

Viral Pandemics Throughout History and What We Have Learnt from Them

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ABSTRACT

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In the course of global history, infectious disease outbreaks have occurred intermittently, causing long-lasting effects on human societies which then subsequently went on to change the very course of history. These outbreaks, whether they be globalized or ubiquitous have lent us the power to alter socioeconomic, political, religious, and cultural aspects of human civilization. Pandemics have shaped modern medicine through the creation of systematic frameworks for epidemiological study, and prevention of disease through pharmaceutical (drugs, mass vaccination) and non-pharmaceutical interventions (quarantine, handwashing and hygiene techniques). Thus, we are constantly striving to overcome the threat of emerging as well as reemerging infectious disease outbreaks. In the last 40 years, we have faced most notably, the Spanish Flu (from 1918 to 1919), HIV-AIDS (from 1981 to present), SARS-CoV (from 2002 to 2003), Swine Flu (from 2009 to 2010) and most recently, COVID-19 (from 2019 to present). Most viral pandemics were caused by zoonoses transmitted through practices of breeding, hunting and global trading leading to increased human-animal contact. By understanding the pathophysiology and pathways of transmission of pathogens to humans, we can discover newer and better methods to controlling and even preventing infections. 40 years back when the plague struck, public health preparedness and interventional measures such as quarantining, isolation, and strict border control were critical in containing the spread of outbreaks and maintaining the structural infrastructure of human society. These non-pharmaceutical containment methods are still found to be effective in controlling the COVID-19 pandemic to this day. Newer technologies for quick diagnosis with disease severity markers and contact tracing as well as mass production and distribution of vaccines are required for effective response. Medical historians opine that studying earlier pandemics and our response to them may help further our insight into infectious diseases in the 21st century. Amongst the advancements made in the healthcare sector, public health response seems to be mostly unchanged.

Keywords: Viral Pandemics, COVID-19, Spanish Flu, SARS, HIV-AIDS, H1N1, Public Health Strategies, Pharmaceutical Interventions, Non-Pharmaceutical Interventions

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INTRODUCTION

The worldwide spread of an infectious outbreak is defined as a pandemic.¹ Historians have recorded multiple outbreaks and pandemics throughout history however the authenticity of these records is disputable. The deadliest ever recorded outbreak previously was the Spanish Flu which occurred in 1918. This was followed by subsequent novel strains of the influenza virus, even those spread from animal reservoirs such as pigs and poultry. In 1981, a particular cross-species transmission event involving a simian immunodeficiency virus (naturally infecting African primates) may have contributed to the evolution and mutation into the

human immunodeficiency virus; the principal cause of the HIV-AIDS pandemic. In late December 2019, a new coronavirus strain was reported in China similar to the 2003 SARS virus. The virus spread rapidly worldwide via mainly droplet transmission and was named the SARS-CoV-2 or the novel Coronavirus. At present, research is still underway regarding the impact of COVID-19 presently and for upcoming generations on the healthcare system including physical and mental health, economy and society as a whole. Various non-pharmaceutical interventions have existed since recorded history to prevent the spread of disease and these are presently being enforced in the view of the current situation, such as staying home, avoiding

