and invest in leading technologies and strategies around communication in order to remain effective.

## 7. R&D aimed at rapid vaccine development for novel threats and distributed surge manufacturing should be a top global pandemic planning priority.

**Medical Countermeasures (MCM) Research and Development**

- There are a range of promising approaches to accelerate rapid vaccine development that should be concomitantly pursued and funded given the uncertainty in knowing which might bring the most important leaps forward.
- Traditional approaches of big pharma and biotech to vaccine and medicine development for infectious diseases will remain fundamentally important in the near term, though this process is expensive and time-consuming.
- Nucleic acid (RNA and DNA)–based vaccines are widely seen as highly promising and potentially rapid vaccine development pathways, though they have not yet broken through with licensed products.
- Advancements in non-nucleic acid–based platform technologies offer some hope of improving the speed with which vaccines for novel pandemic threats are developed and should be expanded.
- Contemporary advances in sequencing and structure function analysis—aided by artificial intelligence and big data analytic approaches—are yielding improvements in both speed and precision of immunologic design and should be supported.
- Similar gains are evident in the antimicrobial arena; as machine learning enters the drug discovery field, approaches to identifying appropriate targets for microbial control are shortening the times to leads and subsequent sensitivity and specificity studies.

**Distribution and Dispensing**

- Mass vaccination strategies should be developed and put in place to increase immediate access. A standing collaboration among international organizations, national governments, and the private sector will be needed to enable and coordinate global distribution to ensure maximal effectiveness and equitable access.
- The uptake of novel, needle-free administration technologies—specifically, those that enable either simplified or, potentially, self-administration—should be a priority to improve our collective ability to administer these countermeasures in clinically relevant timeframes.

- Industry, national regulatory bodies, public health authorities, and other stakeholders should invest in and promote the use of technologies that enable a rapid, streamlined approach to the administration of MCMs.
- WHO should encourage and support the creation of a public-private partnership dedicated to planning for and executing the prioritization and distribution of MCMs in a severe outbreak.

**Surge Manufacturing in Crisis**

- Regulatory agencies should consider regulating some platform technologies by platform, rather than by product.
- The relevant regulatory bodies, global authorization agencies, and public and private manufacturers should develop and exercise response plans.
- National regulatory agencies should establish mechanisms dedicated to decreasing timelines associated with regulatory requirements for MCMs in emergencies, while continuing to ensure safety and efficacy.
- WHO, industry, national regulatory bodies, and other stakeholders should work together to enable and radically increase MCM surge production and access globally. Localized distributed manufacturing could be one solution to this need if the technology and regulatory challenges can be addressed.
- Given the current geographic disparities in where such production and manufacturing efforts are conducted, access and benefit-sharing agreements will be needed.

**Other Research and Development**

- During an event involving a high-impact respiratory pathogen, there will be a critical need to conduct clinical and operational research to inform the response.
- Though there has been important progress in facilitating the conduct of emergency clinical trials, more work needs to be done to prepare to do them in very difficult conditions and rapidly.
- The absence of dedicated mechanisms to facilitate operational research during outbreak responses can result in a failure to collect and analyze valuable, ephemeral data that are crucial for continued learning in the field and generalized improvement of outbreak response.
- WHO, member countries, and philanthropies should develop dedicated resources and plans for the conduct of operational research during outbreaks, epidemics, and pandemics. To enable critical research to proceed without impeding response activities, pre-event planning is needed to identify priority research questions and evaluate potential research protocols.
- Pre-identified networks of researchers could help facilitate and prioritize research that is conducted.

## 8. Frameworks and plans articulating the evidence and role for nonpharmaceutical interventions need to be established.

- Nonpharmaceutical interventions (NPIs) have a greater likelihood of being implemented effectively if well analyzed ahead of time than if considered ad hoc during a crisis. Countries and international organizations need to better analyze the potential value and impact of NPIs; determine in which contexts, if any, a particular NPI would be effective; and conclude in which contexts they are likely do more harm than good.
- WHO and other public health authorities should have the capacity to provide risk/benefit analysis to national governments, driven by scientific evidence where it exists, *before* NPIs are initiated in a crisis.
- During an emergency, it should be expected that implementation of some NPIs, such as travel restrictions and quarantine, might be pursued for social or political purposes by political leaders, rather than pursued because of public health evidence. WHO should rapidly and clearly articulate its opposition to inappropriate NPIs, especially when they threaten public health response activities or pose increased risks to the health of the public.
- WHO and national authorities will need to provide strong evidenced-backed reasoning for the necessity of NPIs in order to effectively implement them and to communicate their role and necessity to the public, especially for NPIs such as social distancing that inherently limit civil liberties. Therefore, they should undertake directly or support research on NPIs and disseminate their findings on these analyses.

## 9. National governments should strengthen biosaftey around high-impact respiratory pathogens.

- Biosafety needs to become a national-level political priority, particularly for countries that are funding research with the potential to result in accidents with pathogens that could initiate high-impact respiratory pandemics.
- All nations should be advised to adopt national-level comprehensive biosafety norms for research involving high-impact respiratory pathogens.
- Countries that fund such research should have oversight systems in place that consider the risks and benefits of this kind of work, and they should have maximally stringent biosafety requirements for any laboratory that is allowed to pursue this type of research.
- WHO should develop stronger interest and capability in monitoring research with the potential to result in accidents involving high-impact respiratory pathogens, and it should advise member nations about the risks and benefits related to this work.

## 10. National governments need to prepare for the deliberate use of a respiratory pathogen.

- Preparation for a deliberate event must include recognition that the deliberate release of a high-impact respiratory pathogen could substantially add to the extraordinary consequences that would follow a naturally occurring pandemic event with the same agent.
- The United Nations (UN), WHO, and the international community will need to take steps to better understand their respective roles during a deliberate event, including greater clarity on which international agency would lead the response.
- Countries should support the adoption of synthesis screening approaches intended to identify work being done on high-impact respiratory pathogens.
- National governments and WHO should plan to engage in a coordinated and collaborative response to deliberate events. For example, pre-event planning is needed among public health officials, military, law enforcement, and/or intelligence communities in order to set expectations about appropriate roles and responsibilities and best practices for data sharing.
- Continued research into the science of attribution, as well as the strengthening of surveillance systems, international collaboration, and implementation of treaty agreements, particularly the Biological Weapons Convention (BWC), are all needed for an effective response to the deliberate use of a biological weapon with a high-impact respiratory pathogen.

## RISKS POSED BY HIGH-IMPACT RESPIRATORY PATHOGENS

The far-reaching tolls of epidemics and pandemics caused by high-impact respiratory pathogens[*] have been documented throughout history. Just over 100 years ago, a new influenza virus spread across the globe, sickened an estimated one third of the world's population, and killed upwards of 50 million people. The toll of this event extended well beyond its health impacts. High burdens of illness and rapid transmission led to high rates of worker absenteeism, which had effects on communities' abilities to maintain public safety and basic infrastructure.[1] Occurring in the midst of a world war, influenza and pneumonia killed more soldiers than did armed conflict, according to US military reports, and the need to care for the sick and the dead diverted resources from combat operations.[2]

Though there have been many medical advances since 1918 that would aid in a response to a high-impact respiratory pathogen event, were such an event to occur again, it would still have severe societal consequences. Today's global population is more than 4 times greater than it was 100 years ago. In 1918, shipping played an important role in spreading influenza around the world, but today's travelers can travel anywhere in the world in less than 36 hours, meaning that global spread would be likely to be far more rapid.[3,4] The World Bank has estimated that a severe pandemic such as the one that occurred in 1918 could cost the modern economy from 1% to 4.8% of global gross domestic product. Even if the next pandemic is not as severe as the one in 1918, it will likely have significant consequences. The World Bank estimates that "mild" and "moderate" pandemics, such as those that occurred in 1957 and 1968, could still cause more than 10 million deaths and reduce global economic activity by 0.7%.[5]

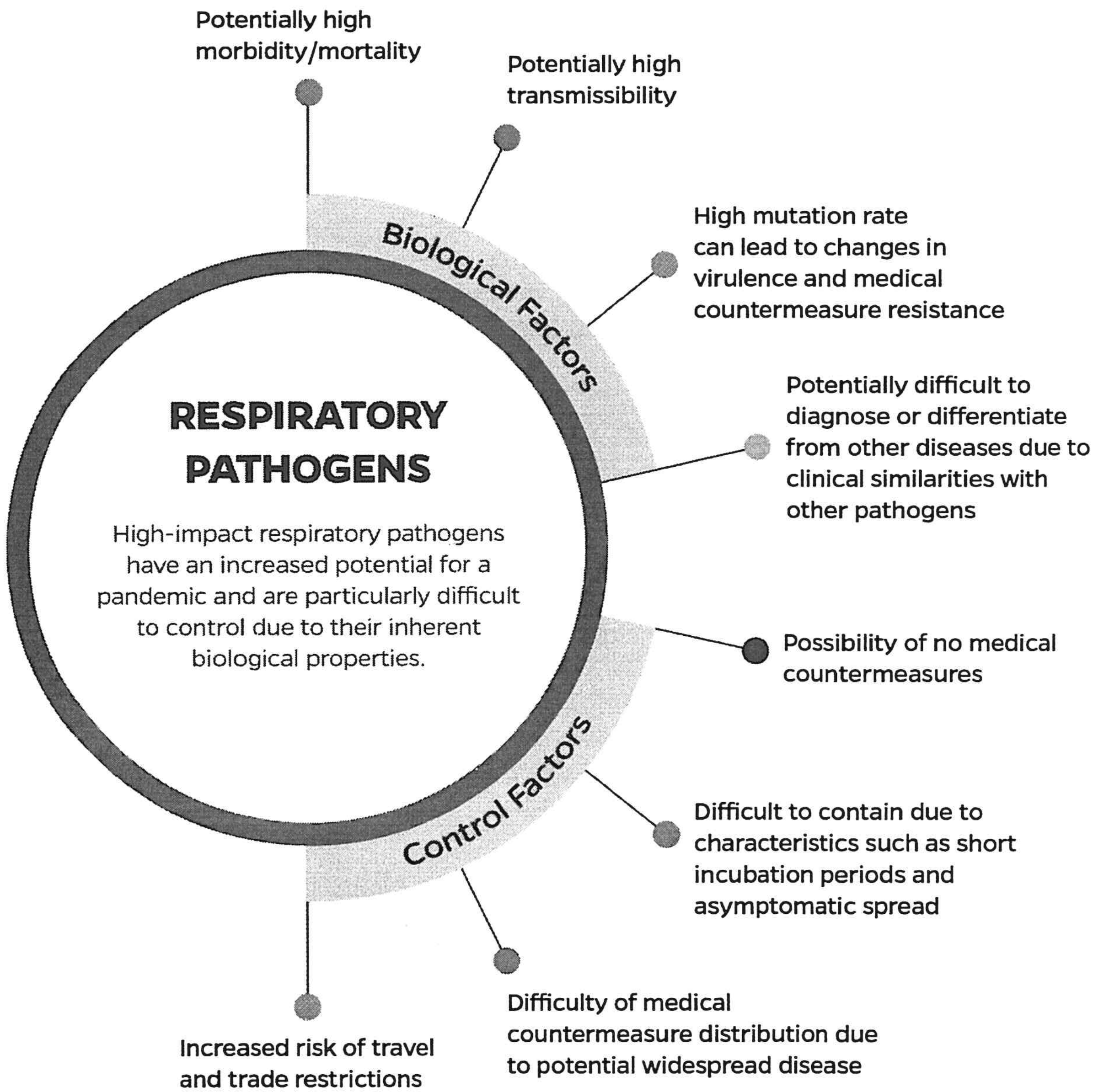
National and regional epidemic events, though geographically limited in scope, are capable of taking significant tolls and causing major international disruption. The Ebola epidemic in West Africa in 2014-2016 sickened more than 30,000 people and is estimated to have cost the 3 affected countries $2.8 billion in lost GDP.[6] The 2003 SARS epidemic spilled over national borders to sicken more than 8,000 people in more than 20 countries and is estimated to have cost the global economy upwards of $40 billion.[7] Had the virus been more easily transmissible outside of clinical environments, the public health impacts of this event would likely have been much greater.

