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Predicting pandemics: past disease outbreaks and what they teach us about preparing for the next pandemic

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Predicting Pandemics: Past Disease Outbreaks and What They Teach us about Preparing for the Next Pandemic

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Glossary of Acronyms

CDC	Center of Disease Control and Prevention (United States)
ebolavirus	Virus Causing EVD
ECDC	European Centre for Disease Control
EU	European Union
EVD or Ebola	Ebola Virus Disease
GID	The CDC's Global Immunization Division
IHR	International Health Regulations
MMR	Measles, Mumps, and Rubella Vaccine
NIAID	National Institute of Allergy and Infectious Diseases
NIH	The National Health Institute
OIHP	Office International d'Hygiène Publique
PPE	Personal Protective Equipment
SARS	Severe Acute Respiratory Syndrome
WHO	World Health Organization

Introduction

On April 27th, 2018, philanthropist Bill Gates presented at the Massachusetts Medical Society's annual meeting his growing concern of the next large-scale pandemic. Using a simulation created by Institute for Disease Modeling, Gates hoped to open the public's eyes to the growing threat influenza and other infectious diseases pose to the world. This simulation predicted that a pandemic new influenza strain similar in severity to the 1918 Spanish Influenza would likely kill 30 million people worldwide within six months[1]. Gates, like many other public health officials and researchers, believes that infectious diseases represent a very real global security threat and should be treated through this lens. Such a threat, though, cannot be eliminated through negotiation and affects more than just a handful of countries. The next pandemic is capable of changing the foundations of the global community, and is a threat that many experts feel the world is not ready to face.

Pandemics are officially defined by the World Health Organization (WHO) as the world wide spread of a new disease, although many ancient outbreaks, such as the Black Death, have been given this designation based more on severity of the disease than global reach[2]. Most pandemics occur due to infection by a novel virus, emergence, or reemergence of bacterium. Regardless of the characteristics of pandemics, all tend to have large impacts on both infected countries and the world as a whole. These diseases have claimed millions of lives, created large economic losses, and interrupted the growth and development of numerous countries.

Influenza virus strains remain the most commonly observed and largest reaching pandemics in history[3]. On average, two flu pandemics occur each century, although the 1900's

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[1] Bill Gates. "Shattuck Lecture - Bill and Melinda Gates Foundation." 2018.
[2] WHO. 2015. "What Is a Pandemic?" *WHO*.
[3] Ibid.

saw three major outbreaks suggesting we may see an increase of influenza pandemics in the future[4]. But these numbers fail to address the numerous non-influenza pandemics seen throughout history, such as HIV/AIDs pandemic which started in the 1981. Since the turn of the current century the world has already witnessed two pandemics: the 2002 severe acute repository syndrome pandemic (SARS) and the 2009 swine flu pandemic. SARS gained the designation of the century's first pandemic not for its high infection rate (only 8,422 people contracted SARS), but rather its quick spread to over 29 countries in seven months[5]. Meanwhile swine flu infected over 60 million people in the United States alone during the 2009 flu season[6]. While both pandemics infected varying numbers of people, their ability to reach numerous countries around the globe highlights both the continued rise in urban areas and the growing interconnectedness of the world. These attributes of our modern world create a greater risk of disease spread and death compared to any historic pandemics, leaving the globe at a more vulnerable position than ever for the next big pandemic.

The growing risk of such a pandemic coupled with the projected spread and death tolls of the threat creates the need to stop this global disaster before it occurs. The best way to stop a large-scale pandemic is to prevent such a disease from spreading to and through human populations. Prevention, however, requires the global health community to accurately predict what the culprit pathogen and provide the proper resources to either completely stop the spread of the novel pathogen to humans or contain the disease as a local outbreak. This thesis will

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[4] Edward Hill, Michael Tildesley, and Thomas House. 2017. "How Predictable Are Flu Pandemics?" *Significance* 14 (6): 28–33.
[5] James D Cherry, and Paul Krogstad. 2004. "SARS: The First Pandemic of the 21st Century." *Pediatric Research* 56 (1): 1–5.
[6] Harvey V. Fineberg. 2014. "Pandemic Preparedness and Response — Lessons from the H1N1 Influenza of 2009." *New England Journal of Medicine* 370 (14): 1335–42.

evaluate the resources utilized in predicting the next pandemic and the global public health system's ability to fight against novel pathogens. In the first chapter, I will set the stage by describing past pandemics and their effects on society, as well as how improving public health has changed the threats posed by future pandemic diseases. The second chapter will provide background on some of the major organizations that play key roles in pandemic preparedness and response. From there, I will evaluate our current inability to predict and respond to disease outbreaks and the repercussions of such failures using the 2014 West Africa Ebola epidemic as a case study. The fourth chapter will look at using molecular modifications as a method of predicting pandemics and explore the practicality and ethics behind such techniques. In my final chapter, I will assert that we cannot predict pandemics. Rather, I will propose improvements to our current public health system that emphasizes surveillance, finding molecular similarities between viruses, and improving vaccine technologies in order to best prepare for the next pandemic.

Chapter 1: Past Pandemics and the Current State of Global Public Health

When the first World War ended in 1918, over 37 million people worldwide died due to the conflict. The end of this historic war, though, did not mean the end of death and despair. 1918 also marked the beginning of the modern world's most severe influenza pandemic. Although the origins of the disease still remain unknown, some speculating it emerged in China[7], while others believe a military base in Kansas[8], this pandemic virus became the worst human natural disaster in history. Caused by a then new-to-humans strain of avian influenza virus A,

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[7] CDC. 2018. "Remembering the 1918 Influenza Pandemic | Features | CDC." 2018.
[8] Ibid.

H1N1, this pathogen infected more than a third of the world's population and killed over 50 million people[9]. It has been just over a century since this deadly flu outbreak, and while recent influenza pandemics have not come close to the infection rates and death toll associated with the Spanish Influenza, many public health experts fear a big one is coming.

These mounting fears of the next large-scale pandemic often seem unwarranted with improvements in both public health and medical technology over the last century. In 1918, no influenza vaccine existed and the discovery of penicillin was still a decade away. Physicians of the time were at a loss on how to treat the disease, and were using all possible medical treatments, ranging from the ancient art of bleeding patients to administering oxygen[10]. Only blood transfusions from those who recovered appeared to have any real effect on treating new patients, but not to the extent needed to curb the mortality rate. Now, the world has an arsenal of medical and public health advances that has helped limit the spread of infectious diseases worldwide, and stopped pandemics from reaching the level of infection and death observed in 1918. These improvements include the discovery of penicillin in 1928 and the creation of the inactivated flu vaccine in the 1940s, technological advances thought to have saved millions of lives[11].

Despite these massive improvements in the technology used when treating people with infectious diseases, concerns surrounding a highly lethal pandemic should not be ignored. The 1918 Spanish Influenza is not the only large-scale pandemic in human history that killed millions of people, suggesting that diseases of similar severity could occur again. Furthermore, pandemics

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[9] Ibid.

[10] Knobler, S., Alison Mack, Adel Mahmoud, and Stanley M Lemon. 2005. "The Story of Influenza." *Institute of Medicine (US) Forum on Microbial Threats.*

[11] Claude Hannoun. 2013. "The Evolving History of Influenza Viruses and Influenza Vaccines." *Expert Review of Vaccines* 12 (9): 1085–94.

have larger impacts on society than just the number of infections and deaths. Throughout history, pandemics of infectious diseases have left their imprint by influencing the economics, politics, and social structure of numerous nations and the international community, shaping the world we know today.

A: Past Pandemics and Their Effects on Society

The Justinian Plague was one of the first recorded pandemics in human history, and the first with a confirmed pathogen: the bacterium *Yersinia pestis*. Occurring over a 200-year period between 530 and the mid-700's, this pandemic started in Ethiopia, and quickly spread to Europe and Asia[12]. The Plague reached a peak in 542, killing nearly 5,000 people a day in the capital of the Byzantine Empire, Constantinople[13]. During a four-year span from 541 to 544 alone, over 100 million people were thought to have died across Asia, Europe, and Africa[14]. The Justinian Plague did more than just kill millions, though, this plague pandemic affected the social and economic fabric of the medieval world.

Once the plague reached Constantinople, trade routes allowed for the bacterium to travel to the furthest reaches of the Byzantine Empire, killing millions. These deaths not only caused the elimination of small villages, but also dwindled the empire's armies, leaving regions further from the capital more vulnerable to enemy attacks. By 568, northern Italy had fallen to the Lombards, and as the disease persisted through the 8th century, the provinces located in North Africa and the near East were absorbed by the rising Islamic Empire[15]. The plague further

[12] John Frith. 2012. "The History of Plague- Part 1. The Three Great Pandemics."
[13] Ibid.
[14] Ibid.
[15] Ibid.

weakened the Empire by decimating its agricultural and economic systems. Demand for a sustainable amount of food, as well as the same level of taxes pre-plague put an enormous strain on the now much smaller population. Farmers who survived began to over work the fields in an attempt to produce the meet the food demanded, leading to an eight-year famine[16]. The survivors struggle to purchase both food and pay their taxes, eventually fragmented the Byzantine Empire into the nations of Medieval Europe.

The disappearance of the plague in mid-8th century, and its repeated reemergence in both the 1300's and late-1800's in Europe and Asia continued to shape the societies of these regions. The Black Death during the 14th century killed a quarter of Europe's population and once again lead entire villages becoming uninhabited and created a shortage of laborers[17]. Furthermore, the Black Death shaped societal interactions which continue today by shrinking the divide between the rich and the poor to make way for a middle class[18]. Meanwhile the Third Plague pandemic of 1894 demonstrated the new interconnectedness of the world by spreading the plague via its host, the brown rat, from a rural province in China across the globe to Africa, Australia, and South America[19].

The disease that truly shaped our modern world's view of pandemics and acts as the baseline of what the next large-scale pandemic may look like is the 1918 Spanish Influenza outbreak. Although the origin of said pandemic remains hotly contested[20] , no one can argue the extent of influenza's reach. During the virus's outbreak from 1918 to 1919 over 500 million

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[16] Ibid.
[17] Green, Monica. 2015. *Pandemic disease in the medieval world: rethinking the Black Death.* Vol. 1. Kalamazoo: Arc Medieval Press.
[18] Ibid.
[19] Firth, 2012.
[20] CDC. 2018. "Remembering the 1918 Influenza Pandemic | Features | CDC." 2018.

people fell sick, a third of the global population. More so, over 50 million people around the world died from the flu pandemic, adding to the 37 million deaths from World War 1, which ended the year the pandemic began. Like the war itself, the Spanish Influenza killed primarily young adults, aged 18 to 40, who generally remain the healthiest during flu epidemics[21]. This discrepancy in the most affected age group likely stemmed from the fact that, unlike other flu outbreaks of the period, the Spanish Influenza was caused by an H1N1 strain. Variants of the H1 and N1 proteins had been present in flu epidemics prior to the birth of this age group, meaning that older generation's immune systems were more likely have antibodies better suited for combating the pathogen[22]. In contrast, young adults lacked the same exposure and therefore an immune response, to the H1N1 pandemic strain, causing their immunity against the disease to better model an infant[23]. The large number of deaths in this age group though, coupled with the death toll already associated with the first World War, shaped society for the rest of the century in a way that often gets ignored.

The Spanish Influenza infected people of all races, economic standings, and gender, leading to large disruption across social groups. The most noticeable of these issues stemmed from the growing number of orphans due to the influenza outbreak[24]. Since the majority of those who died were between the ages of 18 and 40, many children lost both parents to the disease. The rise of orphans forced some children to step up and accept adulthood at a young age, while others became wards of their extended family or the state, creating a sense of not-belonging. In

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[21] Shanks, G Dennis, and John F Brundage. 2012. "Pathogenic Responses among Young Adults during the 1918 Influenza Pandemic." *Emerging Infectious Diseases* 18 (2): 201–7.
[22] Ibid.
[23] Ibid.
[24] Bristow, Nancy K. 2010. "'It's as Bad as Anything Can Be': Patients, Identity, and the Influenza Pandemic." *Public Health Reports (Washington, D.C.: 1974)* 125 Suppl (Suppl 3): 134–44.

some families the flu only claimed one parent, forcing the remaining adult to undertake a role not normally accepted by society. Widows who primarily stayed home and raised the children joined the workforce, or forced their children to do so in their place in an effort to make enough money to survive. Single fathers, meanwhile, had to embrace the role of raising children in a society that viewed men's intervention in children's lives as improper. While a number of state social services, heralded by Jane Addams, aimed to reduce the burden these new roles caused for families, they remained not fully effective of reducing the stigmatism associated with the structure of the family[25].

In the United States during the pandemic period, the 1918 pandemic had it largest effect on groups already marginalized by society: African American communities and the poor. Throughout most of the 20th century, highly prevalent Jim Crow laws barred many African American communities from receiving treatment at more affluent and better staffed hospitals. During the 1918 pandemic, these laws allowed for the allocation of resources needed to treat the disease and prevent spreading of the virus away from African American hospitals towards more affluent white hospitals. By barring African American communities from receiving proper treatment during the outbreak, more of those infected succumb to the disease compared to their white counterparts. The denial of better care for sick black Americans and the subsequent higher death rates was rationalized by white America due to lower infection rates in African American communities, strengthening the belief of equality in such treatment[26].

These struggles with inadequate resources to combat the pandemic were further hampered by the fact that African American communities tended to be poorer than white ones.

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[25] Michals, Debra. 2017. "Jane Addams." National Women's History Museum.
[26] Ibid.

Individuals living at or below the poverty line often experienced greater hardships when trying to combat the disease than their wealthier counterparts, regardless of race. Taking time off of work to help sick family members often meant losing one's job, leading to more financial hardship and the eventual need for outside aid. While some aid programs attempted to help the poor through changing the social systems that contributed to poverty, others blamed individuals for their misfortune. In the early 1900's, eugenics and social Darwinism formed a dominate school of thought in the United States and blamed the poor for their misfortune, rather seeing them as dirty alcoholics who could not care for themselves or their children. Therefore, even when groups supporting eugenics provided aid, it was often at the expense of losing one's child to the state or having to completely build a new life to be deemed "worthy" enough to receive adequate help[27]. These marginalized groups, be it by race or wealth, therefore rarely received the aid they needed when facing the pandemic, all while reinforcing stereotypes of both black Americans and the poor that persist in our society today.

