MEDICINE AND SOCIETY

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Global Health Law for a Safer and Fairer World

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Once considered defeated by modern medicine, infectious diseases continue to devastate populations worldwide. The Covid-19 and mpox pandemics recently joined the HIV pandemic and outbreaks ranging from Zika and Ebola to wild polio. Advances in synthetic biology may create opportunities for cutting-edge interventions, but they also introduce risks from accidental or intentional releases of pathogens.

Recent health emergencies have revealed major gaps in the rules of global cooperation and the institutions overseeing them. In May 2024, the World Health Assembly will consider adopting a historic pandemic treaty and revised International Health Regulations (IHR) that could transform global health governance for a post-Covid era. It's important to understand the major gaps in global preparedness, the critical capacities needed to create a safer and fairer world, and the international instruments required for realizing them.

"DEEPER" PREVENTION OF ZOONOTIC SPILLOVERS AND BIOHAZARDS

Over the past century, 75% of all emerging infectious diseases have originated with zoonoses, animal pathogens infecting humans in spillover events.[1] Most viral pandemics have zoonotic origins. The great influenza pandemic of 1918 was caused by an H1N1 virus with genes of avian origin.[2] Humans acquired HIV from cutaneous or mucous-membrane exposure to infected body fluids of apes,[3] and HIV/AIDS has killed approximately 40.1 million people.[4] Though there are several theories regarding the origins of SARS-CoV-2, the most plausible is a spillover event at the Wuhan Huanan Seafood Wholesale Market.[5] Zika, the Middle East respiratory syndrome coronavirus (MERS-CoV), and Ebola are additional zoonotic diseases that have caused outbreaks in humans. The increasing prevalence of chronic wasting disease in deer and elk in the United States, though caused by prions rather than a virus, is of urgent concern, given research suggesting "that the barrier to a spillover into humans is less formidable than previously believed."[6]

Beyond the risk of death, emerging infectious diseases leave many survivors with life-long disabilities and struggles with emotional and mental health.[7] Long Covid, which affects at least 10% of people infected with SARS-CoV-2, is associated with fatigue, muscle pain, mobility and functionality problems, and mental problems including difficulty with recall and understanding[8]; it affects 10 to 13% of infected children, potentially leading to lifelong disability.[9] And millions of people live with disability from HIV/AIDS, Ebola, Zika, or MERS.

Spillover events have increased owing to human activity, including deforestation, human–animal interactions, wild animal markets and trade, and a growing global population. As pathogens spread by means of international travel and mass migration, spillover events can quickly cause pandemics.

Overuse of antibiotics in farmed animals has led to new threats even from known pathogens. Antimicrobial resistance is increasing worldwide. Countless additional lives would have been lost were it not for the rapid development of effective vaccines and therapeutics; if our medical countermeasures lost their effectiveness, the next pandemic would prove far more devastating than Covid-19. Prudent use of agricultural antibiotics should therefore be required by any pandemic agreement.

Human-driven changes to land result in major disruptions to animal habitats, contributing to zoonotic spillovers. A recent analysis of more than 3.2 million records from several hundred ecological studies revealed "that the populations of species known to host diseases transmissible to humans — including 143 mammals such as bats, rodents and various primates — increased as the landscape changed from natural to urban, and as biodiversity generally decreased."[10] The degradation of forests also precipitates a climate crisis that forces species and people to migrate. Reversing deforestation and forest degradation, especially in tropical and subtropical areas, would reduce spillovers. The Global Biodiversity Framework developed by the Convention on Biological Diversity calls for 30% of the earth's land and sea to be conserved by 2030, by means of establishment of protected areas and other conservation measures.[11]

Substantial evidence suggests that regulating wildlife trade and markets, particularly commercial trade in birds and mammals for food, pets, and medicine, would significantly reduce zoonotic spillover events.[12] Though the Convention on International Trade in Endangered Species of Wild Fauna and Flora aims to ensure that trade in animals and plants does not threaten their survival in the wild, it doesn't address zoonotic spillovers and pandemic preparedness. Similarly, the Convention on Biological Diversity provides rules for protecting biodiversity and limiting deforestation. A new agreement could advance health security by regulating deforestation, the sale and trade of wild animals, and overuse of antimicrobials in agriculture.

