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Preparedness, Policy And Patients – Learning From The Pandemic

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By Adrienne Rivlin and Martin Billman

THE COVID-19 PANDEMIC IS SERVING AS a catalyst to draw attention to other destructive infectious diseases that continue to ravage communities across the world. This is to be welcomed, but we must also ask what we have learnt from our recent experiences that can be deployed to help accelerate approaches to fighting other, similarly devastating, established and emerging infectious diseases.

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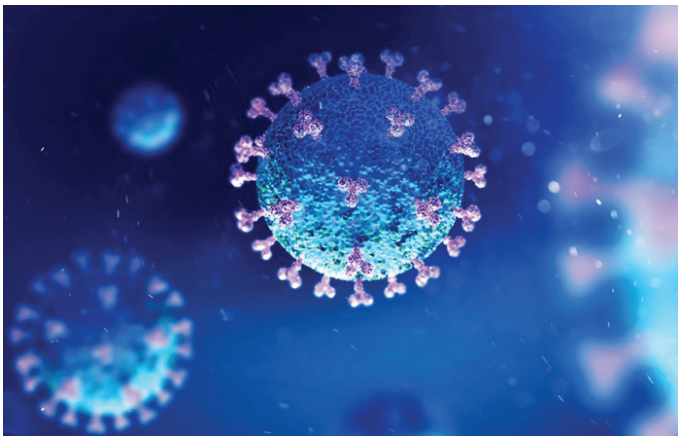
Notwithstanding COVID-19, existing infectious diseases wreak significant health, social and economic havoc across the world each year (see Exhibit 1).

According to a recent analysis by the National Bureau of Economic Research, HIV, tuberculosis and malaria cause millions of deaths and an estimated $4.5trn in economic damage per year, greater than Germany's total annual economic output. According to data from a 2019 Harvard analysis, seemingly innocuous disease such as seasonal influenza kills 390,000 people per year on average, including 27,000 to 130,000 individuals in the US and Europe, whilst an estimated 20 to 40 countries experience significant new disease outbreaks each year, a trend that has been increasing since 2010.

