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EDITORIAL

COVID-19: the United States experience

Gregory R. Ciottone

In 2020, the world woke up to the devastating consequences of a global pandemic involving a highly infectious novel respiratory virus with a death rate more than 10 times that of seasonal influenza. In December 2019, SARS-CoV-2 escaped early containment, the most powerful tool we have to prevent infectious disease transmission, and rapidly spread across our highly connected planet. We have not seen a pandemic of this predicted magnitude since the 1918 influenza pandemic (H1N1), when 500 million people were infected globally, resulting in more than 50 million deaths worldwide and 500,000 deaths in the US [1]. While the 1968 influenza pandemic (H3N2) caused approximately 1 million deaths globally and 100,000 in the US [2], it did not reach the enormity of 1918. What is more concerning, in light of the current COVID-19 pandemic, is that both had a second wave that caused more deaths than the first.

As of this writing, there have been approximately 5 million confirmed SARS-CoV-2 infections and 325,000 deaths globally [3]. While there is still much we have to learn about this novel virus, including its variable expression of clinical disease and degree of postinfectious immunity, the best estimates now put its R0 value (measure of transmissibility) at approximately 2.6 [4], and case fatality rate (CFR) between 1.1% and 7.2%, depending on the region [5]. In comparison, the seasonal influenza virus can vary by strain but has a slightly lower R0 and an approximate CFR of 0.1%–0.2% [6]. In the absence of a vaccine, we should expect continued global spread, the degree of which will be dependent on the success of non-pharmaceutical interventions (NPIs).

Once community transmission of an infectious disease has occurred, containment becomes much more difficult, and if no vaccine or effective therapeutics exist, the public health response relies almost entirely on NPIs, particularly social distancing measures. It is worth noting that the 1968 H3N2 pandemic, while more deadly than seasonal influenza, did not come close to the cumulative infections and death toll of the 1918 H1N1 pandemic, despite very limited social distancing measures being implemented. This is likely due to the wide availability of an influenza vaccine, which was not the case in 1918. An interesting comparison can be made from the 1968 data that may shed light on the current COVID-19 pandemic. While vaccinations were available, it was estimated that only 86% of school children in the US had been vaccinated in 1968. This allowed for comparisons to be made between vaccinated and non-vaccinated children, in the context of the near-complete absence of social distancing measures. One such comparison demonstrated an infection rate in Tecumseh, Michigan, where children were vaccinated, one-third less than that of the bordering towns where children were not vaccinated [7]. This supports the effectiveness of vaccines and their ability to produce "herd immunity", thereby decreasing the number of susceptible people in society able to transmit the disease.

What we also learned from the 1918 and 1968 pandemics is that when and how NPIs are triggered matters. This was well demonstrated by the comparative data from the Philadelphia and St. Louis experiences during the 1918 influenza pandemic. Within 2 days of the first cases being reported in St. Louis, the city implemented drastic social distancing measures by closing schools, playgrounds, staggering work shifts, and banning gatherings of more than 20 people. By contrast, once Philadelphia saw its first cases of influenza, the city did not implement social distancing measures until 11 days later, allowing a city-wide parade to occur in the interim. The resulting experiences with the pandemic were dramatically different, with Philadelphia having a significantly higher rate of infection and number of deaths than St. Louis [8].

At this point in the COVID-19 crisis, the US is struggling with decisions around the downregulation of social distancing measures that some argue were implemented too late and too inconsistently. It appears now that while we were restricting travel from China beginning January 31, 2020, many more cases were coming into the US through travel from Europe, which was not restricted until March 11. This, combined with a delayed, inconsistent start of NPIs and insufficient testing capabilities, led to an early rapid "seeding" of the US, with scattered areas of simultaneous community spread going undetected and unabated. Some interesting new data have recently come out around the idea of measuring a value called the

Correspondence to: Gregory R. Ciottone
Department of Emergency Medicine, Beth Israel Deaconess Medical Center, Boston, MA.
Email: gciotton@bidmc.harvard.edu
Full list of author information is available at the end of the article.
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dispersion factor (*K*) that reflects the apparent disparity in how the SARS-CoV-2 seems to cause disease in clusters. When some clusters of infections are examined, they can be traced back to gatherings of people in relatively small indoor settings and performing possibly droplet-generating activities. Examples being used are a choir practice in Mount Vernon Washington that resulted in a large number of infections, and a Zumba class in South Korea that did the same. At the same time, other events, tending more to be held in outdoor settings, did not lead to clusters, but rather saw the infectious outbreaks die-out on their own. This has led to the comparison of SARS-CoV-2 transmission to a bonfire throwing sparks, some of which ignite the surrounding grass and some simply extinguish themselves. The setting of gatherings and which activities are being performed may greatly influence transmission, helping to guide the procedures for downregulation of social distancing measures and the opening of economies.

Due to widely variable implementation of NPIs, as well as differing population densities around the country, some urban areas in the US have experienced exploding infection rates and subsequent strain on healthcare systems, while other more rural areas have very manageable levels of transmission. As a consequence, either healthcare systems are currently in the hot zone and fully engaged in handling the markedly increased patient load or they are in the preparedness phase in regions that have not yet experienced a surge, and perhaps never will as NPIs keep the transmission rates down. This has resulted in the paradox of a dramatic and nearly overwhelming surge on healthcare systems in some regions, while others are experiencing significantly decreased patient volumes due to concern for contracting the disease. The contrast of these experiences is further demonstrated by the use of some degree of crisis standards of care in the hotspots, including utilization of field hospitals for inpatient treatment, while other healthcare systems are underutilizing their facilities and workforce. Fortunately, social distancing measures have now succeeded in decreasing the transmission of the coronavirus and "blunting the curve", so that the hotspot healthcare systems are better able to manage the patient load.

The US now faces the additional burden caused by implementation of the necessarily draconian NPIs, resulting in an enormous economic strain by forcing many businesses to close and unemployment to rise to levels not seen since the Great Depression of the 1930s. This raises the question: Is the cure worse than the disease? We are now working through the very difficult but mandated task of keeping rates of infection manageable through NPIs in order to safely bridge society to vaccines and effective therapeutics, balanced with the reopening process and recovering a decimated economy. It is this looming economic disaster that is driving the decision to do a phased reopening in the US, despite the fear of either causing a resurgence of infections or it leading to a second surge in the autumn that, based on historical precedence of the 1918 and 1968 pandemics, may be worse than the first.

This is no easy task, and it highlights how devastating global pandemics can be in today's highly integrated world. Infectious disease outbreaks over the past 100 years have taught us how effective early containment of an infectious disease can prevent spread and possible pandemic, and how when containment fails it can be globally devastating. Even in the Ebola outbreak of 2014–15, when the virus spread to West Africa where it caused devastating loss of life, it was able to be secondarily contained in the region and did not get a foothold toward a global pandemic anywhere else. We must heed the lessons of the past and understand that dangerous infectious diseases do transcend borders, and we, therefore, must take a global approach to rapid response and containment. I fear if we do not, we may not have many more chances to get it right. Imagine a novel virus with the transmissibility of rubella or mumps (nearly 10 times higher R0 than SARS-CoV-2), and the CFR of Ebola (50%–70%) or rabies (close to 100%). Without early containment, a global pandemic of such a virus would decimate healthcare systems and could threaten our very existence as a species.

Warm Regards,

Prof. Gregory R. Ciottone

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