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Review

Global public health security and justice for vaccines and therapeutics in the COVID-19 pandemic

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ABSTRACT

A Lancet Commission for COVID-19 task force is shaping recommendations to achieve vaccine and therapeutics access, justice, and equity. This includes ensuring *safety and effectiveness* harmonized through robust systems of global pharmacovigilance and surveillance. G*lobal production* requires expanding support for development, manufacture, testing, and distribution of vaccines and therapeutics to low- and middle-income countries (LMICs). Global intellectual property rules must not stand in the way of research, production, technology transfer, or equitable access to essential health tools, and in context of pandemics to achieve increased manufacturing without discouraging innovation. *Global governance* around product quality requires channelling widely distributed vaccines through WHO prequalification (PQ)/emergency use listing (EUL) mechanisms and greater use of national regulatory authorities. A World Health Assembly (WHA) resolution would facilitate improvements and consistency in quality control and assurances. *Global health systems* require implementing steps to strengthen national systems for controlling COVID-19 and for influenza vaccinations for adults including pregnant and lactating women. *A collaborative research network* should strive to establish open access databases for bioinformatic analyses, together with programs directed at human capacity utilization and strengthening. *Combating anti-science* recognizes the urgency for countermeasures to

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vaccine development
global governance

address a global-wide disinformation movement dominating the internet and infiltrating parliaments and local governments.

1. Introduction

A global response is underway for the development, testing, and production of safe and effective vaccines to prevent COVID-19, together with new therapeutics for treatment or prophylaxis. The urgency for COVID-19 vaccines and therapeutics is clear in the face of the ongoing loss of human life, with estimates that COVID-19 will soon become the leading infectious cause of mortality [1] in low- and middle-income countries (LMICs)[2]. We need safe, effective, affordable, and available vaccines and treatments that will reduce the severity of illness, save lives, and reduce or halt virus transmission worldwide to levels that will sufficiently ease the pressure on strained health systems, which are impacting non-COVID-19 health support [3].

Beyond the health and cost-saving benefits of COVID-19 vaccines and therapeutics, investments in these interventions yield major societal benefits related to the global economy and security [3,4]. New estimates from the International Monetary Fund (IMF) indicate that more than 100 million people were thrown back into extreme poverty because of the direct and indirect effects of COVID-19, with the largest number in India, Nigeria, and DR Congo [5]. Through reductions in hospitalization and requirements for non-pharmaceutical interventions (NPIs), effective COVID-19 vaccines and therapeutics could help restore progress on sustainable development goals (SDGs) and overwhelmed health systems severely impacted by COVID-19 and return vulnerable populations to previous favourable economic trajectories.

1.1. Overview of global governance during the COVID-19 pandemic

The current COVID-19 vaccine and therapeutics development, production, and deployment ecosystem is global, complex and heterogenous. On the development side, vaccine technologies based on mRNA, adenoviral vectors, nanoparticles, or other approaches, are now under evaluation by research institutes, biotechnology and/or multinational pharmaceutical companies (MNCs). Similar evaluations are occurring with innovative monoclonal antibodies and new chemical entities (NCEs) such as molnupiravir [6], leading to new treatments and prophylaxis. New animal models adapted to SARS-CoV-2 were developed and better predict the efficacy of repurposed or new therapies [7]. Better understanding of the disease pathophysiology has helped to refine treatment strategies that must target different clinical objectives depending on the phase of the disease. In parallel, member organizations of the Developing Country Vaccine Manufacturers Network (DCVMN) develop and produce vaccines and in some cases, biologics that often employ traditional approaches and/or have partnered with MNCs to scale-out some or all aspects of the manufacturing continuum. Since created by the World Health Organization (WHO) and partners in April 2020, the Access to COVID-19 Tools-Accelerator (ACT-A) has served to coordinate the global efforts by supporting the development and deployment of diagnostics, treatments, and vaccines, and for health systems strengthening [8]. The ACT-A efforts also led to the development of a framework to promote the fair and equitable allocation of these tools [9].

COVID-19 Vaccines Global Access. The vaccine pillar of ACT-A, also known as COVID-19 Vaccines Global Access (COVAX), is led by Gavi, the Vaccine Alliance (Gavi), the Coalition for Epidemic Preparedness Innovations (CEPI), and WHO. It was established to accelerate access to, maximize equity in, and establish transparency when providing affordable COVID-19 vaccines to all countries, especially LMICs, in anticipation of the emergency authorization and release of safe and effective vaccines [10]. As components of COVAX, the Gavi-coordinated pooled procurement mechanism or COVAX Facility, intends to ensure fair and equitable access to vaccines using an allocation framework formulated by WHO, while the COVAX Advance Market Commitment (AMC) was established as the financing instrument aimed at supporting the participation of LMICs in the COVAX Facility [11]. For instance, CEPI signed agreements with Biofabri (Spain) and GC Pharma (Republic of Korea) to manufacture more than 1 billion doses of COVID-19 vaccines for distribution through the COVAX Facility [12].

ACT Accelerator Therapeutics Partnership. Given the low global vaccines coverage and the rapid emergence of variants of concern, therapeutics will remain essential to combat COVID-19. Led by UNITAID and Wellcome Trust, the ACT-A Therapeutics Partnership, which also includes the Bill & Melinda Gates Foundation, the Global Fund, and WHO, aspires and works to develop, manufacture, and globally distribute COVID-19 treatments to those in need. Expanding access to treatments at all stages of the diseases is urgently needed, whether for steroids and oxygen, repurposed drugs, new chemical entities (NCEs), or monoclonal antibodies [13]. This strategy includes identifying treatments to be tested in multinational platform trials such as ANTICOV, an 'adaptive platform trial' in Africa in mild-to-moderate COVID-19 patients or other clinical trials [9]. ACT-A's goals include the ability to shorten the time from development to availability via its access workstream while enhancing collaboration and coordination. This pillar seeks investment collaborations to assess candidates, test, validate and repurpose already approved therapies, and compile scientific evidence via coordinated clinical trials. Ultimately, regulation, production capacity, pricing, and adequacy for deployment in all countries and all settings are critical to ensure global availability and equitable distribution. In February 2021 the ACT-A Therapeutics pillar launched a COVID-19 Oxygen Emergency Taskforce in partnership with WHO due to recognized global emergency of the insufficient access to oxygen in LMICs [11].

In summary, the objective of this review is to highlight the status of the COVID-19 pandemic through the lens of health equity and access. Specifically, we provide a list of recommendations requiring a combination of short-term (one-year) and mid-term (multi-year) actions. These actions encompass areas of knowledge sharing, health system strengthening, capacity building and training, global governance, and international diplomacy, which are urgently needed to achieve effective global COVID-19 vaccine and therapeutic security, justice, and equity [Table 1].

2. The platforms: vaccine and therapeutic technologies

The development of COVID-19 vaccines and therapeutics was built upon a foundation of largely publicly funded research and some private philanthropic support that began after the emergence of SARS in 2003. The open access disclosure of the complete sequence of SARS-CoV-2 on BioRxiv in January 2020 allowed the scientific community to rapidly initiate efforts to identify potential targets for new vaccines, diagnostics, and therapeutics.

Vaccines. Consistent with the long-standing promise that nucleic acid-based vaccines was a rapid development platform, the mRNA approach proved the quickest to bring an investigational vaccine to the clinic. Despite being a novel platform without any previously licensed vaccine products, mRNA vaccines advanced quickly through

Table 1
Task force one-year and multi-year recommendations.