The numerous lasting effects that past pandemics have had on national and international societies suggest some ways another large-scale pandemic may influence society. While we live in a "modern" world, our lives are filled with racism, sexism, and classism. Despite the persistence of classifying people based on their attributes, pandemic diseases do not discern these differences. Therefore, the rise of such a deadly disease holds the potential to completely rework the very intricacies of our current society. Not picking and choosing who contracts a disease does not mean that everyone will experience a pandemic equally. If history is an indicator of the future, lower-resourced nations and communities will likely experience the effects of a pandemic more severely.

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[27] Ibid.

B: The Changing Threat of Pandemics with Improving Public Health

During the 1918 Spanish Influenza pandemic, the vast majority of those who died did not succumb to their flu symptoms. Rather, most of the deaths associated with the influenza outbreak were caused by secondary bacterial infections causing pneumonia[28]. Pneumonia infections are no longer death sentences, though, due to the modern innovation of antibiotics. In 1928, a doctor in London discovered that the presence of *Penicillium* mold inhibits the growth of the bacterium *Staphyloccous aureus*. Following this discovery, researchers at Oxford successfully isolated the compounds in the mold which killed a variety of bacterium, and began testing the purified sample, named penicillin, on mice[29]. Penicillin became the first of many commercially available antibiotics that have the potential to not only stop infections caused by *Staphyloccous aureus*, but also other bacterium borne diseases including pneumonia and plague.

Improvements to vaccines have also aided in limiting disease caused by influenza virus infection. Rudimentary vaccines have existed since 1796 when Edward Jenner determined that injecting pus caused by cow pox into a young boy provides immunity against small pox, but a similar flu vaccine did not exist during the Spanish Influenza pandemic[30]. In fact, it was not until 1933 when scientists isolated and identified that the microbe causing influenza was a virus, that flu vaccine development truly became a large focus of the medical community[31]. The first flu vaccine was administered to members of the U.S. army in 1945, and has been annually used

[28] Shanks. 2012.
[29] Markel, Howard. 2013. "The Real Story Behind Penicillin." PBS News Hour. 2013.
[30] Stern, Alexandra Minna, and Howard Markel. 2019. "The History of Vaccines and Immunization: Familiar Patterns, New Challenges."
[31] Smith, Wilson, C.H. Andrewes, and P.P. Laidlaw. 1933. "A Virus Obtained from Influenza Patients." *The Lancet* 222 (5732): 66–68.

to vaccinate the general public since 1946[32]. Although the flu vaccine currently requires modification each year to prepare for the most prevalent form of influenza in seasonal outbreaks, researchers have been investing time and resources into developing a universal vaccine. Such a vaccine could provide protection to all strains of influenza that could pass through human populations and last for multiple years, fixing the major shortcomings of the currently used variant[33].

Despite improvements in combating infectious diseases, especially when faced with influenza outbreaks, these new technological tools do not eliminate the risk of a large-scale pandemic that could kill millions. For every step forward the global health community appears to take in battling infectious diseases, a new obstacle appears. Although the development of antibiotics has helped lower the risk of secondary infections and epidemics caused by bacteria, these microbes are gaining resistance to a variety of drugs commonly used as treatment. The rise of antibiotic resistance, sped up in part by the overuse and misuse of bacterial killing drugs, has created strains of bacteria which are difficult, if not impossible, to kill[34]. Antibiotic resistant bacteria are therefore an emerging global threat, causing over 23,000 deaths a year in the United States alone[35]. The rise of such bacteria therefore increases the risk of wide spread infection and death caused by bacterial pathogens such as plague and cholera, and secondary infections often seen with influenza outbreaks[36].

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[32] Donnelly, Grace. 2018. "The Flu Shot: Its History and Common Misconceptions | Fortune." Fortune.

[33] Cohen, Jon. 2018. "Universal Flu Vaccine Remains 'an Alchemist's Dream'." *Science*, November.

[34] CDC. "About Antimicrobial Resistance | Antibiotic/Antimicrobial Resistance." CDC. 2018.

[35] CDC. "CDC Global Health - Infographics - Antibiotic Resistance the Global Threat." 2018.

[36] Ibid.

Even vaccines, a tool that has been utilized in the prevention of both viruses and bacteria, have lost traction in a number of countries. After a successful vaccination campaign leading to the eradication of smallpox in 1980, the global health community believed that vaccines were the key to stopping all infectious diseases. Smallpox lent itself to eradication not only due to its high visibility and short incubation period, but also because humans are the virus's only host[37]. These aspects of the *variolavirus* separate smallpox from other diseases, such as polio and measles, that continue to persist despite similar eradication efforts[38]. On top of these intrinsic difficulties with eradicating other infectious, difficulties have risen in vaccinating high enough proportions of the global population to stop the spread of these viruses. Many diseases that have been targeted for eradication remain endemic in regions around the global with weak health care systems, political insecurity, and poor sanitation[39]. Weak health care systems and political insecurity make it difficult for the global groups working on eradication to vaccinate the needed percentage of the population to make virial transmission of these pathogens impossible[40].

Vaccine rates in countries where these pathogens were once eliminated have also decreased. Citing reasons varying from religious beliefs to believing that vaccines cause developmental disorders such as autism, certain populations have failed to keep vaccine rates high enough to stop once eliminated diseases from reappearing. Resistance to vaccination has been especially prevalent in Western countries, such as the United States and the United Kingdom, following Andrew Wakefield's 1998 *Lancet* paper connecting the development of

[37] The College of Physicians of Philadelphia. 2018. "Disease Eradication." The History of Vaccines.
[38] Ibid.
[39] WHO. 2018. "10 Facts on Polio Eradication." *WHO*.
[40] GPEI, 2019.

autism to receiving the measles, mumps, and rubella (MMR) vaccine[41]. Although Wakefield's paper has since been retracted, skepticism surrounding the MMR vaccine has remained prevalent, causing large outbreaks across the globe in countries where the disease was once eliminated[42].

Establishing vaccination capabilities in areas with systematically healthcare systems and the refusing vaccination for non-medical reasons therefore represents some of the largest risks to the reemergence of eliminated diseases, and why a large-scale pandemic could still occur[43]. Providing a new universal vaccine to populations already struggling to receive well established vaccines may prove difficult, allowing for influenza to persist at high rates in these regions. [44]. Even if a universal flu vaccine were to be administered at high rates around the globe, pockets of resistance against vaccines, especially relatively novel ones, could still allow for highly infectious strains of the disease to rapidly spread. It is therefore not unreasonable to observe a similar occurrence with a pandemic infectious disease, with certain areas of the world being especially hard hit due to low vaccination numbers.

While low vaccination rates persist as a threat to global health security, they still are a lifesaving technology. Vaccines, though, often prove useless during outbreaks of novel viruses due to development time following the identification of a new pathogen. It currently takes ten to fifteen year to create and have a vaccine undergo all of its need clinical trials once the agent of a

[41] Wakefield, A. J., S. H. Murch, A. Anthony, J. Linnell, D. M. Casson, M. Malik, M. Berelowitz, et al. 1998. "Ileal-Lymphoid-Nodular Hyperplasia, Non-Specific Colitis, and Pervasive Developmental Disorder in Children." *Lancet (London, England)* 351 (9103): 637–41.

[42] Hussain, Azhar, Syed Ali, Madiha Ahmed, and Sheharyar Hussain. 2018. "The Anti-Vaccination Movement: A Regression in Modern Medicine." *Cureus* 10 (7): e2919.

[43] WHO. 2019. "Ten Threats to Global Health in 2019." Emergencies.

[44] Find paper about it being top 10 public health risk

disease is first discovered (seasonal flu vaccines not included)[45]. The emergence of a new infectious disease therefore represents a widespread epidemic or pandemic risk due to the severe gap in time between the virus spreading and having a vaccine against the pathogen[46]. This lapse in creating and deploying these vaccines would allow highly pathogenic and transmissible viruses the time needed to reach pandemic status and possibly kill upwards of 30 million people worldwide[47]. In order to avoid such a global catastrophe such vaccines would already need to be in development, or ideally through clinical trial phases. A well-established plan to distribute these vaccines also would already need to be in place to ensure that every person have equal access to protection from such diseases, regardless of their wealth or where they reside in the world. In order to have these pre-established public health protocols and resources, the global community must be able to predict possible pandemic diseases, as well as cooperate as in an interconnected network to ensure an efficient containment of these pathogens.

Chapter 2: Understanding the Role of Health Organizations in Pandemic Preparedness and Response

In 1946, the sixty-one members present at the International Health Conference following World War II determined that health was a human right[48]. This decision inspired the creation of an international health organization, whose entire purpose was to ensure that good health was an international commodity, not just one prevalent in affluent countries. Establishing the World Health Organization (WHO) though, is not the first instance of international health cooperation.

[45] Association of American Universities. 2010. "Vaccines Today: Faster Than Ever."
[46] Gupta, Sanjay. 2018. "The Big One Is Coming, and It's Going to Be a Flu Pandemic - CNN." CNN.
[47] Gates, 2018.
[48] WHO. 2011. "Origin and Development of Health Cooperation." *WHO*.

In July of 1851 marked the first international discussion focusing on public health was held at the International Sanitary Conference in Paris[49]. Following 1851, International Sanitary Conferences began to gain regularity and expanded to tackling infectious diseases commonly associated with poor living conditions, such as cholera and plague[50]. These meetings eventually led to the formation of the first international health organization, the Office international d'Hygiène publique (OIHP), in 1907. The OIHP was a committee of public health officials from member countries who aimed to tackle many of the health issues brought forth during the Sanitary Conferences. Following World War I, the League of Nations also formed an international health organization, the League of Nations Health Committee and Health Section, which co-existed with the OIHP until their eventual merger following the creation of the United Nations and the WHO in the mid-1940's[51].

Since its formation in 1948, the WHO provides support for its 192-member countries around the globe in improving public health[52]. Many of the WHO efforts, though, have been supported by regional, national, and privately funded public health organizations that also hope to improve the standard of living for the communities they serve. All four types of public health organizations therefore play a role in pandemic preparation and response on a global level. Understanding the structure, procedures, and limitations of these groups in response to pandemic diseases provides insight into the current state of global health preparedness for a large-scale pandemic. I will highlight the different roles and procedures that specific national, regional, and privately funded organizations provide in the scope of national and global public health. I will

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[49] Ibid.
[50] Ibid.
[51] Ibid.
[52] WHO. 2017. "WHO's Work with Countries." *WHO*.

also place these types of organizations in context with the WHO, the single international, publicly funded organization that aims to provide the human right of health to the entire globe.

A: National Health: The Center for Disease Control and Prevention

Across the globe, a number of publicly funded organizations exist with the main goal of predicting, preventing, and responding to disease outbreaks in specific countries. These groups are generally publicly funded by a single nation, and work on global health problems that solving benefits the organization's country of origin. Such agencies include the Public Health England Centre of Infectious Disease Surveillance and Control (PHE), the Chinese Center for Disease Control and Prevention, and the Center for Disease Control and Prevention (CDC) in the United States. Although these three organizations vary on protocols, resources, and objectives due to their different country's of origin, understanding one nations program for disease control and prevention provides a basic understanding of the role similar national agencies play. Due to the United States prominent role in the politics of the international community, especially with their dominance in medical technologies and improvement, I will provide specifics on how the CDC aids in pandemic preparedness and response.

Formed in 1946 in Atlanta, Georgia, the CDC originally began under the U.S. Department of Health and Human Services as a program to stop the spread of malaria in the United States[53]. The small program gradually began to take on more challenging problems associated with improving public health surrounding communicable diseases in the United States, increasing the agencies jurisdiction and budget. The CDC is now one of the highest

[53] CDC. 2012. "Our History - Our Story." About CDC. 2012.

funded and well-staffed national health programs and plays a dominate role in improving public health around the globe. The CDC approaches infectious diseases and other challenges to public health as a security risk with their militaristic mission statement of "working 24/7 to protect America from health, safety and security threats, both foreign and in the U.S.", and has achieved these goals by creating three strategic priorities[54,55]. These priorities, improving health security both in the United States and abroad, preventing the leading causes of illness, injury, disability and death, and strengthening public health and health care collaboration, have all generated funding and programs for preparing against and combating potentially pandemic infectious diseases[56].

Currently, the CDC's largest program focusing on pandemic preparedness is the influenza pandemic plan. The first iteration of this plan came out in 2005 following a pandemic scare of the highly pathogenic avian H5N1 influenza strain[57]. While H5N1 failed to become a worldwide pandemic, the CDC continues to update the pandemic influenza plan in anticipation of a novel strain with similar capabilities[58]. The preparedness plan looks to improve influenza diagnostic and vaccination technologies, healthcare and scientific infrastructure, communication with the public, and communication with the global community[59]. Improving monitoring systems both in the United States and abroad is particularly stressed in order to identify particularly pathogenic strains of influenza before they become pandemic[60]. The CDC's

[54] CDC. 2018. "CDC-Budget Request Overview."
[55] CDC. 2019. Mission, Role and Pledge | About | CDC.
[56] CDC. 2018. CDC Strategic Framework | About | CDC.
[57] White House. 2005. "The National Strategy for Pandemic Influenza."
[58] Office of the Assistant Secretary for Preparedness, HHS. 2017. "Pandemic Influenza Plan - Update IV (December 2017)."
[59] Ibid.
[60] Ibid.

pandemic influenza plan also aids the global monitoring program of influenza headed by the WHO[61]. The agency provides surveillance information surrounding the presence and prevalence of different influenza strains in the United States to the international health community and helps improve the monitoring stations in fifty other countries[62].

While the preparedness plan has emphasized improvements in technologies and surveillance policies focusing on influenza, much of the infrastructure also has uses in preparing for possible pandemics caused by other infectious diseases. The systems utilized by the CDC to detect influenza circulation in the United States gathers similar information on all diseases currently present. Furthermore, the efforts of the CDC, in conjunction with other national health organizations including the National Institute of Allergy and Infectious Disease (NIAID), to improve influenza vaccine development and administration has also aided in improvements to vaccines of other common pathogens, leading to the elimination of both measles and polio in the United States[63,64]. The CDC has also helped increase vaccination rates against the flu and other diseases moving towards elimination by providing information on all vaccines utilized in the United States to both health care providers and patients, as well as purchasing and distributing required vaccines for underserved children[65,66]. The agency encourages the continuation of such technological advancements by providing a number of grants and cooperative agreements focused on vaccine development and distribution[67].

