Rethinking Global Pharmaceutical Policy

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Chapter 1: The Global Health Crisis

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The original meaning of the word "crisis" was a point of uncertainty or inflection in the progress of an illness – in other words, the point at which a sick person starts either to recover or to worsen irrevocably. Over time, the meaning of the word expanded to refer to any highly unstable, difficult, or dangerous situation – such as the Cuban missile crisis of 1962 or the global financial crisis of 2008-2009.[1] The current situation with respect to global public health can fairly be described as a crisis, both within the original meaning of that term and within the modern meaning.

The crisis has two dimensions. First, the threats to human health posed by many diseases are currently increasing, alarmingly. Second, the disease burdens borne by poor countries radically exceed the burdens borne by rich countries – and the threats on the horizon may increase that disparity. In short, the first dimension involves growing threats to the health of all people in the world. The second involves inequality of access to the means of preserving health. As will soon become apparent, these two dimensions are intertwined, but the moral questions they raise – and some of the ways in which they might be addressed – are different. Thus, it's important to differentiate them.

The first section of this chapter defines some terms that will prove useful in describing the crisis. The second surveys the threats we all face. The third discusses inequality.

A. Vocabulary

To measure the crisis, we'll need some metrics.

Life Expectancy at Birth is an estimate of how long a person born at a particular moment would live if the conditions affecting health did not change during that person's lifetime.

Healthy Life Expectancy adjusts simple life expectancy downward to take into account periods of time in which people spend in ill health.

Ill health, in turn, is conventionally measured using yet another metric, known as *Disability Adjusted Life Years*, commonly abbreviated "DALYs." One DALY is best understood as one lost year of healthy life. The way the DALY metric works is perhaps best seen through example. If you lose a finger and then live that way for a year, that's treated as a loss of 0.03 DALYs, reflecting a modest diminution in the quality of your life.

[1] The Oxford English Dictionary, for example, defines "crisis" as follows: "Originally: a state of affairs in which a decisive change for better or worse is imminent; a turning point. Now usually: a situation or period characterized by intense difficulty, insecurity, or danger, either in the public sphere or in one's personal life."

By contrast, a year of blindness is treated as a loss of approximately 0.2 DALYs, and a year suffering from an advanced form of Alzheimer's is treated as a loss of 0.67 DALYs. The methodology that has been used to identify these fractions is controversial, but it's currently the most widely used tool in the field of global public health and thus is the best way of comparing countries. More subtle ways of measuring ill health will be introduced in due course.

Deaths should be obvious: the number of people who died from a specific cause, usually measured with reference to a year or other time period.

Mortality Rate measures the percentage of the relevant population who died from a specific cause. It's usually expressed as a number per year, per 100,000 people in the relevant country or group.

Prevalence is the percentage of persons in a population who have a particular disease at a specified moment or over a specified period.

Incidence, by contrast, refers to the occurrence of new cases of disease in a population over a specified period of time, typically a year.

Age Standardization refers to a method of adjusting a metric, such as mortality or prevalence, to control for the facts that (a) the age distribution in two jurisdictions (or in the same jurisdiction at two points in time) are likely to be different and (b) that the prevalence of many diseases (such as cancer) vary by age. There are two main ways of making such adjustments. Either one population is mathematically adjusted to have the same age structure as the other; or both populations are mathematically adjusted to have the same age structure as a standard population. Age standardization facilitates comparisons – enabling us to say, for example, that a disease is worse in country A than in country B or that the situation in a given country is getting worse or better.

In addition to these metrics, we need a few basic categories:

Infectious diseases are those that are "caused by the entrance into the body of organisms (such as bacteria, protozoans, fungi, or viruses) which grow and multiply there."[2] Such organisms are collectively known as *pathogens*.

Communicable diseases, a subset of infectious diseases, are those that are readily transmissible from one person to another through direct contact with an affected individual's discharges or indirectly, such as through a *vector*. Common vectors include mosquitos, flies, and fleas.[3]

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[2] Merriam-Webster dictionary.

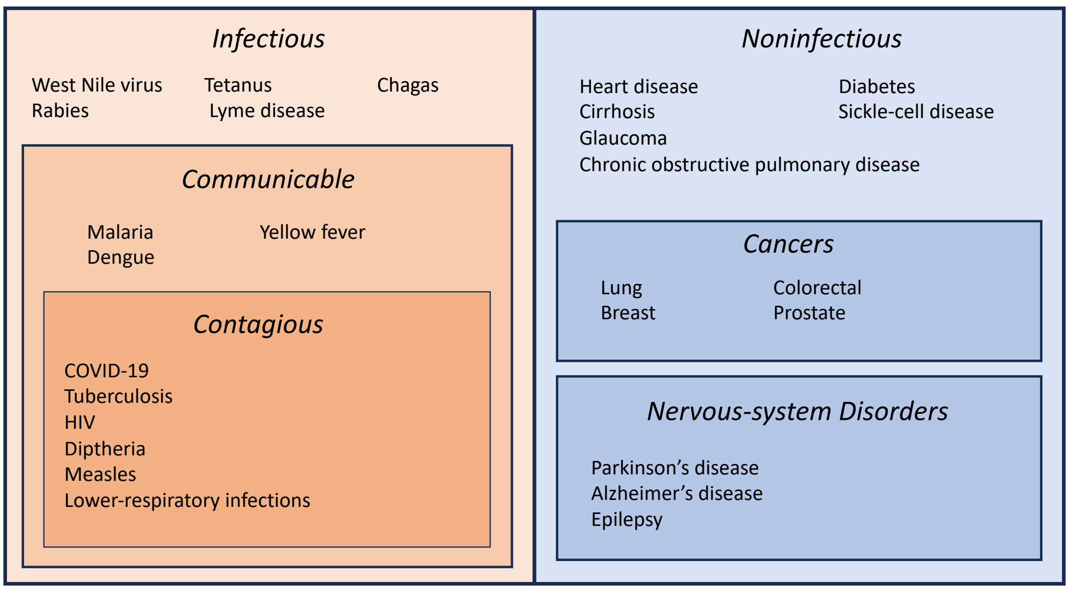
[3] Some scholars and texts include in the category of communicable diseases those that are transmitted, not from one person to another, but from animals or plants to persons. This expanded definition treats "communicable" as synonymous with "infectious." We will try to avoid conflating the categories, in part because (as will be seen) their members differ with respect to the measures best designed to prevent them.

Contagious diseases, a subset of communicable diseases, are those that are "communicable by contact with one who has it, with bodily discharges of such an individual, or with an object touched by such an individual or contaminated by bodily discharges."[4]

Noninfectious diseases are of course those that are not infectious, and *noncommunicable diseases* are those that are not communicable.[5]

Two subsets of noninfectious diseases that are often treated as sufficiently distinct to merit separate treatment are *cancers* and *nervous-system disorders*. The latter refers to diseases that affect the brain or other components of the nervous system, including mental illnesses.

Some common diseases that fit into these various categories are indicated in the following chart:



A disease is *endemic* when it is consistently present in a particular country or area.

An unexpected increase in the prevalence of a disease in a particular area is known as an *epidemic*.