Activities	One-year horizon	Multi-year horizon
Access and affordability	Achieve full funding for ACT-A and the COVAX Facility, with expanded funding for global childhood vaccinations through Gavi, the Vaccine Alliance, WHO, UNICEF, and other international agencies.	Establish and adopt an international treaty signed by all WHO member nations and states to promote international vaccine and therapeutics, quality, equity, and diplomacy, with plans to address this at a future UN General Assembly culminating in a World Health Assembly resolution.
	Establish a transparent and realistic portfolio of vaccines and therapeutics for global health, with the recognition that many may be unavailable for some LMICs due to cost, scalability, or the logistical cold chain challenges.	A mechanism must be established to fully embrace global financing to create a next-generation vaccine and therapeutic ecosystem for current and future pandemic threats.
Safety and effectiveness	Implement a robust system of global post-licensure (phase 4) pharmacovigilance and surveillance for safety and effectiveness.	Maintain and expand the robust system of global post-licensure (phase 4) pharmacovigilance and surveillance for safety and effectiveness of vaccines and therapeutics.
Global production	Support members of the DCVMN and other vaccine and therapeutics manufacturers from LMICs to scale-up production and test products developed or produced locally.	
Implement plans to assess global demands and produce sufficient COVID-19 vaccines for the world's LMICs.	Build, strengthen and expand capacity to access innovation for members of the DCVMN, especially for mRNA vaccine platforms and for the development of new therapeutics both NCEs and monoclonal antibodies to developers and manufacturers in LMICs.	
Quality	Strongly encourage organizations from Russia and China to work through WHO emergency use listing and prequalification mechanisms	Establish and adopt a World Health Assembly resolution/to promote international vaccine and therapeutics, quality, equity, and diplomacy, and with plans to address this at a future UN General Assembly and culminating in an international treaty.
	Expand the assessment of adenovirus-vectored vaccines or conventional vaccines such as WIVs or protein-based vaccines ensuring their review by "functional" national regulatory authority and/or through the WHO emergency use listing and prequalification processes.	
Allocation	Discourage processes through bilateral agreements to avoid vaccinationalism and replace them with successful global governance mechanisms.	Establish and adopt an international treaty signed by all WHO member nations and states to promote international vaccine and therapeutics, quality, equity, and diplomacy, with plans to address this at a future UN General Assembly culminating in a World Health Assembly resolution.
Global health systems	Achieve 60–80% vaccine coverage for global interruption of virus transmission including the need of completing step down studies in children and adolescents, initiating vaccinations for COVID-19, while in parallel launch "catch-up" vaccination campaigns for measles and other childhood illnesses.	Strengthen global systems for adult vaccination programs including vaccines indicated for use during pregnancy and lactation. Prepare and strengthen global systems for therapeutics.
Collaborative vaccine research	Establish and operationalize a new open access database derived from dozens of phase 3 trials conducted in 2020–21for bioinformatic analysis.	Maintain a new open access database derived from dozens of phase 3 trials conducted in 2020–21 for bioinformatic analysis.
	Establish a network of vaccine and therapeutic scientists for sharing best practices, with special emphasis on linking scientists with production and members of DCVMN and others	Maintain a network of vaccine and therapeutic scientists for sharing best practices, with special emphasis on linking scientists with vaccine production and members of DCVMN and others
Combating global anti-vaccine activities	Recognize and address the world's imminent threat from aggressive antivaccine and antiscience movement linked to both governmental and non-governmental organizations.	A UN interagency task force must be created that goes beyond the confines of WHO, Gavi, and health related agencies, recognizing the role for international trade and commerce, legal and business frameworks, an urgency to halt anti-science aggression.

clinical evaluation with subsequent large-scale deployment to the public in high-income countries (HICs) through an emergency authorization from regulatory bodies in the US, Canada, UK, and EC. However, the complexity of manufacture, lack of early technology transfer planning, difficult scale up of production, inherent stability challenges, and freezer chain distribution requirements have severely limited distribution of mRNA vaccines to LMICs. Two adenovirus-vectored vaccines from multinational companies have obtained emergency authorization through stringent regulatory authorities and WHO EUL. Both are being produced and distributed, at least in part, by members of the DCVMN. There are also several protein-based vaccines in late clinical development that will likely follow a regulatory pathway through WHO EUL and then WHO PQ [14].

This leaves COVAX with a substantial but still limited and vulnerable vaccine portfolio to address the pandemic in LMICs. Outside of COVAX, several additional COVID-19 vaccine candidates are in pivotal trials and under review by national regulatory authorities (NRAs). For instance, Whole Inactivated Virus (WIV) vaccines from India and China; adenovirus-based vaccines from China and Russia; and a protein subunit vaccine from China were granted emergency use approval from their local regulatory agencies prior to demonstration of safety and efficacy. All but the Chinese protein subunit vaccine have subsequently reported acceptable safety and efficacy and are available in the country of manufacture, and others, under emergency use approval. The WIV vaccines from China and the Russian adenovirus vaccines were extensively distributed through contractual or binational agreements that currently bypassed COVAX and WHO PQ. However, two Chinese WIV vaccines have just received WHO EUL [15], with the expectation that additional and productive discussions with COVAX are ongoing [16].

The vaccines released through EUA are showing high levels of protective efficacy against symptomatic illness caused by original SARS-CoV-2 strain(s). Empirically a 70% level of population coverage is necessary for herd protection against SARS-CoV-2, however major concerns remain of the performance of many of the COVID-19 vaccines against emerging SARS-CoV-2 'variants of concern' (VOCs). Evidence shows that at least one mRNA vaccine and two adenovirus vaccines induce strong protection against asymptomatic infection

[17], and may protect against at least severe disease caused by VOCs [18]. Vaccines should be further evaluated, because the level of protection may be influenced by vaccine efficacy, force of infection, impact of vaccines on transmission, and impact of VOCs [3,19]. Furthermore, effectiveness trials are needed to evaluate the vaccines in real world settings [20], as well as where in the absence of robust health care delivery, vaccines may be one of very few options for practical control of COVID-19 [21].

Major questions remain [22]. How durable is protection? How will long-term safety compare? All vaccines so far have limited durability information. How many doses of vaccines can be manufactured for deployment within the next year and will the logistical challenges of deploying vaccines requiring ultra-low temperature storage, or even refrigerated storage, complicate use? How protective is one dose of a two-dose series in the long term? How effective are vaccine regimens that combine different types of vaccines, be they the same or different vaccine platform technologies, to complete 2-dose series and/or provide for booster doses (in prime-boost approaches) to extend the duration or expand the breadth of protection [23], especially given global vaccine shortages? For global deployment, vaccines must be selected not only for safety and effectiveness, but practical realities that drive use – cold chain, logistical requirements including number of required injections, availability, price, and vaccine acceptance in different populations.

