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COVID-19: Where we've been, where we're going

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This paper offers a brief history of viral pandemics and the science of the COVID-19 virus. After reviewing COVID-19's economic, social, psychological and political impacts, we touch on the implications for health care. Finally, we look at the need for a global, integrated approach that requires new multi-disciplinary thinking, and what this means for policy makers.

We begin with an appeal for the global public to acknowledge a stark reality: COVID-19 is here to stay. Neither science, nor history, nor politics, alone can solve this crisis. We must learn how to live with it, and either we will manage it effectively or it will manage us.

This paper offers a brief history of viral pandemics and the science of the COVID-19 virus. After reviewing COVID-19's economic, social, psychological and political impacts, we touch on the implications for health care. Finally, we look at the need for a global, integrated approach that requires new multi-disciplinary thinking, and what this means for policy makers.

A brief history of global disease

Disease has been with us since the dawn of history. The Black Death decimated Europe and Asia in the early centuries of the last millennium, and regular outbreaks of smallpox killed millions over millennia. Smallpox, however, was the first disease for which a vaccine was developed, in 1796, and the first to be declared eliminated by the World Health Assembly in 1980.[1] Nevertheless, despite ongoing medical and public health advances, new diseases have continued to emerge and threaten human well-being.

The first major new disease of modern times was the 1918 influenza pandemic. Caused by the H1N1 virus, the "Spanish flu" was exceptionally virulent and eventually penetrated every community in the world. Over a two-year period, nearly one-third of the global population — or an estimated 500 million people — had been infected, with estimated deaths ranging between 25 and 50 million people. This was one of the deadliest pandemics in human history and, like COVID-19, it spread in waves.[2]

It was not until 1981 that the next new virus emerged as a global health threat. This was the human immunodeficiency virus (HIV) pandemic, which caused acquired immunodeficiency syndrome (AIDS). It emerged when viruses crossed into humans from chimpanzees and sooty mangabey monkeys. To date it has resulted in an estimated 79.3 million cases and 36.3 million deaths.[3]

Since the onset of the HIV/AIDS pandemic, there have been other zoonotic viral outbreaks[4] but, prior to COVID-19, none was uncontrolled. The first was severe acute respiratory syndrome (SARS), caused by the SARS coronavirus (SARS-CoV-1), which began in China in 2002. The outbreak ended in June 2003 with only 422 cases and 774 deaths recorded, and a case fatality rate of 11%.[5]

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[1] World Health Organization, Smallpox Eradication Programme – SEP (1966-1980), accessed January 26, 2022, https://www.who.int/news-room/feature-stories/detail/the-smallpox-eradication-programme---sep-(1966-1980).
[2] Kolata, Gina. *Flu: The Story of the Great Influenza Pandemic of 1918 and the Search for the Virus that Caused it*. New York: Simon & Schuster, 2001.
[3] UNAIDS, "Global HIV & AIDS statistics — Fact sheet," accessed February 9, 2022, https://www.unaids.org/en/resources/fact-sheet.
[4] A zoonotic disease is an infectious disease that has jumped from an animal to humans. The pathogens may be bacterial, viral or parasitic.
[5] World Health Organization, "Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003," accessed February 8, 2022, https://www.who.int/publications/m/item/summary-of-probable-sars-cases-with-onset-of-illness-from-1-november-2002-to-31-july-2003.

The H1N1/09 — or swine flu — pandemic started in Mexico in April 2009 and spread rapidly, reaching pandemic proportions within weeks. This pandemic was declared a Public Health Emergency of International Concern (PHEIC) by the World Health Organization (WHO) on April 25, 2009. In early August 2010, it was declared over. It is estimated between 700 million and 1.4 billion people were infected, but only 18,449 lab-confirmed deaths were reported to the WHO.[6] The feared levels of mortality broadcast to concerned publics and policy makers did not emerge and, as a result, the public grew less trusting of public health services and the urgency of their messages.

Middle East Respiratory Syndrome (MERS) is a viral respiratory infection caused by the Middle East respiratory syndrome–related coronavirus (MERS-CoV). It spread from camels to humans and was first reported in Saudi Arabia in 2012. The number of infections was small, fewer than 3,000. Despite rarely spreading from human to human, MERS-CoV has a high case fatality rate of approximately 35%. Due to its low transmissibility, however, it has not become a global threat.[7]

The Ebola virus spread to humans from fruit bats and was first identified in 1976. There continue to be sporadic outbreaks, primarily in Central and West Africa. The most recent major outbreak was from 2014 to 2016. It began in Guinea, then spread to Sierra Leone and Liberia, with small numbers of cases in Nigeria and Mali. On August 8, 2014, the WHO declared the epidemic a PHEIC. Leading up to May 2016, 28,646 suspected cases and 11,323 deaths were reported from this outbreak. The case fatality rate can be between 25% and 90%, but is generally accepted to be about 50%. Sporadic new outbreaks have been contained, except for a major outbreak that occurred primarily in the Democratic Republic of the Congo. The Kivu Ebola epidemic of 2018-2020 was also declared a PHEIC. Due to its high mortality rate and the speed with which it kills its hosts, Ebola virus has not yet become a global health threat.[8]