The meaning of *pandemic* is contested. The World Health Organization defines the term succinctly as "the worldwide spread of a new disease." Most scholars define it more narrowly, but disagree concerning the limiting conditions. In this book, we will try to

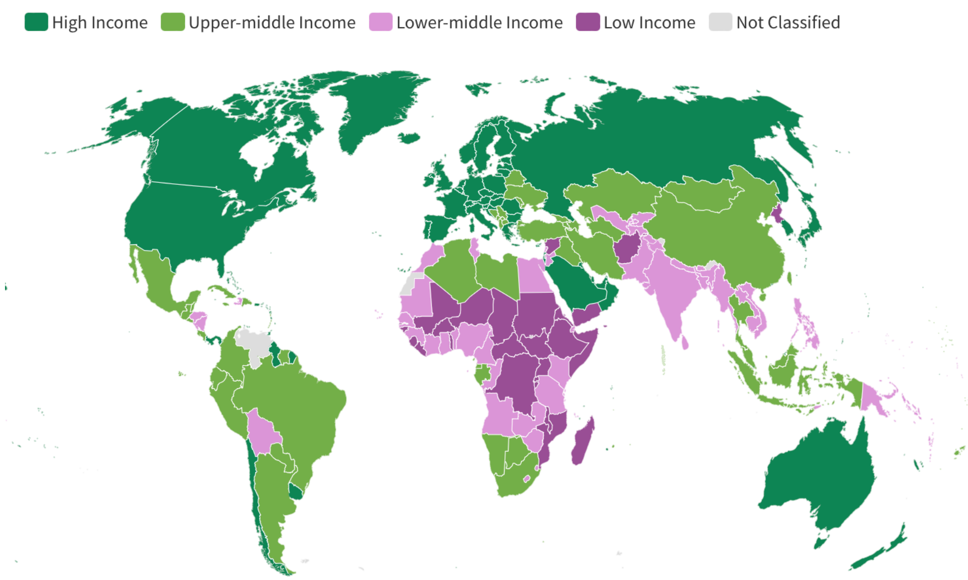
[4] As will soon become apparent, the boundaries of the subcategories of infectious diseases are not watertight. For example, some diseases that are primarily transmitted from one person to another through vectors are occasionally transferred directly. But the divisions are crisp enough to make them useful.

[5] Unfortunately, it is customary to treat "noninfectious" as synonymous with "noncommunicable," and we will often defer to that convention, even though (as indicated above) it is misleading.

describe as pandemics outbreaks in which the disease (a) is highly contagious, severe, and relatively novel and (b) spreads rapidly over a wide geographic area (relative to the zone occupied at the time by humans).[6]

We will be concerned in the book with two types of pharmaceutical products. A *vaccine* (as we will use the term) is a drug used to prevent a disease or disorder.[7] A *therapy*, by contrast, consists of a drug used to relieve or heal a disease or disorder.

Finally, in this chapter and throughout the book, we will often rely on the typology of countries developed by the World Bank. That typology, revised every year, divides countries into four groups on the basis of their gross national incomes per capita – specifically using the "Atlas method."[8] The members of the four groups for 2024-2025 (which are based on countries' GNIs in 2023) are shown below.[9]



[6] This definition roughly tracks the factors emphasized by a gathering of epidemiologists, convened in 2009 by the National Institutes of Health. See Silvio Daniel Pitlik, "Covid-19 Compared to Other Pandemic Diseases," *Rambam Maimonides medical journal* 11, no. 3 (2020).

[7] Historically, the term vaccine had a narrower meaning: "material prepared from the causative agent of a disease, or a product of such an agent, for use in immunization." Oxford English Dictionary (2022). We will use the term to include all drugs used for immunization, regardless of how they are prepared.

[8] The bank explains: "For the current 2025 fiscal year, low-income economies are defined as those with a GNI per capita, calculated using the World Bank Atlas method, of $1,145 or less in 2023; lower middle-income economies are those with a GNI per capita between $1,146 and $4,515; upper middle-income economies are those with a GNI per capita between $4,516 and $14,005; high-income economies are those with more than a GNI per capita of $14,005." World Bank Country and Lending Groups, https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups.

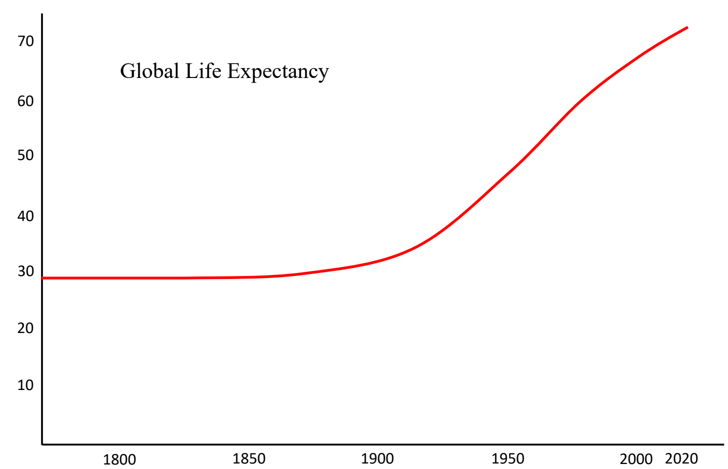
[9] Source: World Bank country classifications by income level for 2024-2025, https://blogs.worldbank.org/en/opendata/world-bank-country-classifications-by-income-level-for-2024-2025. [Recheck the map before publication.]

The last three categories are sometimes combined into "low and middle-income countries," conventionally abbreviated "LMICs." Using such a capacious category is problematic for several reasons,[10] and we will avoid doing so. Instead, we will use the abbreviation, "LMIC," to refer to lower-middle-income countries. The meanings of HICs, UMICs, and LICs should be obvious. When appropriate (as in Chapters 6 and 8), we will construct and apply some custom categories – but for now the World Bank's clusters will suffice.

It's now time to put these tools to work.

B. Threats

Until recently, it was widely thought that the human race was winning the war against disease. That confidence derived in part from observation of the long-term trend of average global life expectancy. For millennia, people lived, on average, between 20 and 30 years. Starting approximately in 1800, average life expectancy began to creep upward. After 1900, the rise accelerated. In the 1980s it slowed somewhat, but the march upward seemed inexorable. By 2000, it had reached 66 years. By 2020, over 72.[11] The arc looked roughly like this:



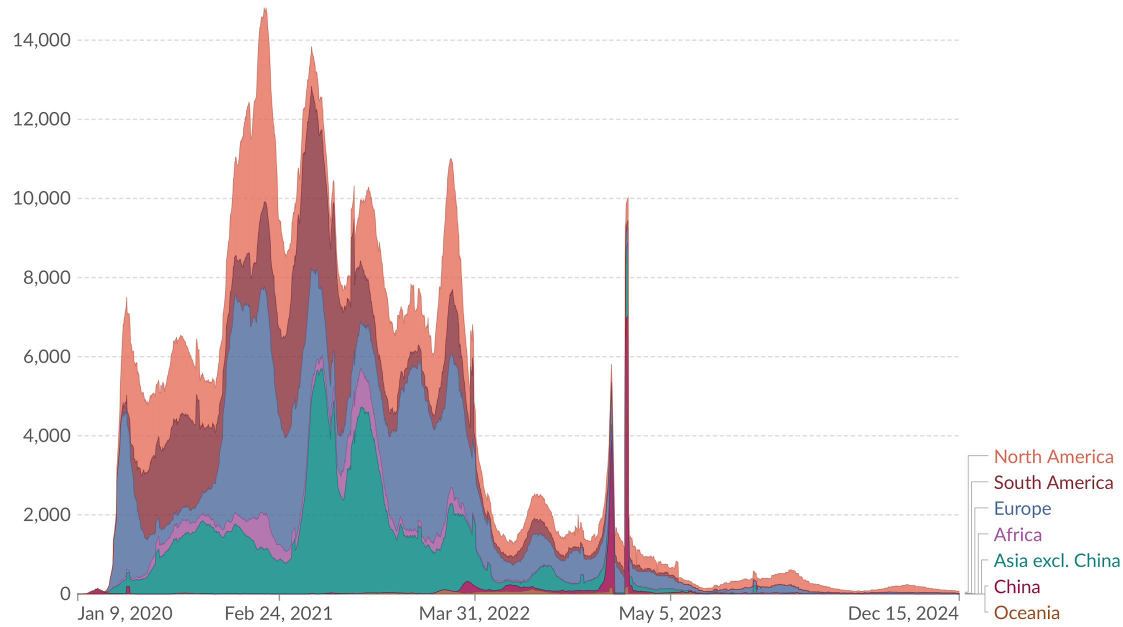
[10] See Raphael Lencucha and Sujaya Neupane, "The Use, Misuse and Overuse of the 'Low-Income and Middle-Income Countries' Category," *BMJ global health* 7, no. 6 (2022).