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[61] CDC. 2019. "Monitoring for Influenza Viruses." Pandemic Influenza (Flu).
[62] Ibid.
[63] CDC. 2019. "Partners." Vaccines and Immunization.
[64] CDC. 2018. "U.S. Polio Elimination." Global Health. 2018.
[65] CDC. 2019. "Educational and Promotional Resources for Partners." For Immunization Partners.
[66] CDC. 2016. "Questions on Vaccines Purchased with 317 Funds." For Immunization Mangers.
[67] CDC. 2019. "About CDC Grants." Grants.

The CDC also helps strengthen the national defense against pandemics through the Global Health Security Agenda by improving disease control and prevention of countries with weaker health systems[68]. The CDC is currently working with thirty-one countries to improve disease surveillance and outbreak response, emergency management, diagnostic abilities and safe laboratory systems[69]. These countries achieve these goals through the CDC's implementation of guidelines utilized by countries with successful health care systems, as well as provision of technology and resources needed to support said guidelines[70]. By participating in the Global Health Security Agenda, the CDC and the United States government hopes that countries with weak health care systems that are at high risk for novel infectious diseases could eventually gain the ability to stop the spread of these diseases before they become a public health emergency of international concern[71].

The CDC has also been at the forefront of providing vaccines to countries who continue to struggle with diseases eliminated in the United States. The CDC's Global Immunization Division (GID) has worked to provide both vaccines and the staff needed to administer the medicine to areas of the world where children are at particularly high risk to contract debilitating and deadly diseases[72]. Currently, funds dedicated to the GID have gone primarily into the global effort of eradicating polio and eliminating measles and rubella[73]. By working on these projects the GID hopes to also introduce other new underutilized vaccines into immunization programs around the world, which could help reduce death in children under five by 40%[74]. Ideally, the

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[68] CDC. 2019. "Global Health Security." Global Health Protection and Security.
[69] CDC. 2019. "Global Health Security: About Us." Global Health Protection and Security.
[70] Global Infectious Diseases Meeting. 2014. "Global Health Security Agenda: Action
[71] Ibid.
[72] CDC. 2016. "Vaccines and Immunization." Global Health.
[73] Ibid.
[74] CDC. 2018. "Introducing New and Underused Vaccines." Global Health.

increase of vaccinations will not only stop the spread of currently endemic diseases, but also promote acceptance of novel vaccines that could lower the risk of new and emerging pathogens from causing epidemics.

Despite the numerous programs that the CDC maintains and supports to help improve public health in both the United States and around the globe, the agency has faced a number of setbacks and failures throughout its existence. Most recently, while the CDC has been aiding in the global elimination of measles, 2019 has already tallied the second highest number of measles infections in the United States since its elimination in 2000[75]. A large reason for this uptick in measles infection stems from the spreading of misinformation surrounding the safety of the vaccine. Most states in the U.S. allow for vaccination exemption due to religious and/or philosophical reasons[76]. While these loopholes were not largely utilized in the early 2000's, a number of individuals have turned to philosophical exemptions in recent years based off of Andrew Wakefield's redacted 1998 paper linking the development of autism to receiving the measles, mumps, and rubella (MMR) vaccine[77, 78,79]. While the CDC has distributed educational information surrounding the safety of the MMR vaccine and encouraged states to deny vaccine exemption for philosophical and religious reasons, the growing number of measles cases demonstrates just one setback the national agency has experienced[80,81,82].

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75 CDC. 2019. "Measles Cases and Outbreaks." Measles (Rubeola).
76 Belluz, Julia. 2019. "Measles Is Back Because States Give Parents Too Many Ways to Avoid Vaccines." *VOX*.
77 Wakefield et al., 1998.
78 Ibid.
79 Bailey, Sarah. 2019. "Some Anti-Vaccination Parents Cite Religious Exemptions. Measles Outbreaks Could Change That." *Washington Post*.
80 CDC. 2018. "Measles, Mumps, and Rubella (MMR) Vaccine Safety." Edited by Mark R. Cookson. Vaccine Safety.
81 Bailey, 2019.
82 CDC. 2019. "Measles Cases and Outbreaks." Measles (Rubeola).

The CDC remains just one example of a national public health organization that tackles problems surrounding infectious disease control and prevention. Nearly every county has an agency that in some way aims to improve the health of its citizens and utilizes techniques to control disease spread similar to the CDC. Furthermore, while countries have their own organizations aimed at improving the health of their country, that does not mean that these groups don't also provide global aid. The CDC plays a role in a number of the WHO's initiatives such as influenza surveillance and the eradication efforts for vaccine-preventable diseases. Regardless of global outreach, though, the CDC and other national health organization emphasizes proper support to address the concerns of their country of origin, rather than the entire world.

B: Regional Health: The European Centre for Disease Prevention and Control

In addition to individual nation's programs for disease control and prevention, publicly funded regional agencies also provide multiple countries support and education with preventing and combating infectious diseases. Such organizations, though, are far less common compared to nationally run programs, due to the need for cooperation between nations[83,84]. The two largest and most established iterations of this regional model of disease control and prevention is the European Centre for Disease Prevention and Control (ECDC) and the Pan-America Health Organization (PAHO). The PAHO provides technical support and coordinates cooperation between its fifty-two-member nations across North and South America to prevent and control diseases, strengthen health systems, and respond to health emergencies and disasters[85]. The

[83] PAHO. 2019. "About the Pan American Health Organization (PAHO)." About PAHO.
[84] ECDC. 2019. "ECDC's Mission and Main Activities." About Us.
[85] PAHO, 2019.

PAHO acts as both an independent organization that aims to improve public health in the Pan-American region, as well as the regional office of the America's for the WHO. Due to its duel function, funding for the PAHO comes from both its member countries and the WHO. In contrast, the ECDC only pulls funding from its member states, functioning independently from the WHO. The ECDC works with and receives funding from all European Union (EU) and European Economic Area countries to respond to public health threats and emerging diseases both in Europe and abroad[86]. Due to its funding being all internally based (i.e. not from other WHO nations such as the PAHO) I will present the ECDC as an example of regionally based public health organizations.

Compared to many nationally run public health organizations and the globally run WHO, the ECDC is relatively new. The ECDC was first voted on in 2004, when the member nations of the EU determined that Europe was lacking the disease control and prevention infrastructure that many similarly wealthy nations had in place[87]. The ECDC began operation in June of 2005, and aims to "identify, assess, and communicate current and emerging threats to human health posed by infectious diseases"[88,89]. The current focus of the ECDC remains on improving and developing new technologies for disease surveillance and early warning systems for fifty-two communicable diseases across Europe[90].

With their focus on disease surveillance and prevention across all member states, the ECDC has organized a number of disease programs aimed to address the varying pathogens that

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[86] Ibid.

[87] Greer, Scott. 2012. "The European Centre for Disease Prevention and Control: Hub or Hollow Core?" *Journal of Health Politics, Policy and Law* 27 (6): 1001–30.

[88] ECDC. 2019. "ECDC's Mission." About Us.

[89] The Lancet Infectious Diseases. 2008. "Strengthening Infectious Disease Surveillance in Europe." *The Lancet Infectious Diseases* 8 (9): 525.

[90] ECDC. 2019. "ECDC's Mission." About Us.

threaten Europe's security. These programs aim to not only provide up-to-date information about different disease risks, but also provides tools to combat said pathogens[91]. Currently, the ECDC funds eight disease programs, which ranges from public health microbiology to emerging and vector borne diseases. Furthermore, like the CDC, the ECDC also has a program focused on providing information surrounding vaccines and improving their safety[92]. Despite parallel initiatives associated with their programs, the ECDC differs from the CDC due to its more limited scope. While the CDC plays a major role in improving the preparedness for novel diseases of countries on every continent, the ECDC mainly focuses on improving the health care system of their member states. Despite these limitations, though, the ECDC has engaged with the global health community when approaching a number of diseases declared as public health emergencies of international concern[93].

Since its formation, the ECDC has already provided resources for two large global health crises: the H1N1 pandemic of 2009 and the 2014 West Africa Ebola epidemic. Due to the relative infancy of the agency compared to other organization that play a large role in global health such the WHO and the CDC, though, the ECDC lagged in providing ample expertise, resources, and general numbers during these crises[94,95]. The 2009-2010 H1N1 influenza outbreak served as the first pandemic the ECDC was forced to confront following its formative years. Although the agency provided adequate risk assessment on the virus in the Europe, it failed to coordinate the purchase and distribution of vaccines and antiviral medicines against the

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[91] ECDC. 2018. "Emerging and Vector-Borne Diseases Programme." Disease Programmes.
[92] ECDC. 2018. "Vaccine Preventable Diseases Programme." Disease Programmes.
[93] Greer, 2012.
[94] Ibid.
[95] The Lancet Infectious Disease, 2008.

pathogen[96]. A large reason for the agency's inadequacies in providing support to the politically contentious issues, such as vaccine purchases, stems from the structure of the organization[97,98]. While it was well acknowledged the program was still quite young, the limitations set on the ECDC has inhibited the program from being a key player in the response to infectious diseases[99]. These restrictions include the relatively small budget of the ECDC of forty million euros, as well as the presence of less than 300 employees across all member states[100].

In order to better serve the member states of the ECDC, the agency's budget has been raised to nearly fifty-nine million euros[101]. Through the provision of more funding, the organization has effectively played a larger role in responding to both epidemics and pandemics on a global scale. Specifically, they have expanded and improved upon their capabilities to provide much needed diagnostic technology during the 2014 West Africa Ebola epidemic[102]. Despite these improvements, though, the resources of the ECDC still remain inadequate for being a point organization in addressing an epidemic or pandemic outbreak[103,104]. Although improvements have been made to the ECDC's budget, it still lacks in comparison to other nationally based organizations such as the CDC, who currently has a budget of over seven billion

[96] Greer, 2012.
[97] The Lancet Infectious Disease, 2008.
[98] Greer, 2012.
[99] Ibid.
[100] The Lancet Infectious Disease, 2008.
[101] ECDC. 2017. "Achievements, Challenges and Major Outputs 2017 Highlights from the Annual Report of the Director." In *Annual Report of the Directors.*
[102] Reusken, Chantal B, Ramona Mögling, Pieter W Smit, Roland Grunow, Giuseppe Ippolito, Antonino Di Caro, and Marion Koopmans. 2018. "Status, Quality and Specific Needs of Ebola Virus Diagnostic Capacity and Capability in Laboratories of the Two European Preparedness Laboratory Networks EMERGE and EVD-LabNet." *Euro Surveillance: Bulletin Europeen Sur Les Maladies Transmissibles = European Communicable Disease Bulletin* 23 (19).
[103] Ibid.
[104] Greer, 2012.

U.S. dollars[105]. Furthermore, the number of employees for the ECDC still remains below 300 for all of Europe[106]. In comparison, the CDC has over 12,000 health care workers, providing services both internally and abroad[107].

Despite these shortcomings the ECDC remains an organization that many public health officials feel has yet to achieve its full potential[108]. The ECDC has the backing of fifty-two countries, a number of which are fairly wealthy, providing the agency with the opportunity to eventually gain the funding and employee base needed to become more influential in global public health. Furthermore, the inclusion of multiple countries funding and interacting with the ECDC gives the agency more input and resources to solve problems surrounding infectious diseases compared to national organizations. While the WHO serves more countries than the ECDC, the smaller member size of the regional agency allows the ECDC to address problems that are more prevalent to its member states in the European region. The ECDC and other regional disease control and prevention organizations can therefore provide broader aid than national programs, but more focused to regional health problems than the WHO.

C: Non-Government Organizations: Médecins Sans Frontières

In contrast to the organizations like the CDC and the ECDC, a number of agencies that are privately funded also provide resources for combating infectious disease. Such groups, including the Bill and Melinda Gates Foundation, CARE International, and Médecins Sans Frontières/ Doctors without Borders (MSF), gather funds either through personal assets or

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[105] CDC. 2018. “CDC At-A-Glance.” About CDC 24-7.
[106] ECDC, 2017.
[107] Ibid.
[108] Greer, 2012.

donations from both individuals and a variety of governments around the globe[109]. Like the publicly funded global health groups, these organizations aim to provide resources for combating infectious diseases in areas of the world that are most at risk. Furthermore, while government-run global health organizations make changes through creating and then enacting different policies, these non-government groups provide a more hands on approach to combating infectious disease and its impact to global health. Médecins Sans Frontières has been one of the leading non-government organizations in providing medical assistance to combat local epidemics and pandemics, and will therefore serve as the main example of what non-government organizations (NGOs) focused on public health bring to protecting the global community against infectious disease.

Médecins Sans Frontières was formed in 1971 in Paris, France following the famine and subsequent war that broke out Biafra, Nigeria[110]. Since its charter, the organization has grown from 300 volunteer doctors, nurses, and other staff based in France, to over 42,000 workers worldwide[111]. Médecins Sans Frontières main goal since its formation has remained providing medical care to whoever is in need throughout the globe, without thought to the effected group(s) race, political views, or religious convictions[112]. Due to their belief that global health is a right that transcends all other aspects of an individual, MSF remains politically, economically, and religiously unaffiliated[113]. Such structure has put MSF on the front lines of global health crisis

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109 School of Public Health, University of Albany. 2018. "What Types of Organizations Are Working in Global Health?" Center for Global Health.
110 Médecins Sans Frontières. 2018. "Who We Are | Our History." Who We Are.
111 Médecins Sans Frontières. 2018. "The MSF Charter." Who We Are.
112 Médecins Sans Frontières. 2018. "Working Principles." Who We Are.
113 Ibid.

ranging from local epidemics, to providing medical care in areas effected by war or natural disaster[114].

In terms of combating epidemic and pandemics diseases, MSF has provided a number of services to countries most susceptible to large outbreaks of certain pathogens due to location and poor public health systems. Médecins Sans Frontières focuses both on short term public health crisis, as well as long term inefficiencies in the public health of different regions[115]. Their short-term efforts generally focus on providing immediate medical care for those in need and informing the global community of the current situation that MSF is encountering[116]. While these projects generally last only as long as the crisis is prevalent, MSF also undertakes long-term projects that sometimes requires the presence of the organization for decades[117]. Such long-term efforts generally begin as short-term projects that lend themselves to MSF staying to either set up or improve the health care systems of the community in need[118]. By undertaking these two distinct length projects, MSF therefore provides immediate response to infectious diseases outbreaks and plays a role in global pandemic preparedness.