The most recent new disease outbreak, prior to COVID, was the Zika virus. This was first reported from Brazil in 2015. A mosquito-borne disease and generally mild, the Zika virus caught global headlines because it can cause severe microcephaly (skull deformity) in the fetuses of infected mothers. In February 2016, the WHO declared the outbreak a PHEIC and ended it on November 18 of the same year, when case rates had dropped.

These global diseases formed the backdrop for the emergence of COVID-19.[9] Public health and medical communities knew an increasing human population, combined with high-density living conditions, poor sanitation, and cohabitation with animals, meant new zoonotic viral diseases would inevitably emerge,

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[6] World Health Organization, "Influenza A (H1N1) outbreak: Overview", accessed January 26, 2022, https://www.who.int/emergencies/situations/influenza-a-(h1n1)-outbreak
[7] Centers for Disease Control and Prevention (CDC), "Middle East Respiratory Syndrome (MERS)", accessed January 26, 2022, https://www.cdc.gov/coronavirus/mers/index.html
[8] Centers for Disease Control and Prevention (CDC), " What is Ebola Virus Disease?", accessed January 26, 2022, https://www.cdc.gov/vhf/ebola/about.html
[9] World Health Organization (WHO), " Zika Virus", accessed January 26, 2022, https://www.who.int/news-room/fact-sheets/detail/zika-virus

and that one would likely become the next pandemic.[10] The WHO had prepared for Disease X, not an "actual disease caused by a known agent, but a speculated source of the next pandemic that could have devastating effects on humanity."[11] Scientists suspected it would be an influenza virus, but this was not the case; what emerged was a coronavirus, officially designated "severe acute respiratory syndrome coronavirus 2," abbreviated to SARS-CoV-2.[12]

In February 2022, two years into the pandemic, with new waves cresting, new variants emerging, large swaths of the world still unvaccinated, and political tensions rising between the vaccinated and unvaccinated, the question emerges: where do we go from here in our fight against COVID-19?

Early responses

There is general consensus that COVID-19 emerged in China late in 2019, while scientific and health communities first became aware of it in early January 2020.[13] The WHO confirmed human-to-human transmission of the virus on January 21 and declared a PHEIC on January 30. By then, the pandemic had spread around the world and cases were rising exponentially.

At first, there were no off-the-shelf drugs known to treat the disease and only symptomatic support was available for patients. The worst cases required ventilators in order to breathe and, once a person was ventilated, there was a 50% fatality rate. When the Government of China made the genetic sequence of the novel coronavirus available on January 12, 2020, scientists swung into action to develop and produce vaccines.[14] At this point, the only prevention tools were so-called non-pharmaceutical interventions.[15] These included reducing contact between people through school and workplace closures; cancellation of public events; limits on gathering sizes; closure of public transport; stay-at-home requirements; and internal movement restrictions. International travel was shut down or greatly reduced. Countries introduced public information campaigns to ensure compliance with these measures, and enforcement by authorities where this was deemed necessary.

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[10] There were various pandemic preparedness exercises at national and multinational levels. For example, it emerged in January 2021 that the British government ran an exercise modelling the impact of a coronavirus outbreak in 2016 and tried to keep it secret. *The Guardian* reported on January 10, under the title "Secret planning exercise in 2016 modelled impact of Mers outbreak in UK": "The previously unpublicised Exercise Alice took place in 2016 involving officials from Public Health England (PHE) and the Department of Health and Social Care (DHSC), and envisioned an outbreak of Middle East respiratory syndrome (Mers), which is caused by a coronavirus."

[11] Huremović, D. "Brief History of Pandemics (Pandemics Throughout History)." In *Psychiatry of Pandemics*, edited by Huremović D., 7-35. Springer, 2019.

[12] World Health Organization. "Naming the coronavirus disease (COVID-19) and the virus that causes it," accessed March 2, 2020, https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it.

[13] Horton, Richard. *The COVID-19 Catastrophe: What's gone wrong and how to stop it happening again*. Cambridge: Polity Press, 2020.

[14] Gilbert, Sarah, and Green, Catherine. *Vaxxers: The Inside Story of the Oxford AstraZeneca Vaccine and the Race Against the Virus*. London: Hodder and Stoughton, 2021.

[15] Liu, Y., Morgenstern, C., Kelly, J. et al. "The impact of non-pharmaceutical interventions on SARS-CoV-2 transmission across 130 countries and territories." *BMC Med* 19 (2021): 40.