[11] The figures set forth in this paragraph were culled from the following sources: Samuel H. Preston, "Human Mortality Throughout History and Prehistory," in *The State of Humanity*, ed. Julian L. Simon, E. Calvin Beisner, and John Phelps (Cambridge, MA: Blackwell, 1995); James C. Riley, *Rising Life Excpectancy: A Global History* (Cambridge: Cambridge University Press, 2001), 1, 33.; Indur M. Goklany, *The Improving State of the World* (Washington, D.C.: Cato Institute, 2007), 31-34.; WHO, "World Health Statistics 2014," http://www.who.int/gho/publications/world_health_statistics/en/.;"World Health Statistics 2019: Monitoring Health for the Sustainable Development Goals," (2019), https://www.who.int/gho/publications/world_health_statistics/2019/en/. Riley, *Life Expectancy*, Chapter 1.; WHO, "Life Expectancy," http://www.deathreference.com/Ke-Ma/Life-Expectancy.html#b.; C.J.L. Murray, Mohsen Naghavi, and Alan Lopez, "Global, Regional, and National Age–Sex Specific All-Cause and Cause-Specific Mortality for 240 Causes of Death, 1990–2013: A Systematic Analysis for the Global Burden of Disease Study 2013," *Lancet* 385 (2015).

This remarkable record of progress had many causes, but one of the most important – it was widely and accurately thought – was increased success in controlling diseases.

COVID has dented that confidence. As readers surely are aware, starting in late 2019, the COVID-19 pandemic swept over the world.[12] At its peak, it killed 100,000 people a week. By the end of 2024, it had killed over 7 million people. Its trajectory is shown below.[13]

Daily Confirmed COVID Deaths[14]



The pandemic is now subsiding. Infections continue (at a pace of roughly 50,000 per week), but, as is apparent from the foregoing graph, the death rate is low and declining. As it fades, most people in most countries are expressing a sense of return to normalcy.[15] Not everyone, of course. Those suffering from so-called "long covid" continue to lament the long-term, perhaps permanent, in some cases catastrophic, changes in their lives.[16] But more and more appear inclined to say, "Covid is over; we can now go back to our lives."

[12] Additional detail concerning the pandemic is provided in Appendix 6.

[13] Source: WHO COVID-19 Dashboard, https://data.who.int/dashboards/covid19/deaths?n=c (last visited, December 9, 2024). These numbers should be used with caution. In particular, the two spikes in January and February 2023 are misleading. Both reflect reports from China. Almost certainly, those reports include deaths that had occurred months or years earlier.

[14] Source: Our World in Data, using data supplied by the World Health Organization – COVID-19 Dashboard (last visited, December 30, 2024).

[15] See, e.g., Megan Brenan, "After Four Years, 59% in U.S. Say Covid-19 Pandemic Is Over," *Gallup*, https://news.gallup.com/poll/612230/four-years-say-covid-pandemic.aspx.

[16] For a sense of the scale of "long covid," see Ziyad Al-Aly et al., "Long Covid Science, Research and Policy," *Nature medicine* 30, no. 8 (2024).

With this shift in sentiment comes a growing confidence that the long march against disease can and will resume. Progress, it now widely believed, will once again be made on all fronts. This optimism is not well founded.

The first step toward a more realistic assessment of our current situation is to recognize that COVID-19 was not an anomaly. Rather, it was just the most recent in a long chain of pandemics. The most important are listed below.

	Dates	**Pathogen**	**Deaths**
Plague of Athens[17]	430-427 BC	Smallpox, measles, or typhus	70K – 100K
Antonine plague[18]	165-180	Smallpox or measles	7M
Plague of Justinian[19]	541-543	*Yersinia pestis*	100M
Japanese smallpox epidemic	735-737	Smallpox	1M
Black death[20]	1334-1353	*Yersinia pestis*	75M - 200M
Western-hemisphere pandemic	1500s	Primarily smallpox	25M - 56M
Italian plague	1629-1631	*Yersinia pestis*	1M
Plague of London	1665-1666	*Yersinia pestis*	100K
Yellow fever[21]	Late 1800s	Yellow fever	100K – 150K
Cholera[22]	1817-1824 1827-1835 1839-1856 1863-1875 1899-1923 1961-present	*Vibrio cholera*	1M
Third plague[23]	1885-1959	*Yersinia pestis*	12M
Russian flu[24]	1889-1890	Influenza A/H3N8?	1M

[17] See Óscar F. Chacón-Camacho et al., "Learning from History in the Midst of the Covid-19: Epidemics/Pandemics of Antiquity up to the Fall of the Western Roman Empire," *Boletin medico del Hospital Infantil de Mexico* 80, no. 5 (2023): 273-74.; Cheston B. Cunha et al., "Great Plagues of the Past and Remaining Questions," (Berlin, Heidelberg: Springer Berlin Heidelberg, 2008).

[18] See Chacón-Camacho et al., "Learning from History," 276.

[19] See Cunha et al., "Great Plagues of the Past."; Björn P. Zietz and Hartmut Dunkelberg, "The History of the Plague and the Research on the Causative Agent Yersinia Pestis," *International journal of hygiene and environmental health* 207, no. 2 (2004): 166-67.; Piret 3

[20] See "History of the Plague," 167-73.; Jocelyne Piret and Guy Boivin, "Pandemics Throughout History," *Frontiers in Microbiology* 11 (2021): 3.

[21] See Pitlik, "Covid-19 Compared to Other Pandemic Diseases," 8.

[22] See S. M. Faruque, M. J. Albert, and J. J. Mekalanos, "Epidemiology, Genetics, and Ecology of Toxigenic Vibrio Cholerae," *Microbiology and molecular biology reviews* 62, no. 4 (1998).; Mohammad Ali et al., "Updated Global Burden of Cholera in Endemic Countries," *PLoS neglected tropical diseases* 9, no. 6 (2015). Piret 4-5

[23] See Piret and Boivin, "Pandemics Throughout History," 3.; Zietz and Dunkelberg, "History of the Plague," 173-75.