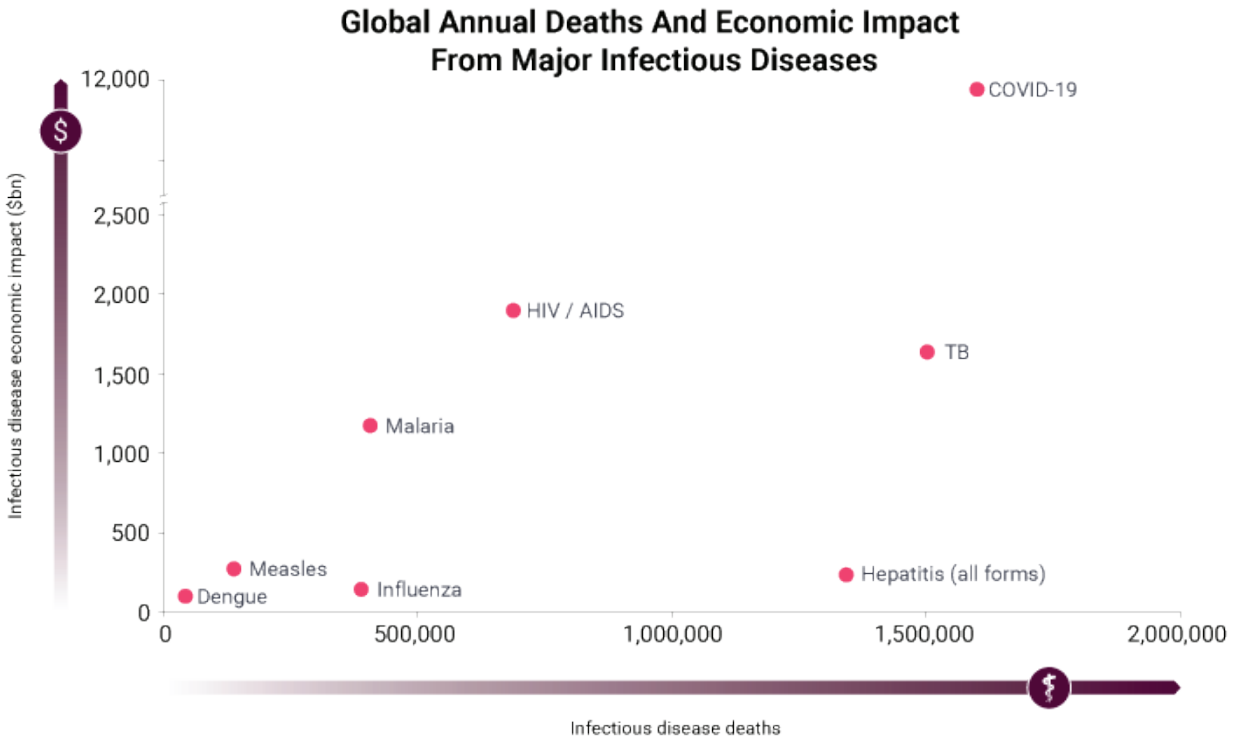


Furthermore, of the 20 neglected tropical diseases prioritized for intervention by WHO, 19 are bacterial, parasitic, viral and fungal infections such as Chagas disease and leishmaniasis, affecting over one billion people worldwide, causing countless millions of deaths a year and contributing to enormous social and economic burden from social stigma, physical disabilities, disfigurement, blindness, discrimination, loss of social status, malnutrition, growth failure and impaired cognitive development.

As Benjamin Perry from the Drugs for Neglected Diseases initiative states: "The human and economic cost of infectious diseases, especially neglected ones, is underrecognized and of a truly astonishing magnitude."

Given the staggering breadth and toll of these figures, and the likelihood that they will, without substantial intervention, continue to increase, it is important that future, as well as ongoing pandemics, are prioritized in the same way as COVID-19, both in terms of financial funding and in the public consciousness.

Exhibit 1.



Source: Dobson *et al.* 2020; Bloom *et al.* 2020; L.E.K. Research

To draw out the lessons we should learn from the COVID-19 pandemic, we interviewed a range of infectious disease and public health specialists from around the world, including leading scientists and clinicians, pharmaceutical and diagnostic company industry experts as well as funders and NGOs active in the space. We also spoke to advisors counseling governments' responses as well as clinicians and managers on the front-line of the fight against COVID-19, influenza, TB, HIV, hepatitis C and neglected diseases. Finally, we covered all aspects of the value chain from early-stage research, clinical development, manufacturing, supply chain and logistics. We have summarized key lessons from the COVID-19 experience for other infectious diseases into three themes: pandemic preparedness; policy; and patients (see Table 1).

Pandemic Preparedness

Lesson 1: Monitor For Emerging Threats And Prepare A Rapid Coordinated Response

Robust surveillance systems are a critical component of pandemic preparedness because they help to identify and define the landscape of potential future disease outbreaks.

According to Professor Charles Bangham, co-director of the Institute of Infection, Imperial College London: "While it is inherently unpredictable which new disease will emerge and when, it is clear where diseases are coming from: areas with zoonotic transfer from birds, animals such as bats, bushmeat hunting, and ecological disturbance."

The early detection of diseases as they emerge

maximizes the chance of an early response and controlling an outbreak before it can spread out of control. It is therefore unfortunate that funding for monitoring programs tasked with identifying viruses which could cause global public health emergencies, such as USAID PREDICT, is often deprioritized once the immediate crisis has passed. Hopefully, the scale of the COVID-19 impact will serve to reinforce the importance of longer-term funding for national and international monitoring systems.