Once tests were developed, widespread testing was introduced. There was "contact tracing" (establishing detailed histories of physical interactions among persons and groups), and quarantining of people who were infected or who had been in contact with infected people. Mask wearing was made mandatory in many public settings, and increased hygiene measures were encouraged. Levels of compliance were extraordinary in most countries, but economic activity plummeted as shops and factories were forced to close. The closures led US president Donald Trump to tweet such statements as: "We cannot let the cure be worse than the problem itself."[16] Such views were echoed by a number of world leaders and had a huge impact in the United States, where any government intervention into economic and personal matters — even if backed by countless health experts — was viewed with suspicion and as an encroachment on political freedoms and personal agency.

The science of COVID-19

Why were we unprepared?

The global response to the current virus outbreak would have been very different if the emergent virus had been an influenza virus. The swine flu outbreak of 2009, for example, went from emergence of the virus to vaccine availability in eight months.[17] This speed was possible because an influenza virus vaccine platform (or design strategy) had been established and proven safe and effective. Tamiflu, an antiviral drug to treat unvaccinated, infected individuals, was also available. The virus that emerged in 2019 was not an influenza virus, as scientists had expected, but a coronavirus, which challenged existing knowledge and experience.

Coronaviruses are an understudied virus family. With only seven species infecting humans and three causing serious disease,[18] coronaviruses never garnered the research dollars or academic attention of "sexier" viruses such as HIV or influenza. Indeed, many university-level virology textbooks do not even discuss coronaviruses. Given this absence of study, most virology labs in the world had to pivot from their popular "virus of interest" to understudied coronaviruses, overnight. And, at a time when the world desperately needed antiviral drugs or vaccines for coronaviruses, none were available.

The optimal approach to combatting virus transmission without limiting human interaction is through vaccination. Most of the vaccines used to combat viruses in humans are based on a live attenuated or inactivated virus platform.[19] These platforms require the ability to produce massive amounts of virus in order to attenuate (weaken) or inactivate (kill) the virus prior to injection into humans. For these vaccines,

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[16] Haberman, Maggie, and Sanger, David E. "Trump Says Coronavirus Cure Cannot 'Be Worse Than the Problem Itself." *The New York Times*, March 23, 2020.

[17] Centers for Disease Control and Prevention. "2009 H1N1 Pandemic Timeline." Last updated May 8, 2019. https://www.cdc.gov/flu/pandemic-resources/2009-pandemic-timeline.html.

[18] Centers for Disease Control and Prevention. "Human coronavirus types." Last updated February 15, 2020. https://www.cdc.gov/coronavirus/types.html.

[19] Wodi, A. Patricia, and Morelli, Valerie. "Principles of Vaccination." In *Epidemiology and Prevention of Vaccine-Preventable Diseases*, edited by Hall E., Wode A.P., Hamborsky, J. et al., 1-8. Washington DC: Public Health Foundation, 2021.

the virus is intact but not able to replicate (or replicate only in a limited capacity), and so the immune system recognizes the virus and mounts an immune response that results in the development of immune memory.

This platform works well for viruses that can be produced in large quantities, but there are several reasons why these inactivated, or attenuated, vaccines were not the first choice for coronaviruses. First, coronaviruses do not replicate in embryonated eggs like influenza viruses and are difficult to grow in culture,[20] making it problematic for manufacturers to produce high levels of coronaviruses. Second, there was a serious concern, based on the SARS-CoV-1 vaccine trials, that an attenuated coronavirus vaccine could produce eosinophilia of the lungs, a type-2 inflammation that would make this vaccination strategy unsafe.[21] Third, attenuated or inactivated virus vaccine approval for a new virus would take time, as the complexities of an intact virus interacting with the human immune system would be difficult to ascertain quickly. Scientists deemed that it was better to focus on simpler vaccine strategies, such as mRNA vaccines, where the host cell is forced to produce one virus protein, thus having less complex interactions with the immune response. Less complex interactions would mean less likelihood for safety concerns, and a faster vaccine to market.

The result was two incredibly efficacious and safe mRNA vaccines (mRNA-1273; Moderna and BNT162b2; Pfizer-BioNTech) and one non-replicating viral vector vaccine (Oxford AstraZeneca) produced by OECD countries. In addition, China quickly had three vaccines and Russia, one.[v] Despite choosing a simple vaccine platform with lower likelihood of side effects, the rapidity with which the vaccines were developed unfortunately led to portions of the global population being skeptical as to the safety of an as-yet-untested vaccine platform.[22]