[24] See Piret and Boivin, "Pandemics Throughout History," 5-8.; Patrick R. Saunders-Hastings and Daniel Krewski, "Reviewing the History of Pandemic Influenza: Understanding Patterns of Emergence and Transmission," *Pathogens* 5, no. 4 (2016): 3; Alain-Jacques Valleron et al., "Transmissibility and Geographic

Spanish flu[25]	1918-1920	Influenza A/H1N1	50M
Asian flu[26]	1957-1959	Influenza A/H2N2	1.1M
Hong Kong flu[27]	1968-1970	Influenza A/H3N2	500K – 2M
AIDS[28]	1981-present	HIV	35M – 51M
Swine flu[29]	2009-2010	Influenza A/H1N1	200K
Ebola[30]	2014-present	Ebola virus	11K
COVID-19[31]	2019-present	*SARS-CoV-2*	7M

Many of these of these pandemics had devastating impacts. For example, the Antonine plague decimated the Roman Empire and contributed to its decline. Four centuries later, the Plague of Justinian overran the Eastern Roman Empire (the principal remnant of the original form) and halted Justinian's effort to restore the scope of the empire. In the late Middle Ages, the Black Death killed 30% of the residents of Europe, provoking fundamental changes to the economy and society of the region. The sixteenth-century western-hemisphere pandemic, caused by the introduction of "old world" viruses into South and then North America, killed roughly 80% of the indigenous population, enabling the radical acceleration of European conquest and colonization. The Spanish flu, the first truly global pandemic, infected half of the world's population and hollowed out an entire generation. Last but not least, AIDS was catastrophic for the populations of many countries, especially those in subSaharan Africa. The following chart shows the magnitude of its impact in just ten countries as of 2012.

Spread of the 1889 Influenza Pandemic," *Proceedings of the National Academy of Sciences - PNAS* 107, no. 19 (2010).

25 See Piret and Boivin, "Pandemics Throughout History," 5-8.; Niall P. A. S. Johnson and Juergen Mueller, "Updating the Accounts: Global Mortality of the 1918-1920 "Spanish" Influenza Pandemic," *Bulletin of the History of Medicine* 76, no. 1 (2002); Saunders-Hastings and Krewski, "The History of Pandemic Influenza:," 3-5.; C. W. Potter, "A History of Influenza," *Journal of applied microbiology* 91, no. 4 (2001). But cf. Peter Spreeuwenberg, Madelon Kroneman, and John Paget, "Reassessing the Global Mortality Burden of the 1918 Influenza Pandemic," *American Journal of Epidemiology* 187, no. 12 (2018).(arguing that the total number of deaths was not as high as is commonly thought).

26 See Piret and Boivin, "Pandemics Throughout History," 5-8.; Saunders-Hastings and Krewski, "The History of Pandemic Influenza:," 7-8; Cécile Viboud et al., "Global Mortality Impact of the 1957–1959 Influenza Pandemic," *Journal of Infectious Diseases* 213, no. 5 (2016).

27 See Piret and Boivin, "Pandemics Throughout History," 5-8.; Saunders-Hastings and Krewski, "The History of Pandemic Influenza:," 8-9.

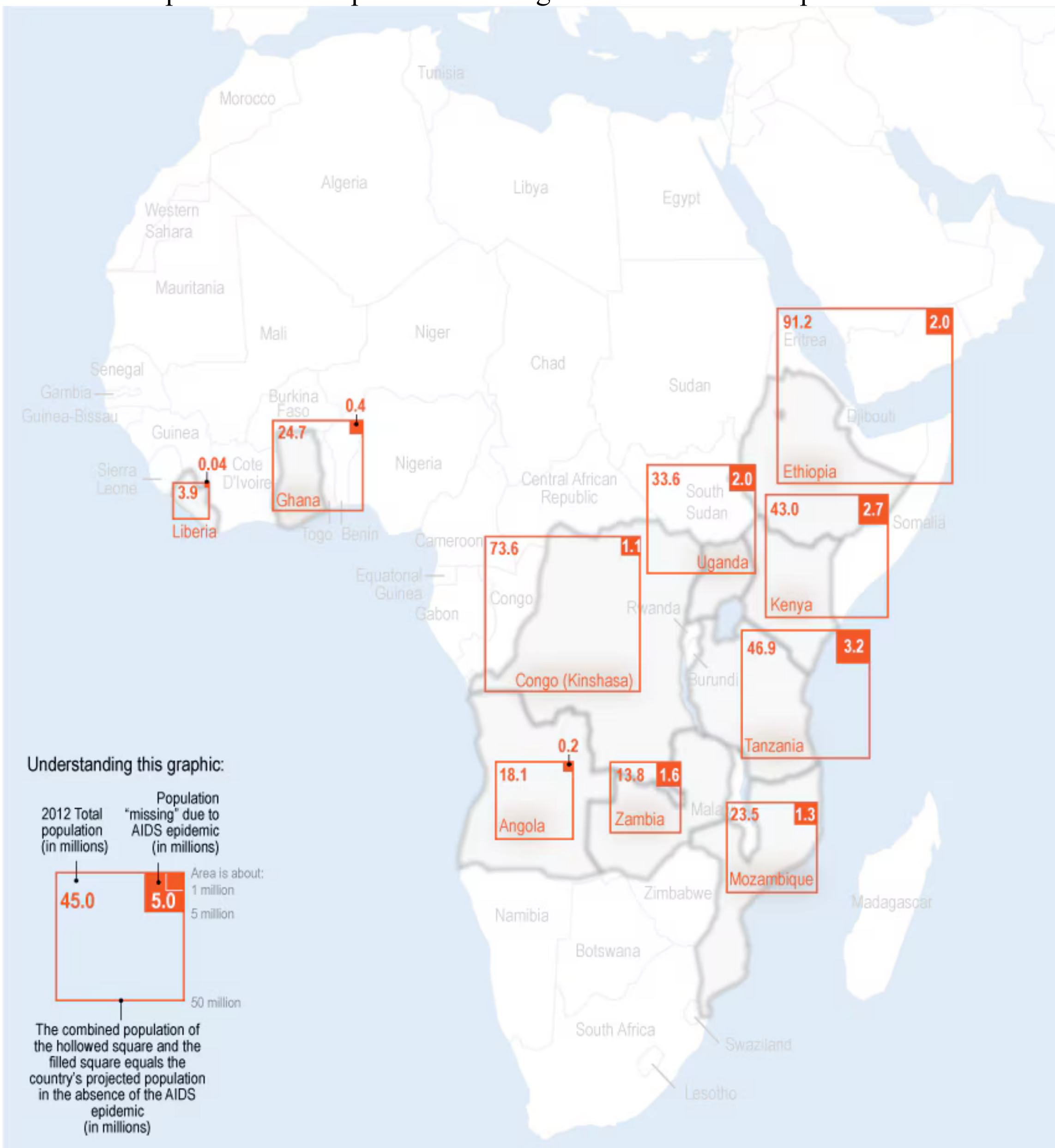
28 See Appendix 3: HIV/AIDS.

29 See Piret and Boivin, "Pandemics Throughout History," 5-8.; Saunders-Hastings and Krewski, "The History of Pandemic Influenza:," 11-12; Lone Simonsen et al., "Global Mortality Estimates for the 2009 Influenza Pandemic from the Glamor Project: A Modeling Study," *PLoS Medicine* 10, no. 11 (2013).

30 See Appendix 5: Ebola.

31 See Appendix 6: COVID-19.

Total Population and Population Missing Due to HIV/AIDS Epidemics: 2012[32]



Most of the pathogens that caused these pandemics are still with us. Some have been contained, but not all. The plague, for example, continues to infect hundreds of people a year, most of them in Africa. The current footprint of cholera is larger; it can be found

[32] Source: U.S. Census Bureau, International Data Base, and unpublished tables, https://www.census.gov/dataviz/visualizations/062/. Explanation: "The HIV/AIDS pandemic has impacted the populations of many African countries. Ten countries in Africa with recent population projections were selected for Figures 1 and 2. These countries have suffered the combined loss of more than 14.5 million people. The scales of the epidemics vary, with some countries more heavily impacted than others. The population missing due to HIV/AIDS represents nearly 12 percent of Zambia's current population."

in many poor or war-torn countries – and kills roughly 100,000 people per year.[33] Last but not least (again), the AIDS pandemic is far from over. To be sure, the number of deaths it causes globally has been declining since roughly 2005. But it still kills over 600,000 people a year. And because the rate of new infections, though diminishing, exceeds the death rate, the total number of people living with AIDS is still rising. It is now over 39 million. Finally, in some parts of the world, the favorable trends with respect to HIV do not hold. In the Middle East and North Africa, the number of new infections was 110% higher in 2023 than in 2010, and in Eastern Europe and Central Asia, the number of annual deaths attributable to HIV/AIDS rose by 34% over the same period.

