Rethinking Global Pharmaceutical Policy

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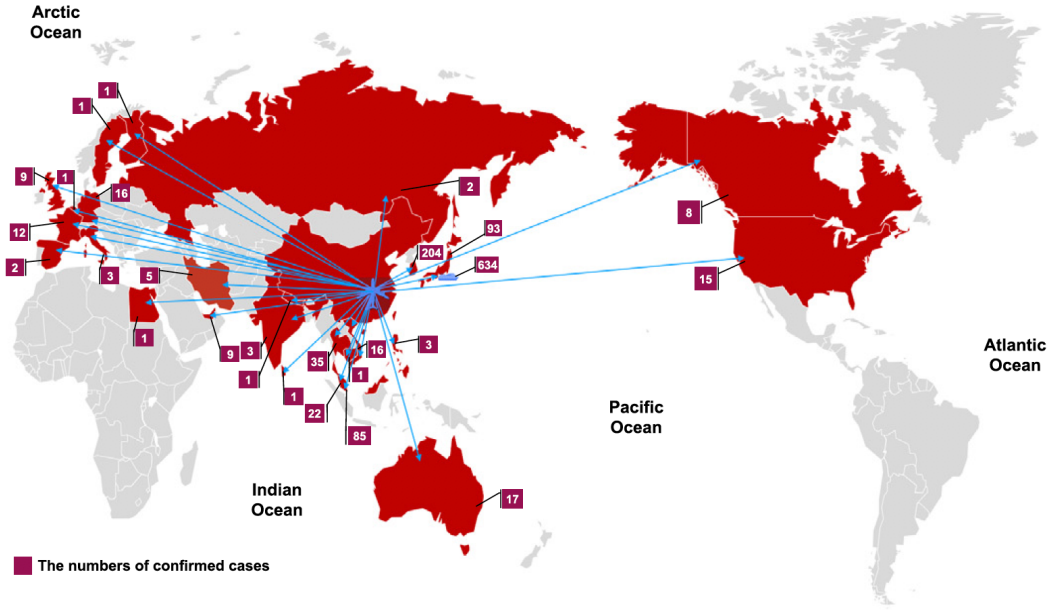
Appendix 6: COVID-19

(version 1, December 2024)

In December of 2019, a small group of people in Wuhan City, China, contracted a hitherto unknown disease. Exactly how they acquired it remains uncertain (and sharply contested), but the leading explanation is that one or more of them came into contact with an infected wild animal in an outdoor "wet" market.[1] The disease proved to be highly infectious and soon spread rapidly through the population of the city. In January of 2020, cases began to appear in other cities in China and then in other countries to which residents of (or visitors to) Wuhan had traveled.[2] The footprint of the disease two months after its initial appearance is shown below.

Figure 1: The Spread of COVID-19 as of February 20, 2020[3]



It was quickly determined that the cause of the disease was a coronavirus -- a class of viruses that often causes intestinal and respiratory disorders in both animals and humans. (The "SARS" outbreak, which killed 8000 people in 26 countries during 2002-2003, was caused by

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[1] For some of the contributions to the ongoing debate over the origins of the pandemic, see Kristian G. Andersen et al., "The Proximal Origin of Sars-Cov-2," *Nature Medicine* 26 (2020).; Jesse D. Bloom et al., "Investigate the Origins of Covid-19," *Science* (2020), https://science.sciencemag.org/content/372/6543/694.1.; Edward C; Holmes et al., "The Origins of Sars-Cov-2: A Critical Review," (2021), https://zenodo.org/record/5112546#.YSTUdS-cYxk.; Xiao Xiao et al., "Animal Sales from Wuhan Wet Markets Immediately Prior to the Covid-19 Pandemic," *Scientific Reports* 11 (2021); Ellen Nakashima, Yasmeen Abutaleb, and Joel Achenbach, "Biden Receives Inconclusive Intelligence Report on Covid Origins," *Washington Post*, August 24, 2021.

[2] See Jiumeng Sun et al., "Covid-19: Epidemiology, Evolution, and Cross-Disciplinary Perspectives," *Trends in Molecular Medicine* 26, no. 5 (2020): 484.; Di Wu et al., "The Sars-Cov-2 Outbreak: What We Know," *International Journal of Infectious Diseases* 94 (2020).

