccination alone – it will require a continued, robust and multi-faceted approach to disease treatment and prevention.

**Keywords:** coronavirus, COVID-19, SARS-CoV-2, vaccine.

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#### Commentary

The effects of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus responsible for coronavirus 2019 disease (COVID-19), continue to affect the world, with more than 96 million people infected globally and approximately 2 million perishing from this devastating virus.<sup>1</sup> Although the medical community is learning more about this highly contagious virus, the most reliable methods for prevention still continue to be wearing a mask, employing proper hand hygiene and remaining socially distant. However, these methods are met with constant resistance from members of the public and political spheres; additionally, we must now also fight against 'COVID fatigue' as we begin 2021.

Although effective treatment options are still being developed and researched, each week is met with another over-the-

counter medication, supplement or prescription that holds promise with minimal or no data in reducing one's risk of acquiring COVID-19, causing people to buy these agents in mass quantities and taking these products without medical supervision. The first approved medication for the management of COVID-19, remdesivir,<sup>2</sup> has been met with conflicting data regarding its true efficacy and place in treatment. In addition, emergency use authorization (EUA) for monoclonal antibody therapy has quickly been adopted as another potential treatment option.<sup>3</sup> Furthermore, the quest to develop and distribute the first vaccines is well under way with a high degree of confidence placed in phase III clinical trials. Despite the ongoing research, there is an urgent need for treatment and prevention options for COVID-19.

The introduction of Operation Warp Speed (OWS) sounded the starting gun for the accelerated race towards the development,

manufacturing and distribution of 300 million initial doses of safe and effective COVID-19 vaccines in the United States by January 2021.<sup>4</sup> An undertaking like this is quite extensive but significant progress was made. Various pharmaceutical companies rapidly created experimental vaccines that are currently undergoing rigorous phase III randomized, placebo-controlled clinical trials, with some recently approved by the Food and Drug Administration (FDA),<sup>5,6</sup> the European Medicines Agency<sup>7</sup> and the United Kingdom.<sup>8</sup>

## Opportunities

### Vaccine development

The development of a novel vaccine is time consuming, resource and labour intensive, and costly. Prior to FDA approval, a vaccine must first be theorized and tested in a laboratory environment. The resulting product can then be evaluated in phase I clinical trials, which are focused on efficacy and conducted with a minimal number of participants (usually 20–100 healthy volunteers). Phase II clinical trials are the next step, in which safety becomes the primary focus and several hundred volunteers may be included. Phase III is the final step. A vaccine must demonstrate efficacy once again but on a much larger scale, oftentimes, incorporating thousands of participants. Thinking about each moving part that brings a vaccine to the public is incredible. Each step is equally important as the next and must be conducted with the utmost accuracy and integrity to achieve a common goal – the production of a safe, effective and easily mass-produced product to help mitigate disease.<sup>9</sup> Historically, the vaccine development and approval process has taken many years. In the face of a devastating COVID-19 pandemic, this is time we cannot afford.

On May 15, 2020, the US Department of Health & Human Services (DHHS) press office announced the direction and structure of OWS. This initiative is a partnership between various governmental agencies and the private companies developing COVID-19 vaccines and treatments, which streamlines efforts to deliver millions of doses of COVID-19 vaccines by early 2021. As a strategy, OWS is conducting the clinical development, manufacturing scale-up and distribution in parallel rather than in sequence, as is most traditionally done.<sup>4,10</sup> As explained by OWS Chief Advisor, Dr Moncef Slaoui, this allows industry developers to start preparing for phase II and III clinical trials while they file for an Investigational New Drug application to conduct a phase I study and as phase I studies are completed and the FDA deems the product safe, phase II and III studies can immediately commence.<sup>11</sup>

### COVID-19 vaccines

Since the genetic sequencing of the SARS-CoV-2 virus in January 2020, numerous vaccine developers targeted efforts towards the rapid development of a vaccine for the prevention of COVID-19. According to the World Health Organization (WHO), as of January 15, 2021, there were

64 vaccines undergoing clinical evaluation worldwide. There are an additional 173 candidates in preclinical evaluation at the time of writing. This is an impressive increase from the 26 and 139 vaccines undergoing clinical and preclinical evaluation, respectively, as of July 31, 2020, just under 6 months prior. There are currently four vaccines undergoing phase III clinical trials in the United States and an additional 18 in other countries around the world.<sup>12</sup>