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crowds, frequent handwashing and carrying and using of hand sanitizers, avoiding handshakes and any form of hand-to-hand contact, wearing masks, especially in crowded, closed and poorly ventilated settings, keeping a distance of at least 1 meter from others in public locations and preferably avoid touching each other, coughing or sneezing into a bent elbow, and ensuring good ventilation in crowded areas² (**Figure 1**). Handwashing has seen to be a first line of defense in preventing spread of infectious droplets during previous and present viral respiratory pandemics. It is a method of primary prevention which is easy to practice. Proper handwashing technique consists of washing with soap and water for a minimum duration of 20 seconds or using any alcohol based hand sanitizer in the absence of proper handwashing facilities.³ In most countries, handshakes, fist bumps, high fives and hugs are commonly used to greet one another, encouraging physical proximity, which in turn facilitates the rapid propagation of infections. Asian countries, since ancient times have used non-physical greetings such as 'Namaste', a form of greeting in the Indian subcontinent consisting of folding hands together while maintaining fair distance from one another or the practice of bowing in Japan and Korea have proved to be effective in preventing spread of disease while still enabling a greeting between two people.⁴ In 17th century Europe, there have been records of 'plague doctors' wearing beak-like masks filled with herbs like clove or cinnamon and dressed in black cloaks and hats. They symbolized the deathly Middle Age bubonic plague. The masks protected from the spoiled air or 'miasma', which was considered the cause of the bubonic plague epidemic then. This was one of the earliest documented accounts of mouth-nose protection during an infectious disease outbreak.⁵ In the 19th century, as germ theory spread, and scientists discovered germs on dust particles, mouth and nose coverage (veils, scarves, face masks) started to be popularized. In this ongoing pandemic, face masks (surgical, N95 or even cloth-based) or even simply covering one's nose and mouth while in proximity of other persons was recommended by public health officials worldwide to great success. It was seen that the act of covering one's nose and mouth was as effective if not more in preventing spread of infected droplets as compared to wearing full personal protective equipment (disposable masks, gowns, face shields, gloves, shoes). Another crucial measure to slow spread of respiratory viral infections has been social distancing. It enabled society in carrying out day-to-day activities while preventing spread of infection. Edward Hall first coined the term 'proxemics' in 1963. It defined social distancing in

everyday life.⁶ Hall hypothesized that close distance between two individuals increased visual, auditory, tactile and olfactory stimulation and feelings of invasion of privacy space to the point where they may react negatively. Later, social distancing was used as successfully to restrict spread of infections. Without the threat of a viral outbreak, long-term social isolation has been proven to cause 29% increase in mortality risk in chronic conditions like depression, dementia and heart disease.⁷ For families, close confinement can precipitate interpersonal tensions in the absence of coping mechanisms provided by attending mass events like sporting, artistic events or religious ceremonies. Job losses and subsequent financial problems along with the long absence from school are also a part of the trend in rising mental illnesses. All in all, people are resistant to social distancing especially if done for only a short duration, although individuals who already have problems with anxiety, substance abuse, depression etc are most vulnerable. Understanding the goal and benefits of prolonged isolation in such situations and taking pride in following the advice of professionals thus, helping out in the well-being of society may help. Quarantine (taken from the Italian word "quaranta" meaning 40) was always a means of isolation of people, animals and any substances that were exposed to an infectious agent. It has been used effectively as a disease control strategy with the isolation, fumigation, disinfection and regulation of groups of persons who were thought to spread the infection since the 14th century.^{8,9} Since the era of the Black Plague to the pandemics of the 21st century, quarantining has been an essential way to decrease contact between sick persons and vulnerable groups, especially in the absence of proper treatment or cure. Quarantining is and always will be a way to contain emerging and reemerging infectious disease outbreaks and curb public anxiety by controlling infection rates and averting death, and thus maintaining the infrastructure of society. But ironically these strategies have always been and will be debated, perceived as a threat to one's privacy and accompanied in every age and under all political regimes by an undercurrent of suspicion, distrust, and riots, raising a variety of political, social, economic, and ethical questions. It requires a fine balance between public interest and individual rights.^{10,11} The use of quarantine, border controls, contact tracing, and surveillance proved effective in containing the global threat in just over 3 months during the 2003 SARS pandemic. For example, the misuse of isolation to separate infected or those suspected of being infected has most often been carried out among lower classes and marginalized