[3] See Sun et al., "Covid-19 Epidemiology."

another member of the same class.) The new virus was labelled, "SARS-CoV-2," and the disease it produces, "COVID-19" (an acronym for "coronavirus disease of 2019").

The disease is not yet fully understood, but its manifestations are well known: Roughly half of infected people are asymptomatic.[4] When symptoms do appear, they usually resemble those associated with influenza: cough, fever, headache, body aches, and so forth. In a substantial minority of cases, however, the patients experience more severe symptoms: among them, pneumonia, dangerously low oxygen levels in the blood, neurological disorders, and damage to major organs.[5] These are especially common in – but are not limited to – persons with comorbidities, such as obesity, diabetes, heart disease, and compromised immune symptoms. Some of the people with severe symptoms are able to recover, especially if they have access to ventilators, oxygen, hospitals, and high-quality care. Others, however, continue to decline and eventually die. Of those who do recover, some experience serious residual symptoms (collectively sometimes called "long Covid") for months or years.[6]

As the threat posed by this disease became increasingly evident, the leaders of a few multilateral institutions – most notably, the G7 and the World Health Organization – attempted to organize a coordinated international response to it. Had those efforts succeeded, the history of COVID-19 might have resembled that of SARS or Ebola. But they did not.[7] Instead, the governments of most nations adopted various unilateral strategies in hopes of halting the spread of the virus into and within their own populations. Most attempted to limit the entry into their territories of infected persons. Some closed their borders altogether or blocked entry from regions with high case loads. Some instituted and enforced mask-wearing or social-distancing requirements. A few adopted rigorous systems for identifying infected persons, tracing everyone with whom they had come into contact, and imposing quarantine requirements on all of them. Many closed schools, restaurants, places of worship, and workplaces.[8]

In general, developed countries initially fared less well than developing countries – in sharp contrast to the pattern that, as we have seen, characterizes most infectious diseases. In particular, in 2020 the United States and the countries in western Europe had the highest case loads and mortality rates. Not all developed countries fared so poorly; for example, Japan, Norway, New Zealand, and Australia initially seemed to have dodged most of the bullets. But overall, rich countries suffered. By contrast, in the early stages of the pandemic, most poor countries were

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[4] See Daniel P. Oran and Eric J. Topol, "Prevalence of Asymptomatic Sars-Cov-2 Infection: A Narrative Review," *Annals of Internal Medicine* 173, no. 5 (2020).

[5] See, e.g., Julie Helms et al., "Neurologic Features in Severe Sars-Cov-2 Infection," *New England Journal of Medicine* 382, no. 23 (2020).; Victor G. Puelles et al., "Multiorgan and Renal Tropism of Sars-Cov-2," ibid.383.

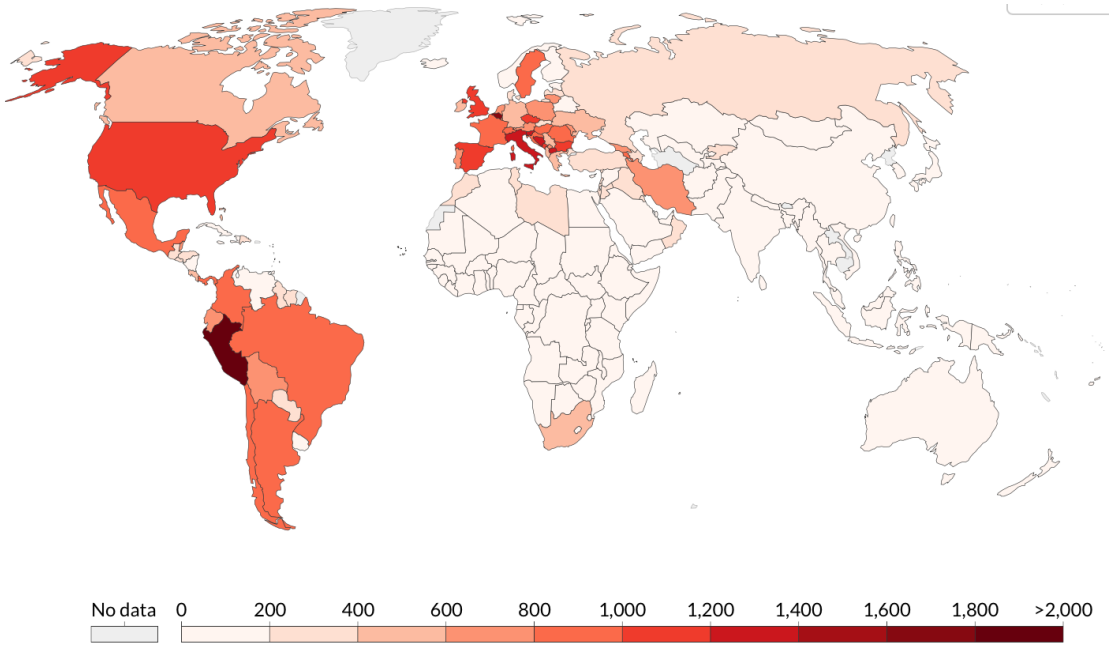
[6] See Bjørn Blomberg et al., "Long Covid in a Prospective Cohort of Home-Isolated Patients," *Nature Medicine* (2021).; Lixue Huang et al., "1-Year Outcomes in Hospital Survivors with Covid-19: A Longitudinal Cohort Study," *Lancet* 398 (2021).

