Preventing and Preparing for Pandemics With Zoonotic Origins

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Introduction

The COVID-19 pandemic has brought the catastrophic threat posed by infectious diseases into sharp focus. With over six million deaths globally, it has raised unprecedented awareness about the need for investments in pandemic prevention, preparedness, and response. Decisions on what, where, and how to invest should reflect factors that drive pathogen emergence and spread.

Emerging Infectious Diseases

"Emerging infectious diseases" is a term used to describe infectious diseases whose incidence has recently increased or threatens to increase in the near future. These diseases include those caused by viruses, bacteria, fungi, and other microscopic biologic agents, often referred to collectively as "pathogens."

Public health and infectious disease experts have been warning since the 1980s that new pathogens are emerging, and that old pathogens are evolving faster than ever before and spreading more easily around the world. The wake-up call was HIV, which likely emerged in the early twentieth century but was not identified until many decades later. Every viral pandemic since 1900—including HIV, influenza, and almost certainly COVID-19—has been the result of the "spillover" of viruses from animals into humans. On this basis, it is reasonable to expect that the next pandemic will also have zoonotic origins.

There is no single pathway by which pathogens spill over from animals to humans. Factors that determine the likelihood of spillover include pathogen prevalence among its host animal species and the frequency and intensity of human contact with those animals. Researchers have identified several human actions that increase the risk of spillover [PDF] by bringing people, animals, and pathogens together, such as land-use change (particularly in the form of deforestation), commercial wildlife markets and trade, and poor infection control when raising farm animals.

Just because a microbe jumps from an animal to a human does not mean that it will cause an epidemic or, if over a large enough international area, a pandemic. Some viruses that spill over cause no illness despite infection and do not readily spread between humans, as in the case of simian foamy virus. Other viruses that spill over can cause severe human disease, but do not readily spread between humans outside of specific circumstances, as in the case of rabies virus. Still others are capable of causing severe human disease and spreading between humans through varying routes such as direct physical contact with infectious materials (e.g., Marburg virus), exposure to respiratory secretions (e.g., Middle East Respiratory Syndrome [MERS] coronavirus), or bites from non-vertebrate animal vectors such as mosquitoes (e.g., Dengue viruses). Even if

a pathogen can spread with ease between humans, other factors, such as crowding and travel, determine whether the initial outbreak will become an epidemic or pandemic.

The 2014–16 West African Ebola epidemic is an example of how these factors can converge to cause a crisis. Before 2014, most Ebola outbreaks occurred in relatively rural areas on the African continent. These outbreaks are believed to have started from human contact with an infected animal and were then amplified during funerals where people touched infectious corpses and in healthcare facilities where infection spread to healthcare workers and other patients. In 2014, these same amplifying factors combined with travel caused widespread community transmission in Guinea, Liberia, and Sierra Leone.

Climate change is a catalyst for many of the factors above. It is accelerating the destruction of landscapes and driving the migration of humans, animals, and vectors such as mosquitoes and ticks. Climate change is expected to greatly increase the burden of most infectious diseases.

Researchers have identified several areas where emerging infectious diseases are most likely to arise. These predictions, however, are highly uncertain, as demonstrated by serious public health threats that have occurred in areas considered lower risk, such as the Middle East (with the coronavirus that causes MERS) and Mexico (with the virus that caused the 2009 influenza pandemic).

Priority Pathogens

Several entities have created lists of "priority pathogens" that public health agencies, academics, and industry should prioritize for research, development, and preparedness. For example, the list of pathogens for rapid research and development from the World Health Organization (WHO) includes:

- Coronaviruses (i.e., SARS-CoV, SARS-CoV-2, and MERS-CoV)
- Crimean-Congo hemorrhagic fever virus
- Filoviruses (i.e., Ebola viruses and Marburg virus)
- Henipaviruses (e.g., Nipah virus)
- Lassa virus
- Rift Valley fever virus
- Zika virus
- Pathogen X (which refers to a pathogen currently unknown to cause human disease)

The Coalition for Epidemic Preparedness Innovations (CEPI), a leading global partnership to develop vaccines to stop future epidemics, has a separate but overlapping list:

- Chikungunya virus
- Ebola viruses
- Lassa virus
- MERS-CoV
- Nipah virus
- Rift Valley fever virus
- Pathogen X

In reality, scientists cannot currently predict with a high degree of certainty which pathogen will cause the next pandemic, though viruses are of greatest concern. Factors that increase the likelihood of a virus causing a large epidemic or pandemic include

- transmission through the respiratory route;

- transmission through *Anopheles* or *Aedes* mosquitoes;
- the ability to spread during the early stages of infection, particularly before onset of symptoms; and
- a lack of prior immunity among humans.