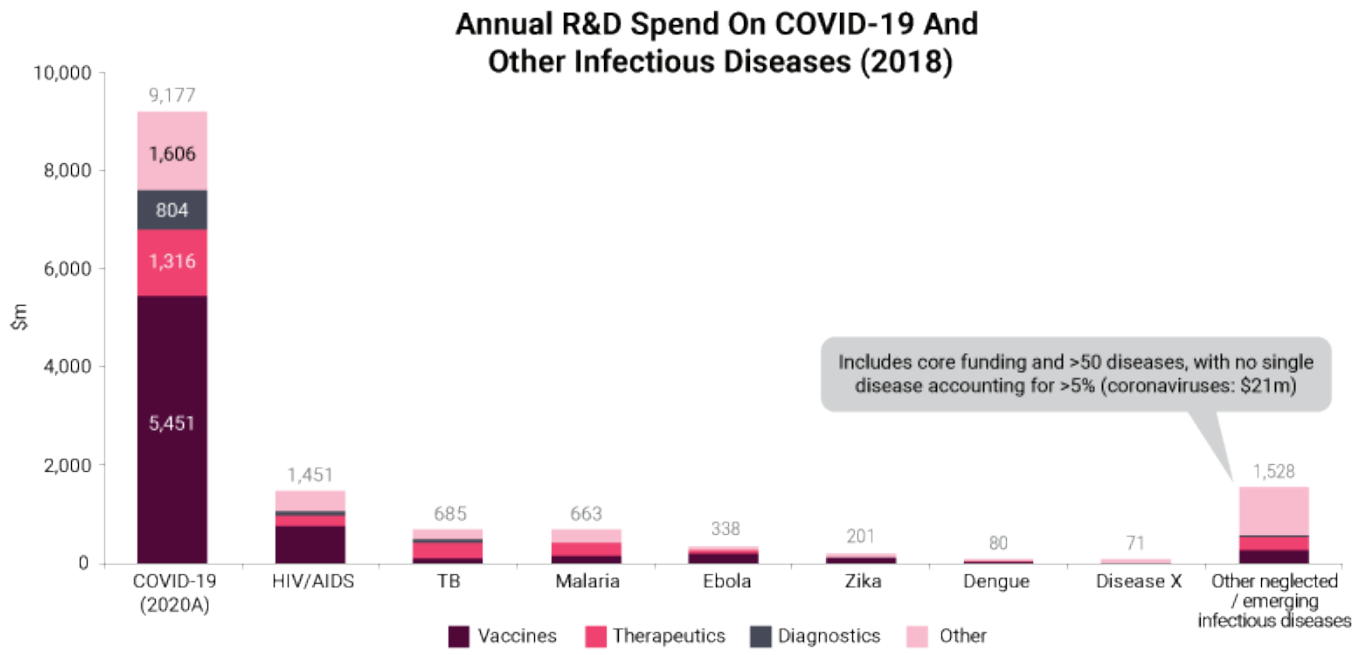
Allied to appropriate monitoring is the need for a rapid, coordinated response within and between nations. At the start of the COVID-19 pandemic, collaboration between agencies within national boundaries as well as between countries and continents was noticeably poor.

A key lesson to be learnt was also the criticality of supra-national agencies in coordinating the pandemic response. Barry Greene, the former managing director, finance and operation at GAVI, said: "I hope that countries recognize the need for transparency, collaboration and a strong WHO as a result of COVID-19."

Lesson 2: Invest In Disease-Agnostic R&D

The world was relatively poorly prepared for a coronavirus outbreak: prior to COVID-19, R&D spend on coronaviruses totaled just $21m in 2018, while disease-agnostic "Disease X" platforms accounted for $71m, according to data from Policy Cures Research. In comparison, by October 2020 approximately $9bn had been spent on COVID-19 R&D. This represents an almost 100-fold increase over the total of the two previous categories in a period of fewer than 12 months (see Exhibit 2).

Exhibit 2.



Source: Policy Cures Research

Disease-agnostic R&D to develop "Disease X" vaccine platforms will hopefully receive a welcome increase in funding given their now well-understood importance.