[7] For an effort to explain the failure of these efforts, see Colin Kahl and Thomas Wright, *Aftershocks: Pandemic Politics and the End of the Old International Order* (New York: St. Martin's Press, 2021).

[8] For descriptions and analyses of the strategies adopted by different governments, see Peter Baldwin, *Fighting the First Wave: Why the Coronavirus Was Tackled So Differently across the Globe* (Cambridge University Press, 2021).; Ho Yeung Lam et al., "The Epidemiology of Covid-19 Cases and the Successful Containment Strategy in Hong Kong–January to May 2020," *International Journal of Infectious Diseases* 98 (2020).; Matteo Chinazzi et al., "The Effect of Travel Restrictions on the Spread of the 2019 Novel Coronavirus (Covid-19) Outbreak," *Science* 368 (2020).

largely spared. Again, there were exceptions; for example, Ecuador, Peru, and (to a lesser extent) South Africa were devastated. But in general, developing countries had many fewer cases per capita. This unusual pattern is evident in Figure 2, which shows the cumulative deaths per million people in each country as of December 31, 2020.

Figure 2[9]



Source: Johns Hopkins University CSSE COVID-19 Data

In 2021, however, the rich countries began to recover, while the poor countries deteriorated. The cause of the improvement in developed countries was not, as one might have expected, the discovery and distribution of drugs that could cure COVID-19. To be sure, many candidates were tried, but few conferred much benefit.[10] Some, such as hydroxychloroquine, proved useless or worse.[11] Remdesivir, an anti-viral drug produced by Gilead, initially seemed capable at least of shortening the duration of patients' hospital stays, but even that benefit proved elusive, and eventually the WHO withdrew its endorsement of the drug as a COVID treatment. [12]

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[9] Source: https://ourworldindata.org/covid-deaths.

[10] See Haiou Li et al., "Updated Approaches against Sars-Cov-2," *Antimicrobial Agents and Chemotherapy* 64, no. 6 (2020).; Dwight L. McKee et al., "Candidate Drugs against Sars-Cov-2 and Covid-19," *Pharmacological Research* 157 (2020).

[11] See, e.g., "FDA cautions against use of hydroxychloroquine or chloroquine for COVID-19 outside of the hospital setting or a clinical trial due to risk of heart rhythm problems" (July 1, 2020), https://www.fda.gov/drugs/drug-safety-and-availability/fda-cautions-against-use-hydroxychloroquine-or-chloroquine-covid-19-outside-hospital-setting-or

[12] For the tangled history of remdesivir, including the efforts, ultimately pointless, to increase its availability in developing countries, see John H. Beigel et al., "Remdesivir for the Treatment of Covid-19 — Final Report," *New England Journal of Medicine* 383, no. 19 (2020).; "Gilead prices remdesivir at $2,340 per patient for developed countries" European Pharmaceutical Review (June 30, 2020); https://www.europeanpharmaceuticalreview.com/news/122592/gilead-prices-remdesivir-at-2340-per-patient-for-developed-countries/ ; Ellen t' Hoen, "Remdesivir developed country price announced," Medicines Law and Policy (June 30, 2020), https://medicineslawandpolicy.org/2020/06/remdesivir-developed-country-price-announced/; JV