Primary Pandemic Prevention

The annual probability of pandemics is expected to increase several-fold in the coming decades. Given the increasing risk of recurring pandemics, the public and private sector should work together to reduce the likelihood and consequences of future pandemics. This requires investments in preventing outbreaks ("primary pandemic prevention"), preventing outbreaks from becoming epidemics and pandemics ("secondary pandemic prevention"), and, if a pandemic occurs despite these preventative efforts, increasing the ability to respond ("pandemic preparedness and response").

Primary pandemic prevention involves interventions to reduce the likelihood of viral spillover, improve laboratory safety, and impede the intentional release of pathogens. While all three of these actions are important, focusing on reducing viral spillover requires the most urgent attention given historic precedent and the ongoing pace of environmental destruction. The frequency of spillovers can be decreased by decreasing the clearing and degradation of tropical and subtropical forests; strictly regulating the commercial trade of live birds and mammals; improving veterinary care and welfare of farm animals; and enhancing the health and economic security of communities living in emerging infectious disease hotspots. All of these actions can be implemented for as little as $20 billion per year globally, a fraction of the millions of lives and trillions of dollars lost from a pandemic such as COVID-19.

Unfortunately, individuals and organizations that dominate pandemic policy discussions—including Bill Gates, the WHO Independent Panel for Pandemic Preparedness and Response, the G20 High-Level Independent Panel, and the Bipartisan Commission on Biodefense—have consistently overlooked primary pandemic prevention in their recent recommendations for addressing pandemics. In fact, some have even gone as far as to actively warn against investing in primary pandemic prevention. However, there are four reasons focusing exclusively on secondary pandemic prevention and pandemic preparedness is problematic.

First, inequity in access to the tools of secondary pandemic prevention and pandemic preparedness, such as vaccines, often hampers these efforts. While many important efforts are underway to address global inequities in access to these tools, it has consistently been the case that those with socioeconomic privilege acquire them before others, as is occurring with COVID-19 and monkeypox. In contrast, primary pandemic prevention aims to prevent an outbreak from occurring at all, thereby protecting everyone—particularly those in settings where access to these tools is limited.

Second, no set of public health interventions is perfect. Over the past two years, COVID-19 mortality has been widespread even in wealthy countries with advanced public health systems. Furthermore, the United States had a high level of preparedness for monkeypox—it has experience handling monkeypox outbreaks since 2003 and has been stockpiling tests, vaccines, and drugs for poxvirus outbreaks since 2001—but currently has the most cases of monkeypox of any country in 2022. Furthermore, in the last decade alone, viruses have defied conventional clinical and public health belief multiple times; this is why priority pathogen lists include a "Pathogen X."

Third, disinformation and rising populism have made proactive communication campaigns less effective. There is no guarantee that an efficacious vaccine or therapeutic will have enough uptake at the population level to abort an epidemic or pandemic if large numbers of people behave in ways that undermine individual and community health.

Fourth, secondary pandemic prevention does not adequately address the threat of "spillback," in which pathogens that spilled over from animals into humans spill back into animals, and then spill over again into humans, increasing the risk of new mutations that add to pathogenicity. Spillback is a leading theory for how the Omicron variant of SARS-CoV-2 emerged and is a major concern for monkeypox. All this underscores why primary pandemic prevention should be pursued alongside secondary pandemic prevention and pandemic preparedness initiatives.

The public health sector has often overlooked primary pandemic prevention. Traditional academic disciplines have likely constrained thinking around complex issues such as infectious disease emergence. Public health leaders often focus on short-term victories that reflect political and funding timelines rather than long-term efforts. It is also difficult to measure the success of primary pandemic prevention because there is no counterfactual for comparison. Finally, there is a bias toward acting only after catastrophe strikes.

All this means that no sector or agency is adequately addressing primary pandemic prevention. Public health experts may assume that the climate sector is already addressing the drivers that lead to spillover, but it is not. Unfortunately, the same biases toward waiting for catastrophe to strike hamper the climate sector as well. For example, nature-based solutions such as keeping forests intact represent 30 percent of the strategy for stabilizing climate, but receive less than 2 percent of climate funds—even though this solution to climate change is already at our fingertips.