In sum, we have not yet suppressed all of the pandemics listed above. But the more fundamental reason to review this history is that there is little reason to think that the pattern will not continue. Indeed, as the planet warms, as the density of human settlements in many areas increases, and as contact between humans and both domesticated and wild animals continues, we can expect novel pathogens to emerge more frequently, not less.[34]

At least one potential pandemic is already on the horizon. The H5N1 influenza virus causes what is commonly known as "bird flu" or "avian flu." It has existed for some time, but has infected people only occasionally. Recently, however, it has begun to pass from birds to humans more often and on rare occasions seems to have passed directly from one person to another. (In other words, it is no longer merely infectious; it has become contagious.) Bird flu has also begun to spread widely in populations of dairy cows (especially but not exclusively in the United States) and perhaps among pigs. That's hazardous for two reasons. First, it increases the risk of transmission to humans (for example, through the consumption of raw milk containing the virus). Second, livestock (especially pigs) have long functioned as reservoirs in which different strains of the influenza virus can exchange genetic information. Because avian flu has a much higher mortality rate than the kinds of influenza with which we are now familiar, the prospect of wide distribution among humans is grim. [35]

Because of their explosiveness, pandemics receive disproportionate attention from the press and the public at large. But the threats posed by the endemic diseases are at least as great. What follows are summaries of the current status of twelve such diseases – six infectious and six noninfectious. More extensive discussions of all twelve can be found in the appendices – to which we will be referring periodically during the book.

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[33] See Piret and Boivin, "Pandemics Throughout History," 5.; WHO

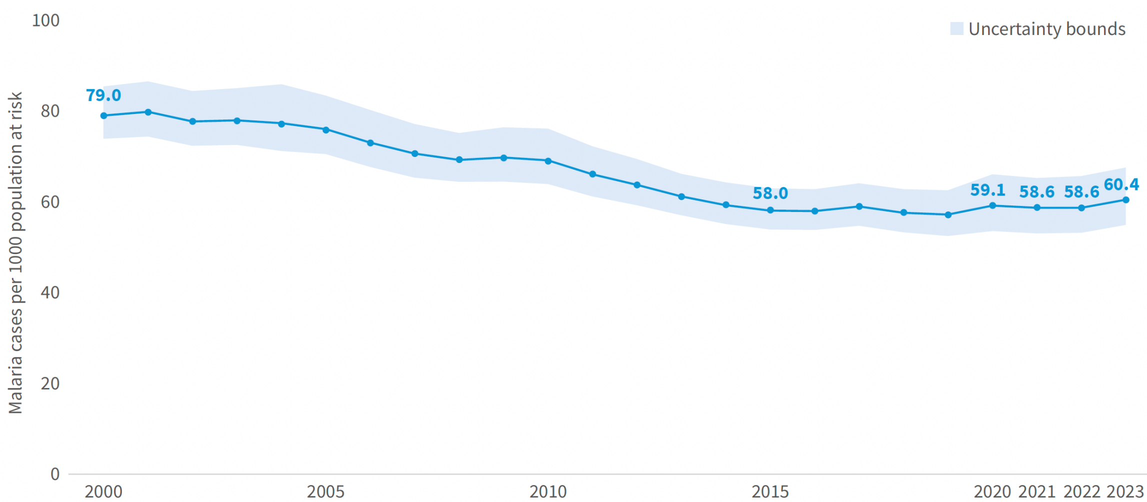
[34] See ibid., 2.

[35] For a variety of perspectives on the threat of a bird-flu pandemic, see U.S. Food and Drug Administration, "Investigation of Avian Influenza a (H5n1) Virus in Dairy Cattle," (2024); U.S. Department of Agriculture, "Report on Avian Influenza," (2024); Center for Disease Control, "Technical Update: Summary Analysis of the Genetic Sequence of a Highly Pathogenic Avian Influenza a(H5n1) Virus Identified in a Child in California," (2024); David Leonhardt, "Bird Flu, Explained," *New York Times*, December 4, 2024 2024; Apoorva Mandavilli and Emily Anthes, "U.S. Milk to Be Tested for Bird Flu Virus," ibid.; Tulio de Oliveira, "The World Is Watching the U.S. Deal with Bird Flu, and It's Scary," ibid., November 19, 2024; Ian Scoones, *Avian Influenza : Science, Policy and Politics* (London; Washington, DC: Earthscan, 2010).

Among the infectious endemic diseases, **tuberculosis** has long been king. It currently kills about 1.23 million people per year. Between 1980 and 2019, that number had been steadily declining – first gradually, then more steeply. With the onset of the COVID pandemic, this favorable trend came to a halt. Total deaths rose significantly in 2021. They have now begun to decline again. Among HIV-negative people, the number is approximately the same as in 2019. Whether it continues to fall remains to be seen.[36]

Two aspects of the recent history of tuberculosis are of particular concern. First, in not all parts of the world are the incidence rates improving. In particular, the rate is rising fast in Latin America.[37] The second is the distressingly high incidence of cases in which the disease is resistant to one or more of the standard antibiotics. In all parts of the world, that number rose rapidly after 1980.[38] Recently, it seems to have stabilized – at approximately 400,000 per year.[39] For reasons that will become apparent shortly, the burdens associated with drug-resistant cases are much more severe than those associated with ordinary tuberculosis.

The state of affairs with respect to **malaria** is similar.[40] Currently, roughly 250 million people are infected with malaria every year, and 600,000 die, most of them children. In the 21st century, both numbers gradually declined until 2014, remained relatively stable between 2014 and 2018, then rose.[41] The recent history of the incidence rate (in the set of 103 countries considered at risk) is shown below.[42]



[36] More detail concerning the history of tuberculosis is available in Appendix 1.

[37] See WHO, "Global Tuberculosis Report," (2024): 7.

[38] See Gwenan M. Knight et al., "Global Burden of Latent Multidrug-Resistant Tuberculosis: Trends and Estimates Based on Mathematical Modelling," *Lancet. Infectious diseases/* 19, no. 8 (2019).

[39] See WHO, "2024 Global Tb Report," 9.

[40] More detail concerning the history of malaria is available in Appendix 2.

[41] See WHO, "World Malaria Report 2024," (2024): Table 2.1.

[42] Ibid., Figure 2.3.

These gross numbers mask large geographic variations. In recent years, at least three countries – Sri Lanka, Uzbekistan and Kyrgyzstan – have been able to eliminate malaria entirely.[43] However, three others – Ethiopia, Madagascar, and Pakistan – saw huge surges.[44] Overall, the campaign to rid the world of malaria seems to have stalled.

The infectious diseases on which we have concentrated thus far – AIDS, Covid-19, tuberculosis, and malaria – are the big killers. Collectively, they cause roughly 70% of the global deaths from infectious diseases.[45] Less well known are infectious diseases that kill fewer but cause large amounts of misery. The global burdens associated with these are reflected better by the DALY metric than by mortality data.