Therapeutics. To date the medical management of COVID-19 with therapeutics has demonstrated a positive impact on patients ill enough to require hospitalization. Some of these interventions include glucocorticoids (i.e., dexamethasone) in those with hypoxaemia, anticoagulants and other anti-thrombotic medications, antivirals, and antibody-based therapies [24–26]. In contrast, a WHO-sponsored "Solidarity Trial" found that additional interventions including remdesivir, hydroxychloroquine, lopinavir/ritonavir, and interferon, produced no clinical meaningful benefit [27]. Studies evaluating ivermectin and other interventions are in progress but to date no intervention has been recommended to treat early cases of COVID-19 and prevent progression to a more severe form of the infection. Symptomatic treatment has been used for early COVID-19 disease [28]. Dexamethasone and additional steroid use can prove harmful if given early in the course of disease in a patient with normal oxygen saturations, in addition to increasing risks of additional infections in patients with underlying comorbidities such as heart disease and diabetes [29]. The two major biologics employed for antibody-based therapies are either those directed at the virus spike protein or those that target host cytokines and other targets of the host inflammatory response (immunomodulators). Regarding the former, convalescent plasma is available in some low resource settings, whereas monoclonal antibodies are still mostly restricted to high-income countries (HICs) and their wide use limited by their IV administration and high prices. To date, access to anti-COVID-19 monoclonal antibodies represents one of the most glaring disparities between HICs and LMICs in the pandemic response. It is vital that systems exist to provide guidelines for safe use of therapeutics during different stages of COVID-19.

Of the interventions highlighted above, only a few are widely available in resource-limited settings and LMICs. They include dexamethasone, anticoagulants and convalescent plasma, in addition to symptomatic treatment with analgesics and inhalers as needed. Oxygen is also necessary in all areas affected by COVID-19 and is in short supply in many resource-limited settings. In August 2020, following an open public consultation, the WHO published a draft of the Target Product Profile (TPP) for therapeutics in hospitalized COVID-19 patients [30]. A second draft TPP for the treatment of non-hospitalized patients was published by the WHO in December 2020 describing the preferred and minimally acceptable profiles for therapeutic agents for outpatient therapy of mild COVID-19 [31]. Multiple gaps persist in COVID-19 therapeutics and require the attention of the global medical and scientific community. If and when those gaps are overcome, equitable access to COVID-19 therapeutics for people in resource-limited settings are and will remain a challenge. Some therapeutic agents were produced with a wide range in price in different countries directly limiting access and leading to illegal importation and use of unapproved drugs, often at exorbitant prices. Adequate availability of fit-for-purpose point-of-care diagnostics are also needed in low resource settings for appropriate COVID-19 case detection and, ideally, supporting approaches that bring testing and treating as close as possible to the primary health care and community level [22].

3. Strengthening health systems for COVID-19 vaccines and therapeutics

Immunization Programs. The COVAX Facility of the ACT-A is working to procure 2 billion doses of safe and effective, WHO EUL/PQ vaccines by the end of 2021 [32]. Two billion doses will provide only about 20% of the vaccine needed in COVAX-participating countries. Ultimately, more than 3 billion people live in the LMICs of Africa, Asia, and Latin America and will require 6 billion vaccine doses as soon as possible [16]. COVAX faces a major challenge procuring this volume of COVID-19 vaccine in a timely manner given the fierce competition amongst high-income countries for the limited supply of authorized vaccines available and the unwillingness, to date, of many of the originator companies to transfer their technology and know-how to enable large-scale production by multiple manufacturers, including in LMICs. Solutions must be envisaged in the very short-term to drastically scale-up the access to safe and effective vaccines globally, inclusive of populations of all ages (adults, adolescents and children) and without regard to which technology or the amount of know-how needed. In addition, there are other important challenges facing LMICs, and ultimately plans are required to produce at-scale the billions of doses required beyond current COVAX targets [16,22].

Depending either on insufficient financing or limited manufacturing capacities, LMICs have approached COVID-19 immunization programs differently. Some developed their immunization programs leveraging the systems used by the Expanded Programme on Immunization established in the 1970s, which focused on vaccine-preventable diseases in children. Others leveraged adult vaccination programs such as the those for the tetanus toxoid-containing vaccines for pregnant women or in some countries the seasonal influenza immunization programs [33]. However, many governments and technical leaders will need to take steps to strengthen adult COVID-19 immunization programs and identify resources to support the development of systems to deliver and monitor the use of COVID-19 vaccines, including strengthening surveillance systems. One suggestion has been to build COVID-19 immunizations on to seasonal flu vaccine campaigns where they exist, or vice versa [31,34,35].

Financing Mechanisms. Most LMICs have faced a significant decline in their gross domestic product (GDP) with reduced business activity and rising unemployment due to the disruptions from the COVID-19 pandemic. Government measures to control the pandemic, care for the many COVID-19 patients, mitigate severe economic hardship, and stimulate economic recovery have increased fiscal imbalances of already heavily indebted countries. Additional funding must be found to support essential research and development (R&D) for essential therapeutics (for COVID-19 and other priorities) and vaccines as well as mechanisms to ensure access as new interventions become available. Those countries that depend on tourism and business travelers are particularly hard hit. Serious consideration must be given by multinational agencies, financial institutions, and the wealthier countries towards a range of measures that could provide financial relief to highly indebted LMICs, beyond concerns about the future access to COVID-19 commodities. However, to ensure universal access to COVID-19 products, governments could rely on some of

the flexibilities offered from the World Trade Organization - Trade-Related Aspects of Intellectual Property Rights (WTO-TRIPS) [36] combined with investments in building biopharma/vaccine manufacturing infrastructure. However, we need to acknowledge that technology transfer, regulation, and construction of facilities to scale-out and -up the manufacture of biological products (like vaccines and monoclonal antibodies) have timelines that do not align with meeting the urgent COVID-19 pandemic needs in the short-term [37]. Other mechanisms could be used such as debt forgiveness or debt swaps, reduced interest on loans or write offs, extended moratorium periods for payment, long term, low interest loans and grants or a Fund related to COVID-19 vaccines and therapeutics. The World Bank (WB) and International Monetary Fund (IMF) need to lead an international initiative to address these concerns and mobilize tangible relief and support to those LMICs in need, because inaction will only further the impact on under-resourced health systems of LMICs, already strained by COVID-19. Some LMICs face special challenges including war, civil conflict, economic crises or natural disasters, forced migration, lack of government cooperation and implementation of mitigation strategies during the pandemic, healthcare systems collapse, huge refugee populations or populations with special needs or vulnerabilities. In the spirit of international solidarity, it is important to facilitate and support national efforts to access to vaccines, similar to the efforts in 2019 to vaccinate war-torn areas of Democratic Republic of Congo (DR Congo) against Ebola virus. Now that COVID-19 is accelerating in the DR Congo, such considerations are more than theoretical.

Cold Chain. By itself, the ultra-cold chain requirements of one of the newer mRNA vaccines is not an insurmountable hurdle outside of major cities where investment in freezers would be needed. However, a considerable investment of resources, including money and health staff, as well as time and effort would be required. For example, the first approved Ebola vaccine (ERVEBO) used widely to avert a catastrophe in DR Congo in 2019 also required setting up an ultra-cold chain for the main distribution point and multiple backup power generators [38]. A lesson learned is that if mRNA vaccines could be provided at large-scale, a freezer requirement is achievable. However, cold-chain logistics and scale-up production challenges suggest that unless these issues are resolved mRNA vaccines may have a limited role for the world's LMICs. As such, other vaccine platforms without complex cold-chain requirements should be encouraged to bridge the existing access gaps for these settings.