Secondary Pandemic Prevention and Pandemic Preparedness

While the risk of spillover can be reduced, not every spillover will be prevented. That is why there should be investment in secondary pandemic prevention and pandemic preparedness. The last three years have shown that the world is unprepared for pandemics. In fact, some would argue that preparedness is now worse than in 2019. To implement secondary pandemic prevention and pandemic preparedness, governments, foundations, and organizations should invest in at least six fundamental areas. These investments are agnostic as to the origins of a pandemic—whether from a spillover, laboratory accident, or intentional release of a pathogen.

First, public health surveillance and data integration should be enhanced. Surveillance is at the core of any public health system, as it allows for ongoing systematic collection of data on diseases in a population with public health significance. Surveillance will not prevent outbreaks, but it will allow for early detection and intervention to prevent them from growing into epidemics or even pandemics. Surveillance should not be limited to humans. Monitoring diseases in domestic and wild animals can provide an early warning of diseases that might spill over into humans. One major challenge with public health surveillance is the limited sharing of data both between government agencies and across governments and sectors. Governments should incentivize and facilitate rapid, transparent data integration, analysis, and dissemination.

Second, diagnostic technologies should be improved. Clinical care and public health surveillance depend on the ability of medical workers to rapidly diagnose illness in patients. Delays in diagnosing highly transmissible pathogens can lead to their spread in both communities and healthcare facilities. Access to rapid diagnostics for emerging infectious diseases, whether in a laboratory or at the bedside, is limited in countries across the income spectrum. For example, a lack of access to diagnostics hampered the U.S. response to COVID-19 and its response to the monkeypox outbreak. There is an urgent need to develop and deploy rapid diagnostics capable of being performed at the bedside for multiple pathogens simultaneously with connectivity to the internet for seamless reporting to public health agencies.

Third, new and improved medical countermeasures such as vaccines and therapeutics should be developed. This includes research and development of medical countermeasures through public-private partnerships and ensuring equitable access to these medical countermeasures. While COVID-19 vaccines became available at record speed, there have been massive disparities in access. For example, over eighteen months after COVID-19 vaccines became available, only 29 percent of the African population has received at least one dose, compared with 81 percent of Americans and Canadians. Access is a function of supply and distribution, both of which need to be addressed to ensure equitable outcomes.

Fourth, public health workers should be recruited and retained. Public health work cannot be done without adequately trained staff. While civil society and academia are important components of a robust public health ecosystem in any country, it is imperative that the staff of national public health institutes (e.g., the Centers for Disease Control and Prevention in the United States) have adequate training and support to carry out their official duties on behalf of the public. The urgency of this need has been made more acute in the midst of COVID-19 given the high rates of burnout among public health practitioners [PDF]. Global experts have set a target of one trained field epidemiologist per two hundred thousand people for all countries globally; indeed, this is a woeful underestimate of the need, given the number of epidemiologists in high-income countries. Furthermore, national public health institutes need to have sufficient legal authority [PDF] and stable funding to act during public health emergencies.

Fifth, the provision of primary care should be enhanced. A robust primary health care system enables people to get care after an exposure to a pathogen, whether or not they have symptoms, thus saving lives and enhancing trust in health institutions. This also enhances the effectiveness of public health surveillance and early containment of outbreaks. Given that healthcare facilities are a common location where infectious disease outbreaks amplify, such as with Ebola, governments should also invest sufficiently in infection prevention and control to ensure the safety of patients who receive care and staff who provide care in those facilities.

Sixth, accurate information should be disseminated effectively. Misinformation and disinformation have cost lives during COVID-19; for example, significant populations around the world refused to get vaccinated for COVID-19. The threat is rising, as social media has given anti-vaccine movements additional reach and strength. Public health messaging is more likely to be received when trusted communicators are used, even if these individuals are not subject matter experts. Governments should ensure their own communicators are sufficiently trained in the science of crisis communications and utilize the full range of channels, including social media.

Conclusion

There is unprecedented support at the highest levels of government to enhance global pandemic prevention and preparedness. The recent decision to create a new fund for pandemics out of the World Bank and the ongoing negotiation for a pandemic agreement within the World Health Organization are potentially transformational. It is critical that comprehensive action be taken quickly through these efforts before the world's collective attention moves on to the next crisis. Failure to do so means future generations will live less healthy and productive lives than we have today.