While unconventional, this is not the first time the scientific community has been asked to develop a vaccine at rapid speed in the setting of an outbreak. Despite the need for speed, safety and efficacy cannot be compromised and the FDA has outlined guidance to address these areas of clinical development.<sup>13</sup> While safety and efficacy are absolute requirements, additional characteristics are also needed for an ideal vaccine. For example, a vaccine with longevity of protection would be preferred, such that patients would only be required to receive an initial single dose or series, unlike the annual influenza vaccine or tetanus vaccine requiring booster injections. An ideal candidate would also be easy to administer, such as orally or as an intramuscular injection, and stable under normal storage conditions. Of particular importance in the setting of a pandemic, an ideal vaccine must be able to be rapidly manufactured and distributed. Finally, an ideal vaccine would retain activity against variants that may emerge or be easily modified to protect against them.

Many vaccine platforms have proven successful throughout history against varying infections. However, in the setting of an outbreak, these platforms present many challenges. For example, live vaccines can elicit a strong immune response but take a long time to manufacture and carry the risk of reversion. On the other hand, inactivated vaccines may not produce a necessary robust immune response. Gene-based vaccines are an attractive platform in the setting of a pandemic given that the time-consuming and costly processes of culturing and fermenting are not necessary.<sup>14</sup>

Of the four vaccines undergoing phase III clinical trials in the United States for SARS-CoV-2, two are mRNA vaccines<sup>12</sup> and are the first RNA virus to get this designation.<sup>15</sup> The other two utilize a viral vector, adenovirus, to transport genetic information. Additional vaccine platforms under clinical investigation around the world include inactivated vaccines, protein subunit vaccines, DNA and virus-like particles.<sup>12</sup>

Two of the four vaccines in phase III clinical trials in the United States were given EUA by the FDA in December 2020: Moderna® (mRNA-1273) and BioNTech/Pfizer® (BNT162b).<sup>5,6</sup> Additionally, the Moderna® (mRNA-1273) vaccine was granted conditional marketing authorization by the European Medicines Agency and the BioNTech/Pfizer® (BNT162b) vaccine was approved in the United Kingdom.<sup>7,8</sup> The other two clinical trials, AstraZeneca® (ChAdOx1 nCoV-19) and Janssen® (Ad26.COV2.S), were temporarily paused due to safety concerns but have since resumed,<sup>16</sup> with the United Kingdom approving the AstraZeneca® (ChAdOx1 nCoV-19) vaccine in

December 2020.<sup>8</sup> All four vaccinations are administered as intramuscular injections. With the exception of the Janssen<sup>®</sup> candidate, which is a single injection, the three others require two doses given 3–4 weeks apart. Patients were randomized in a double-blinded fashion to receive either the vaccine candidate or placebo in all four trials. Target enrollment for each study is over 30,000 participants. The primary efficacy outcome is symptomatic COVID-19 that is virologically confirmed beginning 1–2 weeks after the final vaccination.<sup>17–20</sup>

Limited human data are available for these vaccines at present. The immune response is generally being evaluated by assessing the neutralizing virus-specific T cell response and antibodies, most commonly evaluating the comparison to a human convalescent sample. Phase I data for the Moderna<sup>®</sup> (mRNA-1273) vaccine demonstrated serum-neutralizing activity following a second 100 µg dose, including in patients aged 71 years and older.<sup>21</sup> Subsequently, an interim analysis of phase III data reported by an independent data and safety monitoring board (DSMB) noted a vaccine efficacy rate of 94%. This was based on 196 cases of symptomatic COVID-19; 185 in the placebo group and 5 in the vaccinated group. All 11 cases of severe COVID-19 occurred in the placebo group.<sup>22,23</sup>