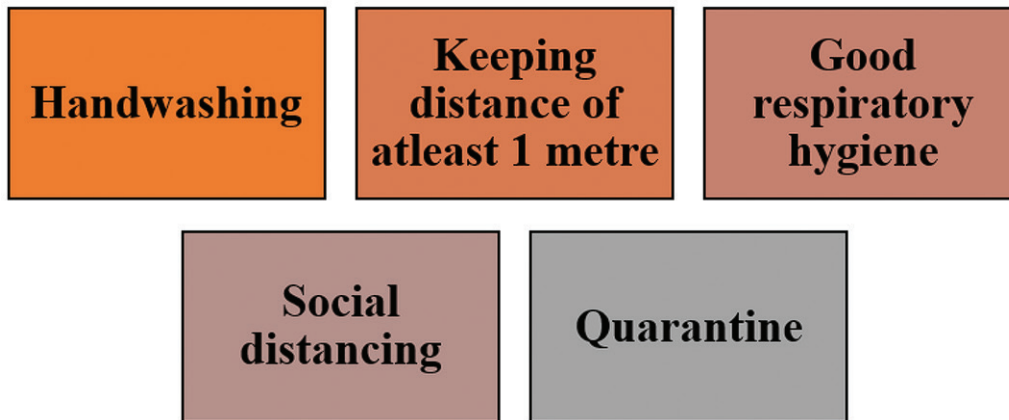


Figure 1. Non pharmaceutical interventions for pandemic preparedness

minority groups, causing them to face stigma and discrimination. During the plague outbreak, this fear of discrimination sometimes led minority groups to escape from affected areas and in the process of travel, contribute to spreading the disease farther and faster. But in today’s globalized world, public panic, augmented by highly inter-connected global media outlets (most notably social media), has the potential to spread further and faster. A historical perspective helps clarify the use and implications of a still-valid public health preparedness strategy such as isolation and quarantine as well as allow us to understand the extent to which panic, connected with social stigma and prejudice, frustrated public health efforts to control the spread of disease.¹² Public trust needs to be gained through regular, transparent, and comprehensive communications in order to avoid intolerance which can happen in prolonged periods of quarantine. The term “cough etiquette” was first described by WHO. It consists of the following components: covering one’s nose and mouth during the act of sneezing and coughing, turning one’s head away while sneezing and coughing, sneezing and coughing into one’s elbow or sleeve, using disposable (paper) tissues, wearing masks to decrease contamination of one’s surroundings.¹³⁻¹⁵

Immunization dates back to hundreds of years and has been a successful pharmaceutical public health prepar-

edness strategy today to reduce infection transmission during outbreaks. In 1796, Edward Jenner successfully managed to inoculate cowpox (vaccinia virus) into a 13 year old boy and demonstrated immunity to smallpox. In 1798, the smallpox vaccine was developed. Systematic implementation of mass smallpox immunization resulted in eradication of smallpox worldwide by 1979; a landmark event in history.¹⁶ The first mass vaccination for COVID-19 started in early December 2020. Preparedness in advance is crucial in reducing impact of the pandemic and ensuring an effective response. Planning for a pandemic requires a multi-disciplinary and global response ranging from public health officials, health care professionals, researchers and scientists. The suspicion of an outbreak generates an immediate need for international, national, state and local governments, public health and health care professionals, corporations, and communities to develop pandemic preparedness plans and strengthen their capabilities to respond to different scenarios of infectious disease outbreaks. Presently we face a prolonged global health crisis, which despite our advanced efforts and continued public health measures is yet to see a decline in case rates worldwide. In this review, we observe the various actions taken to manage viral pandemics in the past in comparison to the current action plans for SARS-CoV-2, which may potentiate interventions for its treatment and prevention.