Interestingly, new data has emerged that the traditional, inactivated vaccine platform from China (Coronavac; Sinovac) produces ten times fewer antibodies compared to BNT162b2.[23] This suggests that traditional vaccine platforms are not as effective as newer mRNA platforms at inducing immune responses, a key factor in establishing both B and T cell immune memory. The suggestion also implies that the Western switch in platform was fortuitous. However, data like this were not sufficient to convince mRNA vaccine skeptics. Fortunately, new vaccines are in the pipeline, including the Janssen non-replicating viral vector vaccine, which was authorized for use in Canada on March 5, 2021.[24]

A second way to combat virus infections is using an antiviral drug to treat infected individuals. This strategy is less effective than vaccines for several reasons. First, it is very difficult to stop a virus infection once it starts, as viruses make thousands to millions of copies of themselves within each cell as they

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[20] Takayama, K. "In vitro and animal models for SARS-CoV-2 research." *Trends Pharmacol. Sci.* 41 (2020): 513-517.
[21] Simon, H.-U., Karaulov, A.V., and Bachmann M.F. "Strategies to prevent SARS-CoV-2-mediated eosinophilic disease in association with COVID-19 vaccination and infection." *Int. Arch. Allergy Immunol.* 181 (2020): 624–628.
[22] Gilbert and Green, op. cit.
[23] Lim, W.W., Mak, L., Leung, G.M., Cowling, B.J., and Peiris, M. "Comparative immunogenicity of mRNA and inactivated vaccines against COVID-19." *Lancet Microbe*. 2, no. 9 (2021): e423.
[24] Chambers, Catharine. "Comparing vaccines: efficacy, safety and side effects." March 11, 2021. https://healthydebate.ca/2021/03/topic/comparing-vaccines.

replicate, which, in turn, infect other cells. Making a drug that can stop every virus particle from replicating and spreading is almost impossible.[25]

Second, viruses mutate quickly, and can mutate to become resistant to antiviral drugs in a short time. This was the case with M2 ion channel inhibitors and seasonal influenza virus.[26] A side effect of this is the probability of rapid virus mutations evading new drugs. This makes risk-averse pharmaceutical companies wary of investing the required millions to launch new antivirus clinical trials.
Third, viruses depend on host machinery to replicate, and finding targets within the cell that negatively impact the virus but leave the host cell unscathed are difficult to determine. This is particularly the case if the virus is understudied. Drugs that negatively affect the virus and the host produce undesirable, toxic side effects. At the writing of this article, only one antiviral drug, Merck's molnupiravir, has been approved to treat SARS-CoV-2. In early November 2021, the UK announced it had approved the use of molnupiravir.[27] Time will tell how effective the drug will be. This lack of available antiviral drugs is of particular concern for unvaccinated individuals or those whose vaccine-mediated immunity is waning, which makes break-through infections possible.

What's next for COVID-19 and its (potential) variants?

Variant emergence

Variants emerge when viruses replicate. This is because viruses make mistakes when they copy their genomes, and these mistakes produce mutations. Some of these mutations are "loss-of-function" mutations, which lead to the viruses losing their capability to infect or transmit. These mutations are often referred to as "dead ends" and do not help the virus evolve. However, some of these mutations become "gain-of-function" mutations, which give the virus an advantage, increasing its ability to replicate, transmit or evade the immune system. Gain-of-function mutations allow a virus to spread between individuals with greater ease, adding fuel to a pandemic's fire. Coronaviruses make a "proofreading" enzyme that fixes some loss-of-function mistakes.[28] It does this to maintain the integrity of its very large RNA genome. The benefit to us, as its hosts, is that it cannot produce as many gain-of-function mutations as some other RNA viruses, such as the influenza virus and HIV. Yet the virus can still mutate, and when there are hundreds of thousands of individual hosts supporting replication, as in the case of a hot spot during an outbreak, the numbers that favour a gain-of-function mutation rise. This can be seen with both the Delta variant and Omicron variant, which both emerged during times of rapid replication

[25] Torrence, Rebecca. "Tamiflu-like drugs face long odds against COVID runaway train." June 24, 2021. https://www.bloomberg.com/news/articles/2021-06-24/tamiflu-like-drugs-face-long-odds-against-covid-runaway-train.
[26] Hussain, M., Galvin, H.D., Haw, T.Y., Nutsford, A.N., and Husain, M. "Drug resistance in influenza A virus: the epidemiology and manangement." *Infect. Drug Resis*t. 10 (2017): 121-134.
[27] Medicines and Healthcare products Regulatory Agency. "First oral antiviral for COVID-10, Lagevrio (molnupiravir), approved by MHRA." November 4, 2021. https://www.gov.uk/government/news/first-oral-antiviral-for-covid-19-lagevrio-molnupiravir-approved-by-mhra.
[28] Robson, R., Khan, K.S., Le, T.K., Paris, C. et al. "Coronavirus RNA Proofreading: Molecular basis and therapeutic targeting." *Molecular Cell* 79, no. 5 (2020): 710-727.

and transmission in India[29] and South Africa,[30] respectively. At the end of January 2022, Omicron was the dominant global strain.