Data published from phase I/II trials for the BioNTech/Pfizer<sup>®</sup> (BNT162b) vaccine suggest robust immunogenicity, with 1.9 to 4.6 times the neutralizing geometric mean titre 14 days after the second vaccine dose of 10 or 30 µg.<sup>24</sup> Similar findings of adequate neutralizing response were observed in a second study out of Germany of participants receiving 1, 10, 30 or 50 µg boosted doses or a single 60 µg dose.<sup>25</sup> Most recently, an interim analysis of phase III data reported by an independent DSMB noted a vaccine efficacy rate of 95% based on 170 cases of symptomatic COVID-19 in the placebo and vaccinated groups. No serious safety concerns were reported and, as required by the FDA, the EUA included safety data from a subset of patients that were followed for a median of 2 months following the second dose.<sup>26</sup>

Preliminary data suggest that the BioNTech/Pfizer<sup>®</sup> (BNT162b) and Moderna<sup>®</sup> (mRNA-1273) vaccines still protect against two of the SARS-CoV-2 variants first identified in England and South Africa.<sup>27</sup> Novel variants are appearing worldwide and are the latest challenge to vaccine developers. Much remains to be discovered before we understand just how well SARS-CoV-2 variants will be able to evade immunity generated from immunization or prior natural infection.

Phase I/II data for the AstraZeneca<sup>®</sup> (ChAdOx1 nCoV-19) vaccine demonstrated appropriate neutralizing antibody responses in most patients following a single dose and in all patients following a booster dose.<sup>28</sup> In a recently available interim analysis of combined phase III data from two dosing regimens, this candidate demonstrated an average efficacy of 70%. When given as a half dose followed by a full dose a month later, efficacy was 90%. However, efficacy was only 62% when two full doses were given a month apart. No serious safety events, hospitalizations or severe cases of COVID-19 were reported by

the independent DSMB in the vaccine group.<sup>29</sup> To date, no human studies have been published for the Janssen<sup>®</sup> (Ad26.COVS.2.S) vaccine candidate.

## The future of vaccine development

The COVID-19 pandemic has challenged not only how we conduct day-to-day activities to mitigate disease transmission but also the current vaccine development process, which has substantial implications for the development of future drug and vaccine products. We are witnessing a rapid paradigm shift as the scientific process and the human spirit are pushed beyond their furthest limits. While the average vaccine may take upwards of 10–15 years for development, emergency approval for a novel COVID-19 vaccine was achieved in under a year.<sup>30</sup>

As many scientists and scholars have alluded to, history often repeats itself.<sup>31</sup> Plagues and pandemics are synonymous with human history and have shaped the landscape in which we live.<sup>32</sup> The COVID-19 pandemic is surely no different. As we move through this crisis and look forward to the return of normalcy, or to a 'new normal', we must think ahead and use the knowledge gained to help prepare for the next pandemic, regardless of how close or far it may be into the future. Within the current COVID-19 vaccines under investigation, there are a multitude of modalities to achieve immunity, each has unique characteristics, which may confer unique benefits. The data accrued from these studies will help focus efforts for future novel viruses when considering the balance of safety and efficacy as well as the feasibility of mass production for population-wide distribution.

## Roles for healthcare professionals

Without an approved vaccine and without widespread access to approved therapies, there was an urgent need for trained healthcare professionals (HCPs) to care for COVID-19 patients due to the quick rise in cases that overwhelmed our healthcare systems early in the pandemic and again during the 'second wave'.<sup>33</sup> In an attempt to relieve pressure from overcrowded hospitals, field hospitals with varying degrees of success were opened around the country. As examples, Chicago's McCormick Place was converted to an alternate care facility with thousands of hospital beds for COVID-19 patients as were US Navy hospital ships docked off the coasts of New York and Los Angeles.<sup>34,35</sup> Additionally, COVID-19 hot-spots, such as New York and California, announced urgent job listings to recruit travel nurses and other HCPs in an effort to meet the massive demands of hospitals. There were also efforts to expand the health workforce against COVID-19 through transitioning retired and non-active HCPs back into clinical practice. Moreover, New York University and other colleges allowed early graduation of fourth-year medical students and nurses nearing graduation in Georgia were granted interim licenses to join the workforce.<sup>36</sup> Despite recruiting all qualified personnel to aid in the COVID-19 response, many healthcare systems are still overburdened.

Thus, the widespread immunity conferred by vaccination provides the promise of relief.