Beyond vaccines, there remains significant untapped potential for "tool-boxes" of molecules against potential pandemic pathogens, as highlighted by Mat Todd, professor of drug discovery at University College London. He said: "Molecules need to be developed in advance. That's possible if you target so-called "conserved" targets that are relatively constant over time. Viruses rely on host machinery to work properly, so you can target that machinery before the virus exists."

Lesson 3: Rapidly Redirect The Focus Of The Biopharmaceutical Industry

The biopharmaceutical industry and its collaborators have demonstrated exceptional agility and speed to focus rapidly on an emerging global crisis. Whether in the rapid repurposing of existing patented molecules (e.g. remdesivir from Gilead Sciences, Inc.), expediting clinical development timelines or in bringing to bear its enormous manufacturing strength and cold chain logistical know-how, the industry has firmly established its credentials in aligning purpose with profit when in the face of a global catastrophe.

For Gilead SVP Jacopo Andreose, there are now two important areas beyond the current pandemic on which the industry ought to continue to focus. The first is the new technologies that have already proven effective, for instance the breakthrough in mRNA vaccinology. "What other new technologies are out there for other infectious diseases that might work?" asks Andreose. The second is the massive effort already undertaken to identify drugs that could work against COVID-19. "Can we say that we have done this as impeccably yet for other infectious diseases?" he questions.

Lesson 4: Invest In Health System Resilience

Initiatives are urgently required to make health systems more resilient against future disruption caused by infectious disease outbreaks to minimize avoidable indirect mortality and morbidity.

This is as true in the more developed health care systems as it is among the developing nations. For instance, an estimated additional 33,890 cancer deaths are predicted to occur in the US in 2021 due to delayed diagnoses, whilst the Global Fund has estimated that up to 1.4 million additional people could die as a result of disruption in the prevention and treatment of HIV, TB and malaria. There is good reason to be worried: during the 2014 Ebola epidemic in Guinea, more additional deaths occurred from disrupted malaria treatments than from Ebola itself.

Potential solutions include increased reliance on telehealth, investment in more robust supply chains, and longer prescriptions, so that patients with daily treatments are less susceptible to health care disruption.

Many of these changes bring benefits outside of a pandemic context as well, as noted by one director of global public health at a large pharmaceutical company who said: "COVID-19 has forced decades' worth of telehealth adoption in a span of months, and it's going to have lasting benefits: reduced person-person risk, lower provider costs, patient travel costs, and even lower carbon costs."

A recent report in Science Magazine, estimated that preventative measures against future pandemics would cost the world approximately $26bn per year. When compared to estimates of the global economic cost of this pandemic of anywhere between $12trn and $28trn, this is likely to be viewed as a reasonable investment.

Table 1.

Summary Of Lessons Learnt From The Current COVID-19 Pandemic

Theme	Lesson	Summary
Pandemic preparedness	• Monitor for emerging threats, and prepare rapid responses	• Monitoring of emerging diseases as well as likely sources of zoonotic transfer • Infrastructure to report and rapidly respond to outbreaks (including through international collaboration)
	• Invest in disease-agnostic R&D	• Further development of platforms able to rapidly develop and test therapeutics, vaccines vs. the next "Disease X"
	• Rapidly redirect the focus of the biopharmaceutical industry	• Ability of industry to scale development, production and distribution of drugs, materials, tests etc.
	• Invest in health system resilience	• Reduction of health systems' and initiatives' susceptibility to COVID-style disruption (e.g. supply chains) • Minimization of indirect additional suffering and deaths
Policy	• Increase R&D funding, and expedite development timelines	• Significant acceleration of development timelines, including by regulatory agencies, without sacrificing efficacy or safety • Manufacturing and distribution scaling at risk
	• Increase data transparency and collaboration	• Consolidation of data sources (e.g. patient demographics, clinical outcomes) for reporting, research and critical disease understanding
	• Improve medical access	• Removal of barriers to access to diagnostics, treatment, mental health care etc., particularly in higher risk groups
Patients	• Boost public health awareness	• Public engagement in non-pharmaceutical interventions ('social distancing', hand washing, mask use etc.)
	• Focus on messaging and maintenance of public trust	• Clarity, consistency, coodination and cadence of messaging from governments and other stakeholders to maintain public trust in interventions, vaccines etc. (including combating of misinformation)
	• Invest in digital health technology	• Digital and technological solutions such as contact tracing, home testing etc.