* For the purposes of this report, we define "high-impact respiratory pathogens" as pathogens that are readily transmissible by the respiratory route (via droplets and airborne transmission); that, due to their typically short incubation periods and high probability of person-to-person transmission, have the potential for widespread (possibly pandemic) spread; and, due to their high observed percent mortality (generally on the order of at least 1%, possibly substantially higher), may have significant public health, economic, social, and political consequences. We expect that, were such a pathogen to emerge, either naturally, or as the result of accidental or deliberate release, many countries would be affected at once, which would require different international approaches than typically occur in geographically limited events.

While the economic impact of pandemics, epidemics, and outbreaks depends, in part, on the severity of the health effects of these events, the actions that countries take in an attempt to control the spread of disease can also exacerbate its tolls. The 2009 H1N1 influenza pandemic, which was generally assessed to be mild in terms of its health effects (and therefore, for this report, would not qualify as a high-impact respiratory pathogen), offers a recent instructive example of this. In 2009, countries that were initially affected experienced drops in tourism revenues as other countries implemented bans and other restrictions on travel in response.

Additionally, some countries responded by employing trade restrictions, which did little to alter the spread of the pandemic but increased its economic costs.[8,9] Such actions are common during significant disease events. For example, during the West Africa Ebola outbreak, more than a third of States Parties to the International Health Regulations (IHRs) implemented restrictions on travel that exceeded recommendations made by the World Health Organization.[10] From these experiences, we can expect that countries would likely be inclined to take similar measures in response to a high-impact respiratory pathogen.

Figure 1: Potential Challenges Posed by High-Impact Respiratory Pathogens



The potential for an epidemic or pandemic caused by a high-impact respiratory pathogen is increasing. Data show that the frequency of outbreaks of newly emerging diseases is rising.[11]

Novel pathogens continue to emerge, often first in animals, then with subsequent spillover into human populations living in close contact with animals, due to changing patterns of animal management and land use. Global conditions enable pathogens to spread widely and quickly in people. International travel, mass displacement, migration, and urbanization enable pathogens to spread in new, susceptible populations.[9] The rising incidence of chronic illnesses and drug-resistant infections place individuals at greater risk of infection and complications from respiratory viruses.[12] Declining levels of protection from vaccines due to the influence of anti-vaccination sentiments in some communities is enabling previously declining respiratory viruses to cause significant outbreaks.[13] Climate-related changes have altered the geography of habitats suitable for spread of certain pathogens and have changed patterns of migration, as humans move to escape consequences of extreme weather events.[14] All of these factors increase the chance that new high-impact respiratory pathogens will emerge and spread, raising the possibility that an epidemic or pandemic will occur.

Novel high-impact respiratory pathogens have a combination of qualities that contribute to their potential to initiate a pandemic (see Figure 1). Respiratory pathogens can be particularly difficult to contain. Their tendency to have short incubation periods and their potential for asymptomatic spread can mean very small windows are available for interrupting transmission. Individuals infected with respiratory viruses may infect many more people at a time as compared to pathogens spread by other means. These factors increase both the pandemic potential of respiratory pathogens and the likelihood that there will be serious public health, economic, and social impacts with their spread. Some viral groups have characteristics that give them a higher probability of being a future source of a novel pandemic pathogen (see Box 1 and Table 1). In anticipating the implications of a high-impact respiratory pathogen, it is useful to consider, as an illustrative disease, the high-impacts of measles in the current world. If we start with naturally occurring measles, and then imagine that measles had an increased percentage of case fatalities and a decreased potential for containment (eg, the absence of a vaccine and the lack of herd immunity), this could reflect the conditions presented by a high-impact respiratory pathogen[15] (see Box 2).

Scientific developments have greatly advanced medical and public health tools to fight epidemic disease, as will be detailed later in this report. But scientific developments have also created the ability for pathogens to be engineered or recreated in laboratories. Should countries, terrorist groups, cults, or scientifically advanced individuals create or obtain and then use biological weapons that have characteristics of a novel, high-impact respiratory pathogen, the consequences could be as severe as or greater than the consequences that would follow a naturally occurring pandemic with such pathogens[16] (see Box 3). Similarly, a laboratory accident involving such pathogens could have a terrible impact if it led to a disease rapidly spreading in a community. Taken together, naturally occurring, accidental, or deliberate events caused by high-impact respiratory pathogens pose pandemic risks that elsewhere have been termed "global catastrophic biological risks."[17]

Global efforts to prepare for significant disease outbreaks have revealed large national and international readiness gaps around detection and containment, including challenges related to tools, personnel, and surveillance systems. After-action reports conducted after recent events, such as the 2014-2016 Ebola epidemic in West Africa and the 2009 influenza H1N1 pandemic, showed systematic failures in global governance and response.[18,19]

High-impact respiratory pathogens—whether they are well known, novel strains of recognized diseases, or as-yet unrecognized (such as a "Disease X" noted by the World Health Organization Research and Development (R&D) Blueprint, or a Clade X, which was the subject of a recent tabletop simulation)—warrant special consideration, given the substantial global risks they pose.[20,21] This report examines global progress toward and gaps surrounding preparedness for high-impact respiratory pathogens, and it provides conclusions to strengthen that preparedness.

## Box 1: Viral Groups Most Likely to Be a Source of Pandemic-Initiating Pathogens

Of the multiple ways in which a microorganism can be transmitted between humans (eg, body fluids, vector-borne, fecal-oral, foodborne, respiratory), the respiratory route poses greatest concern in terms of pandemic risk. As noted in a recent report titled *Characteristics of Pandemic Pathogens*, several features of respiratory transmission are important determinants of pathogen risk.[15]

The primary reason respiratory transmission (which includes pathogens spread by both airborne and respiratory droplet transmission) is the transmission route posing the greatest pandemic risk is that standard public health measures may not easily interrupt transmission. By contrast, each of the other major forms of disease transmission can be interrupted with sanitation, hand-washing, or other forms of intervention. Respiratory transmission can occur with coughing or simply breathing (in aerosol transmission), making containment much more challenging.

Recent high-impact outbreaks of respiratory viruses make this case. In 2009, for example, a novel pandemic influenza virus emerged in Mexico and achieved prolific spread across the planet, causing disruption and widespread illness. Similarly, the 2003 emergence of SARS, caused by a zoonotic coronavirus, was characterized by billions of dollars of economic losses, worldwide circulation fostered by superspreading respiratory events, and severe disruptions. MERS, also caused by a coronavirus of animal origin, bears many of the hallmarks of SARS, including superspreading respiratory events, though it has thus far spread less widely than SARS. These respiratory-borne viruses are testament to the challenges of containment of respiratory pathogens.[22,23]

Another important aspect of pathogen transmission is the timing of transmission. While this is a factor in all modes of transmission, it takes on a heightened role in respiratory transmission because of the relative ease with which respiratory transmission takes place. If an infection is contagious in its incubation period—that is, prior to symptom onset—spread will likely have taken place before awareness of the risk of the infection. This phenomenon is exemplified by diseases like influenza, in which contagiousness precedes symptoms.[24]
Coupled with contagiousness during incubation period is the ability of a microbe to cause a spectrum of illness or have a time course of severity. If a pathogen is capable of causing asymptomatic or mildly symptomatic infections that either do not or only minimally interrupt activities of daily living, many individuals may be exposed. Viruses that cause the common cold, including coronaviruses, have this attribute and are important factors in the widespread nature of the common cold. This mild illness phenotype was also seen in 2 US importations of MERS . Modeling studies have identified this factor as being decisive in outbreak control.[25]

Many respiratory viruses possess RNA (as opposed to DNA) genomes, which may also confer special status on this group in terms of pandemic potential. An RNA genome is often characterized by high degrees of mutability, some of which may confer vaccine escape, antiviral resistance, heightened viral shedding, or increased pathogenicity. RNA viruses also tend to replicate in the cytoplasm of host cells and not the nucleus, a feature that may tie them less to one species and allow more promiscuity of host type (exceptions exist).[26]

Salient features of several classes of respiratory-borne viruses are summarized in the table below. While only a subset of these have caused documented pandemics, these groups all have viruses that have characteristics consistent with increased pandemic potential. Other than influenza and enterovirus, no systematic surveillance occurs for these viruses and there are no vaccines or unequivocally effective antivirals.[15]

**Table 1: Viral Groups with Characteristics Most Consistent with Pandemic Pathogens**

| Viral Group | Important Members | Special Features |
|---|---|---|
| Orthomyxovirus | Influenza | Contagious during incubation period, demonstrated pandemic capacity, airborne and droplet transmission, high mutability |
| Respirovirus* | Human parainfluenza viruses 1 and 3 | Highly contagious, spectrum of illness, capacity to cause severe infection, no countermeasures |
| Henipavirus* | Nipah | Zoonotic origin, limited human-to-human spread, very high mortality, no countermeasures |
| Rubulavirus* | Human parainfluenza viruses 2 and 4 | Highly contagious, spectrum of illness, capacity to cause severe infection |
| Coronavirus | MERS, SARS | Zoonotic origin, human-to-human spread, high mortality, no countermeasures |
| Enterovirus** | EV-D68, EV-D71 | Highly contagious, spectrum of illness, capacity to cause severe infection, no countermeasures |
| Rhinovirus** | Human rhinovirus C | Highly contagious, ubiquitous, spectrum of illness, capacity to cause severe infection, no countermeasures |

*These 3 are paramyxovirus genera.
**These 2 are picornavirus genera.