LMIC R&D capabilities. LMIC-led research needs promotion, especially for the capabilities needed to tackle COVID-19 and future pandemics [39]. The establishment of the Solidarity randomized controlled trial was an excellent initiative and more LMICs must be included in testing the clinical effectiveness of different therapeutic agents. Given the numerous COVID-19 vaccines under development, LMICs must also be supported to participate, if not lead, in future vaccine trials. Furthermore, considering that major pharmaceutical companies have already reserved vaccine production-related resources, securing raw materials required for vaccine technology transfer and manufacturing in LMICs should be addressed. Lastly, the need to accelerate education programs that will target development and mobilization of critical knowhow for vaccine production phases in those LMICs that need it should also be encouraged. The world's LMICs would benefit from technology hubs of scientific excellence related to the chemistry, manufacture, and control (CMC) for multiple vaccine technologies, including mRNA, adenovirus, and vesicular-stomatitis virus (VSV, used to produce the Ebola vaccine for DR Congo), vectors, and even conventional technology such as recombinant protein vaccines.

Regulatory Oversight and Pharmacovigilance. Regulatory authorities in many LMICs need to be strengthened and could benefit from a program of international collaboration as well as regional cooperation and coordination mechanisms. In Africa, the example of African Vaccine Regulatory Forum (AVAREF) illustrates what this model could be. Other similar examples should follow especially for Latin America and Southeast Asia. The introduction of COVID-19 vaccines in LMICs will also require improvements in pharmacovigilance in many of these countries [40]. It will be important to track the safety and effectiveness of different COVID-19 vaccines over time in a variety of populations and settings. Resources to implement effective pharmacovigilance need to be identified and preparation started now, as this is important for our understanding of safety and impact, but also critical for building and maintaining the confidence of society in our public health systems [41].

4. Global supply and capacity

Establishing and maintaining a global plan for COVID-19 vaccines and therapeutics is essential to resilience and sustainability in our world. For vaccines, the COVAX Facility is a valuable initiative, but many agencies including CEPI have warned that COVID-19 vaccines will not be available globally for everyone until 2022 or beyond [42]. Only 83 countries administered at least one dose of a COVID-19 vaccine in excess of 30% of its population, whereas vaccination rate remains below 30% in 133 countries, starkly highlighting the current state of vaccine inequity. The maps in Fig. 1 highlight this inequity, showing the share of people who received at least one dose of COVID-19 vaccine and the share of people fully vaccinated as of July 10, 2021.

The advance purchases from the higher-income countries may make it difficult for COVAX to achieve access and affordable prices for the lower-income countries. For instance, HICs could opt to donate excess vaccines to COVAX rather than starting a booster campaign for those already vaccinated. This could reduce transmission in LMICs also protecting HICs. COVAX, in turn, will have to make complicated decisions about allocation of vaccines for each country [43,44]. Members of the DCVMN have stepped in to produce COVID-19 vaccines including conventional technologies or have embarked on partnerships with multinationals for new technologies. Ultimately, there are insufficient vaccines available through donation mechanisms to meet the global demand. Therefore, a commitment to scale up, produce and deliver the additional billions of doses of COVID-19 vaccines currently required for LMICs should be a priority.

For therapeutics, monoclonal antibodies (mAb) have been shown to be effective in the treatment of COVID-19 in outpatient settings, with Eli Lilly and Regeneron issued emergency use authorizations from the US FDA [45–47]. Global access to monoclonal antibodies is still severely limited, and delivery infrastructure and cost constraints are formidable. Around 85% of the global population from LMICs do not have access to monoclonal antibodies. With the spread of variants of concern globally, it is also vital to understand the efficacy of the various monoclonal antibodies authorized for emergency use as well as the potential need to combine interventions. Ensuring equitable access requires supporting broader registration of antibody products across the globe, including investments in new technologies, establishing business models that enable different market approaches, investing in local manufacturing capacity and strengthening health system infrastructures to promote access. Several platform trials are ongoing including ANTICOV, TOGETHER, PRINCIPLE, ACTIV-6, COVERAGE, and could test new antivirals that treat and prevent severe progression, according to their specific study population.

The pandemic has generated impetus to accelerate the establishment of multiple new publicly owned manufacturing facilities worldwide and many manufacturing technology providers have generated solutions to allow easier installation and operation of vaccine and mAb production facilities [48–53]. The Canadian government is investing $126 million to build a new Good Manufacturing Practices (GMP) compliant Biologics Manufacturing Centre (BMC), in Montréal, which will support the manufacturing of COVID-19 vaccine candidates, accelerate the scale-up production, and prepare the country