While MSF remains unaffiliated to any country, political identity, or religious group, the organization does interact with and contribute to global preparedness and response to infectious disease outbreaks. During the 2014 West Africa Ebola epidemic, MSF doctors were some of the first health care providers to come in contact with EVD patients and alerted the global public health system of the growing threat the then unknown disease had to Guinea[119]. Médecins Sans

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[114] Ibid.
[115] Doctors Without Borders - USA. 2019. “Types of Projects.” How We Work.
[116] Médecins Sans Frontières. 2018. “Working Principles.” Who We Are.
[117] Doctors Without Borders - USA. 2019. “Types of Projects.” How We Work.
[118] Ibid.
[119] WHO. 2015. “WHO | Origins of the 2014 Ebola Epidemic.” *WHO*.

Frontières has also aided the global vaccination effort supported by the WHO against preventable diseases in countries with weaker healthcare systems[120].

Multiple other NGO's also contribute to infectious disease control and prevention, as well as provides on the ground services to medical emergencies in underprepared countries. A number of these groups, though, do not maintain the neutrality observed by MSF, leading to more selective services being provided to those in need[121, 122]. Despite these discrepancies in who receives aids from the NGOs, a large number of these groups do provide effective aid in preparing for and combating infectious diseases[123]. Non-government organizations therefore play an imperative role in global infectious disease and pandemic preparedness, and must therefore be addressed when improving current systems of disease control and prevention.

D: International Health: The World Health Organization

In contrast to national and regional public health organizations, only one publicly funded agency's goal is overall global security from infectious diseases. The World Health Organization (WHO) is currently the only publicly funded international health organization that includes members from every continent (excluding Antarctica). The organization aims to provide knowledge and support to every member country through its international headquarters and its six regional offices (the Americas, Europe, Africa, Southeast Asia, Eastern Mediterranean, and

120 Médecins Sans Frontières. 2018. "Protecting as Many Children as Possible in an Emergency Context." Central African Republic.

121 DeHaven, Mark J, Irby B Hunter, Laura Wilder, James W Walton, and Jarett Berry. 2004. "Health Programs in Faith-Based Organizations: Are They Effective?" *American Journal of Public Health* 94 (6): 1030–36.

122 Bill and Melinda Gates Foundation. 2019. "Foundation Fact Sheet." Who We Are.

123 Ibid.

Western Pacific)[124]. Pre-dated by the League of Nations Health Organization and the OIHP, a unified public health program was suggested during the 1945 conference setting up the United Nations[125]. At this formative meeting, founding members of the United Nations declared health a human right, and therefore made it the goal of this new organization to holistically improve global public health, not just focus on sanitation as its predecessors[126]. In the years following the first meeting, a constitution for this public health agency, known as the World Health Organization, was created and then ratified by members of the United Nations on April 7th, 1948[127,128]. Since its creation in 1948, the WHO has strived to provide the highest standard of health to people all over the globe, which has included helping contain and treat both epidemic and pandemic diseases throughout the past seventy years[129].

With advancements in both public health knowledge, as well as with technologies, the WHO has continued to change throughout the past seventy years, expanding their responsibilities and resources provided to aid in public health initiatives[130]. In terms of infectious disease, the WHO has been a major force behind the eradication efforts of smallpox, polio, and measles among other maladies, providing both technical training and supplies for worldwide vaccinations against these diseases[131]. Most importantly, though, the WHO has been the main organization to mobilize international funds and resources for dealing with public health concerns across the globe, especially in countries with weaker economies and health care infrastructures.

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124 WHO. 2019. "Regional Offices."
125 WHO. 2011. "Origin and Development of Health Cooperation." *WHO*.
126 Ibid.
127 Ibid.
128 WHO. 2019. "Milestones for Health over 70 Years." *WHO.*
129 Fifty-first World Health Assembly. 2006. "Constitution of the World Health Organization." New York City.
130 Ibid.
131 Hopkins, 2013.

In 2005, the first iteration of the International Health Regulations (IHR) was adopted by the 196 countries in association with the WHO (192-member nations plus four others)[132]. These regulations represent an agreement between all signed countries to collaboratively work towards global health security by improving individual nations ability to detect, assess, and report on diseases and making all data gathered public[133]. In making said improvements, the WHO plays a role in coordinating these efforts, working with partners to help raise funds, distribute technologies, and provide knowledge surrounding improving global health security[134]. The creation of the IHR also provided the WHO with power when responding to infectious disease outbreaks that officials view as public health emergencies of international concern (PHEIC)[135]. Public Health Emergencies of International Concerns are decided by a WHO committee based on the risk that an infectious disease poses of spreading internationally and whether a coordinated international response is required[136]. Declaring a PHEIC allows the WHO to directly assess the problem unfolding in the affected regions and respond accordingly by freeing up funds from both the organization and other member nations to properly respond to the crisis at hand[137]. Since enacting the IHR in 2007 only four PHEIC's have been declared, demonstrating the gravity of such a declaration has on the public health community[138].

In addition to meeting the guidelines issued in the IHR, the WHO also works on five other priorities to improve global health security, including noncommunicable diseases and

[132] WHO. 2016. "Health Regulations Third Edition (2005)."
[133] WHO. 2017. "About IHR." *WHO*.
[134] Ibid.
[135] WHO. 2014. "Ten Things You Need to Do to Implement the IHR." *About IHR*.
[136] WHO. 2017. "Frequently Asked Questions about the International Health Regulations (2005)."
[137] WHO. 2016. "Health Regulations Third Edition (2005)."
[138] Bellux, 2016.

increasing access to medical products[139]. These priorities were redefined and strategic plans to achieve these goals were improved upon in 2014 following backlash of the WHO's response to the 2014 West Africa Ebola epidemic[140]. This restructuring of the system has provided the WHO with more funding when responding to PHEIC's by the World Bank, as well as inspired a restructuring of the agencies response system to public health problems in order to better serve countries and communities in need[141].

Despite critiques of the WHO following its responses to a number of public health global security threats, the agency remains the best line of defense against infectious diseases and possible pandemics. The organization combines the expertise of thousands of professionals who are the top of their field when it comes to responding to disease outbreaks, providing the entire globe access to such knowledge[142]. This cooperation through the WHO towards global health provides much needed help in improving the health care and response systems in countries that through war, exploitation, or a combination of both have lagged behind the technological capabilities of nations like the United States. The WHO, though, fails to provide direct intervention, as well as the focused knowledge of a nation's history and relationship with public health. Other national, regional, and NGO's therefore help fill the holes formed by the WHO's broad approach to infectious disease and prevention.

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[139] WHO. 2014. "Twelfth General Programme of Work 2014-2019."
[140] Ibid.
[141] Piot, Peter, Cordelia E M Coltart, and Katherine E Atkins. 2017. "Preface: 'The 2013-2016 West African Ebola Epidemic: Data, Decision-Making and Disease Control'." *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences* 372 (1721).
[142] WHO. 2016. "Health Regulations Third Edition (2005)."

Chapter 3: The 2014 West Africa Ebola Epidemic: Failures of Predicting Pandemics and the International Response

Although numerous organizations combat infectious diseases, their interventions inadequately approach the threat that these viruses pose to global security, failing to stop outbreaks of these diseases. Part of the global health community's current struggles with stopping disease outbreaks may stem from the shift observed in how nations address the risks posed by infectious disease. Throughout history, infectious diseases were primarily viewed as threats to the security of armed forces[143]. In 2007, though, the WHO asserted that infectious diseases also threaten the political and economic stability of individual countries and the world[144]. While the threat that these pathogens have on the fabrics of society have existed for more than the past twelve years, this deceleration led to a shift in how preventing infectious diseases were approached by the global community. Instead of focusing on the global aspect of the novel threats that these pathogens posed, many countries continued to look inwards to improve national programs focused on surveillance, prevention, and treatment. By turning inwards in addressing the threat of infectious diseases, richer countries have vastly improved their ability to prepare for and respond to disease outbreaks. Less affluent countries, though, have been left on their own to face the threat of infectious diseases without the funds or technology that aided their richer counterparts.

West Africa has long been a hot spot for tropical infectious diseases such as malaria, dengue, yellow fever, and Lassa fever. Many of these diseases are caused by viral infections that spill over from animal hosts into humans and have garnered billions of dollars in research due to

[143] Mcinnes, Colin and Kelley Lee. 2012. *Global Health and International Relations.* Cambridge: Polity Press.
[144] Ibid.

their high mortality rates[145,146]. Following 9/11, hemorrhagic fever diseases including yellow and Lassa fever gained the attention of the United States due to fears that these pathogens could be turned into biological weapons for terror attacks. During the Cold War, Lassa virus represents just one virus manipulated by the Soviet Union and the United States into an aerosol weapon, fueling the belief similar virus could again be weaponized[147]. Currently, Lassa fever is endemic in the Mano River Union (MRU) region of West Africa, encouraging the United States to conduct research into the hemorrhagic fever and other viruses in the region that could be weaponized.

First identified in 1969, Lassa fever is a hemorrhagic fever with symptoms similar to Ebola and yellow fever, that spreads through contact with the multimammate rat and human bodily fluids[148]. Unlike other viral hemorrhagic viruses, Lassa fever is endemic in West Africa, infecting hundreds of thousands of people in the region annually. Due to its ease in transmission, and the ability to create an aerosol of the virus during the Cold War, Lassa fever was declared a Category A agent with bioterrorism potential by the U.S. National Institute of Allergy and Infectious Diseases (NIAID) following 9/11[149]. The worries of this disease being used as a bioterrorist weapon, and possibly causing a highly fatal pandemic, encouraged funding from the National Institute of Health (NIH) towards establishing the Lassa Diagnostic Laboratory in the Kenema Government Hospital of Sierra Leone[150]. Built in 2005, this lab tests blood samples of

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[145] Fuller, Jacquelline. 2005. "Funding Commitment to Accelerate Malaria Research." Bill and Melinda Gates Foundation: Press Room. 2005..
[146] WHO. 2016. "WHO | 10 Facts on Malaria." *WHO*.
[147] Groseth, Allison, Steven Jones, Harvey Artsob, and Heinz Feldmann. n.d. "Hemorrhagic Fever Viruses as Biological Weapons." 2005.
[148] WHO. "Lassa Fever." 2017.
[149] Tulane University. 2017. "Viral Hemorrhagic Fevers." Viral Hemorrhagic Fever Consortium. 2017.
[150] Abudullah, Ibrahim and Kamara, A. 2017."Confronting Ebola with bare hands: Sierra

patients suspected to have Lassa fever for diagnosis, as well as sends collected specimens for more in depth analysis by agencies based in the United States[151]. Gathering of such samples has helped the U.S. gain a better understanding of the disease in preperation for a large-scale epidemic or bioterrorist event. Research efforts into Lassa fever in the MRU region, though, failed to predict the real danger lurking in West Africa: Ebola.

A: An Overview of Ebola Virus Disease

First identified in in 1976, Ebola virus disease (EVD) is a hemorrhagic fever caused by the infection of a group of viruses from *ebolavirus* genus within the Filoviridae family. A zoonotic disease, EVD in humans initially presents similarly to other common illnesses such as malaria, Lassa fever, and influenza, with symptoms including fever, fatigue, diarrhea, and vomiting. As the disease progresses, though, more serve symptoms such as impaired kidney and liver functions, as well as internal and external hemorrhaging often occur. Due to the common delay in correctly diagnosing EVD, especially at the beginning of an outbreak, the average fatality rate of EVD is around 50%. Mortality rates in isolated epidemics, though, have ranged between 25% and 90% depending on the virus species and the presence of early supportive care[152]. While highly lethal, EVD transmission requires contact with infected bodily fluids. Education on Ebola coupled with the usage of proper personal protective equipment (PPE) when

Leone's health sector on the eve of the Ebola epidemic" in *Understanding West Africa's Ebola Epidemic,* edited by Ibrahim Abdullah and Ismail Rashid, 112-136. London: Zed Books Ltd.

[151] Ibid.

[152] Tulane University, 2017.

dealing with the virus has therefore allowed for most outbreaks to register case counts below one hundred[153].

Ebolavirus is zoonotic in origin, meaning humans are not the natural reservoir for the virus, and therefore infection occurs through interaction with other animals who either act as a reservoir or carrier. The primary sources of human-Ebola contact occur by residing near previously infected nonhuman primates, or through interactions and consumption of fruit bats, the probable reservoir of *ebolavirus*[154]. Currently, six species in the genus *ebolavirus* are known, four of which have caused human EVD. While the disease was previously known by communities in central Africa, EVD caught the attention of the international community following an outbreak of “a novel hemorrhagic fever” near the Ebola River in the Democratic Republic of the Congo (DRC, formally Zaire) in 1976. This outbreak resulted in 318 cases and 280 deaths, and was linked to a filamentous virus named *Zaire ebolavirus*[155]. A similar outbreak around the same time was later noted in South Sudan (formally Sudan), but with a lower number of cases and death (284 and 151 respectively)[156]. While initially thought to have stemmed from the DRC outbreak, analysis demonstrated that the disease in South Sudan was caused by a distinct virion of the same genus named *Sudan ebolavirus.* Since 1976, two other types of *ebolavirus, Bundibugyo ebolavirus*, and *Taï Forest ebolavirus*, have caused human EVD, with the former being implicated in number of larger outbreaks, while the latter has only caused one

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[153] CDC. 2018. “What Is Ebola Virus Disease? | Ebola (Ebola Virus Disease) | CDC.” 2018.
[154] WHO. “Ebola Virus Disease.” 2018.
[155] J. Burke, R. Declerq, and G. Ghysebrechts. 1978. “Ebola Haemorrhagic Fever in Zaire, 1976. Report of an International Commission.” Bulletin of the World Health Organization. Vol. 56. 1978;56(2):271-293.
[156] WHO. “Ebola Haemorrhagic Fever in Sudan, 1976 Report of a WHO/International Study Team 1.” n.d. Vol. 56. 1978;56(2):247-270.

known case. The remaining two species, *Reston ebolavirus* and *Bombali ebolavirus,* do not cause human EVD, but *Reston* does cause EVD in pigs and other nonhuman primates[157].