## Box 2: Measles Is Bad Enough. What if It Were Worse?

Measles is a highly contagious viral disease that causes serious and sometimes fatal clinical syndromes in children and adults worldwide.[27] Measles is characterized by high fever, runny nose, cough, and a red blotchy rash, among other symptoms.[28] It is spread via droplets, either airborne or through direct contact, when an infected person coughs or sneezes.[29] Deaths due to measles usually occur following complications such as pneumonia or acute encephalitis.[30] These complications are seen more often in children under 5, pregnant women, and people who are immunocompromised.[31] The measles vaccine is safe for most people over 12 months of age and is 93% effective after 1 dose; it is 97% after 2 doses.[27]

With easily identifiable clinical symptoms, lack of carrier state, lack of an animal reservoir, a safe vaccine, and relatively low mortality, measles would be expected to be easily controlled compared to other viruses that commonly cause disease in humans.[30] But while measles was declared eliminated from the United States in 2000, it has since seen a resurgence due to a combination of factors, including the lack of access to care and the rise of vaccine hesitancy.[32,33] Measles has experienced a global resurgence as well, with a tripling of reported cases worldwide in the first quarter of 2019 compared to last year.[34] Its persistence can be explained in part by its high transmissibility. Each person infected with measles is capable of infecting between 12 and 18 additional people.[27] Comparatively, each Ebola case in the 2014 outbreak was only capable of infecting 1.5 to 2.5 additional persons.[35]

With proper medical care and vaccination coverage, mortality from measles is approximately 1% in developed countries, but it can range from 10% to 30% in countries lacking sufficient healthcare infrastructure or where access to health services is limited.[28] These mortality rates are often higher in vulnerable populations, including children, the elderly, and nonvaccinated or immunocompromised individuals.[31]

Measles infection rates and mortality rates were much higher before the introduction of the measles vaccine in 1963, with more than 130 million cases and 7 million deaths annually worldwide.[31] Despite the effectiveness of the measles vaccine, the world continues to experience a global resurgence of cases. It is also important to remember that there is a certain level of baseline immunity to measles, particularly among older generations for whom measles was a practically ubiquitous childhood disease.[28]

What if a disease as transmissible as measles had a case fatality as high as SARS or Ebola, for which there was no effective vaccine and no population level immunity? Analyzing what it would take to control this kind of event helps to crystallize what kind of national and global systems would need to be in place to respond novel, high-impact respiratory pathogens.

## Box 3: Anticipating Challenges During the Deliberate Release of a High-Impact Respiratory Pathogen

Previous epidemics and pandemics caused by high-impact respiratory pathogens, such as the 1918 influenza, showed how such pathogens can lead to widespread health, social, and economic damages.[36] Now, with advances in biology, a high-impact respiratory pathogen could be engineered to create transmissibility and lethality. The deliberate release of such a pathogen could substantially add to the already extraordinary consequences that would follow a naturally occurring pandemic event.

A key difference between deliberate release scenarios and those in which a high-impact respiratory pathogen emerges and spreads via natural mechanisms would be the possibility for there to be multiple attacks, or "reload," in a deliberate event. A sophisticated assailant could use a bioweapon to target areas of public health vulnerability or to deliberately inflict harm on the population or particular segments of it. The ability to effectively respond to such a deliberate event would depend, in part, on an understanding of the risk of subsequent attacks. Activities in the nonhealth domain, such as attribution and interdiction, would be critical capabilities alongside medical and public health response. Currently, there is no clarity on which agency would lead the response to a deliberate event and what responsibilities this would entail (ie, operating the public health response or the investigation and attribution).[37]

Severe epidemics and pandemics have demonstrated how contagious disease emergencies can exacerbate societal divisions, by fomenting social and political tensions and generating stigma against vulnerable groups who may be blamed.[38] The potential for such negative societal consequences could be even worse in a deliberate event. Groups who are perceived as aligned with the perpetrator of an attack may experience backlash.[39] Public fear and uncertainty could be high in the aftermath of a deliberate event, requiring highly effective risk communication and public outreach. Geopolitical ramifications should be expected if countries or terrorist groups were behind such an attack and likely addressed at very high levels, such as the United Nations Security Council.[40] The involvement of the security and intelligence communities may lead to altered or centrally controlled decision-making structures, with implications for the World Health Organization (WHO) and the wider public health response. Currently, no designated position or entity exists in the United Nations (UN) system with a dedicated mandate to coordinate the response to a deliberate event.

In such an event, public health officials would need to interface with law enforcement and/or military personnel, even if their operational goals did not fully align; public health would be attempting to contain the outbreak and identify the pathogenic strain, while national security and law enforcement may consider certain materials or locations to be vital evidence and might think it necessary to limit access to them. Public health and humanitarian workers may be hesitant to operate alongside security personnel in the response, given the possibility or perception that data may be used to further investigations or somehow compromise UN humanitarian principles of independence and neutrality. Security officials may argue that attribution should take priority over the public health response in order to stop a "reload" scenario that could harm others.

Communication, data sharing, outreach, and coordination are key capabilities for managing a response to any severe outbreak, particularly in a pandemic, when many sectors from multiple countries would need to interact openly and honestly with each other to mount an effective response.[41] Data sharing would also need to take place between health and security officials, between international organizations, and among national governments. However, the investigative and intelligence communities may be hesitant to share information with the public health sector due to security issues.

Especially if there were no available medical countermeasures to prevent a disease or treat people after a deliberate event, and if spread could not be readily controlled, national governments may focus on protecting their own citizens rather than cooperating with other countries. The implementation of border closures and travel bans may give governments more credibility among their own citizens for attempting to stop the outbreak, but historical evidence and modeling and public health experts would argue such measures would be unlikely to substantially add to disease control efforts. Prenegotiated bilateral material transfer agreements could help to ensure data and specimen sharing across borders.

Currently, there are few viable avenues for attribution of a deliberate event to a specific actor. Few countries have any existing framework to begin pursuing attribution, and the language of the Biological Weapons Convention leaves much open to interpretation. Continued research into the science of attribution, as well as the strengthening of surveillance systems, international collaboration, and treaty agreements, are all needed for an effective response to the deliberate use of a biological weapon with a high-impact respiratory pathogen.

## WHAT PREVIOUS REVIEWS TELL US ABOUT PREPAREDNESS FOR HIGH-IMPACT RESPIRATORY PATHOGENS

Numerous high-level reviews have been commissioned in recent years to take stock of global preparedness. These reviews—whether comprising a panel of subject matter experts, a written report, or both—have sought to assess current preparedness structures and capabilities, identify existing gaps, and propose recommendations for strengthening outbreak prevention, detection, and response. Assessments from the United Nations, the World Health Organization, the World Bank, the World Economic Forum, the US National Academies of Science and Medicine, nonprofit organizations, and academic institutions have all contributed valuable analyses and recommendations on this topic.

Many of these initiatives* were commissioned following the 2014-2016 Ebola outbreak in West Africa and reflect on the challenges associated with that response.[42-45] While some recommendations from these Ebola-action reviews are generalizable to other epidemic and pandemic events (eg, strengthening IHR implementation), others focus on identifying and recommending improvements needed to prepare for an outbreak of Ebola virus disease or other hemorrhagic fever, and, as such, their findings are not necessarily applicable to high-impact respiratory pathogens.[7,46-51] Some reviews provide recommendations that are intended to be generalizable for any disease outbreak, with the goal of improving overall international and national preparedness capabilities. For example, the National Academy of Medicine report provided recommendations to the World Health Organization, the World Bank, the International Monetary Fund, and national governments to strengthen public health preparedness, improve existing global systems for outbreak response, and increase research and development efforts.[46] A review by the National Academy of Science calls for initiatives such as national governments building information-sharing mechanisms into their institutions, growing the role of nontraditional response actors such as philanthropists, and increasing research and development efforts, particularly with at-home diagnostics.[52]

However, while there is overlap between the systems and capabilities required to respond to any disease outbreak, a high-impact respiratory pathogen poses additional challenges

*Among the reports we considered, those specific to the West Africa Ebola outbreak include the Harvard-LSJTM Independent Panel on the Global Response to Ebola, the European Parliament Report on the Ebola Crisis, the 2015 Ebola Interim Assessment Panel, and the IHR Review Committee on Ebola. Other reports that were commissioned in light of the Ebola crisis and focus on recommendations to improve general preparedness systems include the UN Panel on Protecting Humanity of Future Health Crises; the Global Health Crisis Task Force; the World Economic Forum report, Managing the Risk and Impact of Future Epidemics: Options for Public-Private Cooperation; the International Vaccines Task Force report, Money & Microbes: Strengthening Clinical Research Capacity to Prevent Epidemics; the National Academy of Medicine Report, The Neglected Dimension of Global Security; the International Working Group on Financing Preparedness report, From Panic and Neglect to Investing in Health Security: Financing Pandemic Preparedness at a National Level; and the reports of the Independent Oversight and Advisory Committee for the WHO Health Emergencies Programme.

that deserve special consideration. A small number of high-level reviews do specifically examine global preparedness for a major outbreak of pandemic influenza, such as the report of the Committee on the Functioning of the International Health Regulations in relation to the 2009 H1N1 pandemic, known as the Fineberg Report. Convened following the global transmission in 2009 of the H1N1 virus, the Fineberg Report made several high-level recommendations for improving the IHR and public health emergency response in the context of pandemic influenza. The chief recommendations included: faster implementation of IHR core capacity requirements, the creation of a global public health workforce, building the evidence base for decisions on international trade and travel restrictions, making the IHR Emergency Committee declaration process more transparent, developing uniform and agreed-upon measures to assess the severity of pandemic and seasonal influenza strains, and establishing advance agreements with manufacturers for vaccine distribution.[19]

Of note, several of these recommendations were later adopted, including the committee's calls for agreements on influenza virus sample sharing and access to benefits, which culminated in the Pandemic Influenza Preparedness (PIP) Framework.[53] Another framework, the WHO Global Influenza Strategy for 2019-2030, also followed reports recommending the establishment of robust international and national preparedness capacities for seasonal and pandemic influenza; development of vaccines, antivirals, and treatments; and implementation of measures to increase country prevention, preparedness, and response capacities.[54]