Viruses cannot mutate their proteins indefinitely; there is a limit as to how much a virus can mutate before the protein loses its ability to function. While no one knows yet if Omicron is the optimal variant for SARS-CoV-2, what virologists agree on is that more virus transmission equates to more virus replication, and more replication means more chances for variants to emerge. The biggest question is how this cycle can be halted. Although the simple answer is vaccination, the vaccination process must be global in scale. The virus does not care if a single country is fully vaccinated against current virus strains. If there is a hot spot somewhere on the globe, and a variant emerges in this location that evades vaccine immunity, it may then transmit, spread and cause havoc in vaccinated and unvaccinated communities alike. Governments world-wide should ensure equitable distribution of vaccines to slow down hot spots of virus replication, reduce variant emergence and protect the global community.

Booster shots are inevitable

None of the four seasonal coronaviruses can establish lifelong immune memory. Individuals infected with any of these four coronaviruses can be reinfected with that same coronavirus strain 12 months later.[31] This suggests that the inability to mount long-lasting immunity may be a feature of all coronaviruses, in contrast with other viruses, such as smallpox, whose vaccine produces lifelong immunity.[32] Recent studies have shown that antibody levels drop in vaccinated individuals over time — which would be expected, as an antibody response to a vaccine does not stay elevated forever — and protection against virus infection drops as well. In Israel, patients over 65 who received their vaccines in January 2021 were twice as likely to have severe illness in a July outbreak compared to individuals of the same age who were immunized more recently,[33] while those vaccinated with a booster were much less likely to develop severe disease.[34] Taken together, this evidence suggests that boosters are inevitable if SARS-CoV-2 infections, illnesses and deaths are to be limited. Vaccine boosters are used regularly for other vaccines and are effective at "reminding" the immune system of the virus. At a national level, it makes sense to provide booster vaccinations if much of the world is lagging in providing vaccinations, as there is the potential for variants to emerge.

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[29] Centers for Disease Control and Prevention. "Delta Variant: what we know about the science." Last updated August 26, 2021. https://www.cdc.gov/coronavirus/2019-ncov/variants/delta-variant.html.
[30] Centers for Disease Control and Prevention. "Omicron variant: what you need to know." Last updated December 20, 2021. https://www.cdc.gov/coronavirus/2019-ncov/variants/omicron-variant.html.
[31] Edridge, A.W.D., Kaczorowska, J., Hoste, A.C.R. et al. "Seasonal coronavirus protective immunity is short-lasting." *Nat. Med.* 26 (2020): 1691-1693.
[32] Castellino, F., Galli, G., Del Giudice, G., Rappuoli, R. "Generationg memory with vaccination." *Eur. J. Immunol.* 39, no. 8 (2009): 2100-2105.
[33] Goldberg, Y., Mandel, M., Bar-On, Y.MN., Bodenheimer, O. et al. "Waning immunity after the BNT162b2 vaccine in Israel." *New Eng. J. Med.* 385: e85 (2021): DOI: 10.1056/NEJMoa2114228.
[34] Bar-On, Y.M., Goldberg, Y., Mandel, M., Bodenheimer, O. et al. "Protection of BNT162b2 vaccine booster against COVID-19 in Israel." *New Eng. J. Med.* 385 (2021): 1393-1400.

The WHO has called for a moratorium on boosters until all countries have at least 10% of their population vaccinated.[35] As of January 2022, 10 billion vaccine doses had been administered world-wide, but only 9.8% in low-income countries had received at least one dose. In Canada and the UK, 78% and 71% of the population were fully vaccinated, but in Chad and Haiti the rates were just 0.71% and 0.69%, respectively.[36] If it is critical to vaccinate globally to reduce virus replication hot spots and reduce the chance of variant emergence, the big question governments must now tackle is: do individual nations protect their communities in the short-term by enabling booster shots or should preference be given to longer-term protection by vaccinating in lower-income countries?

Co-infection risks

Unfortunately, viruses do not infect in isolation. More than one virus can infect an individual at the same time. With social distancing and other public health measures in place, naturally seasonal viruses that typically emerge each winter did not materialize at normal levels during the winter of 2020-2021, and possible co-infections between seasonal viruses and SARS-CoV-2 have not yet occurred. A marked example is the seasonal influenza virus, which became almost non-existent in the winter of 2020-2021.[37]

With the loosening of pandemic-fueled restrictions to movement and contact, there were concerns of a "twindemic" of COVID and flu in the 2021-2022 northern winter. However, influenza is not the only virus that could produce problematic co-infections. The respiratory syncytial virus (RSV) causes lung inflammation, mostly in children. RSV infection levels were very low in 2020-2021 winter due to public health measures. Many believed this could lead to a double cohort of RSV-infected children in the 2021-2022 winter; a spike of RSV cases occurred in the summer/fall of 2021.[38] Co-infection concerns are not limited to respiratory viruses. HIV is a virus that may present a co-infection issue in areas such as sub-Saharan Africa. HIV-infected individuals are more predisposed to severe effects of COVID-19,[39] and thus co-infections with SARS-CoV-2 and HIV should be a concern and closely monitored.