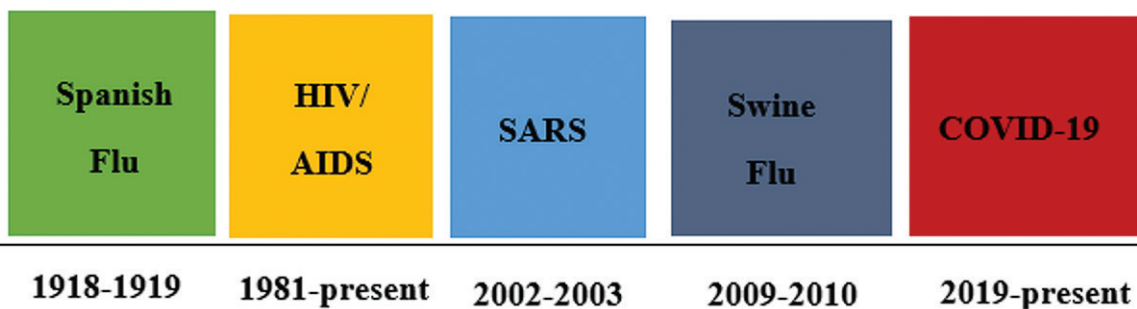


Figure 2. Timeline of viral pandemics throughout history

1. Origin of Viral Pandemics:

For an infectious agent to cause a pandemic, it has to be able to sustain person-to-person spread, cause an infection with high mortality rates and there should be the absence of a readily available treatment or vaccine.¹⁷ Infectious disease agents have been present since the time of dinosaurs and early humans. Some of these infectious agents remain identical even to this day while most have mutated and adapted. Nearly all infectious agents are found to be zoonoses, that is, transmitted from animal to humans. This includes herd and agricultural animals (swine influenza), wild and domestic fowl (avian influenza), and bats (SARS, MERS).¹⁸ Disease outbreaks however were not present in human history till people started living together in large numbers and civilizations under conditions of close contact. This occurred 10,000 years back. It is proposed that the radical change from hunter-gatherers to agrarian close-settled societies may have led to the easy spread of infections.¹⁹ The expansion of trading routes may have led to frequent interaction between humans and animals, thus facilitating the transmission of zoonoses.²⁰ Cross-species transmission was also increased through the practice of hunting, animal farming, meat trade and the exotic pet trade.²¹ Climate change is also thought to play a role in the transmission of pathogens from wildlife to human beings.²² Surveillance programs that are able to detect viral pathogens with greatest potential for zoonotic transmission at the animal-human interface are therefore necessary. The advent of modern forms of transportation has facilitated the spread of diseases globally, especially those that otherwise would not survive long due to their short incubation and communicable period as well as having only human reservoirs.²³

2. Pandemics Throughout History (Figure 2):

2.1 Spanish Flu

In 1918, an influenza pandemic was reported and named the Spanish Flu; a misnomer due to the first reports of outbreaks coming from Spain which was the only western country not under censorship and therefore able to report them. The estimated mortality rate was around 2.5 percent globally.²⁴

2.2. HIV/AIDS

On June 5th, 1981, CDC published case reports of a rare type of pneumonia caused by *Pneumocystis carinii* in five healthy young homosexual males from Los

Angeles. This was later found to be due to an immunodeficiency caused by a virus, named HIV/AIDS.²⁵ 37.7 million people are so far estimated to be HIV-positive with 680,000 deaths from HIV-related causes by the end of 2020. HIV is still a major public health issue globally, having affected 36.3 million people so far. Till this date, there is no proper cure for HIV, however, with easy access to diagnosis, treatment and prevention (especially of opportunistic infections which are also a major cause of HIV-related mortality), it has become a manageable chronic health condition, enabling HIV-positive individuals to lead long lives.²⁶

2.3. SARS

Severe Acute Respiratory Syndrome or SARS is a viral disease affecting the respiratory tract caused by a coronavirus called the SARS-CoV. This disease was first identified in late February 2003 in China. It spread rapidly along routes of air travel and caused severe symptoms.²⁷

2.4. Swine Flu

Sometime in the early months of 2009, a strain of influenza previously unidentified in humans began to spread. The virus (named as H1N1) was first detected in the United States and quickly crossed to other countries. A death rate of 575,400 was estimated worldwide. The flu primarily targeted children and middle-aged (since older adults seemed to have immunity, most likely obtained from prior infection with an identical H1N1 virus). Although the H1N1 Swine flu pandemic ended officially on August 10, 2010, the H1N1pdm09 strain is still around as a seasonal flu, causing sickness and death every year worldwide.²⁸

2.5. COVID-19

The origin of the current global pandemic was reported in early December 2019, when some patients presented with a severe form of atypical viral pneumonia. Most of the early cases reported prior exposure to the local Wuhan market where trade of live animals such as bats flourished. Surveillance systems (put in place after the SARS pandemic) were activated. Nasopharyngeal and oropharyngeal swab samples of these patients were sent to laboratories. It was identified to be due to a coronavirus, named SARS-CoV2 or COVID-19.²⁹ On March 11th, 2020, WHO finally declared COVID-19 to be of pandemic threat. Till now, WHO has reported close to 232,636,622 confirmed cases worldwide with 4,762,089 deaths.³⁰

