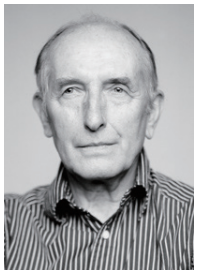
History & Risk



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***Japan SPOTLIGHT* Introduction**

On risk assessment, it is important to compare current risks with similar risks in the past. We need to compare Covid-19 with previous pandemics, in particular with the one in 1918-1919 called the "Spanish flu". People concerned about the future path of today's pandemic may try to see it in parallel with the path of Spanish flu. History can be a useful source of information for assessing the future, but we cannot be certain it will provide us with sufficient data and lessons. To be well prepared for future pandemics, we will need to achieve a thorough assessment of Covid-19 which we are now fighting against so that future generations can take full advantage of it and be prepared for risk mitigation.

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He kindly accepted our request to republish a recent article he wrote about the risks of pandemics from a historical perspective in *Japan SPOTLIGHT*.

Too many people are occupied in modeling the duration and impact of COVID-19. I have no intention of adding to this runaway genre. It is now the first week of April 2020 – too early to make any solid judgments even as far as the first pandemic wave is concerned. It may be dying down in China and sputtering in South Korea, but it is raging in Italy, Spain, and France, and it has only entered its early exponential phase in the United States. Once the first wave recedes, we will still not be sure when the next wave might arrive. That is why I will provide only some important historical perspectives and comparative risk assessments, and list a few lessons that are already absolutely clear.

Looking Back

For several reasons, the 1918–1919 flu pandemic is not the best point of reference. That we still do not know where it began would be irrelevant if we were certain about its global impact and if we could calculate reliable mortality rates for the most affected countries. We can do neither. The most commonly cited estimate of total global mortality is between 20 and 40 million. The World Health Organization put it "upwards of 40 million people" and Niall Johnson and Juergen Mueller go as high as 50 million. Even the lower estimate surpasses all military and civilian deaths of World War I, while the total of 50 million would be almost certainly higher than the toll of the 1347–1351 plague and about equal to another uncertain aggregate, that of all those who perished in the USSR between 1929 and 1953, and in Maoist China between 1949 and 1976.

We will never know how many people were infected, but with 20–40 million deaths within a global population of 1.8 billion, the 1918–1919 pandemic had an average mortality rate of 11 to 22 per 1,000. National mortalities are not highly accurate, but the most likely US count is 550,000. That number is higher than all the deaths sustained by the country's servicemen in all of the twentieth century's wars, and equal to a pandemic-specific mortality rate of 5.3 per 1,000. Both the North American and European data clearly show three successive waves. The British mortality had its smallest peak at just 5 per 1,000 in July 1918, the highest peak at five times that rate in October 1918, and an intermediate wave slightly above 10 per 1,000 during late February 1919. Good epidemiological data are available for several large cities, including New York, Toronto, and Montreal. Between February 1918 and April 1920, New York experienced four waves, together with a heat wave, with peak mortalities shifting from teenagers during the first wave to young adults, with excess mortalities peaking at 28 years of age. Exactly the same age peak was found in Toronto and Montreal in October 1918. Alain Gagnon et al. have argued that this heightened mortality could be explained by an early exposure to the Russian flu pandemic of 1889–1890. The development of early immunological memory may adversely affect the immune response to new strains encountered later in life, and thus increase risk of death.

We know the complete genome and virulence of the influenza virus responsible for the 1918–1919 pandemic; but we also know that most 1918–1919 pandemic deaths were due to bacterial pneumonia. Some 80% of cultures taken from preserved lung-tissue samples contained bacteria causing secondary lung infection. A generation before the development of antibiotics, no treatment was available. Andrew Noymer and Michel Garenne discovered that individuals with tuberculosis were more likely than others to die of influenza; this helps to explain the pandemic's unusual middle-age mortality profile as well as its higher incidence among men, which matches the differential incidence of tuberculosis between the sexes.

Excess mortality in 1918–1919 appears less extreme if some deaths were, in effect, borrowed against future deaths due to tuberculosis. Because neither pre-existing tuberculosis nor bacterial pneumonia have

been important factors in post-WWII pandemics, the Spanish flu is worth studying for its sequence of waves and their growth patterns; but its overall and age-specific mortality were clearly unique.

Comparing Risks

Pandemics are feared because of their relatively high mortalities, but it is impossible to pinpoint those rates while the infection is spreading, and it is difficult to do so even after it ends. The preferred epidemiological approach is to calculate the case-fatality risk, the ratio of deaths to cases. The numerator is not as clear as one might wish because comorbidities are often neglected even when they are noted on death certificates. Still, it is the choice of the denominator that can make a difference in risk assessment as large as two orders of magnitude.