Prior to 2014, all naturally occurring outbreaks of human EVD emerged from the rural tropical rain forest regions of Central and Eastern Africa, except for the one reported case of *Taï Forest ebolavirus* from Côte d'Ivoire in 1994[158]. Furthermore, in all twenty-three non-lab outbreaks of EVD between 1976 and 2014 less than 450 cases were reported, with the 1976 DRC outbreak totaling the largest death toll[159]. Public health officials and locals were therefore unaware of *ebolaviruses* ability to transmit in West Africa from a non-human source, and failed to predict that EVD outbreaks could grow to the size of the 2014 epidemic in Liberia, Sierra Leone, and Guinea.

B: An Overview of the 2014 West Africa Ebola Epidemic

In December 2013, a young boy in rural Guinea fell ill of a disease with an unknown origin causing fever, black stool, and vomiting. Two days later he died[160]. Quickly after the passing of the eighteen-month-old boy, later identified as Emile Ouamouno, his immediate family began showing similar symptoms of this unknown plague. As more fell ill, including a family friend from Sierra Leone, those infected began to travel between towns and neighboring countries, spreading the disease. Those ill also began seeking medical care beyond traditional healers, going to clinics and hospitals which allowed for the swift spread of the disease from the

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[157] CDC. 2018. "What Is Ebola Virus Disease? | Ebola (Ebola Virus Disease) | CDC." 2018.

[158] CDC. 2018. "Ebola Virus Disease Distribution Map: Cases of Ebola Virus Disease in Africa Since 1976 | 2014-2016 Outbreak West Africa | History | Ebola (Ebola Virus Disease) | CDC." 2018.

[159] Ibid.

[160] WHO. 2015. "WHO | Ground Zero in Guinea: The Ebola Outbreak Smolders – Undetected – for More than 3 Months." *WHO*.

rural forests of Guinea into more urban areas such as Conakry[161]. By March of 2014, the outbreak had reached neighboring Sierra Leone and Liberia with a mortality rate of 90%[162]. Despite all of this, the exact virus responsible for the deadly outbreak remained unknown and the communities in these countries had not been alerted to the growing problem. The breakdown in communication between government officials and citizens of these countries likely stemmed from the MRU region being endemic to a number of hemorrhagic fevers, excluding Ebola[163]. Many health officials therefore displayed ignorance towards properly identifying this virus, which not only lead to dissemination of improper information, but also contributed to the poor containment and treatment provided, increasing both Ebola's spread and mortality rate.

It was not until March 13th, 2014 that the Guinean government's Ministry of Health first alerted the national and international communities of the growing unknown threat, over three months since the outbreak began[164]. Following the announcement, the Ministry of Health supported by MSF and the WHO African Regional Office (WHO AFRO) undertook an investigation into diagnosing the exact disease causing such a lethal outbreak. By April of 2014 they discovered the culprit: EVD caused by *Zaire ebolavirus,* the deadliest strain of the known EVD causing viruses in humans[165].

Even with a name to the disease and a protocol established to minimize the spread of EVD across Western Africa, cases continued to occur. The health, cultural, and political infrastructures of the Sierra Leone, Guinea, and Liberia were ill equipped to handle such an

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161 WHO. 2015. "Guinea-Chart-Big.Png (1302×981)." 2015.
162 WHO. 2015. "WHO | Ground Zero in Guinea: The Ebola Outbreak Smolders – Undetected – for More than 3 Months." *WHO*.
163 Elizabeth Bradley, Lauren A. Taylor. "Protecting and Promoting Health in an Interdependent World." Unpublished.
164 WHO. 2015. "WHO | Origins of the 2014 Ebola Epidemic." *WHO*.
165 Ibid.

outbreak alone. The disease began to spread to other countries as well, and not just by traveling on foot. Airplanes flying to international cities contained passengers already infected with EVD, some even growing symptomatic, and therefore contagious, on the flights[166]. EVD successfully made its way not only to nearby Nigeria, Mali, and Senegal through this method of travel, but also into the Global North[167]. By August 2014, the WHO declared the current Ebola epidemic in West Africa a Public Health Emergency of International Concern (PHEIC), providing technical guidance and assistance to the area and emphasizing the need for a coordinated international response to curb the growing problem[168].

Following the PHEIC, the international community responded with donations from countries around the globe, including Cuba, China, the United States, and Great Britain, for treatment centers, as well as the training and deployment of doctors, nurses, and epidemiologists into the affected regions[169, 170]. The aid supplied to Sierra Leone, Guinea, and Liberia helped to eventually declare these regions Ebola free. Liberia was the first country to reach said status in January of 2016, with Sierra Leone quickly following suit[171]. Guinea, though, did not successful stop the spread of EVD until June of 2016, two and a half years after the initial case was

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[166] Nicole J. Cohen, Clive M. Brown, Francisco Alvarado-Ramy, Heather Bair-Brake, Gabrielle A. Benenson, Tai-Ho Chen, Andrew J. Demma, et al. 2016. "Travel and Border Health Measures to Prevent the International Spread of Ebola." MMWR Supplements 65 (3): 57–67.

[167] Ibid.

[168] Jolie Kaner, and Sarah Schaack. 2016. "Understanding Ebola: The 2014 Epidemic." Globalization and Health 12 (1): 53.

[169] Ismail Rashid. "UNMEER and the International Response to the Ebola Epidemic" in *Understanding West Africa's Ebola Epidemic,* edited by Ibrahim Abdullah and Ismail Rashid, 296. London: Zed Books Ltd., 2017.

[170] Kaner, 2016.

[171] Ibid.

discovered. During that time, over 28,000 cases of Ebola were reported, with 11,325 of them resulting in death[172].

C: Slow International Response Rate in 2014 Epidemic Highlights Current Inefficiencies in the Epidemic and Pandemic Response Worldwide

Prior to 2014, an outbreak of EVD had never reported more than 450 cases[173]. The explosion of cases seen in the West Africa epidemic, though, demonstrated the very real threat that infectious diseases have on an increasingly more urban world, and the need for fast response times. Failing to identify *ebolavirus* as the disease-causing pathogen during the first four months of the outbreak allowed the virus to spread unchecked to urban areas of Guinea, as well as surrounding Sierra Leone and Liberia, and simultaneously hinder effective treatment of the disease. While wealthier countries have health systems capable of both identifying infectious diseases in early stages of an outbreak and reducing the spread of the pathogen, Liberia, Guinea, and Sierra Leone lacked the appropriate resources to combat an infectious disease outbreak due to centuries of exploitation by colonial powers[174]. These three effected countries therefore relied heavily on the international community for aid in combating *ebolavirus*. While NGOs such as MSF were quick to provide medical services to the area, the slow mobilization of the WHO and other government funded organizations following identification of *ebolavirus* further hurt containment efforts of the pathogen and exposed just how underprepared the world is when

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[172] Ibid.

[173] CDC. 2018. "Ebola Virus Disease Distribution Map: Cases of Ebola Virus Disease in Africa Since 1976 | 2014-2016 Outbreak West Africa | History | Ebola (Ebola Virus Disease) | CDC." 2018.

[174] Howard, Allen. 2016. "Ebola and regional history: connections and common experiences". *Understanding West Africa's Ebola Epidemic,* edited by Ibrahim Abdullah and Ismail Rashid, 296. London: Zed Books Ltd., 2017.

facing large scale infectious disease outbreaks. The failures in containing the West Africa Ebola epidemic, though, has provided public health officials with a starting place when trying to identify the world's weak spots when it comes to infectious disease preparedness.

The slow response time between the epidemic's start and identifying the viral threat as *ebolavirus* made the West Africa Ebola epidemic not only the largest EVD outbreak ever observed in humans, but was also the longest. Despite the lag in identifying the pathogen responsible for the epidemic, both detection and diagnostic technologies for *ebolavirus* had been readily employed since its discovery 1976[175]. By 2014, real-time reverse transcriptase polymerase chain reaction (RT-PCR) assays and enzyme-linked immunosorbent serological assays (ELISA) were the most the commonly employed techniques, first gaining prominence as diagnostic tools of *ebolavirus* in the early 2000's[176]. While utilizing these techniques requires at least a makeshift laboratory, something that Guinea and Liberia lacked, Sierra Leone was already home to a powerful diagnostic facility at the Kenema Government Hospital[177].

Kenema Government Hospital is home of the Lassa fever diagnostic center, a United States funded laboratory that has the capabilities of analyzing blood samples for the presence of viral pathogens as a diagnostic test[178]. Between 500-700 patients annually from surrounding MRU countries submit blood samples searching for a diagnosis to their aliment. While Kenema has the technologies to diagnose Lassa fever, 60% of patients never receive a diagnosis despite

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175 Broadhurst, M Jana, Tim J G Brooks, and Nira R Pollock. 2016. "Diagnosis of Ebola Virus Disease: Past, Present, and Future." *Clinical Microbiology Reviews* 29 (4): 773–93.

176 Ibid.

177 Abdullah and Kamara, 2016.

178 O'Hearn, Aileen E., Matthew A. Voorhees, David P. Fetterer, Nadia Wauquier, Moinya R. Coomber, James Bangura, Joseph N. Fair, Jean-Paul Gonzalez, and Randal J. Schoepp. 2016. "Serosurveillance of Viral Pathogens Circulating in West Africa." *Virology Journal* 13 (1): 163.

showing symptoms of a hemorrhagic fever[179]. The lack of actually diagnosing patients stems from the hospital only checking for *lassavirus* and ignoring other endemic hemorrhagic fever viruses in the region, such as yellow fever virus[180]. Retroactive studies of these blood samples, though, demonstrated that a number of these undiagnosed cases were caused by *ebolavirus*, putting the pathogen in the region as early as 2006[181]. Both the Kenema Government Hospital and the United States therefore had the ability to identify *ebolavirus* as present in the MRU region at least eight years prior to the epidemic. By focusing too narrowly on expected pathogens instead of viruses that could survive in a region, the global community demonstrated their limitations in actively predicting and preventing disease outbreaks.

While the 2014 Ebola epidemic demonstrated the current weaknesses in predicting epidemics and pandemics on a global level, it more importantly showed the inadequacies in the global community's response to public health emergencies. The health infrastructure of all three MRU countries were highly underdeveloped prior to the 2014 epidemic[182]. The global community had taken notice of the weak health detection capabilities in these MRU countries during the 2005 WHO's International Health Regulations, but placed the burden of improving these systems primarily on the effected countries[183]. The political and economic climates of all three countries, though, remained too weak to actually put any of these recommended improvements into their health systems[184]. Sierra Leone and Liberia saw civil wars end in 2002

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179 Ibid.

180 Abdullah and Kamara, 2016.

181 Schoepp, Randal J, Cynthia A Rossi, Sheik H Khan, Augustine Goba, and Joseph N Fair. 2014. "Undiagnosed Acute Viral Febrile Illnesses, Sierra Leone." *Emerging Infectious Diseases* 20 (7): 1176–82.

182 WHO. 2016. "Health Regulations Third Addition (2005)."

183 Ibid.

184 *Understanding West Africa's Ebola Epidemic,* edited by Ibrahim Abdullah and Ismail Rashid, 296. London: Zed Books Ltd., 2017.

and 2003 respectively, leaving both countries in the midst of rebuilding a politically and economically stable climate during the years leading up to the Ebola epidemic[185,186]. Guinea, while not actively engaged in a war during the 21st century, was still experiencing civil unrest due to years of exploitation by mining and timber companies across the country[187]. The political instability present in all three countries therefore contributed to a lack of internal funding towards improving health systems and for the majority of international aid to go towards rebuilding other infrastructure vital to improve a countries economy and political stability[188].

Funneling money into programs that aided the political climate helped stabilize the MRU countries leading up the epidemic, but the health care and public health infrastructure of the three countries failed to observe such growths. Rather, Sierra Leone, Guinea, and Liberia continued to spend over four times less on health care compared to the global average[189]. All three countries health care systems were therefore too weak to provide impactful treatment against EVD and contributed to the virus's spread. Even in the early months of the outbreak when an endemic hemorrhagic fever was suspected, efficient treatment lacked despite many of the symptoms and the human-to-human transmission remaining the same as EVD[190]. Therefore, as with all viral hemorrhagic fevers, doctors and caretakers of the sick were highly recommended to wear personal protective equipment (PPEs) when treating patients to minimize contact with bodily

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185 BBC News. 2018. "Sierra Leone Profile - Timeline." BBC.

186 BBC News. 2018. "Liberia Profile - Timeline." BBC.

187 WHO. 2015. "Ground Zero in Guinea: The Ebola Outbreak Smolders – Undetected – for More than 3 Months." *WHO*.

188 World Bank Group. 2014. *The Economic Impact of the 2014 Ebola Epidemic: Short- and Medium-Term Estimates for West Africa*. Washington, DC: International Bank for Reconstruction and Development.

189 Abdullah and Kamara, 2016.

190 WHO. 2017. "Lassa Fever."

fluids[191]. A weak health care system, though, meant that most hospitals were underfunded and lacked PPEs, putting health care providers at high risk of contracting the virus[192]. Furthermore, the number of hospitals and doctors in the region were also low due to years of civil wars and unrest pre-dating the epidemic in all three countries[193]. Therefore, many family members and traditional healers without any access to PPEs were the best option to provide treatment to the sick, while running a high risk of contracting the disease themselves[194]. These systematic weakness in the healthcare system help contribute to the quick spread of the virus throughout the region.

The MRU countries poor health infrastructure, coupled by the international community's lack of guidance towards funding and establishing the health systems of these nations led to more losses than the 11,000 lives to *ebolavirus.* The 2014 epidemic also had long term effects on the globes health care system, as well as the economics and social fabrics of Sierra Leone, Libera, and Guinea[195,196,197,198]. By the end of 2015 over 5.1 billion United States dollars in funds had been allotted to helping contain the spread of EVD and provide treatment to the sick[199]. The majority of this funding came as donations from WHO-member countries and the World Bank to

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191 Ibid.

192 Abdullah and Kamara, 2016.

193 Kieh, George. 2016. *Understanding West Africa's Ebola Epidemic,* edited by Ibrahim Abdullah and Ismail Rashid, 296. London: Zed Books Ltd., 2017.

194 Abdullah and Kamara, 2016.

195 Kaner, Jolie, and Sarah Schaack. 2016. "Understanding Ebola: The 2014 Epidemic." *Globalization and Health* 12 (1): 53.