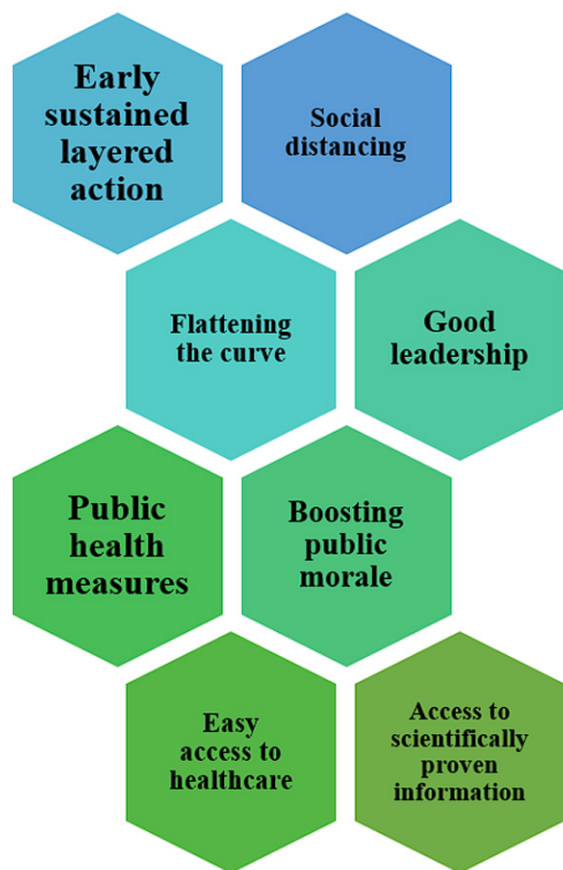


Figure 3. Lessons learnt from past pandemics

3. Lessons Learnt from Past Pandemics: Can history help us understand the present and future?

Before the discovery of viruses in 1940, people were unaware of the etiologic factor in the influenza pandemic. Various theories were put forward such as misalignment of the planets, volcanic eruptions, Russian oats, or even a bacteria discovered early in the lungs of influenza patients (*Bacillus influenza*) which was later found to invade lungs already weakened from influenza.³¹ Studies on the 1918 pandemic showed that as cases began to subside and cities eased restrictions on social distancing, death rates peaked again. Among 43 cities studied in the US, the study notes that no cities were experiencing a second peak of influenza while non-pharmaceutical interventions for the first peak were still implemented.³² While prolonged periods of social distancing can put a strain, especially on those families that require leaving their homes for their (at times) sole source of income, and the economy overall. In 1918, people were very much aware of the risks of not following social distancing. In 1918, during the Spanish flu outbreak, restaurants, schools and businesses had to be closed, public gatherings banned,

and people were told to self-quarantine by staying at home and avoid going out. These efforts contributed to preventing the spread of infection and reducing the overall mortality back then.³³ It is also important to not give up too early. It was seen that giving up on prevention measures led to a consistent rise in flu cases and deaths. Restricting the public was not enough; it had to be enforced strictly by prohibiting public gatherings, and reopening of schools, places of entertainment and restaurants (with some exceptions for essentials like groceries and medications). During the 2003 SARS pandemic, its potential for spread was realized by WHO and the Global Outbreak Alert and Response Network was promptly activated to help send volunteers worldwide to assist severely affected nations. WHO issued mandates to control the outbreaks and prevent further spread. Some lessons from the experiences of this outbreak include recognition of the value of real-time frequently updated information like patient status and any new cases, the difficulties in maintaining symptomatic screening of travellers at both entry and exit health among travellers on a national and international level as well as the implementation of self-quarantine as an effective means to interrupt the chain of transmission.³⁴ Back then, disease outbreaks were common. There hasn't been a major pandemic in a long time, with the most recent example being the HIV/AIDS pandemic, though that didn't require social distancing, just safe sex practices and strict monitoring of blood and bodily fluids for HIV-positive status before blood or organ donations. Good leadership and public health measures make a huge difference. During the Spanish flu pandemic in 1918, the government downplayed the magnitude of the outbreak since it occurred during World War I and they did not want the people to lose hope. But it was too late and by the time people started taking the outbreak threat seriously and the government started establishing rules to prevent spread, lots of preventable deaths had already occurred.