As of this writing, three monoclonal antibodies are showing the most promise as COVID treatments, but their distribution thus far has been too small to make a significant dent in the pandemic. [13]

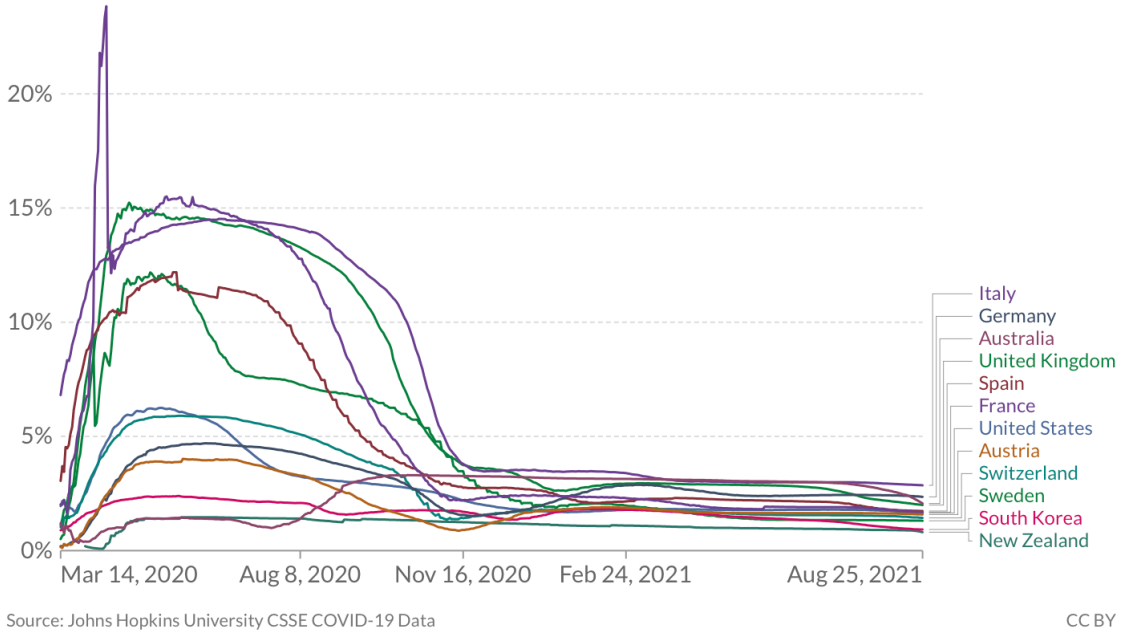
Instead, three factors enabled most developed countries to begin to curb the epidemic. First, as more information about the disease came to light, public-health initiatives designed to impede transmission of the virus slowly became more efficient. Second, health-care workers developed and applied more effective techniques for keeping infected people alive until their bodies could repel the virus.[14] As a result, the case fatality rates in most developed countries plummeted:

Chamary, "The Strange Story Of Remdesivir, A Covid Drug That Doesn't Work" (Forbes (January 31, 2021).; "Gilead, "Voluntary Licensing Agreements for Remdesivir," https://www.gilead.com/purpose/advancing-global-health/covid-19/voluntary-licensing-agreements-for-remdesivir.

[13] See"COVID-19 Treatments and Therapeutics," https://www.hhs.gov/coronavirus/covid-19-treatments-therapeutics/index.html (last visited August 25, 2021).; NIH, "Anti-SARS-CoV-2 Monoclonal Antibodies," https://www.covid19treatmentguidelines.nih.gov/therapies/anti-sars-cov-2-antibody-products/anti-sars-cov-2-monoclonal-antibodies/**;** Harvard Medical School, "Treatments for Covid-19," (2021), https://www.health.harvard.edu/diseases-and-conditions/treatments-for-covid-19.**;** Kevin Weintraub, "After Slow Start, Demand for COVID monoclonal Antibodies Treatment Skyrockets," USA Today (August 25, 2021), https://www.usatoday.com/story/news/health/2021/08/25/monoclonal-antibodies-treatment-demand-skyrockets-covid-cases-climb/5579505001/