INFORMATION SHARING FOR DETECTION, NOTIFICATION, AND RESPONSE

Realistically, the world must also be prepared for what happens when deeper preventive interventions fail. Timely information sharing, combined with measures for building trust in the scientific and lay communities, can help determine whether a localized outbreak becomes a catastrophic pandemic, whether medical countermeasures are rapidly developed and deployed, and whether the world cooperates to stem outbreaks and equitably allocate lifesaving diagnostics, vaccines, and therapeutics.

Rapid detection of novel pathogens in human and animal populations is a prerequisite for effective action. Surveillance capacities, including wastewater and genomic surveillance, are weak in many parts of the world. Similarly, laboratories for testing novel pathogens need to be more advanced and accessible. Portable laboratory technologies could enable faster detection, nearer to affected communities.

Beyond health system capacities, early reporting and information sharing should be firmly established by international commitments. The IHR (2005), the only existing international agreement focused on capacities and binding obligations for detection and rapid notification, proved unequal to the task amid widespread noncompliance during the Covid-19 pandemic. Similarly, Guinean authorities delayed notifying the World Health Organization (WHO) until nearly 4 months after the first Ebola-related death.[13] When the authorities finally admitted how severe the outbreak was, the public was skeptical of the measures recommended by the WHO, the national government, and aid groups.

Ebola, Covid-19, and other recent outbreaks have made evident not only international law's failure to keep pace with the spread of pathogens and the resulting need for sharing scientific data but also the trust that authorities must build in the findings they share. The WHO plays a key role in facilitating open digital platforms that constantly update and share epidemiologic information, enabling near-instant global scientific exchange. Pandemic preparedness could be substantially enhanced if international standards required alert systems and transparent sharing of scientific information. In addition, national governments could identify and work with community, faith, scientific, and public health leaders to ensure that disinformation, misinformation, and conspiracy theories don't undermine evidence-based measures.

ACCESS TO PATHOGEN AND GENOMIC SEQUENCING DATA

Dissemination of biologic and genomic resources is essential for identifying and characterizing an outbreak's causative agent, understanding the nature of transmission, and developing countermeasures.[14] Yet legal and functional barriers inhibit scientific sharing. The 1992 United Nations

Convention on Biological Diversity authorizes governments to regulate access to genetic resources generated within their territories, while the 2010 Nagoya Protocol encourages states to reach agreements regarding access to genetic resources in exchange for benefits for states that provide them.[15] Pathogen genome sequences have become indispensable for emergency preparedness.[16] The law, however, works against rapid sharing: no law currently compels governments to facilitate sharing either themselves or by their corporations and citizens. The only international agreement that fosters pathogen sharing — the Pandemic Influenza Preparedness Framework — is exceedingly narrow, applying only to pandemic influenza strains, and is not legally binding.

Many countries also lack the capacity to sequence and share pathogens. In May 2021, the World Health Assembly encouraged member states to increase their capacities for detecting new public health threats, including by means of genome sequencing.[17] In 2021, the WHO recommended that countries ship at least 5% of their Covid-19 samples to reference sequencing laboratories or continue to produce sequencing data, depending on their capacity.[18] As of November 2021, Africa accounted for just 1% of the more than 3.5 million Covid-19 samples sequenced worldwide[18]; that year, the Economic Community of Central African States contributed to sequencing, on average, 0.9% of all reported cases.[19] When the first Covid-19 case was detected in the WHO Eastern Mediterranean region on January 29, 2020, only 11 of 22 countries in that region had developed next-generation sequencing capacity.[20] These gaps call for a range of efforts, including deployment of artificial intelligence (AI) applications that combine clinical, environmental, lifestyle, and genomic data to provide rich data sets.[21] AI increasingly enables scale-up of sequencing operations and lower-cost production of genomic data.

Even high-income countries face genomic-sequencing challenges,[22] but the hurdles are higher in low- and middle-income countries (LMICs). During the first 2 years of the Covid-19 pandemic, 58% of LMICs sequenced samples in no more than 0.5% of cases, as compared with 21.5% of cases in high-income countries.[23] Lack of sequencing capacity and inadequate infrastructure for shipping samples internationally became major barriers.[20] The problem is especially acute in equatorial zones, where current models suggest the next pandemic pathogen will arise.