Other high-level reviews with a specific focus on preparedness for influenza outbreaks include reviews of the PIP Framework and accompanying processes, such as the Global Action Plan for Influenza Vaccines, the WHO Global Influenza Surveillance and Response System (GISRS), and the WHO Pandemic Influenza Vaccine Deployment Initiative. Numerous recommendations have been made for improving both the PIP Framework and its implementation, including the possibility of adding other diseases (such as animal or seasonal influenza) into the framework; implementation of the Nagoya Protocol to the Convention on Biological Diversity, which could influence influenza virus sample sharing and the equitable distribution of and access to vaccines and other benefits; and ongoing participation of the pharmaceutical sector and other private sector manufacturers in the legal process. It is important to note, however, that the PIP Framework does not apply to respiratory pathogens other than pandemic influenza.[45,53,55]

It should be noted that the 2009 H1N1 pandemic was relatively mild by the standards of other strains of pandemic influenza, such as the 1918 H1N1 pandemic. Thus, its applicability may have limits in the context of a more virulent outbreak of a respiratory pathogen. The Fineberg Report paved the way for subsequent high-level reviews of the global health architecture, especially following the 2014-2016 Ebola epidemic. Many of these high-level assessments have also emphasized the challenges of IHR core capacity implementation and WHO operational response capacity.[18,19,44]

The IHR is the legal framework governing global disease detection and response, including novel strains of pandemic influenza.[56] A consistent strong theme among high-level assessments is the lack of compliance among countries in fulfilling the IHR core capacity requirements. Numerous reviews show that there is wide agreement that IHR implementation for national health systems should be strengthened, including a need for enhanced monitoring and evaluation of core capacity requirements, backed by appropriate financial and technical support and other incentives for country implementation.[18,19,45]

The leadership role and operational capabilities of WHO, which would be expected to lead in the event of a high-impact respiratory disease outbreak, have been widely examined and documented, specifically through the UN Panel on Protecting Humanity from Future Health Crises and the subsequent UN Global Health Crises Task Force.[47,48] While most high-level reviews have reaffirmed the central role of WHO in outbreak response, they have also called for wide-ranging reforms, which culminated in the establishment of the WHO Health Emergencies Programme. Monitoring of WHO's new Health Emergencies Programme and its operational, leadership, and management processes is done through reports of the Independent Oversight and Advisory Committee for the WHO Health Emergencies Programme. Recurring recommendations for WHO from these reports include strengthening emergency response leadership and operations; clarifying public health emergency procedures and accountability; increasing mobilization of financial support for health systems programming; increasing support for country research, development, and manufacturing capacities for medical countermeasures; and enhancing coordination with national governments, the United Nations system, and development and humanitarian actors.[49]

The importance of community engagement and social mobilization has emerged as a key theme among recent assessments. A 2019 report commissioned by the Wellcome Trust and UK Department for International Development (DFID) advocate for "people-centered" approaches to epidemic preparedness and response. The report recommended "making social science a permanent core part of the preparedness and response architecture," including developing social science capacity in organizations such as WHO and the UN, as well as integrating social science with the Joint External Evaluation (JEE).[57] A 2019 Center for Global Development after-action review of the 2014 Ebola epidemic observed the central role of behavior and community-driven methods in scaling up the response. Especially during a global event with millions of cases, during which traditional control strategies may be infeasible or unavailable, the report called for limiting transmission via "a strategic shift toward behavioral interventions," including equipping communities with the basic knowledge and tools needed to protect themselves.[58]

Some of the high-level analyses have argued that community engagement is highly relevant when considering public reactions (positive and negative) to outbreak responses, linking strong equitable health systems to preexisting constructive relationships with communities, and framing risk communication as a means to apply nonpharmaceutical interventions broadly and successfully. Reviews examining pandemic influenza vaccine focus principally on technical or operational challenges for research, development, production, and administration, rather than ultimate population uptake—a social challenge. Still other disease outbreak and health security frameworks and analyses do not address community engagement at all, or they treat it as an unelaborated aspect of risk communication.[19,49,55]

In addition, multiple reports* have recognized that a response to a severe outbreak will increasingly need to incorporate actors from all sectors, including the private and business sectors. Recommendations on this issue consist of engaging with private stakeholders, incorporating private-sector actors into national strategies and preparedness planning, strengthening public-private collaboration for research and development, and using the private sector and businesses for financial and technical support.[7,50-52,59] A review by the National Academy of Sciences specifically references the expertise the private and business sectors contain that can be utilized in response mechanisms, including operations, logistics, and supply chains.[52] Reports have noted that the support the private sector could provide would aid national governments in their preparedness planning and benefit responding agencies in streamlining activities such as procurement processes. In addition, the World Economic Forum report that addresses the risk and impacts of future epidemics strongly advocates for public-private collaboration and provides potential models to optimize private-sector engagement. The World Economic Forum recommends building connections between in-country operators and the public sector; expanding expert-based groups, such as the UN Clusters, to include private sector partners; and developing a platform to improve information flow and increase coordination between the private and public sectors.[50]

In summary, preparedness for a high-impact respiratory pathogen has received little specific focus in these high-level reviews, notwithstanding hundreds of useful recom-

* Reports include the National Academy of Science, Lessons Learned from a Century of Outbreaks; the World Economic Forum, Managing the Risk and Impact of Future Epidemics: Options for Public-Private Cooperation; the International Vaccines Task Force report, Money & Microbes: Strengthening Clinical Research Capacity to Prevent Epidemics; the International Working Group on Financing Preparedness report, From Panic and Neglect to Investing in Health Security: Financing Pandemic Preparedness at a National Level; and the Independent Commission on Multilateralism, Global Pandemics and Global Public Health.

mendations related to strengthening and increasing preparedness systems and structures generally, or specifically related to other forms of outbreak threat. While there has been some focus on improving international and national capacity for pandemic influenza—specifically after the 2009 H1N1 pandemic and subsequent Fineberg Report—there have been few (if any) high-level reviews or recommendations focusing on the possibility of other high-impact respiratory pathogens with pandemic potential.[19,60,61] The lack of global attention to and consideration of this threat illustrates the vital need to address preparedness for epidemics and pandemics that might be caused by high-impact respiratory pathogens.

## HOW CAN THE WORLD BETTER PREPARE FOR OUTBREAKS CAUSED BY HIGH-IMPACT RESPIRATORY PATHOGENS?

### Global Preparedness Mechanisms

Global preparedness mechanisms, which encompass international treaties, frameworks, and agreements, articulate the international roles and national capacities required to prevent, detect, and respond to a high-impact respiratory pathogen event. Published guidance documents, standard operating procedures, and frameworks denote international outbreak emergency response capacities and processes, as well as considerations for data sharing, travel and trade restrictions, and other aspects of the international response.

As many of these international frameworks have been conceived only within the past 20 years, they remain untested during a high-impact respiratory pathogen event that causes serious illness or death in tens or hundreds of millions of people or more. Though not an example of a high-impact respiratory pathogen as defined in this report due to its lower mortality, the emergence and global spread of a novel influenza A H1N1 virus in 2009 provided an opportunity to test modern preparedness mechanisms. The ultimate health impacts of the 2009 influenza pandemic may have been lower than initially feared; however, international conflicts arose about the development and sharing of vaccines and other medical countermeasures and what actions should be taken to limit transmission.[19,45]

It remains to be seen the extent to which the global preparedness system will be prepared to respond to an epidemic or pandemic event caused by a high-impact respiratory pathogen. But as observed in the 2009 pandemic, individual country needs might quickly outstrip international resources and capacities, and national interests might overtake the imperative to adhere to international agreements on sample sharing, vaccine access, and emergency medical assistance.[60] During a high-impact scenario, the limitations of current international frameworks would come into immediate focus.

### The International Health Regulations

The International Health Regulations (2005), an international treaty that outlines WHO's and Member States' responsibilities in disease preparedness and response efforts, represents an important and useful framework for building consensus and aligning global health stakeholders on questions of disease prevention, detection, and response. The revision of the IHR in 2005 can be largely attributed to the emergence and international spread of SARS in 2003. Though the initial call to revise the IHR came during the 1998 World Health Assembly and more there had been an international push to modernize the IHRs for many years, SARS highlighted critical gaps in the authority and scope of the IHR itself, the obligations of WHO and other international bodies, and the duties of countries, specifically their national reporting commitments. The revised IHR requires States Parties to develop core public health capacities to prevent, detect, prepare for, and respond to any disease outbreaks. Unlike its predecessor, the revised IHR includes a focus on novel pathogens that have the potential to spread beyond borders, threaten other countries, and may be considered as a potential Public Health Emergency of International Concern (PHEIC).[56,62]

The capacities that have been identified as core to the IHR are not only useful for the detection of and response to rare events, but, rather, they have day-to-day benefits in helping to identify, measure, and respond to routine health events. For example, a robust national process and a system to enable the collection, analysis, and dissemination of surveillance data is an essential tool for identifying and understanding patterns and drivers behind a wide range of health threats. Similarly, all countries need to be able to communicate with their populaces about health issues and protective actions that they can take. The processes and systems used to conduct risk communication and national surveillance can be multipurpose, serving everyday health priorities, but then tapped, and modified or expanded, if necessary, during emergencies.[56]

Arguably, the IHR's greatest value lies in early efforts of detection and control, before a respiratory pathogen becomes widespread. The IHR requires countries to develop the capacities to detect and report potential PHEICs, with the goal of providing early warning of events that could spread beyond borders and threaten other countries.[63] Past detection of significant zoonotic events, such as Middle East Respiratory Syndrome (MERS) and H7N9, have occurred in a manner that was generally in accordance with IHR protocols, and many countries have adhered to the IHR through transparency in their reporting to WHO. If surveillance and reporting systems can quickly detect and notify WHO of a novel respiratory pathogen that has acquired human-to-human transmissibility, global decision makers may be able to act to limit the spread of the disease by adopting evidence-based nonpharmaceutical interventions. This could, in turn, buy time to mobilize a research agenda to better understand the nature of the threat, collect and share samples, and develop medical countermeasures.

However, the IHR faces challenges in its implementation and content. There is a large disparity in countries' efforts to strengthen their core capacities to prepare for, detect, and respond to potential pandemics. There is a lack of legal provisions to penalize countries for not conforming to WHO recommended measures during emergencies on travel and trade restrictions, and there are concerns related to the criteria for PHEIC declarations.[56,64] The influence of IHR provisions on travel and trade and on a PHEIC declaration during a high-impact respiratory pathogen event would be more limited than in a geographically circumscribed event such as Ebola, since disease would spread quickly across the world.

