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that storage of lyophilized LNPs at ambient temperature or 4°C for 12 weeks did not impact immunogenicity, and storage at both temperatures for 24 weeks yielded a modest decrease in the resultant immunogenicity. Storage of lyophilized LNPs at 42°C resulted in a considerable drop in luciferase production and immunogenicity after storage for all tested timepoints. Together, these results demonstrate that mRNA-LNP activity is clearly dependent on storage temperature and time. The lyophilization procedures used here enabled storage of LNPs at ambient temperature for 12 weeks or at 4°C for at least 24 weeks with no impact to immunogenicity.

Currently, mRNA-LNP vaccines against COVID-19 are stored frozen in their liquid form without lyophilization. This is a great challenge for the long-term storage and transportation of LNPs, both for the COVID-19 vaccines and toward the development and implementation of LNPs for other diseases. The two major mRNA-LNP vaccines, SpikeVax and Comirnaty, have stability reported at ambient temperature for only 12 h and 6 h, respectively.¹² In this article, lyophilization enabled stable storage of the lyophilized PR8 HA mRNA-LNPs for 12 weeks, or reconstituted LNPs for 24 h, at ambient temperature. This is a substantial improvement over the current standard. The stability studies conducted in this article provide important guidelines on the longterm storage, stability, and delivery efficacy

of mRNA-LNPs. Moving forward, it will be valuable to compare multiple lyophilization conditions, such as the type and concentration of cryoprotectant, to enable longer storage at ambient temperature, as lyophilization techniques have been shown to impact LNP stability and performance.⁸ These additional studies, combined with the findings in this article, are critical to the widespread development and implementation of LNPs for longterm disease management. Further, storage at ambient temperatures would enable easier transportation and greater access to LNP therapeutics worldwide.

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Emerging infections and pandemics: The critical importance of global health equity action

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"No man is an island entire of itself; every man is a piece of the continent, a part of the main..."¹

The coronavirus disease 2019 (COVID-19) pandemic has demonstrated the stark reality

of how unprepared the United States and the rest of world were and are for emerging infections that can lead to pandemics. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is unlikely to be the final pathogen that leads to a multi-country epidemic or a global pandemic. A host of other pathogens are waiting in line, ranging from zoonotic

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Table 1. Examples of potential pandemic pathogens		
Viruses ¹³		
	Middle Eastern respiratory syndrome (MERS)	
	SARS-CoV	
Coronaviruses	SARS-CoV-2	
	novel coronaviruses	
	Crimean Congo hemorrhagic virus	
	Ebola virus	
	Hantavirus	
Hemorrhagic fevers	Lassa fever virus	
	Nipah virus	
	Marburg virus	
	Rift Valley Fever virus	
Pandemic influenza		
Novel zoonotic viruses		
	Dengue virus	
Flaviviruses	Yellow fever virus	
	Zika virus	
Togaviruses	Chikungunya virus	
Novel arboviruses		
Antimicrobial-resistant pathogens ^{14,15}		
Multidrug-resistant and extensively drug-resistant tuberc	ulosis	
Methicillin-resistant Staphylococcus aureus		
Carbapenem-resistant Enterobacteriaceae		
Potential biological agents of most concern for bioterror	ism ¹⁴	
Bacteria		
Bacillus anthracis (anthrax)		
Yersinia pestis (plague)		
Francisella tularensis (tularemia)		
Viruses		
Smallpox		
Viral hemorrhagic fevers		
Toxins		
Clostridium botulinum (botulism)		

viruses like SARS-CoV-2 to vector-borne viruses, antimicrobial-resistant bacteria or fungi, and potential agents of bioterrorism (Table 1).