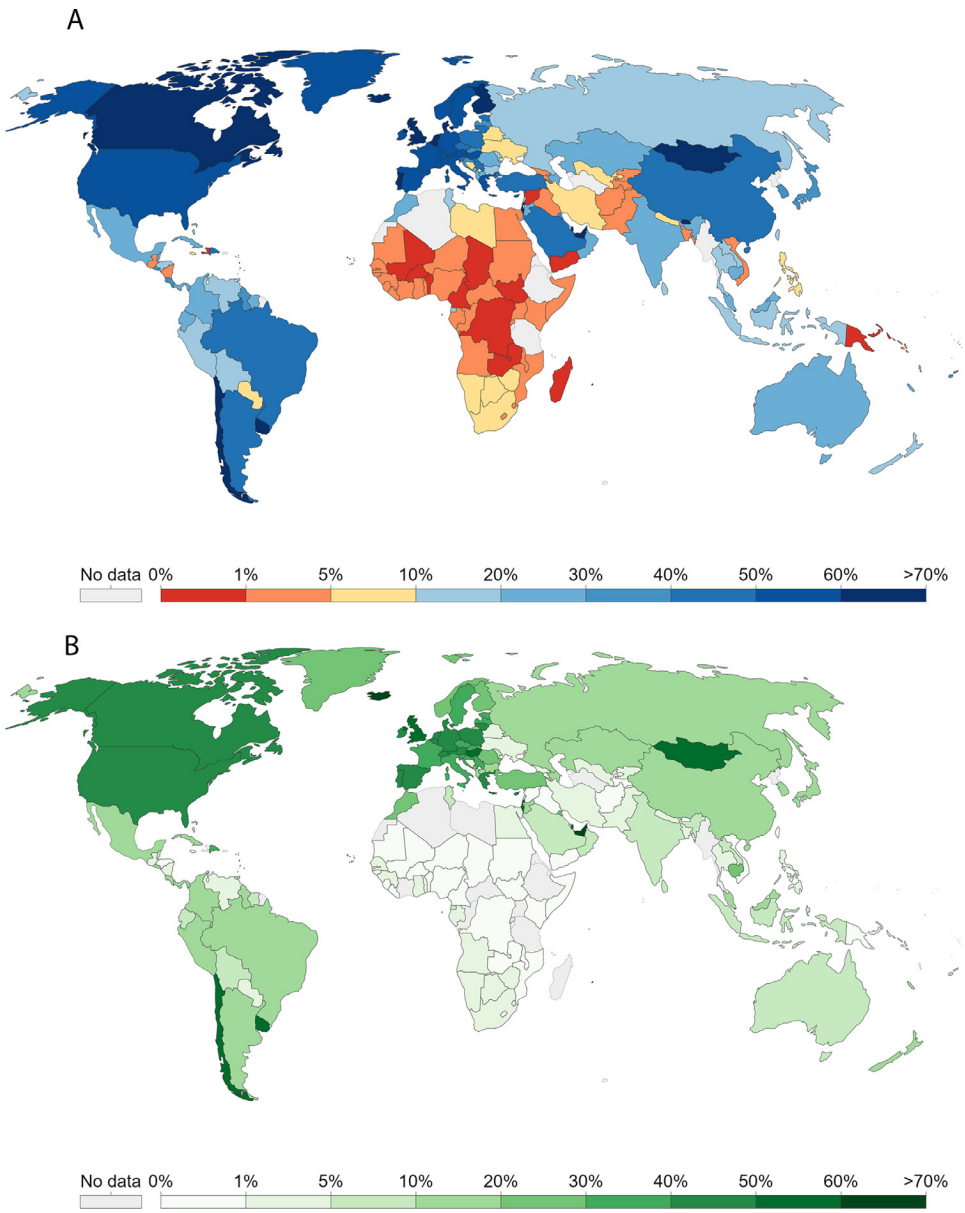

Fig. 1. (A) Share of people who received at least one dose of COVID-19 vaccine, July 10, 2021. Share of the total population that received at least one vaccine dose. This may not equal the share that are fully vaccinated if the vaccine requires two doses. (B) Share of the population fully vaccinated against COVID-19, July 10, 2021. Share of the total population that have received all doses prescribed by the vaccination protocol. This data is only available for countries which report the breakdown of doses administered by first and second doses. From Our World In Data data explorer: https://ourworldindata.org/coronavirus.

for future pandemics [54]. In the UK, the government will invest up to £93 million to build a new Vaccines Manufacturing and Innovation Centre (VMIC), which will be capable of producing large quantities of COVID-19 vaccines to serve the entire UK population [55]. In the US [56], public funding from Biomedical Advanced Research and Development Authority (BARDA) entered into technology investment agreement with Cytiva [57] and awarded US $628 million to Emergent BioSolutions and US $265 million to Texas A&M University (subcontracts the work to Fujifilm Diosynth Biotechnologies) to increase production capacity [58]. Saudi Arabia is establishing the Saudi Vaccine and Biomanufacturing center (SVBC), which will be located in the King Abdullah University of Science and Technology (KAUST) Research and Technology Park, sponsored by King Abdulaziz City of Science and Technology, and operated by SaudiVax [59]. ImmunityBio is working to build capacity in South Africa in collaboration with the DCVMN member, BioVac [60]. Along these lines, the Africa CDC is launching the Partnerships for African Vaccine Manufacturing (PAVM), an initiative that could also serve as a model for other regions in the world including Latin America and Southeast Asia. Finally, the addition of filling and finish facilities for both vaccines and mAbs worldwide can also unlock a bottleneck in manufacturing that will be faced when producing the huge volumes of promised biologics and vaccines to combat COVID-19 [61].

Overall, building new manufacturing plants may be the easier task. However, ensuring that a full trained workforce can operate the plant to deliver consistent, high quality products supported by fully functional national regulatory authorities is another. In the long run, the greater challenge, and one of the reasons for constraints in manufacturing capacity, is establishing a working model for sustaining these facilities in the interpandemic period. If vaccines are priced like commodities, there will not be sustainable “high cost” production at regional manufacturers.

Global health agencies, public sector entities, regulators, and biomanufacturing companies must work together to ensure equitable

and affordable global access to vaccines, efficacious antivirals, oxygen delivery, monoclonal antibodies, and other commonly used therapeutics such as steroids. COVAX and many countries purchasing through COVAX depend on vaccine pre-qualification (PQ) or a time-limited Emergency Use Listing Procedure (EUL) by WHO. For some LMICs having a WHO PQ or EUL facilitates the registration of products in-country. COVAX, vaccine developers, and LMICs vaccine financiers such as the WB should encourage countries to rely on WHO-PQ/EUL and incentivize vaccine sponsors/manufacturers to seek WHO-PQ/EUL.

5. Global justice and equity

The framework of health equity invokes fairness and justice. In the context of COVID-19 vaccines and therapeutics, these principles aspire to reduce or remove obstacles related to power, social status, income, gender, and race or ethnicity [62]. Regarding the distribution of new COVID-19 vaccines and therapeutics, multiple justice and equity issues apply. amongst wealthier G20 economies, people of colour and the poor have been shown to disproportionately suffer from COVID-19 as well as other poverty-related neglected diseases [63]. COVAX has made efforts to avoid a two-tiered system. The default path is that high-income countries receive priority access to vaccine innovations, as well as new NCEs and monoclonal antibodies, such as mRNA COVID-19 vaccines, remdesivir, or monoclonal antibodies. Safe and effective COVID-19 vaccines and therapeutics must also be available to LMICs, concurrently and efficiently, and not years later, especially to avoid the current situation of many low- and middle-income countries having less than 10% of their populations fully vaccinated.

Achieving both balance and equity also requires adequate and sustainable financing, enhanced multilateral vaccine diplomacy, and overcoming vaccine hesitancy and misinformation [16]. Still another threat includes a troubling erosion in vaccine confidence in Africa and the African diaspora (and other groups) due to structural racism, past atrocities, specific targeting by exploitative antivaccine organizations [64], and a complex array of additional factors as well as in the US, in Europe, in Brazil, targeting indigenous groups in the Amazon and in India where misinformation campaigns have also been rampant [65,66]. The COVID-19 vaccines and therapeutics ecosystem are historic for its visionary consideration of health equity. This did not happen by accident. Instead, it reflects extraordinary leadership from selected governments, partners, and champions from academia, NGOs, and civil societies.

6. Sustainability, collaboration and diplomacy

The COVAX Facility is a first global effort to ensure concurrent access to innovative and critical vaccine technology to all countries around the world. It must be strengthened and applied to other vaccines. For instance, is there any reason why, 15 years after approval, 60% of the world's children still do not receive rotavirus vaccine? Importantly, a framework to strengthen health care delivery of necessary COVID-19 diagnostic and therapeutic goods and to distribute them according to priority should be a global priority. Multilateral efforts to enhance health care delivery, strengthen vaccine and non-vaccine prevention, build human and physical capacity, strengthen regional manufacturing and regulatory capabilities, and enhance global R & D cooperation will be necessary to systematically address pandemic needs in the long-term and are fundamental to achieve health and vaccine security. There is urgency to expand vaccine diplomacy activities within foreign affairs and foreign policy missions across the world.

7. Bioinformatics and "big data"

Data sharing will be especially critical given the massive surge of bioinformatics and "big data" expected from dozens of large clinical trials, each deploying unique technologies [67], and massive post-licensure monitoring efforts. Information gained in terms of quantities and types of virus neutralizing antibodies, cellular responses, cytokines, chemokines, and clinical outcomes has the potential to revolutionize the area of systems vaccinology but also to better characterize many aspects of treatments response, resistance development, post-COVID-19 condition monitoring, as was successfully done for malaria with WWARN. As a result, we can now compare host inflammatory and immune responses to mRNA, adenovirus, inactivated virus, live virus, recombinant protein, nanoparticles at a scale never imaginable. Efforts to support standardization of data collection and sharing must be put in place and adequately funded.

8. Vaccine confidence

While overall vaccine confidence remains robust globally, albeit with local variability [68], the rapid development and emergency authorization of COVID-19 vaccines has triggered a significant increase in vaccine misinformation and fuelled already organized vaccine-opposition groups and activists to join with other groups protesting government control measures [56]. Some are connected to far-right political extremism and over the summer of 2020 they helped to ignite protests against COVID-19 prevention in several European capitals [62]. These anti-vaccine activities degrade vaccine security and demand broad-based international action. This means promoting and distributing adequate public messages [69] and building confidence around the efficacy and safety of vaccines and defusing or dismantling anti-vaccine propaganda and interference from state-led activities and entrenched antivaccine groups [70]. Ensuring global vaccine security must go beyond the traditional health sector and the community of vaccine scientists and public health experts. There is urgency to look at new mechanisms and options for countering a globalized antivaccine movement [71]. The COVID-19 pandemic has reminded us of the disruptive power of viruses. A new vaccine security framework embracing vaccine diplomacy, collaboration, confidence, and sustainable financing is paramount. To avoid the further spread of variants of concern globally, it is essential that vaccine hesitancy be addressed immediately.