Policy

Lesson 5: Increase R&D Funding And Expedite Development Timelines

A COVID-19 vaccine was authorized for use by the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK fewer than 300 days after the commencement of clinical trials, demolishing the previous record of four years (Merck's mumps vaccine; see Exhibit 3). This is not just a reflection of investment in vaccine development, but also of coordination and reform amongst regulatory agencies.

The US Food and Drug Administration for instance has streamlined its communications and turnaround times, as well as making greater use of umbrella trials and emergency use authorizations to dramatically accelerate development timelines for all virus countermeasures.

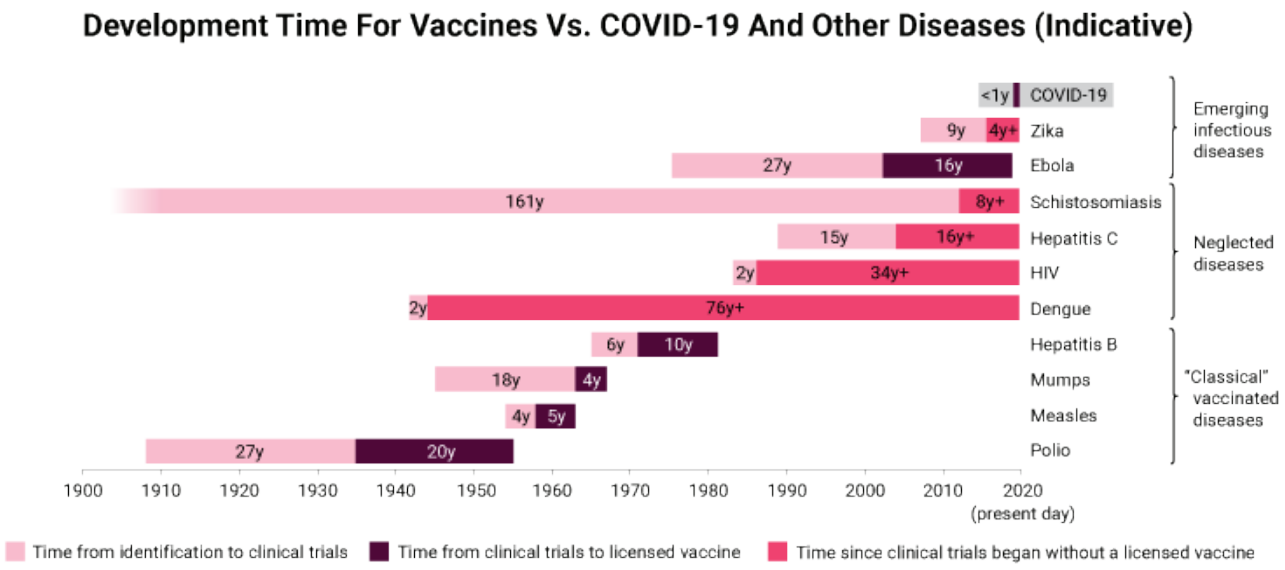
The FDA already plans to make aspects of its acceleration efforts around the pandemic permanent, and the potential for multiple disease areas is exciting. This was noted by one senior executive at a large pharmaceutical company, who commented: "The most impressive thing to me has been the regulatory streamlining and use of EUAs to really accelerate development – why can't we do this in areas with high existing unmet need outside of a pandemic?"

