

## COMMENTARY

# Managing COVID-19 going forward—the lessons from history

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Every fall, we heed the call for an annual flu vaccination tailored to the expected strain of influenza virus for that winter. This was not always the case. There was a time when there was no need for a seasonal vaccine because there were no yearly flu infections. Indeed, the first ‘epidemic’ of respiratory infections resembling influenza was not until the early 16th century, and recurrences, when they occurred, were generational rather than annual phenomena. It was not until the 20th century—heralded by the 1918 ‘Spanish’ flu pandemic—that influenza epidemics became more frequent.

Like coronavirus disease 2019 (COVID-19), influenza is caused by a respiratory virus that evolves in both animal and human reservoirs, and both infections require a level of human activity and interconnectivity that did not exist before the 20th century, with its densely populated cities, modern agricultural practices and networks of international commerce and travel. Seasonal influenza was the result of the linkages we call globalization, and we have managed it well by combining viral surveillance, vaccination and public health measures, with only occasional ‘breakthroughs’, as with the 2009 H1N1 pandemic.

COVID-19 is no different. Coronaviruses have long existed in human and animal populations, causing mostly minor colds. Eighteen years ago, SARS-1 emerged from a coronavirus, followed by MERS, and then SARS-CoV-2 in 2019. Just like seasonal influenza, but more debilitating and lethal, the COVID-19 virus and future variants can be faced down with the same measures that have worked for influenza. A five-step call to arms based on science and history is needed. The strategy is, first, to deploy the tools of emergency response and then to consolidate the

victory by removing the kindling that led to the conflagration in the first place.

First, global viral surveillance: The science of viromics or virus classification has advanced rapidly, augmented to an astonishing degree by cheap, rapid and automated technologies. The positioning of unified virus surveillance and sequencing capabilities, coordinated internationally, would cost little while providing time to identify new variants and produce countermeasures. It has worked for the flu.

Next, vaccines: Like influenza, COVID vaccines will have to be tailored to the latest viral strain. Fortunately, we have had a very lucky break with the RNA vaccines, which are simple to engineer and will become less costly and easier to produce and distribute. Second-generation RNA vaccines requiring lower doses and fewer jabs are in development. They also lend themselves to production facilities suitable to most countries and can be more easily administered at the point of origin of new epidemics.

Third, antiviral drugs: Beyond the deployment of antiviral drugs to reduce disease, computational modeling and antibody engineering make possible the prepositioning of variant-specific antibodies, whose efficacy can be predicted, to protect those at greatest risk to outbreaks of new variants—everywhere in the world.

Fourth, reimagined cities: Epidemiological and historical studies have demonstrated that crowded cities and disadvantaged populations are the front lines in the battle against pandemics. Human vulnerability to such infections correlates with poverty, dense living and working conditions and poor access to

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health care. It is time to reimagine urban land use. Historically, there are strong precedents. In the nineteenth century, pandemics of cholera inspired the transformation of cities during the 'sanitary revolution' that occurred initially in the UK. Britain retrofitted its cities with the sanitary infrastructure of sewers and drains, lavatories, safe drinking water, paved streets and housing regulations. This example spread across the industrial world and two European cities—Naples and Paris—were rebuilt to make them epidemic-proof. Cholera was banished from the developed world, saving millions of lives. The cost was recouped over time by the avoidance of the sickness, death, lost productivity, economic disruption and medical expense.

The current pandemic indeed has provided impetus for an international initiative with the objective of the '30-min city'. To date, the vision of the movement has been most fully realized in Paris. But 40 cities worldwide have declared themselves to its principles of convenient accessibility for all in urban areas, including Barcelona, Seoul, Buenos Aires, Sydney, Los Angeles and Portland, Oregon. The developed world will lead this effort but what about the megacities of Asia, Africa and Latin

America, which will remain ripe for the emergence of new variants and pandemics? What are we waiting for?

Finally, the fifth concern: global equity: The concepts are established. The science, the historical precedents, and the benefits are clear. Much of the scientific infrastructure exists and would need only expansion and reinforcement. But there is the significant final and perhaps a most challenging concern of global inequities and disadvantaged populations, where the costs of urban and rural restructuring would require sustained political will and commitment shouldered by the more advanced economies. Yet, the costs would be more than offset by long-term human and economic gains obtained by preventing or mitigating future pandemics. A sustainable and healthy pandemic-free future requires the implementation of already available and future scientific advances, reapplication of historic public health precedents, and the infusion of significant and sustained resources, equitably distributed to confront and reverse the social and structural inequities that drive historic pandemic vulnerability and the current global crises. There is little time to spare.

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