9. Outstanding questions

The COVAX Facility has been innovative in its ability to promote health equity and access with innovation. It builds on an important precedent set when Gavi, WHO, Wellcome Trust, Gates Foundation and several G7 Governments partnered to accelerate a vesicular-stomatitis-virus-based Ebola vaccine for the DR Congo [72]. That vaccine prevented a humanitarian catastrophe and helped to stabilize Central Africa. Now through COVAX an earnest attempt is in progress to provide access for innovative vaccines to the world's LMICs. However, a stark reality is also emerging.

Ensure COVAX success. It remains an urgent priority to fully fund the COVAX Facility while establishing a transparent and realistic portfolio of vaccines and to assist in a transition to a broader mandate, beyond the original 20% of global COVID-19 vaccine requirement, to ensure that the remaining 80% of vaccine needs will more rapidly be allocated globally, prioritized by need and irrespective of means until vaccination is complete. It means that plans must be implemented to produce sufficient additional vaccine doses to meet these demands.

Support the development and access to new treatments. In parallel, expanding access to new therapeutics, including monoclonal antibodies and new chemical entities is essential together with support

of adaptive platform trials like ANTICOV, particularly those taking place in and led by researchers in LMICs to test repurposed and new drugs.

Over a longer time horizon, we must fully engage all Group of 20 (G20) nations to finance a next-generation ecosystem fully prepared for future pandemic threats. This includes the potential adoption of an international treaty on pandemic preparedness with plans to address at the World Health Assembly (WHA).

Building global governance around pandemics. With each pandemic in this 21st century our scientific community responded by committing resources and infrastructure towards fighting future communicable diseases. For example, following SARS, IHR 2005 was implemented, while a Global Health Security Agenda was established after the H1N1 influenza pandemic. After Ebola in 2014, global leaders convened at the World Economic Forum Annual Meeting in Davos to launch CEPI. As a result, with each pandemic our global governance to address disease outbreaks improve. We currently face a new and evolving ecosystem for pandemic threats. Coronaviruses were here before COVID-19 and will not go away. We have now seen three coronavirus outbreaks in this century and must build in a coronavirus vaccine and treatment preparedness and response infrastructure. This may also include mechanisms for producing a universal coronavirus vaccine and next generation pan-coronavirus therapeutics. Lastly, we also must face pressing issues related to implementation and reach of vaccination programs worldwide and continue to ensure that no program is left behind.

The sequential strengthening of multilateral efforts around pandemics makes an important point about preparedness. The stark and costly lessons of the COVID-19 pandemic should not be lost or repeated. We must gather those lessons, establish consensus around responses/mitigation, and establish the infrastructure and capabilities for effective future responses, enable governments and health care systems to build capacity and infrastructure for future pandemics, and building a more resilient response tomorrow from the crises of today.

10. Search strategy and selection criteria

The sources of the materials to generate this Review were identified by searches of MEDLINE, Current Contents, PubMed, and references from relevant articles using the search terms such as “COVID-19″, “vaccine”, and “therapeutics”.

Author contributions

All authors contributed equally.

PJH and MEB provided the first draft. CB, YBA, OE, JPF, SG, MG, MH, GK, DCK, JHK, BL, HL, DN, TS, SS, AW-S, SOS, NS-W, and PY drafted and edited assigned sections of the review and provided critical feedback, reference sources, and critical revisions for intellectual content and verified the information presented here.

PJH, MEB, JPF, JHK and BL managed the process of review and edits.

Declaration of Competing Interest

MEB and PJH are developers of a COVID-19 vaccine construct, which was licensed by Baylor College of Medicine to Biological E Ltd., a commercial vaccine manufacturer for scale up, production, testing and licensure. MG participates in one of eight SARS-CoV-2 vaccine development projects supported by The Scientific and Technological Research Council of Turkey (TÜBİTAK) since March 2020. SG is cofounder of Vaccitech and has a patent on ChAdOx1 nCoV-19 licensed to AstraZeneca. MH is Founder and Managing Director of SaudiVax. JPF, GK and DCK are members of the WHO SAGE Working Group on COVID-19 vaccines. GK is independent director appointed by the Wellcome Trust, MSD Wellcome Trust Hilleman Laboratories Private Limited and Vice Chair of the Board, Coalition of Epidemic Preparedness Innovations (CEPI). DCK reports grants from Bill and Melinda Gates Foundation (BMGF) and grants from CEPI, JHK reports personal fees from SK biosciences. HL reports grants and honoraria from GlaxoSmithKline for training talks and from Merck as a member of the Merck Vaccine Confidence Advisory Board, grants from J&J outside the submitted work. AWS serves as Consultant to WHO. The views presented here reflect her views and not necessarily those of WHO. TS reports grants from National Institute of Allergy and Infectious Disease and Fast Grants and research contracts from GlaxoSmithKline, and ViiV Healthcare. SS reports grants from Ansun BioPharma, Astellas Pharma, Cidara Therapeutics, F2G, Merck, T2 Biosystems, Shire Pharmaceuticals, Shionogi, and Gilead Sciences, outside the submitted work; and personal fees from Amplyx Pharmaceuticals, Acidophil, Janssen Pharmaceuticals, Reviral, Intermountain Healthcare, Karyopharm Therapeutics, Immunome, Celltrion, and Adagio outside the submitted work.

All other authors declare no conflict of interests. The authors views and opinions in the Commentary do not necessarily represent the views, decisions, or policies of the institutions, universities, or health systems with which they are affiliated.