More broadly, the level of R&D investment in COVID-19 over the past year has dwarfed that seen in other infectious diseases, even those with extremely high burdens (see Exhibit 3). Witnessing the success of development programs with such significant financial backing raises the hope that neglected infectious diseases could also see greater and faster progress

through larger investment.

Furthermore, Joe Simmonds-Issler, chief of staff of the Coalition for Epidemic Preparedness Innovations (CEPI), believes that technologies that have been validated in response to this pandemic, such as mRNA or adenovirus vaccines, may have direct applications for other diseases. He said: "The University of Oxford are working on other diseases for their adenovirus vaccine

Exhibit 3.



Source: Kim *et al.* 2020, Bukh 2016, Pharmaceutical Technology 2018, L.E.K. Research

platform, and their processes will be more validated and streamlined through this experience."

Lesson 6: Increase Data Transparency And Collaboration

This pandemic has also demonstrated the need for, and benefits from, data transparency and collaboration. Michele Robbins, a pharmaceutical executive with more than 20 years' experience working in HIV, said: "We witnessed the importance of sharing scientific and clinical results quickly amongst different organizations and institutions. Sharing the data certainly contributed to finding solutions more quickly and more cost-effectively."

Countries such as the US, the UK, France and Germany have sometimes suffered from having data that is fragmented and hard to access, while researchers stress the need for centralized and simplified sources to track, for example, epidemiology and patient outcomes.

Collaborative efforts to address this problem have, though, been evident, including those arising from pharmaceutical company alliances (e.g. between GlaxoSmithKline plc and Sanofi) and pharma-academia collaborations (e.g. between AstraZeneca PLC and Oxford University), as observed by Jacopo Andreose, SVP, Gilead, who said: "The infectious disease sector has always been relatively collaborative but this level is new – advocates for collaboration within our industry are being really vocal."

These partnerships have allowed companies to focus on their strengths, pool resources and drive innovation, with great potential for progress in other diseases.

COVID-19 has also brought about increased

coordination and collaboration, as well as investment in product commercialization, specifically in manufacturing and distribution. Multiple organizations, most notably CEPI and the US government's Operation Warp Speed, have spent billions of dollars funding the manufacture of vaccines and therapeutics "at risk," to minimize waiting times, if they are found to be effective and safe.

The world is set to reap the benefits of this with billions of vaccine doses likely to be available throughout 2021. Paul Barnsley, of the think tank Policy Cures Research, states that the logic of manufacturing at risk to reduce timelines could be extended to other high-burden diseases: "We are manufacturing at risk to get the vaccine out there as quickly as possible and save as many lives as possible. This argument for saving lives by saving time applies equally to diseases like HIV and TB as well."

Lesson 7: Improve Medical Access For Both Physical And Mental Health

A society's ability to defeat infection is predicated on comprehensive access for its citizens to vaccines, testing and treatment. This is especially true with diseases where patients are infectious before symptoms arise, or where infection is a source of stigma. This is true for COVID-19 but also diseases such as HIV and hepatitis C. Beatriz García Fidalgo, of Abbott Laboratories Ltd comments: "In the absence of a vaccine, defeating these diseases is contingent upon identifying high-risk groups and then proactively screening them and offering treatment; by the time they show up at the doctor's office it's often too late."

COVID-19 has also highlighted the mental health impacts of disease: mental health impairment from the pandemic is estimated to have cost the US$1.5trn so far, according to a recent report in JAMA, either from direct symptoms ("Long COVID") or related to stay-at-home measures. Whilst the burden of COVID-19 is deeply regrettable, there are significant mental health implications of other infectious diseases too, and the focus on the psycho-social elements of these diseases – particularly ones with chronic or extended duration such as HIV, hepatitis and TB – is likely to be welcome.

Patients

Lesson 8: Boost Public Health Measures

Non-pharmaceutical public health measures themselves can often be the most powerful tools against an infectious disease if they are embraced by individuals and groups. The need for, and importance of, public health awareness has never been clearer: a study published by the New York Times in November 2020 showed a striking association between the stringency of US states' containment measures and their relative numbers of COVID-19-related hospitalizations.