An example is **dengue**, a mosquito-borne infection long common in Asian countries and now increasingly common in the western hemisphere. In a majority of the cases, dengue is not manifested at all. In most of the remainder, it produces a set of symptoms resembling the flu: fever, nausea, skin rash, headaches, and severe joint and muscle pain. This constellation of ailments, commonly known as "dengue fever" or "breakbone fever" is debilitating, but typically lasts only 10 days and results in no permanent impairment.[46] However, in a small percentage of cases, the disease progresses into the much more dangerous "dengue hemorrhagic fever" (DHF) in which the person's blood vessels begin to leak plasma into the surrounding spaces in his or her body. If the leakage is severe, it gives rise to "dengue shock syndrome" (DSS), characterized by extremely low blood pressure. If not treated promptly with "vigorous fluid resuscitation," DSS can be fatal.[47]

The number of deaths caused by dengue are relatively modest – currently approximately 24,000 per year. However, the number of DALYs it causes is large – currently approximately 1,750,000 per year. Between 1980 and 2018, both numbers rose steadily. Between 2018 and 2023, they declined,[48] but in the past year, they have

[43] Ibid., 4.

[44] Between 2022 and 2023, the incidence rate in Ethiopia increased by 82%; in Madagascar by 71%; and in Pakistan by 59%. See ibid., 10.

[45] In 2021, the numbers were (646,749 + 8,713,194 + 1,395,228 + 604,620) / (5,020,518 + 11,188,110) = 11,359,791 / 16,208,628 = 70%.

[46] An excellent description of a typical case can be found in Vanesa Barbara, "10 Days of Dengue Fever," *New York Times*, May 1, 2015 2015.

[47] See Ngo Thi Nhan et al., "Acute Management of Dengue Shock Syndrome: A Randomized Double-Blind Comparison of 4 Intravenous Fluid Regimens in the First Hour," *Clinical Infectious Diseases* 32 (2001).

[48] The most recent set of numbers reported by the WHO follow:
2000: 17,786 deaths; 1,563,378 DALYs
2010: 24,925 deaths; 1,991,250 DALYs
2015: 28,798 deaths; 2,186,744 DALYs
2019: 26,235 deaths; 1,907,659 DALYs
2020: 25,510 deaths; 1,853,010 DALYs
2021: 23,932 deaths; 1,755,858 DALYs
More detail concerning the history of dengue is available in Appendix 4.

rebounded. In June of 2024, the CDC reported that "the global incidence of dengue has been the highest on record."[49]

A similar pattern can be found in **schistosomiasis**, a communicable, parasitic disease common in Africa. It comes in two forms. One produces abdominal pain, diarrhoea, and sometimes damage to internal organs. The other damages the genitals and other organs. Together, they cause relatively few deaths (roughly 14,000 in 2021), but almost 2 million DALYs per year.[50] Neither number has changed much since 2000.

Another little known but increasingly dangerous infectious disease is **Japanese Encephalitis**. Encephalitis is a family of diseases, defined by a symptom: inflammation of the brain. Among the factors that can cause such inflammation are viruses, and among those viruses the most potent is a flavivirus closely related to West Nile virus, now known as the Japanese Encephalitis virus. It is typically transmitted to a person by a *Culex* mosquito that previously had bitten an infected wading birds or pig. Most people infected by it do not show symptoms, but those that do are likely to experience a cascade of pain: fever, headache, disorientation, and tremors. Many proceed to coma and death. Those who survive often have permanent neurological damage. There is no treatment for the disease, but it can be prevented by any of three vaccines.[51] Japanese encephalitis was first identified in Japan in 1871. Confirmed cases appeared in Korea (1933), China (1940), the Philippines (1950), and India (1955).[52] It is now endemic in most countries in Southeast Asia.

Currently, there are roughly 100,000 new clinical cases of Japanese encephalitis per year. The disease results in approximately 25,000 deaths and a loss of more than 700,000 DALYs. Administration of the vaccines in some of the affected countries does not seem to have reduced those numbers materially. In addition, the footprint of the disease is now growing. The virus has been detected in pigs in Australia and Italy, and in the former has begun to infect people.[53] Public health authorities are urging increased testing

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[49] Center for Disease Control, "Increased Risk of Dengue Virus Infections in the United States," (2024).

[50] Much the same in distribution is Lymphatic filariasis (elephantiasis), which disrupts the normal functioning of the lymph system, causing disfigurement and pain. It causes almost no deaths, but results in a loss of 1,323,000 DALYs per year. That number declined radically between 2000 and 2010, but has been relatively stable since. See WHO, "Global Health Estimates 2021: Dalys by Age, Sex and Cause," (2024).

[51] See Lance Turtle and Tom Solomon, "Japanese Encephalitis — the Prospects for New Treatments," *Nature Reviews Neurology* 14, no. 5 (2018); Sang-Im Yun and Young-Min Lee, "Japanese Encephalitis: The Virus and Vaccines," *Human vaccines & immunotherapeutics* 10, no. 2 (2014).("Approximately 20–30% of clinical JE cases are fatal, and ~30–50% of survivors experience serious neurologic, cognitive, or psychiatric complications even years later."); CDC, "Japanese Encephalitis: Causes and How It Spreads," (2024); WHO, "Japanese Encephalitis," (2024).

[52] See Yun and Lee, "Japanese Encephalitis," 263.

[53] See P. Ravanini et al., "Japanese Encephalitis Virus Rna Detected in Culex Pipiens Mosquitoes in Italy," *Euro surveillance : bulletin européen sur les maladies transmissibles* 17, no. 28 (2012); Claire Waller et al., "Japanese Encephalitis in Australia — a Sentinel Case," *New England Journal of Medicine* 387, no. 7 (2022).("As f August 1, 2022, a total of 40 cases of infection that had led to 5 deaths had been reported."); H. Zeller, "Is Japanese Encephalitis Emerging in Europe?," *Euro surveillance : bulletin européen sur les maladies transmissibles* 17, no. 32 (2012).

of livestock outside the traditional zone in order to determine the need for more widespread vaccination.

Unlike the Japanese encephalitis virus, the **measles** virus is transmitted easily from one person to another. For centuries, vast numbers of children were infected by it. Most experienced moderate symptoms – a high fever, cough, a runny nose, conjunctivitis, and the telltale rash – but recovered within a few weeks. A small percentage, however, experienced complications, including pneumonia, encephalitis, and blindness. An effective vaccine became available in 1963. Its widespread distribution enabled a radical diminution in the incidence and impact of the disease. By 2021, global deaths per year attributable to measles had declined from 2.6 million to 81,000. The longstanding goal of eliminating the disease seemed within sight.[54]

Measles is now rebounding. The immediate cause seems to have been a disruption of the vaccination programs caused by the COVID-19 pandemic. Unfortunately, the fading of the pandemic has not been accompanied by a resurgence in vaccinations; the percentage of children in the world who in 2023 had received at least one dose of the vaccine was no higher than it was in 2022 – and well below the peak in 2019. The grim results are suggested by the following data.[55]

TABLE 1. Estimates of regional immunization coverage with the first and second doses of measles-containing vaccine administered through routine immunization services, reported measles cases, and reported measles incidence, by World Health Organization region — worldwide, 2000–2023

	Percentage					
WHO region/Year (no. of countries in the region)*	MCV1 coverage†	Countries with ≥95% MCV1 coverage§	MCV2 coverage†	Reporting countries with fewer than five measles cases per 1 million population¶,**	No. of reported measles cases¶ (% of total cases)	Measles incidence¶,**,††
Total (all regions)						
2000 (191)	71	28	17	33	853,479 (100.0)	144.6
2016 (194)	85	42	67	65	132,490 (100.0)	18.0
2019 (194)	86	44	71	44	873,373 (100.0)	118.8
2020 (194)	83	30	71	58	159,073 (100.0)	21.2
2021 (194)	81	30	71	68	123,171 (100.0)	16.4
2022 (194)	83	34	73	61	205,173 (100.0)	28.0
2023 (194)	83	35	74	47	663,795 (100.0)	91.0

The extreme fluctuations in the number of reported cases and the incidence (shown in the last two columns) are probably due in part to the cyclical nature of the disease. There is thus some reason to hope that 2023 was an anomaly. But myriad recent reports of serious outbreaks in many parts of the world suggest that measles has indeed returned with a vengeance.[56]

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[54] See William J. Moss, "Measles," *The Lancet (British edition)* 390, no. 10111 (2017); WHO, "Measles," (2024).