The impacts of the pandemic[40]

We have all felt the effects of the pandemic. For some, this was illness, isolation, and/or the loss of loved ones. For others, in countries with a social safety net, it was periods on furlough, being supported by

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[35] World Health Organization. "WHO Director-General's opening remarks at the media briefing on COVID-19, 8 September 2021." https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---8-september-2021.

[36] Our world in data. "Coronavirus COVID-19 vaccinations." Accessed November 1, 2021. https://ourworldindata.org/covid-vaccinations.

[37] Rubin, R. "Influenza's unprecedented low profile during COVD-19 pandemic leaves experts wondering what this flu season has in store" *JAMA*. 326, no. 10 (2021): 899-900.

[38] Ducharme, J. "Why the respiratory disease RSV is having an off-season surge." *Time Magazine*. July 22, 2021. https://time.com/6082836/rsv-spike-summer-2021.

[39] Centers for Disease Control and Prevention. "What to know about HIV and COVID-19." Last updated November 1, 2021. https://time.com/6082836/rsv-spike-summer-2021.

[40] Spiegelhalter, D., and Masters, A. *Covid By Numbers: Making Sense of the Pandemic with Data*. UK: Pelican Books, 2021.

governments while being locked out of a job. In countries with no safety net, it was a matter of survival. Most people experienced periods of lockdown of varying levels of severity.[41]

In the UK, when under extreme lockdowns, only essential workers were allowed to go to work. Everyone else had to work from home, while juggling other responsibilities. Social lives were massively curtailed, and children, if they were lucky, were home schooled. The world's media showed countless images of misery from the Global South: millions of Indian migrant workers forced to walk great distances to their home states and villages, and the raw earth of new graves stretching into the distance in Manaus, Brazil.[42] The impacts include those we could measure and quantify. The unquantified costs will have the greatest effects, however, and be felt in the long term.

The quantified costs

Deaths, in theory, are the easiest to count. In January 2022, the highest cumulative death rate (per million) was in Peru with 6,143; the United States was 20th with 2,638 deaths; Belgium was at 24th in the ranking with 2,487 deaths per million and the first European Union country to feature; South Africa, the first African country to feature, was ranked at 53rd with 1,576 deaths. Canada was 87th with just 876 deaths per million.[43]

Hospitalizations indicate the number of people requiring care. But since the reasons for hospitalizations may not be clear, better crude indicators of the burden that COVID-19 is placing on hospitals may be the demand for oxygen or ventilators. In January 2022, the good news (in OECD countries at least) could be seen in the steady increase in the number of people vaccinated and — despite the new wave of the Omicron variant — the fact that hospitals had not been overwhelmed, and the proportion of patients requiring intensive care and ventilation remained manageable, without an increase in deaths.[44]

The economic impact of COVID-19 is emerging.[45,46] At the macro level, we still do not know the extent of the economic damage from the pandemic, but there is consensus there will be severe negative impacts on the global economy. "Early estimates predicted that, should the virus become a global pandemic, most major economies will lose at least 2.9 percent of their gross domestic product (GDP) over 2020. This

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[41] FT Visual & Data Journalism Team. "Lockdowns compared: tracking governments' coronavirus responses." Last updated November 15, 2021. https://ig.ft.com/coronavirus-lockdowns.
[42] https://www.theguardian.com/world/2020/apr/30/brazil-manaus-coronavirus-mass-graves, accessed January 28, 2022; Pandey, Vikas, "Coronavirus lockdown: The Indian migrants dying to get home," BBC News, Delhi, May 20, 2020, https://www.bbc.co.uk/news/world-asia-india-52672764, accessed January 28, 2022.
[43] Our World in Data. "Coronavirus (COVID-19) Deaths," accessed January 28, 2022, https://ourworldindata.org/covid-deaths.
[44] Office for National Statistics, "Coronavirus (COVID-19) latest insights: Comparisons," accessed January 28, 2022, www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/coronaviruscovid19latestinsights/Overview.
[45] Jones, L., Palumbo, D, and Brown, D. "Coronavirus: How the pandemic has changed the world economy." January 24, 2021, https://www.bbc.co.uk/news/business-51706225.
[46] Tooze, A. *Shutdown: How COVID-19 Shook the World's Economy*. London: Alan Lane, 2021.

forecast was already restated to a GDP loss of 4.5 percent. To put this number in perspective, global GDP was estimated at around 87.55 trillion U.S. dollars in 2019 – meaning that a 4.5 percent drop in economic growth results in almost 3.94 trillion U.S. dollars of lost economic output."[47] These statistics do not show the increase in poverty, food insecurity and unemployment. The impacts are also gendered, as women are worst affected.