### Joint External Evaluation

The IHR requires signatories to develop core public health capacities to prevent, detect, and respond to any disease outbreaks. The Joint External Evaluation (JEE) process was developed as a voluntary, multisectoral program to assess national-level IHR implementation and identify critical gaps and challenges in national preparedness mechanisms.[65] To date, more than 85 countries have voluntarily undergone a JEE and have published the results, as determined by the number of available JEE mission reports.[66]

While the number of countries that have completed JEEs is encouraging, the small number of these that have followed through to address gaps in their JEEs is concerning and suggests that new strategies are needed to keep countries motivated to complete the intended full JEE process that would result in improved core capacities. Data will be essential to motivating political leaders and to measuring progress. Efforts should be made to ensure assessments of core capacity developments are conducted regularly. Currently, it is planned that the JEEs will be repeated every 5 years. However, given the pace with which JEEs are being conducted and the current level of resources allocated to the JEE process, it is unlikely that this timetable will be met.

The JEE is broadly capacity-focused so that it can address a range of threats. Because of this focus, it does not encourage or call on countries to develop plans specific to the unique needs of high-impact respiratory pathogens.[65] There are additional capacities that would likely be needed during a potential high-impact respiratory pandemic that are currently not captured in the JEE. These include the healthcare system's capability to cope with serious respiratory disease, the capacity to manage continuity of critical government functions despite widespread illness and absenteeism, and the capacity to rapidly acquire medical countermeasures and other equipment when other countries are concurrently seeking the same countermeasures and materials (eg, masks).

### Deliberate Release Scenarios

It is often said that responding to a deliberate biological event would be just like responding to a natural pandemic. While there are a number of similarities related to medical and public health response, there are also critical distinctions that need to be understood and prepared for. The deliberate release of a high-impact respiratory pathogen would complicate application of international frameworks and global decision-making and response models. The activation of national and international security and intelligence apparatuses, which would be called on to identify the source of a deliberate event and attribute blame or responsibility, could interact with the public health response in unforeseen ways. Central involvement of the security sector, the possibility that countries may be less likely to share information during a deliberate event, and the potential for major societal fissures are just some of the elements that would complicate or interfere with current international response frameworks in ways that would make them less effective in addressing the response to a major deliberate event.[67]

The Biological and Toxin Weapons Convention (BWC) prohibits the development, production, stockpiling, and acquisition of biological weapons. This prohibition serves a crucial normative global role. In addition to explicitly committing countries to preventing the development and proliferation of biological weapons for both state and non-state actors, the BWC also includes provisions that promote international collaboration to support capacity building and the prevention of disease. States Parties to the BWC are obligated to provide response assistance in the event of a deliberate biological event, including for respiratory diseases with pandemic potential, but the scope of this assistance is not clarified. Beyond these goals, the BWC also serves as a forum in which countries, international organizations (eg, WHO), and civil society can engage on a range of topics relevant to the prevention, detection, and response to a range of biological threats, deliberate or otherwise. Unfortunately, the BWC remains under-resourced, particularly as it relates to coordinating response assistance in the aftermath of a deliberate event. In addition, the BWC was given neither an investigatory mandate nor enforcement provisions in the event of a deliberate event or state noncompliance.[68]

**Pandemic Influenza Preparedness (PIP) Framework**

The PIP framework provides a global approach to encourage influenza virus sample sharing and to commit manufacturers to equitably providing vaccines, treatments, and diagnostics during influenza pandemics and annually contributing funds to WHO for influenza pandemic preparedness.[53] The PIP framework is widely considered to be a significant global achievement, but it has limits. Neither seasonal nor animal influenza are covered under the framework, limiting its applicability to pandemic influenza strains. Questions persist about which of the remaining countries* will ratify the Nagoya Protocol to the Convention on Biological Diversity, and about the implications of this provision for viral sample sharing. Numerous barriers, ranging from intellectual property restrictions to slow inter-country coordination, limit the speed with which specimens are shared across borders. Slow or nonexistent specimen sharing affects the development, validation, and production of new medical countermeasures, as well as the continuing participation of industry and R&D stakeholders, which expect to benefit from their voluntary contributions to the framework.[55] According to the 2018 Annual Progress Report, only 21

* At the date of this publication, 120 States Parties have ratified the Protocol, including the European Union, which obligates its member countries to be subject to the Protocol's requirements.

countries have received support through the benefit-sharing mechanism of the PIP framework have written, exercised, or begun developing influenza pandemic preparedness plans.[69]

A related, ongoing concern among government and R&D stakeholders is that the deployment of potentially billions of vaccines (were such a stockpile of effective vaccines to be available at some time during a pandemic) to countries will be of questionable benefit if the plans, infrastructure, and distribution networks are not in place to vaccinate their populations. As such, the WHO Global Influenza Strategy promotes stronger country capacity by encouraging countries to implement tailored influenza programs, including national pandemic preparedness plans; establish infection prevention and control practices; and develop better vaccines, treatments, and diagnostics.[54] The Partnership for Influenza Vaccine Introduction (PIVI) provides technical assistance to middle- and low-income countries for routine seasonal influenza vaccination programs. These programs can support local vaccine markets by establishing predictable vaccine demand, while aiding countries in identifying the networks that will be needed to distribute vaccines to high-priority populations during a pandemic.[70] It will be important for WHO to continue to call on countries to develop pandemic influenza preparedness plans, practice sustainable seasonal influenza immunization programs, and prepare a logical system of vaccine allocation within countries and regions.

While agreements exist for influenza preparedness (see Box 4), similar international frameworks that promote preparedness measures (including virus sample sharing) more broadly for other respiratory pathogens do not exist. In the absence of a PIP-style framework for other respiratory diseases, countries seeking access to specimens must negotiate bilateral material transfer agreements with potentially dozens or more countries, a challenging and time-consuming process that is vulnerable to legal bottlenecks. It remains to be seen whether the PIP framework could emerge as an ad hoc model for access and benefit sharing during a severe respiratory epidemic or pandemic or if countries will scramble to arrange their own bilateral agreements.[55]

## Box 4: Pandemic Influenza: A Preparedness Model for Other Respiratory Pathogens?

While a range of high-threat respiratory diseases are known to exist, preparedness for pandemic influenza has received by far the greatest attention from international, national, and local stakeholders. For example, researchers and manufacturers possess the technical know-how and ability to develop, test, and manufacture medical countermeasures for the influenza virus, a capability that does not yet exist for coronavirus, enterovirus, and other contagious respiratory subgroups.

Preparedness for seasonal influenza, including routine surveillance, annual immunization campaigns, and specimen sharing, has contributed to a practical knowledge base and infrastructure that can be leveraged following the emergence of a strain with human pandemic potential. Fears that a pandemic strain may be overdue, especially following the devastation caused by past biological events, including the 1967-68 and 1918-19 influenza pandemics, have also focused global attention on this pathogen.

Pandemic influenza preparedness comprises a range of international and national agreements and frameworks pertaining to areas as diverse as medical countermeasures, surveillance and detection systems, cross-border specimen sharing and access to benefits, infection prevention and control practices, and networks of distribution for medical countermeasures. An interdisciplinary range of stakeholders are actively involved in these processes, including the scientific research community, academia, international agencies, national health ministries, the private sector and pharmaceutical industry, the healthcare sector, intellectual property lawyers, and others. These programs are not without their shortcomings or criticisms, and their effectiveness during a high-impact influenza pandemic remains to be seen. Nevertheless, there exists a stark disparity between the level of readiness for pandemic influenza and other potential high-impact respiratory pathogens. It is important to more fully understand the systems that have been built for influenza and consider the extent to which they would be of value for responding to other high-impact respiratory pathogens, and the extent to which they could be a model for building new systems for other respiratory threats.

**Pandemic Influenza Preparedness (PIP) framework**—PIP was adopted by the World Health Assembly in 2011 to improve sharing of influenza virus samples with human pandemic potential, as well as access to and sharing of other benefits, such as medical countermeasures and surveillance data. Other areas of the framework include laboratory and surveillance capacity building, regulatory capacity building, community engagement and risk communication, and planning for deployment. PIP was negotiated together with WHO Member States and the pharmaceutical industry, which contributes financially to framework implementation and commits to donating a percentage of vaccine product to lower-income countries.[53]

**National Pandemic Influenza Preparedness Plans**—At the behest of WHO, approximately 95 Member States have published national pandemic influenza preparedness plans. These plans articulate the capacities and capabilities needed to respond to an outbreak of pandemic influenza in humans, including intersectoral coordination and partnerships, risk communication, and surveillance and monitoring. However, only 17 countries have published or revised their plans since 2014, and 99 countries are still without a publicly available plan. In addition, national plans vary widely in terms of their level of quality and comprehensiveness.[71]

**WHO 2019-2030 Global Influenza Strategy***—The WHO Global Influenza Strategy provides a framework for WHO, Member States, and other partners to address influenza with the aim of strengthening seasonal prevention and control and preparedness for influenza pandemics. The strategy outlines 4 overarching objectives for the next decade: promoting research and innovation to address unmet public health needs, strengthening global influenza surveillance and data utilization, expanding seasonal influenza prevention and control policies to protect vulnerable populations, and strengthening pandemic preparedness and response for a safer world.[54]

**Partnership for Influenza Vaccine Introduction (PIVI)**—PIVI was established based on the recognition that a strong in-country vaccine delivery system not only reduces the burden of annual seasonal influenza and other vaccine-preventable illnesses, but it can also save lives during a pandemic event. An initiative of the US CDC, PIVI partners with national health ministries to train healthcare workers in flu vaccine delivery and establish networks of vaccine distribution to ensure vaccines can be delivered to the most vulnerable populations.[70]

**Global Influenza Surveillance and Response System (GISRS)**—GISRS is a global monitoring, surveillance, and response system for seasonal, pandemic, and zoonotic influenza. Among its many functions, GISRS acts as a global alert for novel or emerging influenza viruses and recommends the composition of the vaccine for the upcoming influenza season. GISRS is comprised of National Influenza Centers (NICs), WHO Collaborating Centers, Essential Regulatory Laboratories, and H5 Reference Laboratories.[72]

* Examples of other relevant WHO initiatives include the Global Action Plan (GAP) for Influenza Vaccines, the WHO Pandemic Influenza Vaccine Deployment Initiative, the WHO Initiative for Vaccine Research, the WHO National Immunization Technology Advisor Group (NITAG), and other WHO specialized advisory committees.