Apart from the shift in HCPs, there has also been a shift in patients obtaining medical care. A reluctance towards pursuing routine care has been anecdotally observed during the pandemic and reported in several studies.<sup>37–39</sup> Approximately 32% of US adults have avoided routine medical care and 12% have avoided urgent or emergent care due to fear of contracting COVID-19. Failure to seek proper and timely medical care has the potential to increase the morbidity and mortality associated with various medical conditions.<sup>40</sup> Healthcare avoidance also creates an environment for the re-emergence of vaccine-preventable diseases, with a notable decline in paediatric vaccine administration reported since the United States first declared a state of national emergency.<sup>41</sup>

New or expanded initiatives, including telehealth services, are helping increase access to care. During the first quarter of 2020 there was a reported 50% increase in telehealth visits in comparison to 2019.<sup>41</sup> To help remedy low vaccination rates, the US DHHS expanded access to childhood vaccines by granting pharmacists authority to order and administer vaccines to younger individuals, ranging from the age of 3 to 18 years old.<sup>42</sup> Once a COVID-19 vaccine is available, bundling services may be an effective approach to ensure COVID-19 vaccine uptake and normalize rates of routine vaccinations and care that cannot be performed through telehealth.

In addition to administering routine vaccinations to expanded age groups, pharmacists have also been involved in COVID-19 vaccine administration in clinical trials. Once initiatives to vaccinate the general public for COVID-19 take off, there will be a need for qualified HCPs in accessible settings to support the mass distribution and administration of vaccines. Thus, the US DHHS partnered with CVS<sup>TM</sup> and Walgreens<sup>TM</sup> pharmacies for vaccine distribution and authorized pharmacists to administer initial COVID-19 vaccines to prioritized, vulnerable populations such as residents of long-term care facilities.<sup>43,44</sup> Nonetheless, many challenges still exist for HCPs and patients worldwide regarding the successful implementation of a COVID-19 vaccine.

## Challenges

### Risks of fast-tracking

The accelerated development of clinical trials, manufacturing and distribution processes would not be possible without substantial investment by governments and the private industries and volunteers. Industries must take the enormous financial risk of product failure at both early or late phases, while volunteers must risk exposure to an investigational product. Many examples of investigational products with diverging phase II and III study results attest to this risk.<sup>45</sup> Consequently, only vaccine candidates with robust pre-clinical or early clinical data supporting their safety and efficacy were selected by OWS.<sup>11</sup> It is critical for the general public to know

that no corners are being cut, particularly with respect to safety and efficacy. The FDA has been clear on the type of safety and efficacy evidence that are legally required for licensure or EUA and has issued guidance to developers on how to meet these regulatory requirements with respect to COVID-19 vaccines.<sup>13</sup>

The FDA, independent DSMBs, and international regulatory agencies maintain full vigilance over ongoing COVID-19 vaccine studies. For example, based on pre-clinical data in animal models of SARS-CoV-2 and MERS-CoV, the FDA requested safety monitoring with respect to a COVID-19 vaccine-induced enhanced respiratory disease and provided recommendations on appropriate monitoring.<sup>13</sup> Similarly, AstraZeneca<sup>®</sup> and Janssen<sup>®</sup> agreed to temporarily pause their phase III studies for safety data review by the FDA and other regulatory agencies and were allowed to resume after they concluded that serious adverse events observed in two study participants could not be attributed to the study vaccines.<sup>46,47</sup>

Although a great deal of information about vaccine safety and efficacy is obtained during the development process, a significant amount of data are also obtained after its widespread use. Pre-licensure clinical trials (phases I–III) are only able to uncover the most common adverse events occurring soon after vaccine administration. Detecting more rare side-effects requires vaccine exposure in a much larger group of people and over a much longer period of time.<sup>48</sup> Systems such as the Vaccine Adverse Event Reporting System (VAERS) database, the Vaccine Safety Datalink (VSD) and Post-Licensure Rapid Immunization Safety Monitoring (PRISM) programmes aid in phase IV and post-licensure surveillance.<sup>49</sup> A strong surveillance infrastructure and significant co-ordination among these surveillance systems will be required, not just in the United States but globally. Additionally, because these systems rely on voluntary reporting, it will be important to educate both HCPs and the public on their use.