Blythe Adamson, a leading infectious diseases epidemiologist and affiliate professor at the University of Washington, agrees. She said: "The social determinants of health are often overlooked but I think that the COVID experience has engendered greater empathy for their importance."

Non-pharmaceutical interventions, such as "social distancing," undertaken for COVID, also seem to be effective against a broader range of respiratory diseases, including TB and influenza. One senior executive at a large pharmaceutical company said: "If everyone were to follow the same measures for TB as for COVID, we would see astronomical decreases in patient numbers." In the case of influenza, the southern hemisphere's winter spike did not materialize in 2020, and it appears to be significantly curtailed in the beginnings of the northern hemisphere's winter as well.

Lesson 9: Focus On Messaging And Maintenance Of Public Trust

The effectiveness of public health measures, as well as that of vaccines and therapeutics, is contingent on the public's acceptance of them. The need for clear, consistent, and coordinated messaging has been demonstrated in the struggles of multiple countries, as well as the success of nations such as China, South Korea and New Zealand.

Changing behavior can be incredibly powerful but

is also very difficult and requires a lot of focus from governments," said an infectious diseases pharmacist in a UK hospital. This principle applies to all infectious diseases, from controlling STIs to maximizing vaccine uptake for influenza and previously common childhood infections. The same point can also be made for the importance of combating misinformation, which was already an issue for vaccines and other medicines but has been amplified during this pandemic.

Lesson 10: Invest In Digital Health Technology

Digital health technology has proved an important tool during the COVID-19 pandemic. Rapidly developed digital solutions in various fields including screening, clinical management, planning and tracking, medical supplies, contact tracing and quarantine/self-isolation have all played a role in containing or helping to manage the infection rate. There is emerging evidence for countries such as South Korea that indicate that flatter infection incidence curves are attributable, at least in part, to better adoption of digital technologies.

In particular, the innovation in digital solutions that aid patients' fight against disease (with due consideration for data protection) has been notable. Contact tracing apps and the first rapid home tests have been successfully rolled out; these advancements may have lasting benefit in the fight against other diseases. One leading infectious diseases physician said "If we think about some infectious diseases like RSV, there are now rapid tests that can give you results within minutes which are as accurate as samples sent to the lab. For infectious diseases where contact tracing is required, digital health technology could be adopted to improve existing systems."