## Emergency Response Mechanisms

With the establishment of the WHO Health Emergencies Programme following the Ebola epidemic in West Africa, the international response system received an overhaul in the way it responds to disease outbreaks. WHO now provides operational capabilities in addition to its traditional expert technical and normative roles. Through the Health Emergencies Programme, WHO was clearly defined as the coordination and technical lead for any international response to health crises, including managing collaborations with any health partners in the field. Also, with the establishment of the Health Emergencies Programme, a new financing mechanism, the Contingency Fund for Emergencies, was developed to facilitate cash flow and provide the initial funds necessary to mount a response to health emergencies.[73]

In this new approach, WHO leads the international response to major internationally important outbreaks, and it would be the lead agency for the health response to any high-impact respiratory pathogen event. Large-scale disease outbreak response efforts require multisectoral collaboration, and so WHO closely coordinates with the broader UN humanitarian system in these responses. Mechanisms to alert relevant authorities—including the Inter-Agency Standing Committee*, UN country offices, non-governmental organization (NGOs), and private-sector partners—are in place.[73,74] This kind of coordination would be expected and critical in the response to a high-impact respiratory pandemic.

While many processes to initiate and scale up response efforts would apply across all diseases, additional considerations unique to high-impact respiratory pathogens may not be adequately addressed in these response guidelines, including the WHO's Emergency Response Framework.[74] During such a pandemic scenario, regional, national, and local needs could severely outpace existing international capacities and resources, and countries could not expect emergency medical response teams to assist them. Donated medical countermeasures, personal protective equipment, and other technical assistance

* The Inter-Agency Standing Committee is the UN's primary mechanism for coordination of any (UN or otherwise) agencies in a humanitarian assistance. The Inter-Agency Standing Committee is composed of the heads of UN and non-UN organizations that are involved in humanitarian response to emergencies, including health crises (source: https://interagencystandingcommittee.org/).

that they might receive in geographically limited outbreaks might not be available. During a large-scale respiratory outbreak, widespread humanitarian needs might arise, such as food insecurity or poverty associated with job losses. Concerns have been raised regarding the existing mechanisms intended to deal with these issues, citing inadequate coordination and planning among WHO and the broader humanitarian system, including various UN agencies and the UN Secretary-General.[42,52] In a large disease outbreak scenario, there may also be decreased international interest in supporting other countries' responses as nations deal with the health crisis in their own borders (see Box 5).

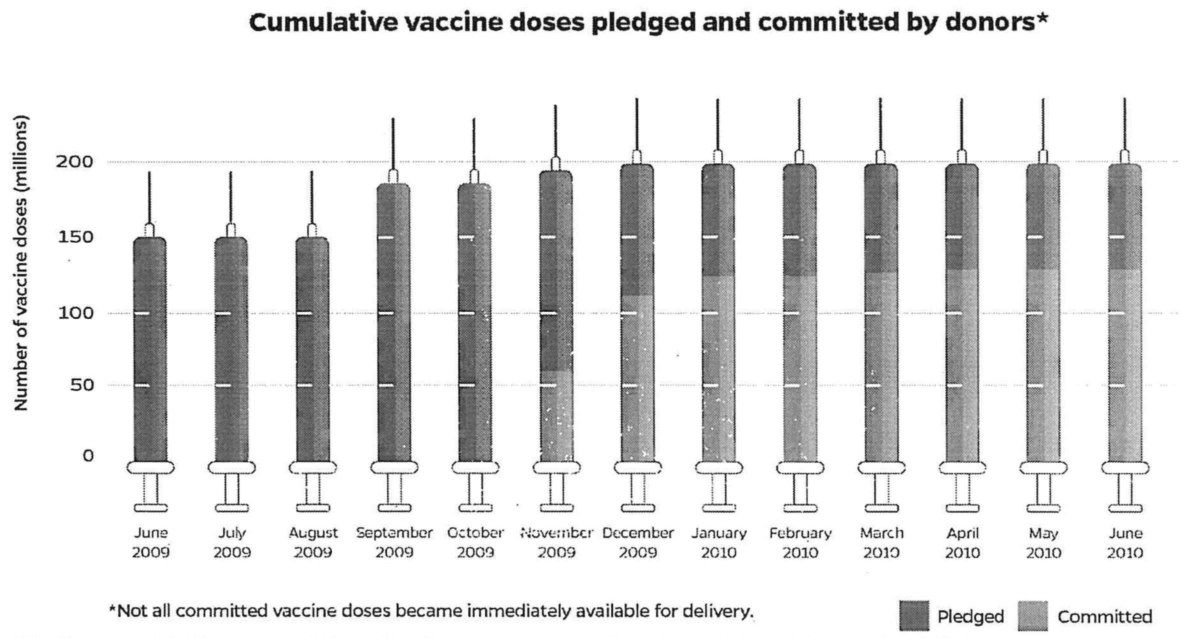
## Box 5: The Potential Problem of National Sovereignty in Pandemics

The landscape of international response for a pandemic may look very different from what is seen for regional epidemics or locally contained outbreaks that are geographically limited. Where outbreaks are geographically more limited, international organizations, NGOs, and other governments can more readily provide personnel, equipment, and financial support to control the outbreak and limit the risk of spread. However, in the event of a high-impact respiratory pathogen causing a pandemic affecting numerous countries around the world, international organizations and NGOs are unlikely to have the capacity to provide support to all countries in need. The capacity of these organizations would likely be exhausted quickly, with little chance of replenishment due to high demand and scarcity of resources. Similarly, other countries would be focused on either combating the disease outbreak within their own borders or ramping up preparedness efforts to prevent the introduction of the disease into their territory. This may include decisions not to share vaccines with other countries until all domestic needs are met, as was seen in Australia during the 2009 H1N1 influenza pandemic when a manufacturing company was told that it had to fill all vaccine requirements for its host country before exporting to other places.[75]

With an expectation of more limited international support in a pandemic, a country would need to rely to a much greater extent on its own ability and resources. Challenges existing in epidemics and smaller disease outbreaks will be exacerbated in a large-scale pandemic, and the issue of scarcity of resources, coupled with high demand, needs to be considered ahead of time.

An example of this issue was seen during the response to the 2009 H1N1 influenza pandemic. While information sharing occurred early in the outbreak, as the cases continued to rise and vaccine production was under way, concerns over equity of access to the vaccine arose. Countries initially announced their support of efforts to provide the vaccine for countries without access and declared they would share a percentage of their vaccine with low- and middle-income countries. However, as shown in Figure 2, the committed number of vaccines shared was considerably lower than the original pledged amounts. While various factors contributed to this actuality, including delay in vaccine production and pledges including amounts to be used in future emergencies, the large disparity between pledged and committed amounts drive home the concern that in a pandemic scenario, a country's national capacity will be even more important as international support, particularly from other affected countries, will be limited and exhausted quickly.[76]

### Figure 2: Vaccine Doses Pledged and Committed During 2009 Influenza Pandemic



## Multisectoral Involvement and Coordination

Preparedness for an epidemic or pandemic caused by a high-impact respiratory pathogen would require the involvement and coordination of multiple sectors. There is a high likelihood that a pandemic caused by a high-impact respiratory pathogen would cause harm that extends beyond the health sector, so it is crucial that other major sectors be involved in both preparedness planning and response efforts.

The possibility of wide geographic spread and/or deliberate use of respiratory pathogens would mean that government human health resources alone would be insufficient to detect and respond to the spread of a novel respiratory pathogen. The continued development and sustainment of operational and effective OneHealth partnerships among human, animal, plant, and environmental health sectors is essential for preparedness. The collaboration among WHO, World Organisation for Animal Health (OIE), and Food and Agriculture Organization (FAO) has shown commitment to the OneHealth approach, and they have recently developed a guide outlining a OneHealth approach to zoonotic diseases.[77] However, many reviews have underscored the continued lack of integration among the human, animal, plant, and environmental health sectors. One example of the consequence of a lack of such integration is the delayed ability of the human health sector to recognize Ebola as the cause of an outbreak in West Africa in 2014, which was in part due to the human health community's belief that the virus was not present in the region—a finding that had been previously predicted by animal health experts.[78]

Preparedness for high-impact respiratory pathogens will also require involvement from nonhealth actors, including other government, private, and nongovernment organizations. This section highlights 3 specific sectors—financial, private sector, and security—that are critical in pandemic preparedness and response.

### Financial

Financing for outbreak preparedness and response will require involvement of public, private, and NGO actors, supporting both international organizations and national health systems across multiple areas, including preparedness and response activities. Though funding for global preparedness has traditionally involved resources from national governments, there have been limits to government-centric approaches to financing, with inconsistent political commitments to funding for preparedness.[7] Estimates from the World Bank suggest that the cost* of developing the core public health capacities needed to prepare for public health emergencies is well below the cost of responding to

* The World Bank notes that for low- and middle-income countries that have costed their National Action Plans for Health Security, the investments needed to develop core public health capacities necessary to prevent, detect, and respond to potential public health emergencies may be less that US$1 per person per year (source: https://www.worldbank.org/en/topic/pandemics).

such events, but governments continue not to make such investments in advance of an emergency. Many assessments have called on national governments to break the cycle of "panic and neglect"—a term meant to describe the episodic way in which national budgets are often used to fund preparedness. There are similar funding shortfalls for advancing preparedness on the global level. While multiple existing mechanisms provide emergency funds for global response operations, such as WHO's Contingency Fund for Emergencies, the UN Central Emergency Response Fund, and the Pandemic Emergency Financing Facility, these funds generally are not available to support preparedness activities.

While national governments should continue to be encouraged to increase and sustain their investments in preparedness, there is also a need to explore the availability of financing from nongovernment sources. New models and sources of financing are needed to increase the availability of resources for preparedness.

**Private Sector**

Beyond the financial sector, there has been acknowledgment in recent years of the need to engage the broader private sector in disease outbreak preparedness activities. A severe respiratory pandemic is likely to devastate economic growth, either directly via trade and travel restrictions or indirectly via high morbidity and mortality and the loss to jobs and industry, such as tourism. Therefore, both out of self-preservation and for reasons of corporate social responsibility, the private sector will need to play a greater role in planning for and responding to such events.

Increasingly, public-private partnerships are being proposed as a model to expand the availability of financial resources for preparedness. The Coalition for Epidemic Preparedness Innovations (CEPI) receives financial contributions from governments and private philanthropists to promote vaccine development for priority pathogens identified in the WHO R&D Blueprint. To date, CEPI intends to invest upwards of $500 million in candidate vaccines for MERS-CoV, Lassa, Nipah, Rift Valley fever, and chikungunya. CEPI is also making investments in platform technologies with the goal of accelerating development of vaccines for previously unrecognized diseases, such as Disease X. Overall, CEPI has set a $1 billion fund-raising target.[79] Another example of public-private partnership, the PIP framework, requires industry stakeholders to pay an annual contribution, of which 70% is used by WHO solely on influenza preparedness activities.[80]

Still more initiatives are required to mobilize financial support to enhance preparedness systems. Identifying new sources of funding for both national preparedness strengthening and research and development of vaccines, diagnostics, and treatments for high-priority diseases is greatly needed.