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References

[1] Institute for Health Metrics and Evaluation. COVID-19 projections. 2021. https://covid19.healthdata.org/global?view=cumulative-deaths&tab=trend. (accessed May 27, 2021)
[2] Charlier P, Varison L. Is COVID-19 being used as a weapon against indigenous peoples in Brazil?, 396. London, England: Lancet; 2020. p. 1069–70.
[3] Bartsch SM, O'Shea KJ, Ferguson MC, et al. Vaccine Efficacy Needed for a COVID-19 Coronavirus Vaccine to Prevent or Stop an Epidemic as the Sole Intervention. Am J Prev Med 2020;59:493–503.
[4] Moghadas SM, Vilches TN, Zhang K, et al. The impact of vaccination on COVID-19 outbreaks in the United States. medRxiv Preprint Server for Health Sciences; 2020 published online Nov. doi: 10.1101/2020.11.27.20240051.
[5] Karas H. The impact of COVID-19 on global extreme poverty. Brookings 2021. https://www.brookings.edu/blog/future-development/2020/10/21/the-impact-of-covid-19-on-global-extreme-poverty. (accessed May 27, 2021).
[6] Fischer W, Eron JJ, Holman W, et al. Molnupiravir, an oral antiviral treatment for COVID-19. medRxiv 2021. doi: 10.1101/2021.06.17.21258639.
[7] Muñoz-Fontela C, Dowling WE, Funnell SGP, et al. Animal models for COVID-19. Nature 2020;586:509–15.
[8] World Health Organization. The access to COVID-19 tools (ACT) Accelerator. 2021. https://www.who.int/initiatives/act-accelerator. (accessed May 27, 2021).
[9] World Health Organization. WHO SAGE values framework for the allocation and prioritization of COVID-19 vaccination. 2020. https://apps.who.int/iris/bitstream/handle/10665/334299/WHO-2019-nCoV-SAGE_Framework-Allocation_and_-prioritization-2020.1-eng.pdf. (accessed May 27, 2021).
[10] World Health Organization. Covax-working for global equitable access to COVID-19 vaccines. 2021. https://www.who.int/initiatives/act-accelerator/covax. (accessed May 27, 2021).
[11] Unitaid. Unitaid and the access to Covid-19 tools accelerator. https://unitaid.org/covid-19/act-accelerator/#en. (accessed May 27, 2021).
[12] CEPI. CEPI expands global manufacturing network, reserving manufacturing capacity for more than 1 billion doses of COVID-19 vaccines. 2021. https://cepi.net/news_cepi/cepi-expands-global-manufacturing-network-reserving-manufacturing-capacity-for-more-than-1-billion-doses-of-covid-19-vaccines. (accessed May 27, 2021).
[13] World Health Organization. COVID-19 oxygen emergency impacting more than half a million people in low- and middle-income countries every day, as demand surges. 2021. https://www.who.int/news/item/25-02-2021-covid-19-oxygen-emergency-impacting-more-than-half-a-million-people-in-low–and-middle-income-countries-every-day-as-demand-surges. (accessed May 27, 2021).
[14] World Health Organization. Regulation and prequalification. 2021. https://www.who.int/teams/regulation-prequalification/eul/covid-19. (accessed May 28, 2021).

[15] World Health Organization. WHO lists additional COVID-19 vaccine for emergency use and issues interim policy recommendations. 2021. https://www.who.int/news/item/07-05-2021-who-lists-additional-covid-19-vaccine-for-emergency-use-and-issues-interim-policy-recommendations. (accessed May 27, 2021).

[16] Hotez PJ, Narayan KMV. Restoring vaccine diplomacy. JAMA 2021 published online May 28. doi: 10.1001/jama.2021.7439.

[17] Dagan N, Barda N, Kepten E, et al. BNT162b2 mRNA Covid-19 vaccine in a nationwide mass vaccination setting. N Engl J Med 2021;384:1412–23.

[18] Rubin R. COVID-19 vaccines vs variants-determining how much immunity is enough. JAMA 2021;325:1241–3.

[19] National Collaborating Centre for Infectious Diseases. Updates on COVID-19 variants of concern. 2021. https://nccid.ca/covid-19-variants/. (accessed May 27, 2021).

[20] Young-Xu Y, Korves C, Powell EI, Zwain GM, Smith J. Coverage and effectiveness of mRNA SARS-CoV-2 vaccines among United States Veterans. medRxiv 2021. doi: 10.1101/2021.06.14.21258906.

[21] Kim JH, Marks F, Clemens JD. Looking beyond COVID-19 vaccine phase 3 trials. Nat Med 2021;27:205–11.

[22] Lancet Commission on COVID-19 Vaccines and Therapeutics Task Force. Urgent needs of low-income and middle-income countries for COVID-19 vaccines and therapeutics, 397. London, England: Lancet; 2021. p. 562–4.

[23] University of Oxford. Com-Cov. Comparing Covid-19 vaccine schedule combinations. 2021. https://comcovstudy.org.uk/home. (accessed July 1, 2021).

[24] Klassen SA, Senefeld JW, Johnson PW, et al. The effect of convalescent plasma therapy on mortality among patients with COVID-19: systematic review and meta-analysis. Mayo Clin Proc 2021;96:1262–75.

[25] National Institutes of Health. COVID-19 Treatment Guidelines. Convalescent Plasma. 2021. https://www.covid19treatmentguidelines.nih.gov/immune-based-therapy/blood-derived-products/convalescent-plasma/. (accessed May 27, 2021).

[26] Libster R, Pérez Marc G, Wappner D, et al. Early High-Titer Plasma Therapy to Prevent Severe Covid-19 in Older Adults. N Engl J Med 2021;384:610–8.

[27] World Health Organzation. "Solidarity" clinical trial for COVID-19 treatments. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments. (accessed May 27, 2021).

[28] Janik E, Niemcewicz M, Podogrocki M, Saluk-Bijak J, Bijak M. Existing drugs considered as promising in COVID-19 therapy. Int J Mol Sci 2021;22. doi: 10.3390/ijms22115434.

[29] Ahmed MH, Hassan A. Dexamethasone for the treatment of coronavirus disease (COVID-19): a review. SN Compr Clin Med 2020:1–10.

[30] World Health Organization. WHO target product profiles for COVID-19 therapeutics. 2020. https://www.who.int/publications/m/item/who-target-product-profiles-for-covid-19-therapeutics. (accessed May 27, 2021).

[31] World Health Organization. WHO target product profiles for COVID-19 therapeutics for non-hospitalized patients. https://www.who.int/publications/m/item/who-target-product-profiles-for-covid-19-therapeutics-for-non-hospitalized-patients#.X8oTXsVXvpo.twit. (accessed May 27, 2021).

[32] World Health Organization. Fair allocation mechanism for COVID-19 vaccines through the COVAX facility. https://www.who.int/publications/m/item/fair-allocation-mechanism-for-covid-19-vaccines-through-the-covax-facility. (accessed May 27, 2021).

[33] Ruscio BA, Hotez P. Expanding global and national influenza vaccine systems to match the COVID-19 pandemic response. Vaccine 2020;38:7880–2.

[34] Gostin LO, Salmon DA. The dual epidemics of COVID-19 and Influenza: vaccine acceptance, coverage, and mandates. JAMA 2020;324:335–6.

[35] Ortiz JR, Neuzil KM. Influenza immunization in low- and middle-income countries: preparing for next-generation influenza vaccines. J Infect Dis 2019;219:S97–106.

[36] World Trade Organization. Amendment to the agreement on trade-related aspects of intellectual property rights (TRIPS). https://www.wto.org/english/tratop_e/trips_e/tripsfacsheet_e.htm. (accessed May 27, 2021).

[37] Hotez P, Bottazzi ME, Yadav P. Producing a vaccine requires more than a patent. Foreign Aff 2021. https://www.foreignaffairs.com/articles/united-states/2021-05-10/producing-vaccine-requires-more-patent. (accessed June 3, 2021).

[38] Sultana J, Mazzaglia G, Luxi N, et al. Potential effects of vaccinations on the prevention of COVID-19: rationale, clinical evidence, risks, and public health considerations. Expert Rev Vaccines 2020;19:919–36.

[39] Preston C, Lou VM, Bond K. Strengthening medical product regulation in low- and middle-income countries. PLoS Med 2012;9:e1001327.

[40] Addo-Atuah J, Senhaji-Tomza B, Ray D, Basu P, Loh F-HE, Owusu-Daaku F. Global health research partnerships in the context of the sustainable development goals (SDGs). Res Soc Adm Pharm 2020;16:1614–8.

[41] Naniche D, Hotez P, Bottazzi ME, et al. Beyond the jab: a need for global coordination of pharmacovigilance for COVID-19 vaccine deployment. EClinicalMedicine 2021;36:100925.