196UN Office of the Special Envoy of Ebola. 2015. "Resources for Results III."

197 Evans, David K, Markus Goldstein, and Anna Popova. 2015. "Health-Care Worker Mortality and the Legacy of the Ebola Epidemic." *The Lancet Global Health* 3 (8): e439–40.

198 Suerie Moon, Devi Sridhar, Muhammad A Pate, Ashish K Jha, Chelsea Clinton, Sophie Delaunay, Valnora Edwin, et al. 2015. "Will Ebola Change the Game? Ten Essential Reforms before the next Pandemic. The Report of the Harvard-LSHTM Independent Panel on the Global Response to Ebola." *The Lancet* 386: 2204–21.

199 UN Office of the Special Envoy of Ebola, 2015.

both the WHO and the affected countries[200]. Although declaring a PHEIC provided the WHO access to some funds and resources, no emergency fund had previously been established to deal with an epidemic of this magnitude[201]. Rather, countries where PHEIC's have previously been declared had enough resources and a healthy enough economy that technological support and minimal funding from the WHO was sufficient in combating these infectious diseases[202]. The economies of Sierra Leone, Libera, and Guinea, though, were much weaker due to centuries of exploitation by the Global North, civil unrest, and recent wars in Sierra Leone and Libera[203]. These economies were therefore underprepared to deal with such an epidemic, resulting in a loss of over 2.2 billion dollars of GDP between the three countries despite these donations[204]. Such a blow to these economies further destabilized the already delicate political climate of the MRU countries and reversed the growing economy observed pre-outbreak.

While the poor health care infrastructure of the three MRU countries played a large role in the economic loss experienced by the 2014 epidemic, many public health officials feel that these losses, and the deaths of thousands, are largely due to the WHO's late and bordering inefficient intervention[205, 206, 207]. The WHO had stated in 2005 that all countries included on the IHR needed effective detection infrastructure for infectious diseases, yet Guinea's ability to

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[200] Ibid.

[201] "WHO | WHO's New Health Emergencies Programme." 2016. *WHO*.

[202] Put citation here

[203] *Understanding West Africa's Ebola Epidemic,* edited by Ibrahim Abdullah and Ismail Rashid, 296. London: Zed Books Ltd., 2017.

[204] CDC. 2014. "Cost of the Ebola Epidemic".

[205] Moon et al., 2015.

[206] Piot et al., 2017.

[207] Coltart, Cordelia E M, Benjamin Lindsey, Isaac Ghinai, Anne M Johnson, and David L Heymann. 2017. "The Ebola Outbreak, 2013-2016: Old Lessons for New Epidemics." *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences* 372 (1721).

detect viral outbreaks in 2014 remained too weak to provide an early response to the disease[208]. The lack of complying to the mandated detection service in Guinea represents the failure of the WHO to properly support its member nations. While a number of WHO nation-states are rich enough to constantly reimagine their disease detection systems and improve upon those of other countries, less affluent members are expected to meet the standards of these richer countries without proper resources[209]. One of the WHO's largest function is to provide technical support to address public health issues and mobilize funds from other nation states to respond to emergencies[210]. By failing to provide the needed expertise and funding to Guinea prior to the 2014 epidemic, the WHO inadvertently allowed for EVD to spread throughout the country for over three months before detection.

Even once the spread of a then unknown disease was reported by Guinea's Ministry of Health and MSF workers stationed in the area due to malaria outbreaks, the WHO was slow to respond. By the time that *ebolavirus* was identified as the disease-causing pathogen in late March of 2014, the virus had already registered sporadic cases to the capital cities of all three MRU countries[211]. Despite EVD reaching multiple capital cities, something unseen in other outbreaks of the virus, the WHO continued to describe the outbreak as "relatively small", much to the vocal disagreement of MSF officials in the region[212]. The WHO disregard to the growing Ebola outbreak persisted for another four months, even as the disease began to sustain transmission in Sierra Leone, Liberia, and Guinea and MSF continued to demand international

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208 Moon et al., 2015.
209 CDC. 2019. "Monitoring for Influenza Viruses." Pandemic Influenza (Flu).
210 WHO. 2011. "Origin and Development of Health Cooperation." *WHO*.
211 Moon et al., 2015.
212 Saliou, Samb. 2014. WHO says Guinea Ebola outbreak mall as MSF slams international response. *Reuters*.

aid[213,214]. It was not until July of 2014, when a number of international organizations including the World Bank, began heading the warnings from MSF and donating both funds and supplies to curb the disease spread[215]. With the larger international community beginning to engage with the outbreak, an International Health Relegations Emergency Committee was formed by the WHO in early August, and subsequently declared a PHEIC[216].

These steps towards helping the affected MRU countries, though, came a little a too late. By the time the international community began to provide adequate aid, thousands of individuals had already contracted *ebolavirus*, and the disease was beginning to spread to countries outside of the MRU region and the continent of Africa[217]. The WHO and the rest of the international community involved in the outbreak now had a larger task ahead of them to stop the spread of the disease compared to if intervention had occurred earlier. The failure to contain the outbreak for another eighteen months after the declaration of PHEIC, as well as the multiple false declarations of countries being *ebolavirus* free demonstrates the difficulties that the WHO and associated organizations faced in truly gaining control of the outbreak[218,219].

The international community's failure to listen to present MSF workers, as well as ignoring the novel aspects of the outbreak, demonstrates major weakness in the global response to infectious disease outbreaks. The WHO is supposed to provide aid and technical services to

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213 Moon et al., 2015.
214 Médecins Sans Frontières. 2014. "Ebola in West Africa: Epidemic Requires Massive Deployment of Resources | Médecins Sans Frontières (MSF) International." Press Release.
215 Moon et al., 2015.
216 WHO. 2014. "Statement on the 1st Meeting of the IHR Emergency Committee on the 2014 Ebola Outbreak in West Africa." *WHO Statement*.
217 *Understanding West Africa's Ebola Epidemic,* edited by Ibrahim Abdullah and Ismail Rashid, 296. London: Zed Books Ltd., 2017.
218 Kaner, 2016.
219 Brice, Makini. 2016. "WHO Declares Liberia Free of Active Ebola Virus Transmission - Reuters." Reuters. 2016.

countries struggling with public health problems, yet they failed to adequately address the weaknesses in the MRU regions health system both prior to and during the Ebola epidemic. The health care infrastructure of Sierra Leone, Guinea, and Libera had long demonstrated inefficiencies in responding to public health emergencies prior to 2014, yet the growing threat of a pathogen previously unknown to the region failed to garner aid from the WHO. While the global health community has called for a restructuring of the WHO in terms of epidemic response, it also should require the WHO to reanalyze its treatment of members states. While the WHO may currently provide equal aid to member countries, the organization should instead look for equity by being quicker to respond to even small disease outbreaks in nations with weak health care systems to avoid repeating the 2014 epidemic.

Chapter 4: The Threat of H5N1: Molecular Modifications as a Predictive Tool

The slow response and subsequent containment of the 2014 Ebola epidemic by the international community resulted in the unnecessary infection of hundreds, if not thousands, of people in Western Africa. While these failures have spurred a change in how international community responds to highly lethal and infectious diseases and a restructuring of the WHO, these policies fail to truly address how unprepared the world continues to be for an epidemic of a known disease. The inability to properly asses the dangers of a disease that has existed in human populations for over forty years reflects poorly on the international communities' ability predict the next large epidemic, let alone pandemic. The failures with predicting the West Africa Ebola epidemic also sparks concerns about a new infectious disease appearing in humans. While the majority of new zoonotic diseases rarely become more than an epidemic, rising global and urban populations means that these new outbreaks could become more severe than previously observed.

The appearance and spread of SARS in 2002 highlight the risk of new diseases appearing in more urban areas, allowing for easier spread throughout the globe. The first chain of SARS transmission occurred in Fosham City, China, a metropolitan area home to more than seven million people[220]. Within four months, the disease had spread to Hong Kong, and quickly accrued cases in 28 other countries across every continent but Antarctica[221]. In contrast, the first outbreak of Ebola appeared and stayed in the rural villages of the DRC's Bumba Zone[222]. The shift in new infectious diseases appearing not in these rural areas, but now highly urban ones, presents the threat of a pathogen with pandemic potential spreading around the world quicker than the international community can respond. The likelihood of this fear becoming a reality with our growing populations emphasizes the need to predict currently epizootic disease, which may turn pandemic in humans. H5N1 represents one such virus currently circulating through numerous bird populations in Southeast Asia with known capabilities to infect humans, but rarely sustains human to human transmission. Fears of a human transmissible airborne strain mutating, though, has prompted monitoring programs for H5N1 as an attempt to predict if and when the virus mutates to become a pandemic risk.

A: An Overview of H5N1

In 1996, a novel, highly pathogenic strain of influenza was isolated in a farmed goose from China. Less than a year later this strain, H5N1, made its first jump to humans, infecting 18

[220] Cherry, 2004.
[221] WHO. 2003. "Summary Table of SARS Cases by Country."
[222] Burke, 1976.

people and killing 6 of them in Hong Kong[223]. As the world entered the 21st century, though H5N1 went from just a rare species of influenza that occasionally infects humans, to a pandemic threat. Late in 2003, countries across Southeast Asia began reporting H5N1 outbreaks among poultry. During this time no human cases were associated with the disease due to the SARS outbreak which was also concurrently affecting the region. It was not until 2006 that a number of deaths associated with SARS between late 2003 and early 2004 in China and Viet Nam were correctly attributed to H5N1[224]. As 2004 progressed more and more countries in the region began reporting outbreaks of the virus in their poultry, spurring people in close contact with the sick birds to get tested for H5N1. Many of those exposed to the sick birds fell ill across Asia, with over 60% of the sick eventually succumbing to the disease[225]. The high mortality rate of H5N1 made the later discoveries of apparent transmission between family members of the virus more concerning, suggesting that the virus mutated to allow for easier human-to-human transmission.

From 2004 until 2006, 263 confirmed cases of H5N1 were confirmed in fifteen countries spanning North America, Africa, and Asia, with a mortality rate of 60%[226]. Luckily, despite earlier fears of human to human transmission of the disease, the interactions needed for the virus to spread were only observed in immediate blood relatives, suggesting extremely close and prolonged proximity to the infected for transmission[227]. The drop in new cases in 2007 further

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[223] Walters, Mark Jerome. 2014. "Birds, Pigs, and People: The Rise of Pandemic Flus." In *Seven Modern Plagues*, 151–73. Washington, DC: Island Press/Center for Resource Economics.

[224] WHO. 2018. "Cumulative Number of Confirmed Human Cases for Avian Influenza A(H5N1) Reported to WHO, 2003-2017."

[225] "Clinical Aspects of Pandemic 2009 Influenza A (H1N1) Virus Infection." 2010. *New England Journal of Medicine* 362 (18): 1708–19.

[226] WHO. 2018. "Cumulative Number of Confirmed Human Cases for Avian Influenza A(H5N1) Reported to WHO, 2003-2017."

[227] "Clinical Aspects of Pandemic 2009 Influenza A (H1N1) Virus Infection." 2010. *New England Journal of Medicine* 362 (18): 1708–19.

proved this fact, with the virus slowly retreating back into birds. Despite the case decrease, though, many leading health organizations continue to monitor this epizootic disease in birds across the globe in an attempt to stop the spread of a more transmissible strain of lethal H5N1[228]. This monitoring system encompasses two approaches: identifying flocks with H5N1 and cataloguing the new mutations noted in the virus. Identifying birds that carry H5N1 gives time for groups such as the WHO to cull the birds, as well as provide prophylaxis to those exposed, in an attempt to minimize H5N1 transmission from birds to humans. Culling infected birds also limits their ability to spread the disease to other mammals that can contract avian influenza viruses, such as pigs, limiting the virus's ability to recombine with other strains of influenza that could cause H5N1 to become develop human transmissibility. Meanwhile, keeping track of viral mutations provides national and international health organizations the ability to quickly produce a vaccine if one of these strains does jump to humans and easily diffuses through the population.

B: The Reality of Using Molecular Modifications to Predict the Next Pandemic

Critics of the virus monitoring program in birds have pointed out that we lack the ability to discern if a mutation in H5N1 makes the disease more transmissible until it is actually spreading through human populations[229]. Therefore, while these monitoring techniques may help speed up the vaccine creation process if the need arises, creating a vaccine could still take upwards of a year in development. By that point in the outbreak, millions of individuals would likely have contracted H5N1, and an untold number of them will have died[230]. Furthermore,

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[228] Fineberg, Harvey V. 2014. "Pandemic Preparedness and Response — Lessons from the H1N1 Influenza of 2009." *New England Journal of Medicine* 370 (14): 1335–42.

[229] Denise Grady, and Donald G. McNeil Jr. 2011. "Debate Persists on Deadly Flu Made Airborne." New York Times. 2011.

[230] Gates, 2018

while public health officials lean on the idea that highly transmissible H5N1, if formed, would be effectively contained to birds through the culling and administrating of prophylaxis process, in 2016-2017 we still saw 13 cases resulting in four deaths[231]. Though this number is small, it still demonstrates that, as an international community, we currently do not possess the tools to stop all bird to human H5N1 transmission. These holes in the WHO and other national and international health agencies plans on H5N1 containment are therefore viewed by some as inadequate for stopping a potential pandemic.

In 2012, a group of researchers based in the Netherlands and the United States provided what some public health officials view as much needed information and others a liability: the mutations needed to make H5N1 mammalian transmissible via airborne routes. Published in the June, 2012 issue of *Science*, a group of researchers at the Erasmus Medical Center in the Netherlands created a stain of H5N1 that can pass in the air between ferrets, using only wild H5N1[232]. Led by Ron Fouchier, this group took naturally occurring H5N1 from a 2005 outbreak of the disease in humans in Indonesia, and induced mutation through the serial passage of the virus in ferrets. The result was five mutations that Fouchier's lab deems as "required" for H5N1 to become transmissible in the air between ferrets. Ferrets have longed been utilized as model organisms for understanding influenza transmissibility in humans, and many results observed in these animals can often be applied to humans. Therefore wild types H5N1's ability to mutate without recombination with other influenza viruses to become airborne in ferrets suggests that a possibly pandemic strain of this viruses could form just over time in humans.