Governments have historically viewed the private sector as a potential source of support for public sector–led operations, including in-kind donations and purchases of equipment, supplies, or medical countermeasures. But the private sector has additional capabilities and expertise that can be tapped to support preparedness efforts.[50] The unique expertise and services of several industries deserve special attention. The first is the pharmaceutical industry, which plays a key role in the research, development, and manufacture of medical countermeasures. The second is the airlines, transportation, and logistics/shipping industries, which can ensure the transfer of medical personnel and equipment for scaling up operations. The third is the medical supply industry, which would also be of high global importance in a pandemic and contribute to R&D and manufacturing of MCMs. And fourth is the global communications sector—both those who provide the hardware and software around communications, as well as those who are global leaders in delivering content and helping to serve public information needs.

Despite its potential, private sector involvement to date has been haphazard and mostly limited to the response phase of a disease outbreak. A key challenge is the lack of advance communication and coordination between public and private actors, which is needed to clarify the appropriate roles, responsibilities, and expectations of each during an epidemic or pandemic. The Private Sector Roundtable and a variety of efforts at the World Economic Forum around private-sector engagement in preparedness and response are notable exceptions in which global business has been leading or participating in the development of new partnerships and potential solutions with WHO and governments.[50, 81]

The partnership between government and the private sector will be most effective if defined and agreed on well in advance of an event. The ad hoc inclusion of private sector services into a health response could conceivably hinder a response in that it could risk public suspicion of private sector involvement for monetary or financial gain. Prenegotiated partnerships and/or memoranda of understanding that transparently define the nature and extent of private-sector involvement are needed.

Private-sector organizations can also meaningfully contribute to preparedness by preparing continuity plans to ensure their continued operations in the event of a potential pandemic.[82] Many communities rely on such organizations to provide essential services. Therefore, these organizations can also serve as extensions of government health response by educating their employees, families, and surrounding communities about recommended protective actions and planning to provide support for employees who become ill.

### Security

The potential for deliberate release of a high-impact respiratory pathogen provides a clear case of an instance when engagement with the security sector is required. However, the need to involve security in disease outbreak preparedness is not limited to deliberate events. The ongoing outbreak of Ebola in the Democratic Republic of Congo has also underscored the importance of having robust partnerships between health and security. Generally, a national or international security sector will include military, law enforcement, and intelligence agencies.

Militaries may have a mandate and well-defined protocols for disaster relief operations, but their experience in disease preparedness and response may be limited. National militaries may have experience in medical countermeasure research and development, transport elements, military health or other surveillance programs, or other initiatives that may prove relevant to outbreak preparedness and response.

Challenges that could prevent or complicate engagement from the security sector include a possible lack of experience with biological or health-related emergency response in a given country's security agencies; a mutual lack of understanding regarding the needs of the response and potential assets that could be brought to bear; a lack of training, equipment, or buy-in from military personnel; and the possibility that security sector involvement could, if improperly implemented, be at cross-purposes with efforts to provide communities with public health or medical interventions.[83,84] On balance, in many countries the security sector could bring valuable expertise and assets to bear, both in terms of preparing for high-impact respiratory pathogens and in the response and in medical countermeasure research and development. Countries should seek to find mechanisms to incorporate the security sector, while planning on avoiding the possible complications of this kind of engagement.

## Surveillance, Monitoring, and Assessment Systems

### Surveillance Capabilities

Reviews of past events have revealed limitations in global and national surveillance capacities. Current systems vary widely in their quality, and many under-resourced settings do not have surveillance systems that could adequately serve those purposes. Furthermore, existing surveillance systems are highly fragmented and local, with data that cannot easily be pooled and analyzed to direct a large-scale response. Enhancing (and, in some under-resourced settings, implementing) surveillance systems would improve capabilities to prevent, detect, and respond to an event from a high-impact respiratory pathogen. A commonly cited limitation is insufficient availability of laboratory testing.[85] Laboratory information is essential for ensuring the availability of accurate and actionable surveillance. In addition to assessing the availability of laboratories that can perform diagnostic testing, countries must also consider the capacity of laboratories to handle testing in the event that there is a large surge in demand. While laboratory networks and surveillance mechanisms including GISRS, FluNet, and WHO Collaborating Centers are vital components of current surveillance capacities, efforts should be made to further strengthen these mechanisms and improve laboratory testing.

Surveillance capacity as measured by the JEE tool requires syndromic surveillance for 3 core syndromes (including severe acute respiratory syndrome) and regular analysis and reporting of surveillance data. Of the countries for which data is available, the average surveillance score is 3.3 out of 5 on the JEE, which suggests that there is room for strengthening the capacity of many countries to detect and monitor outbreaks.[86]

During large-scale events involving a respiratory pathogen, it will be critically important that countries and the international community have ready access to information to support decision making about how best to respond. A key question that is likely to emerge right away is how severe the event is in terms of health impacts (eg, percent ill, percent of cases resulting in death or severe outcomes). As demonstrated in the 2009 influenza pandemic, the answers to these questions are likely not readily available in traditional public health surveillance systems. Health officials should identify additional data sources that may provide insights to these questions and make plans for accessing and analyzing them.[87] To enable this, countries should invest in developing surveillance systems that produce timely, accurate, and highly resolved data that can be easily analyzed and shared. Specific diagnostic information would be of great importance, and countries should have plans for the development or uptake of diagnostic tests. In an event involving a novel pathogen, PCR-based tests are likely to be the first to be available to aid in diagnosis and confirmation. In preparation for this, national public health laboratories and large commercial laboratories should develop a concept-of-operations for how to distribute test kits rapidly to relevant clinical sites and laboratories in areas affected by the outbreak.

In instances in which demand exceeds capacity at available laboratories, policies for testing may change. For example, during the 2009 influenza pandemic, public health laboratories stopped confirming individual cases of influenza once transmission became widespread.[88] Such changes in testing procedures would require pre-event planning to determine criteria for testing and communication about planned protocol changes with clinicians, public health practitioners, and the public.

The information needs and sharing that may occur during deliberate events may vary greatly from a naturally occurring event. For example, there will be a need to assess the risk of subsequent attack—a consideration that is likely to be central in discussions about how to utilize medical countermeasures. It has also been identified that there are insufficient mechanisms to enable rapid information sharing across sectors during a deliberate event response.[37]

Additional gains could be made by further developing modeling capabilities to enable the modeling of surveillance data to gain insights into its anticipated trajectory and potential future impacts of an event, as well as modeling around possible response strategies. Modeling can support public health decision making in a number of ways, including planning and comparing interventions, forecasting the trajectory of the epidemic, and simulating risk scenarios.[89] Models can also transform diverse data streams into a mathematical representation of an outbreak that is more structured and informative than the input data individually. In order to be as useful as possible, modeling capabilities should be implemented in advance of an emergency and closely integrated with the public health decision-making team to facilitate rapid analyses and decision-making cycles. Decision makers also must be informed in advance about the expected limitations of modeling approaches and how uncertainties about existing data may affect model predictions.

**Detection Capabilities and Diagnostics**

In the event of a novel outbreak of a high-impact respiratory pathogen, early detection of the event through regular diagnostic testing may not be possible. Routine tests may not properly identify novel diseases. In these circumstances, clinical recognition that something is not normal and rapid reporting of this to appropriate public health authorities would be critical for enlisting the right specialized diagnostic expertise and for mounting a rapid response. In higher-resource countries, specialized diagnostic tools or approaches could be used in efforts to make a rapid initial, pathogen-specific diagnosis of the first patients, with the time to specific diagnosis depending on the pathogen, the samples, the period between recognition of an clinical anomaly, and the initiation of testing. In lower resource settings, or in healthcare settings where clinical anomalies might not be easily evident, it might take substantially longer to initiate the proper testing for a novel pathogen. In those settings, regional, national, or international laboratories might need to be engaged to make an initial specific pathogen diagnosis.

Once a pathogen responsible for an emerging epidemic or pandemic is definitively identified as the etiology, the use of diagnostic tools would switch. Diagnostics would no longer be needed for detection, but instead they would be needed for event management. In this latter phase, diagnostics become an important tool in event characterization (determining who is affected, who is at risk of severe outcomes) and in clinical management of patients to optimize treatment and to reduce transmission through proper isolation.

In the clinical realm, in a high-resource setting, the approach to a novel diagnosis would be expected to begin with initial confirmation using research-related molecular diagnostics, then would evolve to clinical syndromic surveillance with post facto laboratory confirmation, eventual testing at reference laboratories and major commercial laboratories, and, finally, to widely disseminated diagnostic testing strategies. These processes may be facilitated via pre-established processes to authorize emergency use for nonapproved tests and with national laboratories and public health authorities distributing materials (such as primers) to qualified parties. However, this process is often not seamless nor rapid. In settings without well-developed regulatory frameworks, the process would be more uncertain and depend on local expertise, resources, plans, and perhaps international assistance.

With a truly unknown respiratory viral pathogen, initial cases would fail to produce a diagnosis by conventional means, leading to more sophisticated testing, including next-generation sequencing, to identify any clue as to what type of microbe is present and what characterizes it (ie, what viral family it is most closely linked to). In countries with access to such testing, as the diagnostic test is perfected and the etiologic agent better characterized, the development of serological tests to identify past infections as well as simplified molecular diagnostics (and in some cases point-of-care molecular testing) would occur.[90] These tests might first be available at national public health labs and may or may not diffuse to local health centers. Limitations would include technical ability as well the availability of materials for the construction of testing, such as nucleic acid primers. In the context of a novel respiratory pathogen, many cases would be diagnosed using clinical scoring criteria, with or without eventual laboratory confirmation.

In the event of a deliberate release of a pathogen, the first recognition is likely also to occur following recognition of an anomaly (or anomalies) in the clinical sector, where sick patients are turning up for treatment, with similar processes and challenges to diagnostics as noted above. In addition to clinical diagnostics, assessments of where pathogens may have contaminated the environment could be important for law enforcement activities and efforts at attribution, if there is information available that made such assessments feasible. If these assessments were feasible, then this information could help with determining the scope of initial exposures and determining where there might be environmental contamination.