The unquantified costs

Humans do not tend to function well when isolated. COVID-19 has meant that many elderly people were left on their own, unable to see families and friends, and in the worst cases levels of care were reduced. In many OECD countries, long-term care homes were badly hit and felt abandoned, as did their residents.

The closure of schools meant children missed out on education, socialization and examinations. Countries have now implemented catch-up schemes, but the time lost will be hard to recover. Education for a five-year-old can only be given when the child *is* five. Given that this is the first impact of this type, on this scale, it is hard to estimate the overall damage to society and healthcare systems. In the health sector, routine treatments were postponed and, in the UK, waiting lists are at the highest levels ever. The delays extend from elective surgeries to more urgent cases.

The pandemic has also highlighted and exacerbated socio-economic and educational divides within communities. In the United States, vaccine uptake and viral outbreaks could be contrasted based on whether the county in question had a Democratic base, where people were amenable to being vaccinated, or a Republican base, where more people were resistant to vaccination.[48] This divide between vax and anti-vax communities has been felt not only in federal, provincial and local politics, but also in our places of employment, our schools and our homes. The pandemic has provided an opportunity for individuals to convey their political, religious and scientific (and often non-scientific) opinions on social media platforms, undermining public health measures that require community support for effectiveness. The fracture in our communities from these diverse choices and opinions will be felt for years as emotional and social divides over the efficacy and importance of vaccinations, and will outlast the pandemic itself.

Impacts and silver linings

The pandemic's many impacts — in terms of illnesses and deaths, economic and educational losses, social divisions, and effects on mental health — cannot be overstated. Yet there have also been silver linings. The speed with which scientists came to grips with the pandemic was nothing short of miraculous. Researchers began developing vaccines as soon as the consortium led by Yong-Zhen Zhang of the

[47] Szmigiera, M. "Impact of the coronavirus pandemic on the global economy — Statistics & Facts." September 15, 2021, https://www.statista.com/topics/6139/covid-19-impact-on-the-global-economy/#dossierKeyfigures.
[48] Medina, J., and Gebeloff, R. "The coronavirus is deadliest where Democrats live," *The New York Times*, May 25, 2020, https://www.nytimes.com/2020/05/25/us/politics/coronavirus-red-blue-states.html.

Shanghai Public Health Clinical Center and School of Public Health released the genome sequence.[49] According to Sarah Gilbert, she and other members of the AstraZeneca team were thinking about vaccine development as soon as the reports of the outbreak reached them.[v] Advances that might have taken years were achieved in weeks.

The growth of telemedicine — the diagnosis and treatment of patients using telephone and video communications — enabled some health care to continue. In the long term this could free up resources and change the way care is delivered. Telehealth visits in the United States increased 154% in March 2020 compared to the same period in 2019, clearly demonstrating the impact of the pandemic on this health care practice. Telehealth has multiple benefits, including expanded access to care, reduced risk of exposure to SARS-CoV-2 for patients and health practitioners, and reduced demand on health care facilities. However, it remains to be seen how this new way of providing care will play out long term. Another innovation has arisen in the provision of drugs. For instance, AIDS prescriptions are now being made for longer periods of time, making adherence easier. This will be one gain that we will keep.

The public has become well educated on respiratory virus infections and how they are transmitted. There is a better understanding of the importance of washing hands frequently, choosing to meet outside to reduce the chance of transmission, and increased acceptance of staying home if a person feels sick. The stigma of wearing a mask in public, a common practice in much of Asia to reduce respiratory virus transmission pre-pandemic, has been eliminated in many North American communities. These practices will surely help us reduce transmission of other respiratory viruses (e.g., influenza virus or RSV) once SARS-CoV-2 infections have abated.

Where do we go from here?

A number of key points can be learned from our experiences to date.

1. ***Early warning systems must improve***

Early warning systems worked reasonably well in early 2020, and governments, public health practitioners and the international community became aware of the disease rapidly. The WHO has been criticized, but compared to the normal, sclerotic international agency mobilization, and in light of the unexpected emergency of a coronavirus rather than an influenza pandemic, its actions were commendably speedy. Thus, while the response was commendable, it was not nuanced or detailed, and did not comprehend the gravity of the risks ahead.