In addition to enhancing health system capacities, it's important to develop an effective international system for scientific sharing. Researchers and governments generally share pathogen genomes using data repositories like those of the International Nucleotide Sequence Database Collaboration (INSDC). Their effectiveness, however, depends on the willingness of data producers to upload their sequences in real time, typically before analysis or publication. Unfortunately, INSDC's data-use policy provides no protections for data producers regarding attribution, academic recognition, or collaboration. Some data producers are reluctant to promptly upload data for fear that others may use their data without proper attribution or in ways that threaten future patents or publications.[16] An international agreement could address such disincentives.

Although the IHR obligate countries to inform the WHO, within 24 hours, of all pertinent "public health information" related to any event that may constitute an emergency, samples and genomic-sequence data are not explicitly categorized as public health information.[14] The resulting legal uncertainty impeded access during past health emergencies, including the MERS (2012), West African Ebola (2014–2016), and Zika (2016) epidemics.

The global health community must adequately invest in systems and create binding norms to facilitate sharing of pathogen samples and genomic-sequence data. It will also need to invest in national health systems, including protecting LMICs from the costs of complying with rapid-notification requirements.

FINANCING FOR PANDEMIC RESPONSE

The Covid-19 pandemic exposed gaping financial deficits. A month after declaring Covid-19 a public health emergency, the WHO had allocated just $23.9 million, and 3 months later the United Nations' response plan was just 5% funded.[24] Though an estimated $16 billion was mobilized in 2020, allocation was piecemeal and ad hoc.[25,26] Most important, funding was mobilized far more slowly than the virus spread. By December 2020, high-income countries had already preordered vaccines to cover their populations, but the WHO had raised only $2 billion of

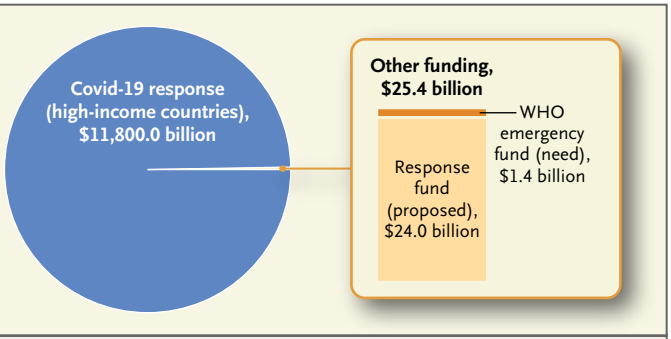

Figure 1. Proposed Global Health Financing as a Portion of Total Covid-19 Spending.

Data are from Kavanagh and Singh[31] and the International Monetary Fund.[32] WHO denotes World Health Organization.

the $10 billion needed to supply vaccines for LMICs.[27]

World Bank financing initiatives have floundered. The bank's Pandemic Emergency Financing Facility was shut down after failing during Ebola and Covid-19.[28] The new World Bank Pandemic Fund is an intermediary that channels funds from donors through 13 different implementing organizations, including Gavi and the WHO. In its first funding round, it made just over $300 million available but was oversubscribed by a factor of eight, with requests for more than $2.5 billion from 133 countries.[24] Moreover, the fund is designated for long-term capacity building, not emergency response.

These flows of funds and their targets should change. As soon as an outbreak with pandemic potential is identified, rapid-response funds should be triggered. The WHO's contingency fund is fit for purpose but receives only about 5% of what it needs each year.[29] States should agree to fund it by assessed contributions, or identify an alternative.

If an outbreak grows and the WHO declares an emergency, a larger pot of rapid funding is needed. We believe a response fund of at least $24 billion should be established; $23.7 billion was mobilized for the Access to COVID-19 Tools Accelerator (a global collaboration to accelerate medical countermeasure research, production, and equitable access),[30] setting a benchmark both for the minimum needed in a pandemic and for what donors are willing to mobilize. That amount is less than 1% of what high-income countries spent on domestic Covid-19 support and response (Fig. 1), but it needs to be available on "day zero."[27,32] To ensure such availability without creating a large pot of idle funding, International Monetary Fund (IMF) reserves could be used when an emergency is declared. To avoid reliance on an ad hoc philanthropic approach, governments negotiating the pandemic treaty could make a binding commitment to repay the IMF according to their ability (much as they already fund the IMF according to a quota formula). Funding could be funneled through existing entities, including the WHO, the Africa Centers for Disease Control and Prevention, and the Global Fund to Fight AIDS, Tuberculosis, and Malaria.