Technological advances are needed to modernize our diagnostic capabilities to become faster and nimbler at the onset of outbreaks, particularly around novel pathogens. Diagnostic tools are required in settings beyond centralized laboratories. Microfluidic devices and other "lab on a chip" devices still in development have the potential to improve diagnostic capacity across a range of settings, shorten the timeline to diagnosis, and ultimately trigger a cascade of other actions needed to isolate and characterize the pathogen.[91] The window for detection for respiratory pathogens would be very short before transmission may become widespread. As such, the development of these sentinel tools can provide the early detection and warning needed to get ahead of an outbreak.

### Outbreak Investigation and Response

An epidemiologic investigation and the accompanying response are the backbone of outbreak control. As seen currently in the DRC Ebola outbreak, efforts to complete contact tracing in that setting are challenging but critically valuable. Contact tracing is highly effective for outbreaks that are mildly to moderately transmissible and of a modest scope. For high-impact respiratory pathogens, contact tracing would quickly become infeasible. It is very difficult to identify contacts when all who may have been in the general vicinity of a case may be at risk. Furthermore, as the number of potential contacts grows, the resources required to monitor those people quickly would become overwhelming. A 2011 assessment of the economic burden of measles outbreaks, for example, found that each case of measles generated many dozens or even hundreds of contacts, requiring thousands of personnel hours to manage.[92] New technologies—for example, those making use of location data or push notifications from mobile phones—could conceivably be leveraged to extend the utility of contact tracing for highly transmissible events, though this should be considered an open research question at this point. Absent widespread availability and effectiveness of such technologies, in the event of a large-scale respiratory outbreak, other nonpharmaceutical interventions (detailed below) may be more practical, though they are likely to be less effective.

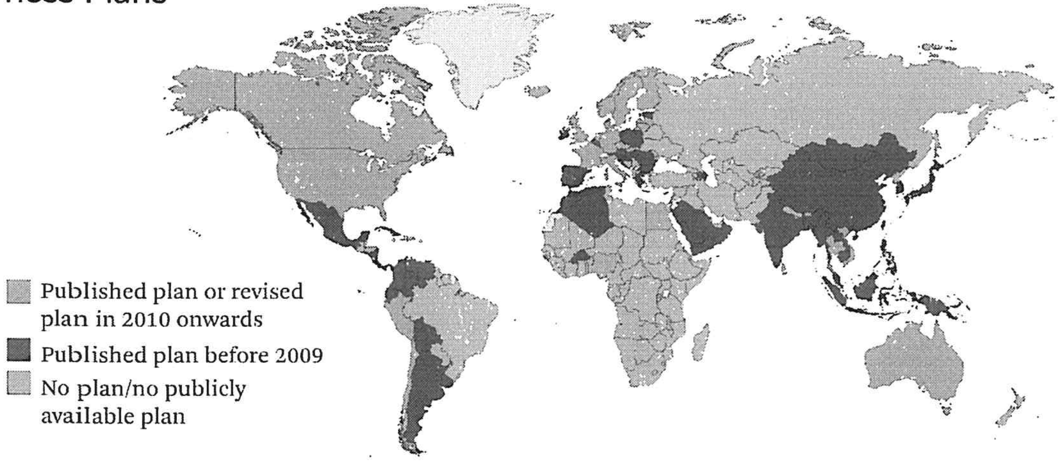
## Health Systems and Infrastructure, Health Services, and Clinical Management

Widespread transmission of a high-impact respiratory pathogen would cause a surge of patients seeking care that would challenge even the most well-prepared health system. As a result, victims of a large-scale outbreak in settings with weak health systems would likely die at a higher rate than would be otherwise expected, due to lack of available modern medical care. Individuals who need to use the overburdened healthcare system for routine care during an outbreak would also likely suffer elevated morbidity and mortality, as available health resources are shifted to the emerging outbreak. As seen in Box 6, absolute mortality estimates for a high-impact respiratory pathogen are much greater today than they were in past decades, which highlights the strain that health systems would be under.

Unprepared or under-resourced health systems could make matters worse by exacerbating disease transmission through nosocomial spread and the inability to promptly diagnose and render care. During the 2003 SARS epidemic, transmission in healthcare settings played a prominent role, accounting for 72% and 55% of presumed and confirmed cases in Toronto and Taiwan, respectively.[93] During the 2013-2016 West Africa Ebola epidemic, healthcare workers were 21 to 32 times more likely than the general public to get infected with Ebola, which had a severe impact on the affected countries' already-depleted healthcare workforce.[94] The provision of routine medical care also suffered setbacks, with an estimated 50% reduction in access to healthcare services during the epidemic, including care for other infectious diseases such as HIV, tuberculosis, and malaria.[95] The ongoing Ebola outbreak in the Democratic Republic of Congo (DRC) has also seen substantial nosocomial spread to healthcare workers, accounting for approximately 6% of all cases.[96]

International initiatives have aimed to improve health system preparedness and response for outbreaks and pandemics of respiratory diseases, focusing largely on influenza, but global preparedness for a high-impact respiratory pathogen event remains inadequate. One of the strategic objectives of the 2019-2030 WHO Global Influenza Strategy is to "strengthen pandemic preparedness and response for influenza," and it includes numerous health system–related efforts, including national planning and exercises; building stockpiling capacities; procurement, deployment, and administration of vaccines, treatments, and supplies; and multisectoral collaboration.[54] Not every country, however, has developed influenza preparedness plans. WHO reports that only 32 countries developed or revised plans after the 2009 H1N1 pandemic, and 99 countries still have no influenza plan that is publicly available (see Figure 3).[71,97] Despite these initiatives, preparedness for high-impact respiratory disease outbreaks such as influenza remains dependent on political will and sustainable human and financial resources-, and, thus, varies from nation to nation.

### Figure 3: Global Map Identifying Countries with National Influenza Preparedness Plans




*Data extracted from WHO Strategic Partnership Portal

Early in a pandemic, isolation of the sick will be critically important to limiting further spread, but most hospitals around the world have very limited isolation capacity, particularly for airborne pathogens, and likely only a fraction of what would be needed in a large outbreak. To adequately prepare for and respond to outbreaks of respiratory pathogens, health facilities would need to increase their capacity for large-scale isolation of patients with highly transmissible respiratory diseases.

While a small number of facilities have dedicated units for the isolation of high-impact infectious disease patients (eg, high-level isolation units), this capacity is very limited, and all facilities need to plan for less resource-intensive yet effective isolation strategies to handle larger patient volume. These include converting regular patient care units into isolation units or cohorting patients who are similarly infected. Plans for just-in-time care or triage facilities (eg, tents or other alternative care facilities) could also provide additional space during emergencies. Once an epidemic is under way, healthcare workers would need to be able to rapidly identify those in need of isolation. Training and education would be required to ensure that frontline healthcare workers, particularly those staffing emergency departments, were fully aware of the emerging epidemic and capable of implementing travel, exposure risk, and symptom screening in order to identify and isolate suspected cases.

Surge capacity planning is another key issue. A large influx of patients during a respiratory pandemic would require additional staff and supplies. Healthcare workers would need to be trained in appropriate infection prevention and control practices, including personal protective equipment (PPE) donning and doffing, and appropriate hand hygiene. The availability of essential basic supplies and equipment must also be included in global planning efforts. There is a severe maldistribution of medical supplies between countries and health systems around the world, and a dedicated effort is needed to determine how low- and middle-income countries would maintain access to critical supplies (eg, masks, respirators, gloves, gowns, IV fluid bags, medical gases) during a large-scale respiratory disease outbreak. Plans to ensure access to other critical logistics and infrastructure—including clean water, electricity, data and telecommunications, and waste management and other sanitation services—during a severe pandemic need to be made.

### Box 6: What Would the 1918 Influenza Pandemic Look Like Today?

In the worst pandemic in recorded history, the 1918 influenza pandemic, the novel virus infected approximately one-third of the global population over a period of 2 years, ultimately leading to 50 to 100 million deaths worldwide. One might imagine that the death rate would be lower today due to the advent of modern medical equipment and procedures that did not exist in 1918, but the global population is now approximately 4 times greater than in 1918. This growth, however, is disproportionately higher in low- and middle-income countries, often the ones with developing health systems. Many—predominantly in Africa, Southeast Asia, Latin America, and the Middle East—have experienced population growths of 1,000% or more since 1918. Crowded urban areas provide prime conditions for the spread of respiratory diseases, and urbanization is increasing globally, including the emergence of 47 "mega-cities" (populations over 10 million). By comparison, London was the world's largest city in 1918, at approximately 5 million people. Additionally, global travel has increased by orders of magnitude compared to 1918. Even then, shipping and population movement (including World War I) played an important role in global spread of the disease, but today, humans can fly anywhere in the world in less than 1 incubation period, meaning that global transmission can be expected to be even faster.

In 1918, the global case fatality ratio is estimated to have been 2.5%, but it was considerably greater in low- and middle-income countries, with some estimates exceeding 10%. Today, some high-income countries would be expected to fare much better because of modern health care, but the case fatality in countries with limited access to healthcare could be as bad as or worse than 1918. Simple arithmetic would suggest the possibility of 100 to 400 million deaths if a 1918-like pandemic were to occur today, but unprepared or under-resourced health systems could further exacerbate disease transmission through nosocomial spread and an inability to promptly diagnose and render care, a particular concern for developing health systems. During the 2003 SARS epidemic, 72% and 55% of presumed and confirmed cases in Toronto and Taiwan, respectively, occurred as a result of healthcare transmission. A similar nosocomial outbreak in which healthcare facilities became amplifiers of the epidemic, this time of MERS, happened in South Korea in 2015.

## Community Engagement

Community engagement entails the collaboration of affected and at-risk populations with policymakers and practitioners in the generation, implementation, and evaluation of measures to safeguard public health and safety.[98] When genuinely operating within a community engagement framework, authorities see themselves as working *with*, rather than *on behalf of* potentially endangered people, and they accord community members both respect and responsibility as actors who have influence over their own well-being.[46,99] Community engagement—comprised of dialogue, power sharing, collaborative decision making, and combined actions among a community, its providers, and its leaders—can strengthen readiness, response, and recovery in the case of a potential high-impact respiratory pathogen outbreak.[100] Once fully engaged in larger systems of disease outbreak planning and consequence management, for instance, community members can offer ideas and insights that enable public health interventions and clinical care to be more culturally competent, attuned to local conditions, and socially acceptable.[46] In addition to their intellectual contributions, the community offers the power of many hands—for example, backfilling depleted responder workforces, complementing care in the formal health sector with care in the home, and standing up mutual aid networks for ill and/or confined people and their families.[100] Lastly, beyond the community's practical offerings are its moral and ethical ones: Leaders faced with extreme conditions and stark choices can elicit community values and views on—and thus secure broader support for—for