Lasting Change

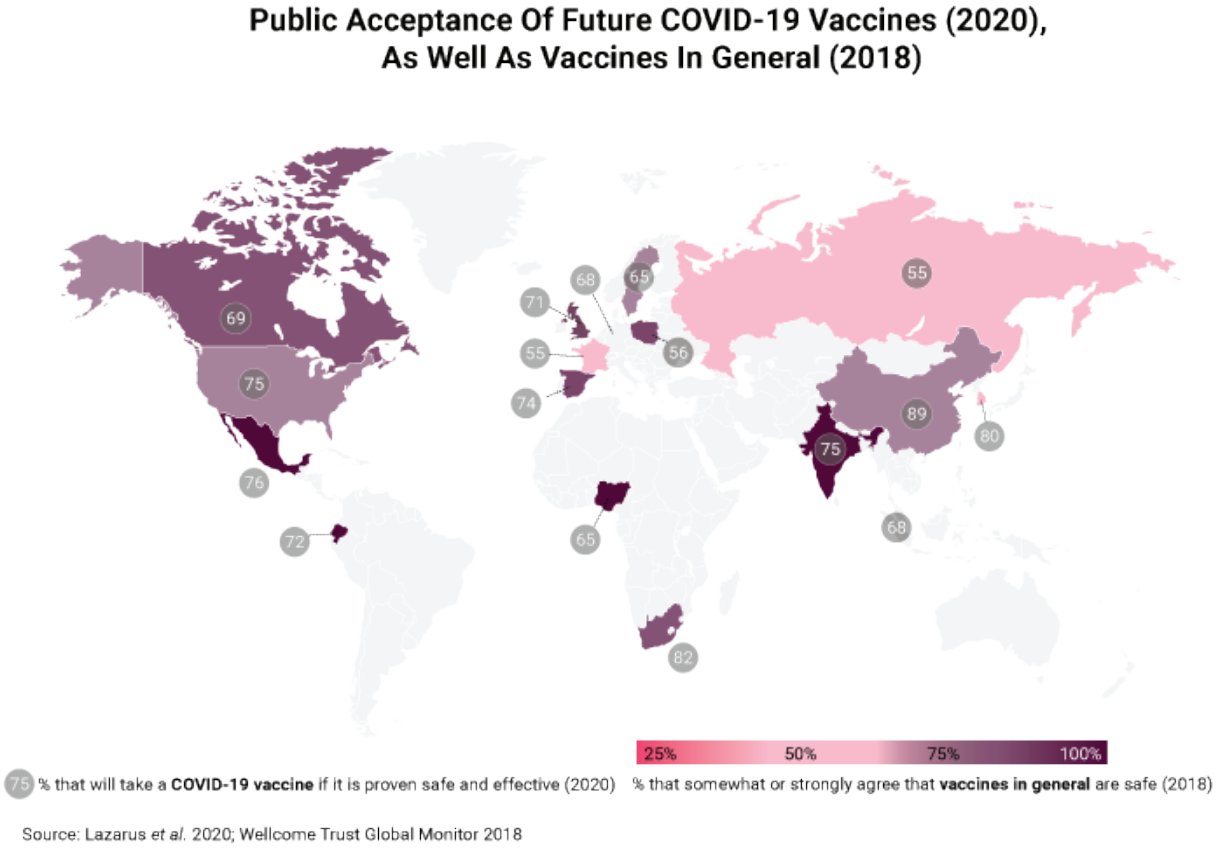
The health care, social and economic effects of COVID-19 will continue to be felt for years, if not decades to come. We have already witnessed a transition away from pre-COVID approaches and behaviors, such as large offices or a reliance on face-to-face health care. Similarly, pre-existing trends around remote working and telehealth have been accelerated. There is also the potential for new practices to emerge from this pandemic, such as R&D and regulatory reforms and new, improved public health strategies.

Countries are about to embark on one of the largest and most logistically challenging vaccine roll-outs ever witnessed and, as they do so, one of the biggest lessons may yet be to come: how to overcome the increasing problem of vaccine "hesitancy." A study published in The Lancet in October 2020 revealed the scale of this challenge in countries such as Russia and France (see Exhibit 4). However, optimistically, in many countries the degree of confidence in a COVID- 19 vaccine was often higher than that generally seen for vaccines overall. We can hope that a successful COVID-19 vaccine roll-out could serve as a reminder of the power and importance of vaccines more generally.

CEPI's Joe Simmonds-Issler said: "We will emerge from this pandemic with new vaccines and platforms, companies and organizations experienced with developing, manufacturing and distributing vaccines, therapeutics and diagnostics at an unprecedented scale, and a society that has lived through the experience of the disruptive power of disease. We will absolutely have more tools against disease, but we will only go as far as our political will and financial investments can take us."

Just as important perhaps as any individual new technology or policy is the potential for a greater understanding, both among decision makers and the public, of the disruptive and destructive potential of disease at the societal and personal level. This burden can be felt just as keenly for more familiar infectious diseases such as influenza, HIV or TB, as well as non-communicable diseases such as diabetes and cancer. There are an abundance of lessons and new tools for us to learn from and use as a result of this pandemic; it is then a question of how well we choose to use them.

Exhibit 4.



This article was written by Adrienne Rivlin, partner, and Martin Billman, senior life science specialist, leveraging the Global L.E.K. Healthcare Insights Center, and additional research support from Thomas Pangia.