4. Future of Pandemic Response

The world we live in today is much more interconnected thus facilitating rapid transmission of information. One thing that has grown common around the world is the spread of misinformation. The spread of COVID-19 worldwide has been followed by the spread of conspiracy theories and misinformation such as preventive measures like vaccination, social distancing, and face masks being used as political strategy. We live in more densely populated cities than before

which may contribute to the rapid spread of infectious diseases. But we have also made great strides in the field of healthcare with the ready availability of treatments and vaccines in all parts of the world. Looking at how far we have come in comparison to pandemics throughout history and the present pandemic, the most remarkable thing is the inaction in preparation for the COVID-19 pandemic, despite the knowledge of its spread early on in China. This begs the question: if just early dissemination of information was not the only thing needed to manage the crisis, then what more do we need to do? Prompt and open reporting of cases with potential for international spread was one of the most important lessons we have learnt from earlier viral epidemics. This is very easily done in the highly interconnected world of today. International talks are immensely important in the aftermath of the pandemic, with scientists and public health experts worldwide joining hands. A country's top priority lies in its healthcare facilities, especially during inter-epidemic periods. To illustrate, the 2003 SARS epidemic exposed requirements for prolonged intensive care, isolation wards and quarantine facilities, mass screening, active surveillance and contact tracing, and overall weak and ill-equipped healthcare facilities. Implementing surveillance programmes worldwide for quick detection of viral spillover in the animal-human interface is the need of the hour. An integrative approach called the One Health concept was launched to promote health for humans, animals and the environment alike.³⁵ Environmental effects from climate change and urbanization increased the risk of spillover of viruses from animals to humans, thus, emphasizing the need for such an approach in surveying zoonosis.^{36,37} A systematic characterization of virus diversity in wildlife species can decrease the time between detection and response during the outbreaks.³⁸ Another is the Global Virome Project which detects and identifies viruses that can potentially infect and threaten human health. It does so by determining the viral host range, identifying the pathogenicity markers as well as the transmission for high-risk viruses, identifying typical factors that favor animal-human spillover and finally establishing a worldwide network for surveillance.^{39,40} Next generation metagenomic sequencing analysis of viruses was done using nasal/throat swabs from individuals at the highest risk of zoonotic infections. The results of this analysis were also used to expand search for novel viruses that could potentially affect humans, especially

from spillover as well as understand the viral population in the respiratory tracts of humans who were in close contact with animals.⁴¹

CONCLUSION

Outbreaks and pandemics will continue. The global population will be shaped by these infectious disease outbreaks. What we have learned from them will inform our response to the epidemics to come. In 1918, when the Spanish Flu struck, people were unaware that it was caused by a virus, and they couldn't treat it properly with medications or vaccines; mostly relying on quarantining and isolation. Today, we have been able to quickly identify the etiologic agent of COVID-19 and have already developed and administered multiple types of vaccines for it. But that makes it more remarkable that non-pharmaceutical interventions like quarantining, social distancing, and the simple acts of wearing a mask and practicing proper handwashing were a success which implies that such strategies, despite their simplicity and intrusiveness, can help save millions of lives. If we were able to follow them with effect before, there's no doubt we can do it now.

END NOTE

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Abbreviations:

- H1N1 : A strain of the influenza virus (Swine flu)
HIV-AIDS : Human Immunodeficiency Virus causing Acquired Immunodeficiency Syndrome
SARS CoV : Severe Acquired Respiratory Syndrome caused by coronavirus
COVID-19 : Coronavirus disease 2019 caused by SARS CoV2

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