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[231] WHO. 2018. "Cumulative Number of Confirmed Human Cases for Avian Influenza A(H5N1) Reported to WHO, 2003-2017."

[232] Sander Herfst, Eefje J. A. Schrauwen, Martin Linster, Salin Chutinimitkul, Emmie de Wit, Vincent J Munster, Erin M Sorrell, et al. 2012. "Airborne Transmission of Influenza A/H5N1 Virus Between Ferrets HHS Public Access." *Science* 336 (6088): 1534–41.

Fouchier's results have provided the world the exact mutations H5N1 may need to become transmissible through the air to humans, a major concern of the global health community. Fouchier's experiments, though, also demonstrated that by acquiring these mutations for air transmission H5N1 becomes less pathogenic[233]. Therefore, these results provide not only a possible approach to monitoring H5N1, but also the knowledge that even if such a strain were to appear, the mortality rate would be lower than in previous H5N1 outbreaks. Furthermore, a study published in the same issue of *Science* looked into the probability of this pandemic strain of H5N1 mutating in humans. The paper found it highly improbable for a strain of H5N1 with none of these mutations to gain the modifications necessary to become airborne and infect humans[234]. Despite the low probability of these mutations occurring, two of the needed five mutations are already common in currently circulating forms of H5N1 in birds and another mutation sporadically appears[235]. The remaining two mutations have yet to appear in the virus's RNA, although both were present in the H2 and H3 strains of avian flu that caused the 1957 Avian Flu and 1968 Hong Kong Flu pandemics.

C: The Ethics of Using Molecular Modification to Predict the Next Pandemic

The creation of such an easily transmissible strain of H5N1, although helpful for anticipating future possibly pandemic diseases, became a hotly contested topic both in the scientific and public health communities. In 2010, Fouchier and his group first reported that they

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[233] Ibid.

[234] Russell, Colin A., Judith M. Fonville, André E. X. Brown, David F. Burke, David L. Smith, Sarah L. James, Sander Herfst, et al. 2012. "The Potential for Respiratory Droplet–Transmissible A/H5N1 Influenza Virus to Evolve in a Mammalian Host." *Science* 336 (6088): 1541–47

[235] Ibid.

had created an airborne form of the highly pathogenic avian flu, and quickly gained the attention of many public health organizations around the globe. Despite this ground-breaking discovery many high-ranking officials, ranging from leaders of various nations and the WHO, urged the group to not publish their findings, claiming that this research should never have occurred[236]. Critics of Fouchier's work believed not only that terrorists could utilize this mutated form of H5N1 as weapon, but also that the pathogen could escape the lab. Publishing the results and methods of creating such a strain would only strengthen these fears of H5N1 being used as a bioweapon or more research groups utilizing the mutant, since the paper could act as a template to recreate the virus.

Despite these mounting fears, though, Fouchier and his group published their findings in a 2012 *Science* article. Although initially requiring censorship for publication, three months prior to releasing the paper, a WHO panel decided that Fouchier's work should remain uncensored, citing that the benefits from such a paper outweighed the risk[237]. The reversal on the committee's take on the paper emphasizes the risk that many felt H5N1 could become pandemic. Experts in the field have described H5N1 actively circulating within bird populations as similar to "living on an active fault line", highlighting the need to understand the virus rather than hope the needed mutations never occur[238]. Idealistically, knowing the specific mutations for H5N1 to become airborne will help improve the surveillance of the virus circulating in birds and activate an eradication effort of the disease if the more transmissible strain ever does appear. The efficiency of such a response, however, is debated. Although countries in Southeast Asia, where the H5N1

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[236] Grady, 2011.

[237] McNeil Jr., Donald G. n.d. "H5N1 Bird Flu Research That Stoked Fears Is Published - The New York Times." New York Times. 2012.

[238] Ibid.

strain is most prevalent in bird populations, have better health infrastructure than the countries affected by the Ebola epidemic, they are also more populous. China, where the disease was first discovered in birds, has a population over 140 times the size of Sierra Leone with 1.38 billion people. The effect of these possibly pandemic viruses appearing in dense areas means that even if the response to airborne H5N1 was fast and efficient, it still may be too slow to stop the disease from spreading to millions of people in China alone.

Furthermore, the approval of the WHO committee to publish their research on airborne H5N1 does not mean Fouchier's lab, and groups doing similar work on other diseases, should ignore the implications their research has on an ethical level. Even without publishing a paper, such work creates the risk of these dangerous pathogens escaping the laboratory setting. Although rather rare in occurrence, even in recent years researchers have accidently inoculated themselves with a number of viruses, included eradicated *vaccinavirus*[239]. While these accidental injections of pathogenic viruses do not guarantee exposure to civilians in the area, it does increase their likelihood. This situation may be problematic if these individuals are unaware, and therefore not consenting, of their proximity to these viruses.

The publishing of Fouchier's paper also raises ethical concerns since the piece details how to create the airborne variant of H5N1, a possible biological weapon. Although groups wishing to create such a weapon could do so without government funded research, publishing papers that detail the method of creating said strain provides a blueprint to these groups quicker than through unguided research. Even if the global community has yet to observe the creation of

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[239] Moussatché, Nissin, Mari Tuyama, Sayuri E M Kato, Ana Paula V Castro, Brian Njaine, Regina H Peralta, José M Peralta, Clarissa R A Damaso, Paulo F Barroso, and Paulo F. Barroso. 2003. "Accidental Infection of Laboratory Worker with Vaccinia Virus." *Emerging Infectious Diseases* 9 (6): 724–26.

weaponized H5N1, this does not minimize the possibility that such a strain exists[240]. The probability of releasing a weaponized strain remains low, though, due to difficulties in controlling influenza infections[241]. Despite these difficulties, people are not always rational and betting on those creating biological weapons to realize the fallacies of using H5N1 remains a global security risk. The publishing of such a paper therefore places many civilians at threat for exposure of the pathogen as an act of biological terrorism, as well as creating a pandemic of airborne H5N1 through an unnatural manner.

Despite these threats to global security and the ethics behind conducting such research, understanding the mutations that could affect the spread of H5N1 remains a powerful tool in pandemic preparedness. Currently it takes five to six months to develop an influenza vaccine after identifying a possibly pandemic strain[242]. While in the timeline of outbreaks like the 2014 Ebola epidemic that lasted two and a half years, the first six months may not seem imperative, researchers at the Institute of Disease Modeling have predicted that a particularly pathogenic strain of influenza could kill 30 million people during that time[243,244]. Having information surrounding possible mutations of H5N1, and other worrisome avian strains of influenza that may lead to a pandemic variant, could allow for the production of vaccines prior to the disease spilling over into humans, potentially saving millions.

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[240] Groseth, 2005.
[241] McNeil, 2012.
[242] WHO. 2015. "Pandemic Influenza Vaccine Manufacturing Process and Timeline." *Emergencies Preparedness, Response*.
[243] Gates, 2018.
[244] Karner, 2016.

Chapter 5: Preparing for the Next Pandemic

As the world continues to wait for the next pandemic, we appear no closer to predicting the exact virus that will cause the outbreak. While many believe that the deadly virus will likely be caused by a novel strain of influenza, other infectious diseases, such as Ebola, continue to threaten global security. Furthermore, while technology has improved to let the global community better identify mutations that cause more pathogenic influenza strains, many are still wary of the ethical implications. All of these factors suggest that when the world is faced with its next large pandemic, we will not know what it looks like until possible millions are already infected. In order to minimize the spread and death associated with a pandemic virus therefore requires a system that not only recognizes a threat once it emerges in a human population, but also ensures that it will not spread to other regions around the globe. The best line of defense against a pandemic infectious disease therefore remains improving preventive measures against a variety of infectious diseases.

If the 2014 West Africa Ebola epidemic taught us anything, an efficient disease surveillance system in every country remains a great tool in catching possible pandemics while the disease is smoldering in the human population. To install such an interconnected system will require the cooperation nations around the globe, as well as organizations such as the WHO and MSF to mobilize the funds and resources needed. Some areas, such as the United States and Western Europe, already have highly sophisticated health care and public health systems that rely on just improving their technologies and general maintenance for effective disease detection and response. For others, such as Liberia, Guinea, and Sierra Leone, the health care and public health sectors of the countries are under developed due to years of systematic exploitation and histories of conflict, and therefore require more foreign aid to establish. Lastly, there are countries such as China and India, that have developed health care and public health services, but are hotspots for emerging infectious diseases due to climate and high populations[245]. These countries therefore require more support than equally as developed, but less at-risk nations, to ensure effective detection and containment of emerging infectious diseases.

To better prepare for the next pandemic the global health community must combine aspects of global cooperation and technological innovation learned from past disease threats, epidemics, and pandemics. Past influenza pandemics have demonstrated the power that new technological assets, such as vaccinations and antibiotics, have in minimizing both mortality rates and the spread of these diseases. By coupling these advances in medical treatments with early response systems in particularly susceptible countries for emerging viral pathogens, the global health community can ensure rapid containment of infectious disease outbreaks.

Furthermore, the WHO, as the sole government funded international health agency, must play a large role in directing improvements to infectious disease preparedness, as well as allocating resources to countries that are at the greatest risk for outbreaks. The recent slowness in the WHO and the rest of the international community's response to the 2014 Ebola epidemic has demonstrated the systemic inefficiencies this organizations had in actually mobilizing resources to help combat infectious diseases. Changes to the global disease control and prevention procedures must be undertaken to curb these past failures and minimize the risks of a pandemic killing millions of people around the world.

In order to better improve the global plan pandemic preparation, I propose a three-part approach that builds off the global public health community's inability to predict what the next

[245] Jones, Kate E., Nikkita G. Patel, Marc A. Levy, Adam Storeygard, Deborah Balk, John L. Gittleman, and Peter Daszak. 2008. "Global Trends in Emerging Infectious Diseases." *Nature* 451 (7181): 990–93.

pandemic pathogen will look like and where it will emerge, as well as inefficiencies in the global disease response to the 2014 Ebola epidemic. The first part of preparation will come from ensuring that every country has a functional and robust early disease detection system for humans, birds, and other mammals. Utilizing these early detection systems, the second part of this plan will analyze the genetic composition of novel pathogens to identify any similarities between past viruses that caused disease outbreaks. Finally, early vaccine development will begin for viruses that appear capable of and have the genetic markers of a virus causing a human disease outbreak. Together, these three steps of a novel emerging virus response will help limit the spread and severity of both epidemic and pandemic disease outbreaks.

A: The Importance of an Early Detection Systems

The majority of pandemic diseases originate in animals before a spillover event allows the virus to jump from their original host into humans[246]. A number of these eventual pandemic pathogens therefore circulate in non-human species for an unspecified amount of time before they are identified in humans, providing a possible window for public health officials to identify these pathogens prior to human infection. In order to achieve early identification of these diseases, though, every country must have a virus detection system in place not only in humans, but also in other possible hosts. Already, the international community has emphasized the need for such a robust detection system with the 2005 International Health Regulations[247]. With the signing of the IHR, each of the 196 nations present agreed to instate a disease surveillance

[246] Morse, Stephen S, Jonna A K Mazet, Mark Woolhouse, Colin R Parrish, Dennis Carroll, William B Karesh, Carlos Zambrana-Torrelio, W Ian Lipkin, and Peter Daszak. 2012. “Prediction and Prevention of the next Pandemic Zoonosis.” *Lancet (London, England)* 380 (9857): 1956–65.

[247] WHO. 2016. “Health Regulations Third Edition (2005).”

system within the next five years[248]. In 2014, though, the Ebola epidemic demonstrated that a number of countries had failed to fulfill the IHR, exemplified by Guinea's inability to catch the presence of *ebolavirus* for over three months. In order to gain an advantage against possibly pandemic diseases, the global health community must work together for the rigorous implementation of high functioning disease surveillance systems in every country.

Currently, many wealthy countries already have highly sophisticated disease surveillance systems with multiple automated centers allowing for larger data sets and quicker response times when looking for infectious diseases[249]. Every year many of these surveillance systems are improved upon in order to better monitor these outbreaks, with the 2014 Ebola epidemic inspiring changes to simplify notifiable disease reports [250]. In contrast, the surveillance systems of less affluent countries either severely lack in identification abilities or do not exist at all[251]. While these discrepancies have widely been acknowledged in the wake of the 2014 epidemic and international groups, such as the CDC, have provided both funding and technical advice towards improving these countries surveillance and reporting systems, many systems still prove inadequate in identifying viral outbreaks[252]. A new way of implementing surveillance for disease outbreaks must be used to ensure that countries are actually receiving benefits from these technologies.

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[248] Ibid.

[249] Vlieg, Willemijn L, Ewout B Fanoy, Liselotte van Asten, Xiaobo Liu, Jun Yang, Eva Pilot, Paul Bijkerk, et al. 2017. "Comparing National Infectious Disease Surveillance Systems: China and the Netherlands." *BMC Public Health* 17 (1): 415.

[250] CDC. 2018. "Notable Milestones." Surveillance and Data.

[251] WHO. 2016. "Health Regulations Third Edition (2005)."

[252] Sambala, Evanson Z, Tiwonge Kanyenda, Chinwe Juliana Iwu, Chidozie Declan Iwu, Anelisa Jaca, and Charles S Wiysonge. 2018. "Pandemic Influenza Preparedness in the WHO African Region: Are We Ready Yet?" *BMC Infectious Diseases* 18 (1): 567.

To better implement surveillance and reporting systems for infectious diseases on a global level, international agencies must intervene and help set up these systems for nations lacking both the funding and knowledge to do so independently. While some organizations, such as the CDC, already provide such technical advice surrounding these systems, the failure to note any real changes in these countries surveillance abilities' highlights the need of a more hands-on approach. Although such a model for setting up the surveillance of another country may seem to unethically over step the role of international aid, other methods of providing partial funding and support has allowed for these systems to continue to fail. While the global community has remained complacent in not establishing a connected network of disease detection and reporting, it places people all over the world at risk of a disease spreading and reaching pandemic levels before the international community becomes aware of its existence. Direct intervention by the WHO or other nations with more sophisticated systems may therefore exist as the best option for getting struggling countries surveillance systems off the ground.