Despite a 2-year-plus period with the COVID-19 pandemic, the critical role of global health equity in preventing and controlling pandemics has received far too little attention. A major manifestation of this inequity is in access to COVID-19 vaccine supply in the global effort to reach herd immunity. The World Health Organization (WHO) has set a benchmark of 70% popula-

tion-level coverage for COVID-19 vaccination for all countries by mid-2022.² At the time of writing, COVID-19 vaccination rates among adults over 18 years in high-income countries range from ~65% to >90%, while the overall vaccination rate for low- and middle-income countries is significantly lower: 60% in South America and abysmally low at 25% across the African continent.³ Furthermore, while COVID-19 vaccine coverage in the United States is >20% for 5–11 year olds and approaching 60% for 12–17 year olds,⁴ the vast majority of 5–17 year olds in African countries have not yet been cleared to access vaccines and have not received a single shot.⁵

Similarly, the availability and accessibility of COVID-19 diagnostics and treatments has greatly lagged for low- and middle-income countries compared with high-income countries.^{6,7} The results of this inequity have played out in many deleterious ways: substantial morbidity and mortality in both high- and low- and middle-income countries;8 development of more infectious variants, such as Delta and Omicron, that have greatly prolonged the pandemic; and xenophobic travel bans from high-income countries that often disproportionately and unjustifiably target low-income countries, with substantial costs to those countries in terms of supplies needed to combat COVID-19.

Within high-income countries, the human costs of COVID-19 have also been borne disproportionately by historically disadvantaged and minoritized populations. For example, early in the pandemic in the United States, Hispanic or Latin, Black, and Native American communities each had mortality rates more than twice those in non-Hispanic white populations: 2.8-, 3.6-, and 2.2-fold higher mortality, respectively.⁹ These disproportionate burdens did not spare children, especially with respect to mortality: in the early pandemic, Hispanic, Black, and Native American children, who comprise 41% of the population, bore 75% of child deaths from COVID-19.¹⁰

Sadly, this was not unexpected, as disadvantaged populations in both high-income and low- and middle-income countries have historically suffered significant disparities in a number of other health conditions. However, with COVID-19, the glaring inequities experienced within countries and across continents have highlighted the need for global health equity action for children and adults during this pandemic and to prevent or alleviate the severity of the next one. These efforts are needed to bridge the gap between high- and low-income countries and between privileged and marginalized populations worldwide. As we have seen with the recent development Commentary

Table 2. Ten steps for equitable pandemic responses through global health action		
Step	Category	Action
1	Coordination: global, regional, national, and subnational incident command	Fund an at-the-ready center to support population-level pandemic prevention and control
2	Inclusion	Ensure high-level participation by low- and middle-income country participants and participants from other marginalized groups' in the pandemic center's operations
3	Equitable and timely resource allocation	Prioritize the vulnerable in response time, data collection, and allocation of resources
4	Sharing knowledge and resources	Incentivize vaccine and medication patent sharing and low-cost production in low and middle-income countries
5	transparent communication and building trust	Communicate effectively with the general public and pre-emptively combat misinformation
6	Addressing prejudice and harm	Identify and eliminate racism and discrimination in the pandemic response
7	Inclusion and building trust	Establish rapid response pathways to address public concerns and channel these concerns into risk communication and policy making
8	Improving access to technology	Support research and development for low-cost, low-tech vaccines and therapeutics in low and middle-income countries
9	Improving access to prevention and control interventions	Support the manufacture of vaccines and therapeutics in low- and middle-income countries
10	Improving access to prevention and control interventions	Develop and strengthen supply chain and healthcare infrastructure in low- and middle- income countries

of SARS-CoV-2 variants of concern, a slow and inequitable response to a pandemic increases the risk for everyone, everywhere.

With these goals in mind, we propose ten key steps for public health institutions at the subnational, national, regional, and global level to prevent and control pandemics through promotion of global health equity, highlighted in Table 2.

1. Fund an at-the-ready center to support population-level pandemic prevention and control. In September 2021, the World Health Organization (WHO) established its new Hub for Pandemic and Epidemic Intelligence to strengthen global preparedness and response to disease outbreaks. The Hub's Equity Statement is as follows: "The WHO Hub will work for the benefit of all populations and address unfair and avoidable differences in access to pandemic and epidemic intelligence tools, insights, and participation, irrespective of social, economic, demographic, or geographic factors."11 This globally focused center must be actively funded and supported by all member nations and given authority to obtain data from all partner countries, conduct studies of potential for emerging infections, develop policy that will ensure equity in the pandemic

response, and have authority to call on member nations, particularly high-income countries, to live up to their obligations to ensure global health equity. Centers established at lower geographic levels (i.e., regional, national, and subnational) should operate in similar fashion.