[55] Source: Anna A. Minta et al., "Progress toward Measles Elimination — Worldwide, 2000–2023," *Morbidity and Mortality Weekly Report* 73, no. 45 (2024).

[56] See, e.g., CDC, "Measles Cases and Outbreaks," (2024); Joshua Cohen, "As Measles Spreads through U.S., Cases in Europe and Central Asia Surge," *Forbes*, April 15, 2024 2024; CDC Newsroom, "Measles Cases Surge Worldwide, Infecting 10.3 Million People in 2023," (2024); Pan American Health Organization, "Paho Issues Epidemiological Alert for Measles Cases in the Americas," (2024); Gouvernement du Québec, "Measles Outbreak," (2024); UNICEF, "Measles Cases across Europe Continue to Surge, Putting Millions of Children at Risk," (2024); Stephanie Nolen and Arlette Bashizi, "Tiny Coffins: Measles Is Killing Thousands of Children in Congo," *New York Times*, December 18, 2024.

It should by now be apparent that these infectious diseases are idiosyncratic. However, two troubling factors are common to many of them. First, many of the pathogens and the vectors are evolving in ways that make it more difficult, using our existing tools, to control the diseases they cause. We have already seen one example: the emergence of variants of the tuberculosis virus that are resistant to one or more of the available antibiotics. There are many more.

The history of treatments for malaria is illustrative. Starting in the early nineteenth century, the drug used most often was chloroquine, derived from the bark of a tree native to the Andes and later farmed in parts of Southeast Asia.[57] In the 1950s, *Plasmodium falciparum* parasites (one of the four species) began to exhibit resistance to chloroquine, so many health-care systems in regions of the world dominated by that species switched to sulphadoxine-pyrimethamine (SP).[58] Resistance to SP emerged soon thereafter.[59] Today, most health services outside of Latin America use artemisinin-based combination therapy (ACT) as the primary means of treatment.[60] Fortunately, artemisinins are less likely than their predecessors to provoke resistance, apparently because they kill off the parasites more rapidly and thus shorten the window for mutation.[61] But, despite this advantage, resistance to them is now showing up increasingly often. The problem is exacerbated by continued sales of oral artemisinin monotherapies (which lead to resistance more quickly than the combination therapies) by some Indian generic companies, despite opposition to the practice by the WHO.[62]

An analogous struggle can be seen in efforts to control the mosquitos that transmit the parasites. Two strategies are employed for this purpose: supplying residents with bed nets treated with insecticide to shield them from bites while sleeping; and reducing the number of mosquitos in homes by spraying the walls with insecticide. The first of these initiatives has been the most extensive and successful. In the past decade, bed nets treated with insecticides (ITNs) have been widely distributed (usually for free) in malaria-endemic countries. Roughly 50% of the population in those countries now sleeps under nets.[63] They are inexpensive to produce, and their effect is dramatic. Studies suggest that they reduce malaria incidence by half.[64] The second approach – known as "indoor residual spraying"

[57] See James L.A. Webb, Jr., *Humanity's Burden: A Global History of Malaria* (New York: Cambridge University Press, 2009), 92-126.

[58] In Central America, where most malaria cases are caused by *P. vivax*, chloroquine remains the drug of choice. Recently, however, some resistance to that drug has been observed, prompting health-care services to shift increasingly toward ACT – described below.

[59] See David Bell and Peter Winstanley, "Current Issues in the Treatment of Uncomplicated Malaria in Africa," *British Medical Bulletin* 71 (2004): 31.

[60] *See* Robert Ridley, *Winning the Drugs War*, NATURE Vol. 430 at 942 (Aug. 19, 2004). Forty-two malaria endemic countries have switched to ACT. *See* WHO: *First Global Report on Efforts to Roll Back Malaria*, available at: www.who.int/mediacentre/news/releases/2005/pr17/en/index.html (May 3, 2005). For the WHO's current recommendations concerning their use, see WHO, "World Malaria Report," (2014): 24.

[61] See Bell and Winstanley, "Treatment of Malaria in Africa," 32.

[62] See WHO, "Malaria Report 2014," 28.

[63] See "World Malaria Report," (2019), xvi, 28-29, 46-48.

[64] See Lengeler C. Insecticide-treated bed nets and curtains for preventing malaria. Cochrane Database of Systematic Reviews, 2004 (2):CD000363 [*recheck]. For slightly less favorable assessments of the efficacy

(IRS) – is equally effective but less widely used; indeed, usage appears to be diminishing, rather than increasing.[65] Unfortunately, both of these approaches are threatened by increases in the resistance of the pertinent species of mosquitos to the most commonly used insecticides.[66] To slow the development of this resistance, the WHO recommends that distributors of the chemicals used in IRS and the manufacturers of insecticide treated bed nets rotate the insecticides they employ. Some countries abide by this guideline, but most as yet do not.[67]

The second of the recurring factors is that climate change is making things worse. One unsurprising reason is that, as the planet warms, the regions hospitable for the types of mosquitos that serve as vectors for many infectious diseases expand. This helps explain the growing footprint of dengue, for example. A recent study of this effect in the western hemisphere and Asia reported that: "Our findings indicate that historical climate change has already increased dengue incidence 18% (12 - 25%) in the study region, and projections suggest a potential increase of 40% (17 - 76) to 57% (33 - 107%) by mid-century depending on the climate scenario, with some areas seeing up to 200% increases."[68]

A less obvious reason is that extreme weather events can create conditions conducive to the spread of the diseases. For example, in 2022, floods in Pakistan linked to climate change provoked an outbreak of malaria, which caused the number of cases to increase by fivefold over 2021.[69]

Some noninfectious diseases pose even greater threats than the infectious diseases we have highlighted. Especially worrisome are the six summarized below.

Diabetes is manifested by excessive amounts of glucose in the blood. It comes in two forms. Type 1 is caused when the body's own immune system destroys the clusters of cells within the pancreas that produce insulin, a hormone that regulates blood-glucose levels. Type 2 is caused by abnormalities in both the secretion and the processing of insulin.[70] If not controlled, diabetes often leads to serious complications, including cardiovascular or neurological damage, blindness, and limb amputations.[71]

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of ITNs, see Mark Musumba, Aklesso Egbendewe-Mondzozo, and Bruce A. McCarl, "Analysis of the Cost of Malaria in Children and Use of Insecticide-Treated Bednets in Africa," African Development Review 26, no. 1 (2014).

[65] See WHO, "2019 Malaria Report," xvi, 48-49.