The FDA, regulatory agencies and the private industry must not neglect the basic principle in epidemiology of good public relations and communication, which include transparency, listening, communication planning and evaluation.<sup>50</sup> The Pew Research Center noted a significant decline in the number of surveyed adults in the United States who would probably or definitely get a COVID-19 vaccine from 72% in May to 51% in September 2020, with those who would definitely get the vaccine accounting for the change.<sup>51</sup> In this survey, the decrease in willingness to get the vaccine was consistent across political party affiliation, gender, race/ethnicity, age, and education level, with a majority of adults thinking that the vaccine will be used without full knowledge of its safety and efficacy. For those not planning to get the vaccine, concerns about side-effects or wanting to know more about its efficacy were identified in the survey as the main reasons. Media reports also show the growing mistrust that the public has on the FDA and the government and the rising anti-vaccination movement in the country.<sup>52</sup> Moreover, epidemiologists across the country have warned of the deterioration in the public's



trust on vaccines and public health authorities that could occur because of a misguided COVID-19 vaccination campaign.<sup>53</sup>

## Politicization of the vaccine

The COVID-19 pandemic has incited political divides in unprecedented ways. Moreover, the politicization of the COVID-19 vaccine trials has re-ignited widespread mistrust of the medical community among the general public, especially in marginalized populations. This distrust is often traced to the infamously tragic Tuskegee Syphilis Study<sup>54</sup> and is compounded by scepticism of vaccinations in general and by the escalating conflicts between the political and scientific spheres. Unfortunately, the Former President leaned on the promise of a COVID-19 vaccine to improve his electoral prospects in the race for re-election. This was evident by his repeated overstating of the possibility that a vaccine would be available before Americans cast their votes in the presidential election on November 3, 2020.<sup>55,56</sup> As a world leader, the US President affects public opinion and policy not only domestically but also abroad. Additionally, other world powers have sown the seeds of doubt by operating outside of scientific evidence. Jair Bolsonaro, the Brazilian President, dismissed COVID-19 vaccines as untrustworthy without providing any backing.<sup>57</sup> The Russian Ministry of Health formally approved an under-tested COVID-19 vaccine in early August.<sup>58</sup>

Fortunately, to combat rising concerns about COVID-19 vaccines in the face of political pressure, the FDA and biopharmaceutical companies stepped-up to reassure the public. Although initially delayed by the White House Budget Office,<sup>59</sup> the aforementioned FDA EUA guidance provides an ethical and scientific strategy for vaccine approval.<sup>60</sup> Unfortunately, Former President Trump continued his attempts to undermine the scientific process. Just hours after the guidance document was released, he called it “just another political hit job!” in a Tweet addressed to FDA Commissioner Stephen Hahn.<sup>61</sup> The CEOs of AstraZeneca®, BioNTech®, GlaxoSmithKline®, Johnson & Johnson®, Merck®, Moderna®, Novavax®, Pfizer® and Sanofi® came together to issue a historic pledge to the world in which they make a “united commitment to uphold the integrity of the scientific process.”<sup>62</sup> It is paramount that vaccines are not approved until they are deemed safe and effective. Premature authorization has the potential to fuel vaccine hesitancy, thus prolonging the pandemic and igniting disastrous consequences.

## Vaccine allocation, distribution and accessibility

The development and distribution of a safe and effective vaccine for COVID-19 is a primary focus around the globe and has required the development of a new infrastructure. It is imperative that anticipated obstacles are considered, including an inadequate supply, transport and storage, and patient adherence, especially if more than one dose is required.

Globally, the WHO developed a framework endorsed by the Strategic Advisory Group of Experts (SAGE) for the allocation and prioritization of COVID-19 vaccines between and within countries.<sup>63</sup>

In the United States, the determination of the optimal allocation of vaccines throughout the country is made by the Centers for Disease Control and Prevention (CDC) in collaboration with the Advisory Committee on Immunization Practices (ACIP). Recommendations for the COVID-19 vaccines were driven by multiple independent organizations, including Johns Hopkins Bloomberg School of Public Health, The National Academies of Sciences, Engineering, and Medicine, and the WHO<sup>64</sup> and considered epidemic trajectory models that predict the total averted burden with different targeted populations.<sup>65</sup> Initial reports from the ACIP and CDC recommend that HCPs be vaccinated starting with essential workers and continuing with patients with high-risk medical conditions and adults 65 years of age and older.<sup>66,67</sup> Subsequently, ACIP provided a more specific recommendation for group 1a (HCPs who are especially at risk for exposure and residents or employees of nursing homes and similar facilities) to be vaccinated first.<sup>68</sup> With national recommendations as a guide, many state and city governments in the United States, such as those of Illinois and Chicago, respectively, developed local guidelines to best meet their specific needs.<sup>69,70</sup>