[42] Oxfam. Rich nations have bought up more than half the future supply of leading COVID-19 vaccine contenders. https://www.scoop.co.nz/stories/WO2009/S00120/rich-nations-have-bought-up-more-than-half-the-future-supply-of-leading-covid-19-vaccine-contenders.htm. (accessed May 27, 2021).

[43] Medical Xpress. Why 'vaccine nationalism' could doom plan for global access to a COVID-19 vaccine. https://medicalxpress.com/news/2020-09-vaccine-nationalism-doom-global-access.html. (accessed May 27, 2021).

[44] Lieberman A. A global COVID-19 facility could prevent 'vaccine nationalism' — But the challenges are steep. https://www.devex.com/news/a-global-covid-19-facility-could-prevent-vaccine-nationalism-but-the-challenges-are-steep-97905. 2021.

[45] Byrne J. Lilly's monoconal antibody is the First to be authorized for use in treating Covid-19. BioPharma-Reporter.com. https://www.biopharma-reporter.com/Article/2020/11/10/Lilly-s-monoclonal-antibody-is-the-first-to-be-authorized-for-use-in-treating-COVID-19. (accessed May 27, 2021).

[46] Arthiur R. Regeneron Submits Request for EUA for Covid 19 Antibody Cocktail. BioPharma-Reporter.com. https://www.biopharma-reporter.com/Article/2020/10/08/Regeneron-submits-request-for-EUA-for-COVID-19-antibody-cocktail. (accessed May 27, 2021).

[47] Wellcome. Expanding access to monoclonal antibody-based products: a global call to action. https://wellcome.org/reports/expanding-access-monoclonal-antibodies. (accessed May 27, 2021).

[48] Kis Z, Kontoravdi C, Dey AK, Shattock R, Shah N. Rapid development and deployment of high-volume vaccines for pandemic response. J Adv Manuf Process 2020;2:e10060.

[49] DNDi. Covid-19 Accelerating research, advocating for accountability. https://dndi.org/diseases/covid-19/. (accessed May 27, 2021).

[50] GE. Think Inside The Box: Pfizer Will Use GE's mobile biotech factory to make next-generation drugs in China. https://www.ge.com/news/reports/pfizer-will-use-ges-modular-factory-to-make-next-generation-drugs-in-china. (accessed May 27, 2021).

[51] Merck Millipore. Integrated bioprocess solutions. 2016 https://www.merckmillipore.com/Web-IN-Site/en_US/-/EUR/ShowDocument-Pronet?id=201605.055. (accessed May 27, 2021).

[52] Cytiva. KUBio prefabricated Manufacturing facilities for monoclonals. https://www.cytivalifesciences.com/en/us/solutions/bioprocessing/products-and-solutions/enterprise-solutions/kubio/kubio-mab-manufacturing-facility. (accessed June 23, 2021).

[53] Sun News. Melbourne vaccine manufacturing facility announced as hope for coronavirus vaccine continues. https://www.abc.net.au/news/2020-11-16/new-vaccine-facility-melbourne-coronavirus-anti-venom/12886346. (accessed May 27, 2021).

[54] Government of Canada. COVID-19 response: building the infrastructure. https://nrc.canada.ca/en/covid-19-response-building-infrastructure. (accessed May 27, 2021).

[55] PA Media. Government to invest £93 m in UK vaccine manufacturing centre. https://www.theguardian.com/society/2020/may/17/government-to-invest-93m-in-uk-vaccine-manufacturing-centre. (accessed May 27, 2021).

[56] Lancet Commission on COVID-19 Vaccines and Therapeutics Task Force. Operation warp speed: implications for global vaccine security. Lancet 2021;9:E1017–21.

[57] Connolly C. Cytiva enters into technology investment agreement with BARDA. https://www.cytivalifesciences.com/en/us//news-center/cytiva-enters-into-technology-investment-agreement-with-barda-10001. (accessed May 27, 2021).

[58] Bowman C. How BARDA locked up COVID-19 vaccine manufacturing capacity for operation warp speed. https://bioprocessintl.com/bioprocess-insider/global-markets/how-barda-locked-up-covid-19-vaccine-manufacturing-capacity-for-operation-warp-speed/. (accessed May 27, 2021).

[59] KAUST News. Groundbreaking for first R&D vaccine center in the middle East takes place at KAUST. https://innovation.kaust.edu.sa/groundbreaking-for-first-r-d-vaccine-center-in-the-middle-east-takes-place-at-kaust/. (accessed May 27, 2021).

[60] Wingrove J. World bank announces deal to fund vaccines for South Africa. Bloomberg 2021 https://www.bloomberg.com/news/articles/2021-06-30/world-bank-announces-deal-to-fund-vaccines-for-south-africa. (accessed July 1, 2021).

[61] African Union and Africa CDC launches Partnerships for African Vaccine Manufacturing (PAVM), framework to achieve it and signs 2 MoUs. https://africacdc.org/news-item/african-union-and-africa-cdc-launches-partnerships-for-african-vaccine-manufacturing-pavm-framework-to-achieve-it-and-signs-2-mous/. (accessed May 27, 2021).

[62] P B., Arkin E., Orleans T., Proctor D., Plough A. What is health equity? robert wood Johnson found. https://www.rwjf.org/en/library/research/2017/05/what-is-health-equity-.html. (accessed May 27, 2021).

[63] Hotez P. Poverty and the impact of COVID-19: the blue-marble health approach. Project Muse; 2020. https://muse.jhu.edu/book/75688 (accessed May 27, 2021).

[64] Africa Union. COVID 19 Vaccine Perceptions: A 15 country study. https://africacdc.org/download/covid-19-vaccine-perceptions-a-15-country-study/. (accessed May 27, 2021).

[65] Lazarus JV, Ratzan SC, Palayew A, et al. A global survey of potential acceptance of a COVID-19 vaccine. Nat Med 2021;27:225–8.

[66] Hoffman J. I Won't Be Used as a Guinea Pig for White People. New York Times; 2021. https://www.nytimes.com/2020/10/07/health/coronavirus-vaccine-trials-african-americans.html. (accessed May 27, 2021).

[67] Raeven RHM, van Riet E, Meiring HD, Metz B, Kersten GFA. Systems vaccinology and big data in the vaccine development chain. Immunology 2019;156:33–46.

[68] de Figueiredo A, Simas C, Karafillakis E, Paterson P, Larson HJ. Mapping global trends in vaccine confidence and investigating barriers to vaccine uptake: a large-scale retrospective temporal modelling study. Lancet 2020;396:898–908.

[69] Lancet Commission on COVID-19 Vaccines and Therapeutics Task Force. Correcting COVID-19 vaccine misinformation. Lancet EclinMedicine 2021. https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00060-2/fulltext.

[70] Broniatowski DA, Jamison AM, Qi SH, et al. Weaponized health communication: twitter bots and Russian trolls amplify the vaccine debate. Am J Public Health 2018;108:1378–84.
[71] Hotez P. COVID vaccines: time to confront anti-vax aggression. Nature 2021. https://www.nature.com/articles/d41586-021-01084-x. (accessed July 1, 2021).
[72] United States Food and Drug Administration. First FDA-approved vaccine for the prevention of Ebola virus disease, marking a critical milestone in public health preparedness and response. https://www.fda.gov/news-events/press-announcements/first-fda-approved-vaccine-prevention-ebola-virus-disease-marking-critical-milestone-public-health. (accessed May 27, 2021).