EQUITABLE ACCESS TO MEDICAL COUNTERMEASURES

Inequitable access to lifesaving countermeasures impedes outbreak responses. After effective HIV therapies became available, deaths in high-income countries fell dramatically, but approximately 12 million people in Africa died waiting.[33] During the first year Covid-19 vaccines were distributed, just 1% of doses were delivered to low-income countries.[34] Last year, the Democratic Republic of Congo (DRC) reported more than 13,000 mpox cases and 600 deaths, yet vaccines were deployed in high-income countries, not in the DRC.

These inequities are longstanding. In 1995, the newly established World Trade Organization gave strong protections to pharmaceutical patents and trade secrets, with minimal regard for the effect on public health. The results were global monopolies on drugs and prices too high for many countries to afford. After early failures, HIV-drug prices were reduced by more than 99%, while production expanded worldwide[35] — governments compelled multinational corporations to license drugs to local companies, encouraged pooling of patents, and invested in low-cost manufacturing.[36] During Covid-19, by contrast, cumbersome voluntary procurement through the COVID-19 Vaccines Global Access program (COVAX) undermined access initiatives, and only limited intellectual-property waivers were extended. High-income governments hoarded both vaccines and technological know-how.[31]

Going forward, international legal agreements could ameliorate longstanding inequities. Agreements could include commitments to share medical technology. The WHO has already invested in

hubs for mRNA vaccine production in Africa, Asia, and Latin America, building on experience developing influenza-vaccine production capacity worldwide.[37] Just as biologic-weapons treaties give all state parties the right to the scientific and technological information needed for controlling such weapons, a pandemic agreement could provide rights with respect to development and allocation of medical countermeasure technology.[38]

An international agreement could also establish a norm for governments to link their public research funding with global pandemic preparedness. The United States, for example, invested tens of billions of dollars to develop mRNA Covid-19 vaccines, but without agreements for developers to share technology and know-how during health emergencies, the publicly funded technology was monopolized by manufacturers.[39] A global version of President Joe Biden's recently announced legal measures requiring public access to government-funded medical technology could help.[40]

Relatedly, an international agreement could specify that global intellectual-property rules will be waived in emergencies so each country can decide whether to enforce patents on relevant technologies. During Covid-19, the World Trade Organization's patent-waiver process took years, applied narrowly to vaccines, and ultimately resulted in little or no benefit to LMICs.[41] A better model is the U.S. Public Readiness and Emergency Preparedness Act, which enables the secretary of health and human services to issue emergency declarations that automatically create flexibility in legal rules to facilitate response — for example, creating a fund to cover the costs of severe adverse events in people receiving medical countermeasures or a modified process for making diagnostics, therapeutics, and vaccines available.

IMPLEMENTATION, COMPLIANCE, AND ACCOUNTABILITY

Good governance for health requires legal agreements, general compliance, and accountability for failures. Covid-19 revealed noncompliance with the IHR, which is why the United States — joined by many countries — proposed compliance-enhancing mechanisms. Any new pandemic agreement would have to ensure compliance.

The WHO has little power to police member states to ensure cooperation and compliance with international law. But well-designed agreements can use a range of mechanisms to coax countries to comply.[42] Potentially effective measures include independent rapporteurs empowered to report on violations; "shadow reporting," as in human-rights treaties, to enable civil-society organizations to attend and present results of investigations; formal mechanisms for resolution of disputes between countries; and a platform for requesting assistance needed for compliance. As in the framework conventions on tobacco control and climate change, an empowered conference of the parties could draw attention to emerging health security threats, boost implementation and compliance, and advocate for additional protocols with built-in enforcement and accountability.[43]

Deep prevention, transparent information sharing, and synergistic research collaborations shaped by regard for equity can all be achieved with thoughtful revision of international rules and negotiation of a new pandemic agreement. Undergirded by robust financial commitments and compliance measures, the world can be made safer and more resilient to pandemics. Working together, the world's governments can meet these daunting challenges; they require only the political will and foresight to do so.

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