Attempting to implement such technologies in multiple nations will be both time consuming and cost the global health community more than they can afford if such work occurs all at once. In order to minimize the cost while still ensuring that the global community is receiving pertinent information on diseases, the implantation of these surveillance systems should occur in waves. The first countries that should receive these technologies are ones that exist in regions where new zoonotic diseases are most likely to emerge from. These countries, such as the MRU countries most affected by the Ebola epidemic, exist at lower latitudes and are tropical in climate[253]. Special attention should be paid to nations with higher populations in these

[253] Jones, Kate E., Nikkita G. Patel, Marc A. Levy, Adam Storeygard, Deborah Balk, John L. Gittleman, and Peter Daszak. 2008. "Global Trends in Emerging Infectious Diseases." *Nature* 451 (7181): 990–93.

areas, since a highly pathogenic strain could infect more individuals in these countries over a shorter amount of time. After addressing these hotspots for emerging diseases, surveillance systems should them be installed based on its affluence, with the most exploited and ignored countries getting preference for these surveillance systems over more affluent nations. Ideally, the countries that receive aid in setting up these technologies are ones that are completely lacking such infrastructure, meaning that they gain more knowledge from these technologies than the slightly more affluent nations with weak surveillance systems. By filling in the gaps of countries currently lacking functional surveillance systems, the global health community will be provided with information not only about what diseases are present in humans, but also in the surrounding animal populations.

B: Genetic Analysis in Identifying Potentially Pandemic Viruses

By installing these surveillance systems into every country, the WHO and other disease control and prevention centers will know currently circulating pathogens that pose a risk of becoming epidemic or pandemic. While this information can prove invaluable, expanding these surveillance systems past humans could help the global community get in front of an infectious disease outbreak before it even occurs in humans. While this can also be helpful in identifying if viruses already known to infect humans are likely to reemerge in people based on its circulation in other animals, it can also help identify the risk of completely novel animal pathogens. In order for such information to actually have meaning other than the diseases present in non-humans, these new viruses must be genetically compared to past pathogens that have spread to humans and caused outbreaks.

Such an approach to identify future zoonotic viruses would employ some of the same principles as Ron Fouchier's lab's research on H5N1. Although his research looked to identify the mutations required to make avian H5N1 air transmissible between ferrets by repeated transmission, Fouchier's work also began to identify a common mutation present in other airborne avian influenza strains. By running a genetic analysis of both the newly created H5N1 strain and the pandemic influenza strains of 1957 and 1968, Fouchier identified two mutations common in all three types of the virus[254]. These commonalties could indicate a mutation required for all avian flus to gain air transmissibility in humans, an aspect of new influenza viruses that often raises concerns of the strain becoming pandemic.

Other similarities between infectious diseases in both genetic make-up of pathogens that have caused disease outbreaks could be also be identified within viral families. These patterns could then be applied to newly discovered animal viruses of the same family to determine the likelihood of a spill over event occurring, as well as the severity of the human disease. Although the genetics of a virus is not the only determining factor of a spillover event[255], nor will every new pathogen discovered resemble past disease-causing viruses in humans, the accumulation of this information could prove valuable in preparing and even stopping potentially pandemic diseases.

C: Technological Advances on Medical Care: The Role of Vaccines in Pandemic Preparedness

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[254] Fouchier et al., 2012.

[255] Plowright, Raina K, Colin R Parrish, Hamish McCallum, Peter J Hudson, Albert I Ko, Andrea L Graham, and James O Lloyd-Smith. 2017. "Pathways to Zoonotic Spillover." *Nature Reviews. Microbiology* 15 (8): 502–10.

The most important part in preparing for a pandemic disease remains the response once an outbreak of a pathogen actually occurs. During the 1918 Influenza pandemic, millions of civilians died worldwide due to ineffective ways of treating the disease caused by the virus and secondary infections by bacterium. While many of ill received treatment from medical providers either in a hospital or a home setting, the majority of these methods proved ineffective[256]. Therefore, in order to stop people from dying due to infection, doctors and public health officials attempted to stop the spread of the disease using a number of non-pharmaceutical interventions, including isolation both of the sick and the healthy[257]. Forcing people to refrain from social interactions proved difficult to enforce, leading to the high death toll associated with the 1918 outbreak.

In the century since the deadliest pandemic in modern history, there have been numerous improvements in medical technologies that have aided in reducing the mortality rates of subsequent influenza pandemics. The discovery of anti-viral drugs has helped limit the viral load of an infected induvial, increasing their chances of survival, while antibiotics have been imperative for the prevention of secondary bacterial infections linked with the majority of deaths during flu outbreaks. Since the 1918 pandemic, a number of preventive measures have also been improved upon. The most influential continues to be the flu vaccine, which first became readily available in 1946. The influenza vaccine causes the body to produce antibodies against the viral strain present in the vaccine, providing protection against subsequent infection by virus[258].

While the influenza vaccine has provided at risk populations protection against developing the flu, such benefits only occur if the correct strain of the virus has been vaccinated

[256] CDC. 2018. “1918 Pandemic (H1N1 Virus).” Pandemic Influenza. 2018.
[257] Ibid.
[258] CDC. 2019. “Different Types of Flu Vaccines.” Influenza (Flu).

against. The decision of what strains are included in each version of the flu vaccine occurs twice a year by the WHO Collaborating Centers for Reference and Research on Influenza; once in February to determine the composition for the northern hemisphere and again in September to decide the same for the southern hemisphere[259]. The make-up of said vaccines are based off of the data collected by the 113 countries with influenza centers[260]. The previous season's vaccine is then modified according to the most prevalent strain of influenza circulating in the human populations before distribution. Over the past fifteen years, the effectiveness of these vaccines in the United States have varied between 10 to 60%[261]. Therefore, while receiving the influenza vaccine can decrease one's likelihood of developing the flu, it does not guarantee that every vaccinated individual will not get sick from the pathogen. The inability to correctly identify influenza strains present each flu season therefore continues to present shortcomings in utilizing this medical technique as a preventive measure against the virus.

The turnaround time needed to develop the seasonal flu vaccine following the strain identification is not indicative of the overall ability to produce efficient vaccines against other emerging infectious diseases, including pandemic strains of influenza. For completely novel diseases deemed to require a vaccine, development of these lifesaving medicines can take between ten to fifteen years to become publicly available[262]. For the *ebolavirus* Zaire subtype, research and development of the vaccine has occurred since 2000, and while the vaccine has

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[259] Stierwalt, Sabrina. 2015. "How Are Seasonal Flu Vaccines Made?" Scientific American.
[260] Ibid.
[261] Belongia, Edward A, Burney A Kieke, James G Donahue, Robert T Greenlee, Amanda Balish, Angie Foust, Stephen Lindstrom, David K Shay, and Marshfield Influenza Study Group. 2009. "Effectiveness of Inactivated Influenza Vaccines Varied Substantially with Antigenic Match from the 2004-2005 Season to the 2006-2007 Season." *The Journal of Infectious Diseases* 199 (2): 159–67.
[262] The College of Physicians of Philadelphia. 2018. "Vaccine Development, Testing, and Regulation." The History of Vaccines.

been employed in the 2018-2019 Democratic Republic of the Congo outbreak, it has yet to be formally approved for general use[263, 264]. Although creating a vaccine against possibly pandemic strains of influenza take less time following the identification of the variant than with other novel pathogens, the average vaccine development time of five to six months is enough time to accumulate 30 million deaths worldwide[265, 266]. Current development times of vaccines therefore makes it difficult to avoid the spread of possibly pandemic pathogen utilizing just this technology.

Aware of the limitations that vaccine development times presents researchers have begun turning their attention towards creating a universal influenza vaccine. While this vaccine does not negate the slow development time observed with emerging non-influenza viruses, it does provide immediate protection against possibly pandemic influenza variants[267, 268]. A universal influenza vaccine works by inducing the creation of antibodies that target the highly conserved head of the HA proteins in both human and avian strains of influenza A[269]. In April, 2019, the National Institute of Health (NIH) approved the first in-human trail of a universal influenza vaccine[270]. If the vaccine proves at least 75% effective against both types of influenza A viruses

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[263] Sullivan, Nancy J., Anthony Sanchez, Pierre E. Rollin, Zhi-yong Yang, and Gary J. Nabel. 2000. "Development of a Preventive Vaccine for Ebola Virus Infection in Primates." *Nature* 408 (6812): 605–9.

[264] Branswell, Helen. 2019. "WHO: Experimental Ebola Vaccine in the DRC Has Saved Countless Lives." Stat News.

[265] WHO. 2015. "Pandemic Influenza Vaccine Manufacturing Process and Timeline." *Emergencies Preparedness, Response*.

[266] Gates, 2018.

[267] NIH. 2018. "Universal Influenza Vaccine Research." Influenza Vaccines.

[268] NIH. 2019. "NIH Begins First-in-Human Trial of a Universal Influenza Vaccine Candidate." News Releases.

[269] NIH. 2018. "Universal Influenza Vaccine Research." Influenza Vaccines.

[270] NIH. 2019. "NIH Begins First-in-Human Trial of a Universal Influenza Vaccine Candidate." News Releases.

and provides protection for at least a year, it will likely progress to a stage-two clinical trial as early as 2020[271]. The implications of an efficient universal influenza vaccine would not only save millions of lives during the early stages of an otherwise pandemic influenza, but it also would provide protection against all seasonal variants, saving resources in predicting and designing potentially ineffective vaccines.

Creating a universal influenza vaccine is just one step towards protecting the world from witnessing another pandemic as severe as the 1918 Spanish influenza, not a full solution. As previously mentioned, the universal influenza vaccine is only effective in limiting the spread of influenza, not other emerging infectious diseases. The information gathered through the genetic analysis of monitored viruses in both humans and animals around the world will prove valuable both for identifying potential outbreaks of viruses in humans and for creating new vaccines against these emerging threats. As mentioned, the entire process of creating a new vaccine from discovering pathogen to the drug being approved for general use takes between ten and fifteen years. By identifying viruses in animals that may eventually spill over into humans, though, the innovation process for creating a vaccine against said viruses could begin long before the pathogen even appears in humans. Research into such vaccines should not occur with every novel virus found in animals in an effort to save funds. Rather, interest should only go into a small number of pathogens that show high likelihood for spill over based on their molecular make-up, as well as other epidemiological factors commonly observed in such events[272].

Furthermore, even if a universal influenza vaccine was highly efficient and durable, it could only stop the spread of pandemic influenza if a large enough portion of the global

[271] Ibid.
[272] Plowright et al., 2017.

community were vaccinated, as is the case with a number of other infectious disease vaccines. Acquiring high enough vaccination rates to fully protect a population against an infectious disease remains a difficult problem for the global health community with established vaccines, therefore a new vaccine may prove even more difficult during its formatives years in reaching at risk populations. The world saw *vacciniavirus* (smallpox) eradicated in 1980, yet no other virus has followed suite due to difficulties in distributing vaccines for diseases such as measles and polio[273]. Regions of the world that have been successful in eliminating the above diseases have also experienced setbacks in achieving high vaccination rates, causing a resurgence in these pathogens due to the spread of misinformation surrounding vaccines[274]. Therefore, while vaccines remain a powerful tool in helping prevent the spread of epidemic or pandemic diseases, the global community still struggles with the efficient administration. Improvements into vaccine education and changing laws requiring vaccinations against preventable diseases may help raise vaccination rates in countries where these pathogens were once eliminated. For administering the vaccines where disease persists due to poor living conditions, war, and/or systematic oppression, continued efforts by the WHO and other international organization may prove the best way to eradicate these pathogens. Regardless of these difficulties, though, the creation and use of new vaccines remains the best way to prevent the next pandemic.

[273] CDC. 2018. "U.S. Polio Elimination." Global Health.
[274] Hussain et al., 2018.

Conclusion

The world is not prepared for the next pandemic. The gap between rich and poor nation's health systems allows for pathogens to slip through the cracks, increasing the risk of an infectious disease emerging and spreading through the world before adequate protective actions can take place. Although public health officials can try to predict the next pandemic, diseases the Western world views as threats have distracted them from other possibly pandemic pathogens. Even with technological improvements in molecular modification and computer programs that can model which pathogens may become pandemic, none of these results are ever guaranteed. Therefore, we cannot accurately predict the next pandemic, and rather must rely on public health initiatives and sophisticated health care systems to minimize the damage a pandemic virus could do around the world.

Since the 1918, the global community has yet to observe another pathogen that infects or kills as many individuals as the Spanish influenza, largely due to the numerous improvements in both prevention and treatment of diseases caused by viruses and bacterium. These improvements, while lowering the risk of new and emerging infectious diseases from becoming pandemic, do not guarantee that a similarly severe pandemic will never occur. Rather, our technological advances, both against pathogens and the natural world around us, has allowed the global population to boom since the mid-1700's[275]. This exponential population growth puts more people in urban areas and closer to potential animal reservoirs and vectors for pathogens than ever before[276]. Furthermore, with the growing population, humans are producing more

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275 Bavel, J Van. 2013. "The World Population Explosion: Causes, Backgrounds and -Projections for the Future." *Facts, Views & Vision in ObGyn* 5 (4): 281–91.

276 Senthilingam, Meera. 2017. "Seven Reasons We're at More Risk than Ever of a Global Pandemic." Edited by David Joseph Diemert. *CNN*.

greenhouses gases than ever, contributing to the increase in global temperatures and the range of pathogens previously identified as tropical[277].

Together, these conditions allow for the perfect storm of a pandemic outbreak. Humans are contracting more viruses from animals than ever before, and spreading them with more ease to one and other. While we cannot predict the exact viruses that emerge from these animals and that develop into epidemics or pandemics, the global health community can improve public health policies to better prepare for these outbreaks. Past epidemics and pandemics have illustrated just how far our technology has come in preventing widespread deaths by viruses with vaccines, antivirals, and antibiotics against secondary infections. They also have identified holes in our current approaches to diseases outbreaks. Learning from these failures remains our best chance in preventing public health emergencies like the 1918 Spanish influenza pandemic or even the 2014 Ebola epidemic. In order to prevent repeating out history, though, we must continue improving upon on technologies in regards to public health. Early detection systems of viruses spreading both in humans and animals gives the public health community an idea where the next outbreak may occur, helping mobilize resources before they're even needed. Gathering these data too can aid in finding patterns in which pathogens cause these outbreaks, possibly helping create vaccines against these viruses before they even emerge in humans. Even with these recommendations, work is needed to better prepare for the next pandemic. By implementing these ideas, though, the risk for a pandemic is a little less.

[277] Ibid.

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