[14] See, e.g., Eric K. Wei, Theodore Long, and Mitchell H. Katz, "Nine Lessons Learned from the Covid-19 Pandemic for Improving Hospital Care and Health Care Delivery," *JAMA Internal Medicine* (2021), https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2782429; Donna Marbury, "3 Ways to Improve Healthcare Tech for Better Covid-19 Care," *HealthTech* (2020), https://healthtechmagazine.net/article/2020/11/3-ways-improve-healthcare-tech-better-covid-19-care; Ann Kavannah et al., "Improving Health Care for Disabled People in Covid-19 and Beyond: Lessons from Australia and England," *Disabiliity and Health Journal* 14 (2021); National Institutes of Health, "Coronavirus Disease 2019 (Covid-19) Treatment Guidelines," (2021), https://files.covid19treatmentguidelines.nih.gov/guidelines/covid19treatmentguidelines.pdf.

Figure 3: Case Fatality Rate in Representative Developed Countries: March 2020 to August 2021[15]



Last but not least, a huge investment of money and human resources resulted in the remarkably rapid development of several effective vaccines, large quantities of which were purchased by the governments of developed countries and made available to their residents.[16]

Unfortunately, the benefit that developing countries could reap from these three factors was limited. With respect to the first factor, several conditions common in those countries made it difficult to adopt or sustain public-health initiatives: houses are often close together (especially in the poor sectors of urban areas); most residents have neither savings nor credit and thus must go to work to survive; meager Internet access limits opportunities to work at home; lack of refrigeration necessitates daily shopping; and limited sanitation inhibits the adoption of protective measures.[17] With respect to the second, most developing countries lacked enough hospital beds and health-care workers to provide infected persons the kind of care that was increasingly available in high-income countries. With respect to the third, the bulk of the first wave of effective vaccines

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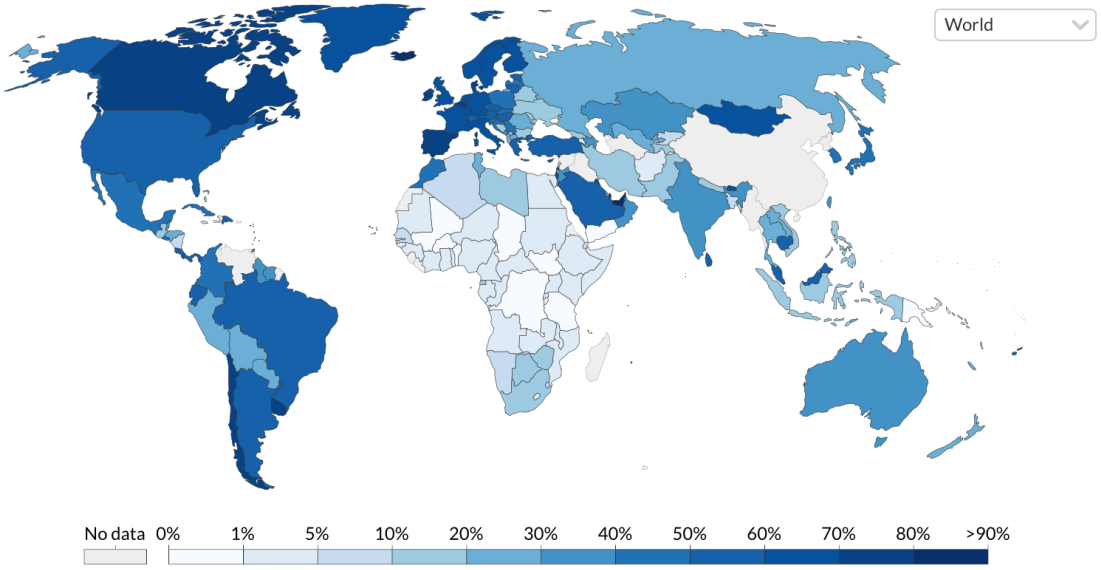
[15] Source: https://ourworldindata.org/mortality-risk-covid.