While the reporting of the SARS-CoV-2 emergence was prompt, case numbers were, and still are, clouded by political agendas. Examples include the very low official number of cases reported from China

[49] Wu, F., Zhao, S., Yu, B., Chen, Y.-M., Wang, W. et al. "A new coronavirus associated with human respiratory disease in China." *Nature*. 579 (2020): 265-269.

and the Tanzanian president's denial of the existence of the disease.[50] It is clear that we need a global early warning system for emerging zoonotic viruses. The Global Influenza Surveillance and Response System provided by the WHO is a global platform for reporting and monitoring influenza virus strains.[51] This type of surveillance and reporting needs to be extended beyond influenza viruses, certainly to coronaviruses, but perhaps to other respiratory viruses. This system would hopefully provide a politics-free platform to report emerging cases in real time. Increased funding toward global surveillance and reporting of viruses circulating in common virus reservoirs, such as bats, would be helpful. It could monitor levels of viruses likely to become zoonotic. This would enable scientists and public health professionals to be proactive instead of reactive to emergent zoonotic viruses.

2. ***Global solidarity is lacking***

Throughout the pandemic, global solidarity has been lacking. There was an undignified scramble by governments to protect their populations at the expense of others. This was seen early in the pandemic in the over-purchasing of personal protective equipment for frontline workers, and later, with vaccine hoarding. The inability of poor countries to source vaccines shows this regrettable tendency continues.

Global pandemics require global transparency. The current pandemic has highlighted how politics can hamper scientific communication, the adoption of public health measures, and vaccination rates. What if the power were taken out of the hands of politicians and social media were used instead to promote global solidarity? Instead of government reports, tainted with political agendas, blocking the flow of information between countries, globally accessible apps or social media platforms could allow for self-reporting of infected individuals and highlighting of hot spot outbreaks. Individuals could have access to COVID-19 infections rates in their community, their country, their world, in real time, with information that can be fact-checked and moderated.

3. ***Decision making must be based on more disciplines***

One of the key questions in the battle against COVID-19 is how to inform the public while also getting them involved in decision making, rather than having seemingly arbitrary and illogical rules imposed. By the end of 2021 in the UK, for example, cinemas and theatres reopened by the end of 2021 and the wearing of masks was voluntary, even while all passengers on aircraft had to wear masks. Similar inconsistencies are seen throughout the world. In January 2022, in Ontario, Canada, children were allowed to attend elementary or high school in person, but universities were teaching remotely, while restaurants and gyms remained closed.

The authors of this paper are, respectively, an economist and a virologist. We know what works in preventing transmission and we know that the science will evolve. We are not specialists in effective

[50] Dickens Olewe, "John Magufuli: The cautionary tale of the president who denied coronavirus." BBC News, https://www.bbc.co.uk/news/world-africa-56412912.
[51] World Health Organization, "Global Influenza Surveillance and Response System (GISRS)", accessed November 15, 2021, https://www.who.int/initiatives/global-influenza-surveillance-and-response-system.

public health messaging or the equitable administration of global vaccination programs. Multi-disciplinary approaches will be more effective at addressing all aspects of a pandemic response, hence, the importance of the historical, ethical, and multi-perspectival insights offered here.

4. ***Science needs more: money, time, data!***

Current funding opportunities in Canada have focused on putting large numbers of grant dollars into developing vaccine technologies and producing effective public health measures. These are excellent venues for funds. However, more money needs to be allocated to basic coronavirus research. The more we understand this virus family, the better the vaccines and antiviral drugs we will design.

Clearly, we need more anti-coronavirus therapeutics. Health regulators moved more nimbly than usual to provide access to cutting-edge vaccines while still ensuring safety protocols were being adhered to. This process needs to be extended to antiviral therapeutics, to allow for new antiviral drugs to be released quickly, but with all safety standards still in place.

We also need to know more about our new coronavirus vaccines. As discussed, these vaccines will need booster shots, perhaps yearly or bi-yearly. Improvements should be expected and communicated to the public as being normal, and this should not become something that further detracts from a positive public opinion and understanding of scientific technology.

5. ***Increasing trust in science is vital***

During this pandemic, politicians have assumed that the public could not understand scientific findings, and so these findings have not been communicated widely (with the exception of epidemiological curves, which were shared with abandon, mostly to shore up public support for stringent public health measures). The public can and should be taught what is happening from a scientific perspective.

The messaging provided needs to be uniform across the country, and two-way in nature to allow for questions from the public to be addressed. Messaging needs to be open and transparent, easy to understand and provided with humility. Instead of declaring "Behold, this is the truth, listen to us!," scientific communications and public health measures should be delivered as: "This is what we know now, this is how we know it, and this information may change as we learn more." This kind of messaging will be more effective at reducing "rogue science" perpetuated across social media and increase faith in the scientific process and its inexorable flux. Messaging should work to humanize scientists, making them people too, who can and will make mistakes. Increasing public faith in science is an incredibly important task. Without science, a virus — either this one or the next — will win.

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