From a global perspective, it is reasonable to anticipate that vaccine acquisition, distribution and administration in low- and middle-income countries may be difficult as is the case with many other vaccines.<sup>71</sup> Organizations such as Shot at Life work to increase vaccine access in low-income countries that remain plagued by diseases that have been eradicated in most areas of the world.<sup>72</sup> However, needing to build the supply of a newly developed COVID-19 vaccine adds a further challenge to the existing obstacles faced by low- and middle-income countries. To help combat this, COVAX was developed as one of the three pillars of the Access to COVID-19 Tools (ACT) Accelerator. Their focus is to guarantee equitable access to COVID-19 vaccines and treatments for all people worldwide, regardless of their country's wealth.<sup>73</sup> However, high-income countries have pre-ordered the majority of the world's COVID-19 vaccine doses. COVAX has only secured an estimated 700 million of the 2 billion vaccine doses they want to provide by the end of 2021. This may leave low- and middle-income COVAX member countries reliant on donations from high-income member countries and jeopardize equitable distribution.<sup>74</sup>

A prominent concern regarding COVID-19 vaccine distribution is transportation and storage, including temperature requirements. Notably, one of the vaccines currently in phase III trials in the United States, the BioNTech/Pfizer® (BNT162b) vaccine, requires storage at  $-70^{\circ}\text{C}$ .<sup>75</sup> In addition to challenges in maintaining the correct temperature during transport, the physical storage of the vaccines once at the desired location may pose a problem for many healthcare facilities.<sup>76</sup> Most

pharmacies, physicians' offices and other common vaccine delivery locations are not prepared with the appropriate equipment to store vaccines at this temperature, which means that they would have very limited time to administer stock once delivered.<sup>77,78</sup> This has led to concern that vaccines will need to be administered at large events and centralized locations, thereby reducing accessibility for patients.

Accessibility is further complicated by the fact that three of the four vaccines in phase III clinical trials in the United States require two doses. Prior data have shown incredibly low adherence rates to multi-dose vaccine series, particularly when administered to adult patients.<sup>79,80</sup> Non-traditional, easily accessible vaccination sites, such as pharmacies, can increase accessibility for patients and theoretically make it more likely that patients will return for their second injection.<sup>81,82</sup> Reduced geographical availability as well as potentially longer wait times may lead patients to be less likely to complete the entire vaccine series. Data regarding "some protection" after a single dose of the BioNTech/Pfizer® (BNT162b) vaccine candidate is emerging.<sup>83</sup> However, these data must be interpreted with caution, as initial and long-term protection are equally important.

Last but not least, the cost of COVID-19 vaccine products could prohibit fair worldwide accessibility. AstraZeneca® stated that

they will provide their ChAdOx1 nCoV-19 vaccine at ~US\$3–4 per dose and on a not-for-profit basis to low- and middle-income countries in perpetuity and for the duration of the pandemic to others. The Janssen® d26.COVID.S vaccine will also be provided on a not-for-profit basis during the pandemic, but it is priced at ~US\$10 per dose. Moderna's® mRNA-1273 and BioNTech/Pfizer's® BNT162b vaccines are priced at US\$25–37 and ~US\$19 per dose, respectively.<sup>83,84</sup>

## Conclusion

While the hope of widespread vaccination against SARS-CoV-2 appears to be on the horizon, it will likely be met with challenges as well as certain optimism that society can return to some sense of normalcy. At least for the foreseeable future, continued masking, hand hygiene and social distancing will be necessary to prevent viral transmission, regardless of location, socioeconomic status or political affiliation. In the United States and many other places around the world, some of us are living with the unfortunate results of 'COVID fatigue', relaxed social distancing requirements and a false sense of security as we attempt to survive the 'second wave' of COVID-19. To overcome this pandemic, we cannot rely on vaccination alone. We must continue a robust multi-faceted approach to disease treatment and prevention.

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