- 2. Ensure high-level low- and middle-income country participation in pandemic centers' operations. Pandemic centers will not meet their objectives without high-level, functional participation and decision-making input. This includes meaningful leadership and participation from low- and middle-income country experts in the global center and for relevant but historically neglected constituents in centers at lower geographic levels.
- 3. Prioritize the vulnerable in response time, data collection, and allocation of resources. For example, prioritize people who are marginalized and/or living in the lowest income contexts, children, pregnant women, and people with underlying health conditions when evaluating pandemic risk factors and outcomes and allocating resources to combat the pandemic.
- 4. Incentivize vaccine and medication patent sharing and low-cost production. The unwillingness to share pandemicresponsive intellectual property ex-

hibited by those empowered to do otherwise has been an unethical and unacceptable example of global health inequity in action.

- 5. Communicate effectively with the general public and pre-emptively combat misinformation. Misinformation and disinformation have cost hundreds of thousands of lives, perhaps more, in the current pandemic, as people have refused vaccination and mask wearing, two interventions proven to greatly reduce SARS-CoV-2 infection and disease, on the basis of misinformation and outright lies spread by multiple sources. Public health sources were and still are slow to understand how to better communicate information, relying often on "the data speaking for themselves," when the pandemic has clearly shown that data alone are insufficient to convince many people. Governments and health organizations must invest in scientific communications training and in supporting experts and behavioral scientists to understand the root causes for successful spread of misinformation and to engage with the public in successful risk communication.
- Identify and eliminate racism and discrimination in the pandemic response. This should be done at all levels: subnational, national, regional, and global.

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- 7. Establish rapid response pathways to address public concerns and channel these concerns into risk communication and policy making. This work would go hand in hand with providing accurate information and combating misinformation.
- 8. Support research and development for low-cost, low-tech vaccines and therapeutics. An excellent recent example is the patent-free, low-cost Corbevax COVID-19 vaccine. This protein-based vaccine was developed by a team of scientists from the Center for Vaccine Development at the Texas Children's Hospital in Houston, Texas.¹² The scientists have shared the technology with manufacturers in India, whose government has granted emergency use authorization for the vaccine.¹² Data from these trials had not been publicly released at the time of writing. This is perhaps because smaller organizations do not have the resources to do the rapid analysis and quality control of data that large, forprofit pharmaceutical companies do. Given the hesitancy surrounding mRNA vaccines in some areas, nonprofit government funding of trials for vaccines like Corbevax that use traditional low-cost vaccine components and technologies should be a priority, as these vaccines can be much more easily given in low- and middle-income countries.
- 9. Support the manufacture of vaccines and therapeutics in low- and middle-income countries. Globally, and among resource-limited settings, countries in sub-Saharan Africa continue to have the lowest vaccination rates against COVID-19 (~25%). A major reason for this is that there are few vaccinemanufacturing facilities in this region.⁷ Similarly, most medications in Africa are imported from other countries, with limited manufacturing capability within Africa. The scientific, engineer-

ing, and business workforce within many African countries can now support vaccine and drug manufacture. Initiatives like the African Vaccine Manufacturing Initiative (http://www. avmi-africa.org) should be strengthened and supported.

10. Develop and strengthen supply chain and healthcare infrastructure in lowand middle-income countries. Vaccines, medications, and prevention measures are ineffective without the resources and systems within which to provide them. General strengthening of supply chain and healthcare infrastructure in low- and middle-income countries is critical to the success of prevention and treatment efforts in a pandemic.

Conclusion

Global health equity, with focus on the most marginalized and underserved populations within and across high- and low- and middle-income countries is at the heart of SARS-CoV-2 infection and disease prevention and of COVID-19 treatment in the current pandemic. Global health equity will remain an issue in future pandemics, which, given the realities of our interconnected world, will continue to occur. Achieving global health equity will require substantial input of resources and time but will yield substantially better health, economic, and well-being outcomes for *everyone*.

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