Studies of the 2009 influenza A(H1N1) pdm09 pandemic used three different case definitions: laboratory-confirmed cases, estimated symptomatic cases, and estimated infections (based on serology or on assumptions regarding the extent of asymptomatic infections). As expected, laboratory-confirmed approaches yielded the highest risk of death – mostly between 100 and 5,000 per 100,000; symptomatic approaches were in the range of 5 to 50 per 100,000; and approaches based on estimated infections yielded risks of just 1 to 10 per 100,000. The first approach showed fatalities up to 500 times higher than the last.

These considerations are pertinent as the COVID-19 pandemic unfolds. The number of tested cases is reported daily, but we can only estimate how many asymptomatic people have been or will be infected, and once the infection wave spends itself the best we can do is to estimate that total by relying on post-pandemic population serological studies. The most prominent example illustrates the uncertainty. By April 3, 2020, official Chinese statistics listed 50,007 cases of COVID-19 in Wuhan, the pandemic's epicenter, and 2,553 deaths, implying a case-fatality rate of about 5.1%. But the denominator included only tested or tested *and* symptomatic cases. Wuhan has a population of 11.1 million: 50,000 cases would mean a 0.5% infection rate, and this is impossibly low. Until we can make, at least, a good estimate of actual infections, we might compare risks by relying on the demographic approach to mortality: deaths from specific causes per 1,000 people. Assuming that the worst of Wuhan's 2020 COVID-19 is over, the deaths of 2,553 people would imply a pandemic-specific mortality rate of 0.23 per 1,000.

According to the Centers for Disease Control, influenza in the United States will affect 38–54 million people in 2019–2020, with 24,000 to 62,000 deaths. Assuming mean fatalities of 43,000, the influenza-specific mortality rate would be 0.13 per 1,000, compared to 0.23 per 1,000 for Wuhan COVID-19. Wuhan's COVID-19 mortality rate is thus almost twice as high as the 2019–2020 seasonal flu mortality rate in the US. Obviously, this comparison holds only if the Chinese data are reasonably accurate.

Clear Lessons

Perhaps the most obvious consequence of the latest pandemic is to expose the delusionary nature of recent claims concerning the human mastery of life. The entire lineup of near-miraculous advances has been exposed as irrelevant, and the notion of *Homo deus* boldly charting the destiny of a godlike species has imploded. What benefits have we derived from the Singularity? How useful are those endlessly touted, all-encompassing powers of artificial intelligence? Have our abilities to engineer organisms at will or rapidly produce objects by 3D printing contributed to preventing, moderating, or managing the COVID-19 pandemic? Where are the powers and decisive contributions of the entire high-tech, Silicon Valley world? What difference do these technologies make for doctors in New York City or Milan when they need ordinary rubber gloves, and when 92% of their global supply comes from Malaysia, Thailand, and China? The only solid promise is the development of a vaccine. Having it within 18 months would be historic, but, by then, the pandemic may well have spent itself. The best we can do is to imitate the residents of Italian medieval towns: stay away from others, stay inside for 40 days, *quaranta giorni*.

The COVID-19 pandemic has also exposed an astonishing degree of strategic incompetence in the US, and in other countries, as well. Since the attacks of 9/11 in 2001, which killed 2,977 people, the US has spent trillions of dollars domestically and abroad to prevent another attack. But despite the certainty of another pandemic in the near future, the US remains astonishingly unprepared to manage similar circumstances in an effective and resolute way.

The shortage of gloves, masks, shields, and gowns has been shocking, outrageous, and predictable because the US chose to outsource its manufacturing to Asia in general and to China in particular. While taking this strategically self-defeating step, it also failed to amass sufficient domestic stocks of needed equipment. The United States Conference of Mayors concluded that more than 90% of American cities did not have enough face masks for their first responders and medical personnel. This mindless, profit-driven outsourcing goes far beyond simple manufactured products: it includes basic chemicals, pharmaceutical ingredients, and commonly prescribed drugs. How are such strategic blunders possible? More than $700 billion a year is spent casually on the military, an utterly useless institution in fighting a pandemic, while domestic manufacturing capabilities for indispensable healthcare items remain utterly neglected. Previous financial, military, or public health blunders have gone unpunished. There is no reason to suppose, with respect to the COVID-19 pandemic, that anyone will be held responsible. A reversion to engrained habits is likely. The world did not take any resolute steps after the pandemics of 1958–1959, 1968, and 2009. Why should we assume it will be different this time? Governments will not make adequate provisions for the next pandemic; companies will keep putting profits above security; people will resume their mindless, endless flying and cruising; and, in places where such foods are sought-after delicacies, buyers will continue to eat any imaginable kind of wild animals thus ensuring that sooner, rather than later, one of the animal viruses will jump again to people and start a new pandemic. Some *Homo deus*!

This article is reproduced as originally published in Inference International Review of Science, April 3, 2020.

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