[16] As of this writing, seven COVID vaccines are included in the WHO's emergency use listing, and 19 have been approved by at least one national authority. *See* UNICEF, "Covid-19 Vaccine Dashboard," https://www.unicef.org/supply/covid-19-vaccine-market-dashboard (last accessed 30 June 2021). The remarkable story of the rapid development of these vaccines can be traced in Florian Krammer, "Sars-Cov-2 Vaccines in Development," *Nature* 586 (2020).; L.A. Jackson et al., "An Mrna Vaccine against Sars-Cov-2 — Preliminary Report," *New England Journal of Medicine* 383, no. 20 (2020).; L.R. Baden et al., "Efficacy and Safety of the Mrna-1273 Sars-Cov-2 Vaccine," ibid.384, no. 5 (2021). The funding strategies that made this possible are described in Chapter 2, Section A.1, below.

[17] See Matthew E Levison, "Covid-19 Challenges in Developing Countries," *Merck Manual* (2020).; Terrence McCoy and Heloísa Traiano, "Brazil's Densely Packed Favelas Brace for Coronavirus: 'It Will Kill a Lot of People.'," *Washington Post*, Masrch 21, 2020.; Yasmeen Serhan, "Where the Pandemic Is Only Getting Worse," *The Atlantic* (2020).; Brett Walton, "Healthcare Facilities in Developing Countries a High Risk for Coronavirus Transmission," *New Security Beat* (2020).

were purchased (typically well in advance of their manufacture) by developed countries, leaving little for the developing world.[18] As of this writing, the supply of vaccines to developing countries is at last gradually increasing, in part because of efforts by the COVID-19 Vaccines Global Access Facility ("COVAX") to secure vaccine batches on their behalf and in part because of modest donations by developed countries of doses that they find they do not need. But the flow remains insufficient to meet demand. As one might expect, the net result (evident in figure 4) has been radical disparity among countries in the administration of vaccines.

Figure 4: Share of the Population that has Received at Least One COVID-19 Vaccine Dose, August 14, 2021[19]



The fruit of this combination of factors: most countries in Latin America are now suffering at least as badly as those in North America and Europe, and variants of the virus are spreading rapidly in Africa, India, and Indonesia.[20] A short video, showing the erratic but seemingly inexorable shift in the concentration of COVID deaths from the developed to the developing world is available at [insert COVID_Deaths.mp4].

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[18] *See* Megan Twohey, Keith Collins, and Katie Thomas, "With First Dibs on Vaccines, Rich Countries Have 'Cleared the Shelves'," *New York Times*.; Padmashree Gehl Sampath, "Covid-19 and the Need for a New Global Health Diplomacy, *Harvard Public Health Review, 2021 (29),* available at: https://harvardpublichealthreview.org/29-article-gehlsampath/#_ftn1

[19] Source: https://ourworldindata.org/covid-vaccinations. Note, in particular, the dire situation in Africa. In the United States, despite the resistance of many people to being vaccinated, over 60% of the population has already received at least one dose; in Africa, the number currently is under 2%. Ibid.

[20] See, e.g., Johns Hopkins Coronavirus Resource Center, "Mortality in the Most Affected Countries," https://coronavirus.jhu.edu/data/mortality (showing that, as of August 22, 2021, total deaths per 100,000 population in Peru, Brazil, Colombia, Argentina, and Mexico exceed the number in the United States); Richard C. Paddock and Muktita Suhartono, "No Longer 'Hidden Victims,' Children Are Dying as Virus Surges in Indonesia," *New York Times*, July 31, 2021.; Jinshan Hong, Randy Thanthong-Knight, and Jason Scott, "It's Not Just India: New Virus Waves Hit Developing Countries," *Bloomberg* (2021).

The proliferation of variants of the virus and ongoing struggles over vaccination practices and public-health initiatives makes it difficult to predict how the pandemic will progress in each nation. But there is little doubt that, for the foreseeable future, developed countries will continue to have disproportionate access to the tools necessary to combat the virus. As a result, both infections and deaths will soon be concentrated in the developing world[21] -- just as they are with respect to tuberculosis, malaria, HIV, dengue, and Ebola.

[21] See Indermit Gill and Philip Schellekens, "Covid-19 Is a Developing Country Pandemic," *Brookings* (2021), https://www.brookings.edu/blog/future-development/2021/05/27/covid-19-is-a-developing-country-pandemic/.; United Nations, "As Developed Nations Spring Back to Life, the World's Most Vulnerable Struggle on the Sideline," (2021), https://www.un.org/ohrlls/news/developed-nations-spring-back-life-worlds-most-vulnerable-struggle-sideline.