[66] *See* Stephen Hoffman. *Save the Children*, NATURE Vol. 430 at 940 (Aug. 19, 2004); Michelle L Gatton et al., "The Importance of Mosquito Behavioral Adaptations to Malaria Control in Africa," *Evolution* 67, no. 4 (2013).

[67] See WHO, "Malaria Report 2014," 16-17.

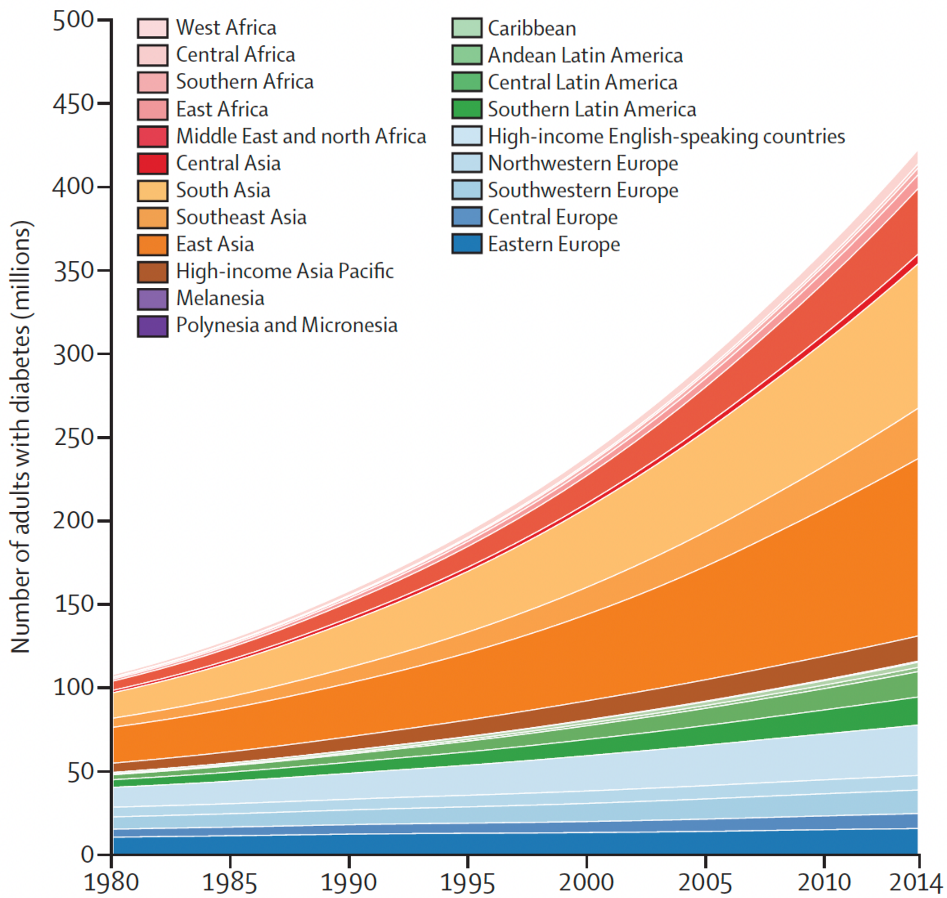
[68] Marissa L. Childs et al., "Climate Warming Is Expanding Dengue Burden in the Americas and Asia," *medRxiv (Cold Spring Harbor Laboratory)* (2024).

[69] See WHO, "World Malaria Report 2024," 4-5.

[70] See Ralph A. Defronzo, "From the Triumvirate to the Ominous Octet: A New Paradigm for the Treatment of Type 2 Diabetes Mellitus," *Diabetes* 58, no. 4 (2009).

[71] See Marianna Karamanou et al., "Milestones in the History of Diabetes Mellitus: The Main Contributors," *World journal of diabetes* 7, no. 1 (2016).

Although it has afflicted humans for millennia, diabetes was long uncommon. In the late twentieth century, however, its prevalence began to increase rapidly. A comprehensive study conducted in 2016 found that "From 1980 to 2014, worldwide age-standardised adult diabetes prevalence increased from 4.3% to 9.0% in men and from 5.0% to 7.9% in women."[72] When combined with the increase and aging of the global population, this trend produced astonishing increases in the total number of people suffering from the disease.[73]



Since 2014, the distressing trends have continued. In 2021, over 500 million people had diabetes. It caused 1.6 million deaths and a loss of 80 million DALYs.[74] By 2045, the total number of affected persons will likely approach 800 million. The annual costs to treating diabetes, already close to a trillion dollars a year, globally, will likely keep rising.

In 1900, **lung cancer** was rare. The increasing popularity of cigarette smoking and worsening of air pollution led to rapid increases in its incidence, especially among men –

[72] Bin Zhou et al., "Worldwide Trends in Diabetes since 1980: A Pooled Analysis of 751 Population-Based Studies with 4.4 Million Participants," *THE LANCET* 387, no. 10027 (2016): 1516.

[73] This figure is reprinted from ibid., 1523.

[74] Data derived from WHO, "Global Health Estimates 2021: Estimated Deaths by Cause and Region, 2000-2021," (2024); "Global Health Estimates 2021: Dalys by Age, Sex and Cause."

first in the United States in Europe, then in Asia. It now kills more people per year than any other cancer. In 2022, the number was roughly 1.8 million. The age-standardized incidence rate has now begun to decline in most HICs and in China, but continues to rise in many LMICs and LICs.[75] Because lung cancer disproportionately affects older people, and because the global population is both growing and getting older, the aggregate burdens associated with the disease will continue to rise for some time. In 2050, it is projected to cause 4.62 million new cases and to lead to roughly 3.5 million deaths.[76]

A similar story can be told concerning **colorectal cancer**, currently the cause of the second largest number of cancer deaths. Like lung cancer, its incidence increased dramatically during the 20th century. It too first became common in high-income countries, but now is spreading most quickly in poorer countries. Currently, roughly 5 million people in the world are living with the disease. Roughly one million people die from it each year – double the number in 1990.[77]

The global burdens associated with colorectal cancer are also expected to continue to increase. The current and projected incidence of its principal subtypes are listed below.[78]

	2020	2040
Colon	1,148,515	1,916,781
Rectal	732,210	1,160,296
Anal	50,865	77,597
Total	*1,931,590*	*3,154,674*

The WHO predicts that, by 2040, it will kill 1.6 million people a year.[79]

Cancer is perhaps the most frightening of all diseases, but even more worrisome is the rising prevalence of disorders of the central nervous system. The CNS disease that is growing most rapidly is **Parkinson's**. In 1990, 2.5 million people had the disease. By

75 See Jialin Zhou et al., "Global Burden of Lung Cancer in 2022 and Projections to 2050: Incidence and Mortality Estimates from Globocan," *Cancer epidemiology* 93 (2024): 2; Chao Li et al., "Global Burden and Trends of Lung Cancer Incidence and Mortality," *Chinese medical journal* 136, no. 13 (2023): 1584; Rajesh Sharma, "Mapping of Global, Regional and National Incidence, Mortality and Mortality-to-Incidence Ratio of Lung Cancer in 2020 and 2050," *International journal of clinical oncology* 27, no. 4 (2022); Isaac Adler, *Primary Malignant Growths of the Lungs and Bronchi: A Pathological and Clinical Study* (New York [etc.: Longmans, Green, and co., 1912); Javier Cortes et al., "Enhancing Global Access to Cancer Medicines," *CA: A Cancer Journal for Clinicians* 70, no. 2 (2020).

76 See Zhou et al., "Global Burden of Lung Cancer," 9.(predicting 3.55 million deaths); Sharma, "Mapping of Lung Cancer."(predicting 3.2 million deaths)

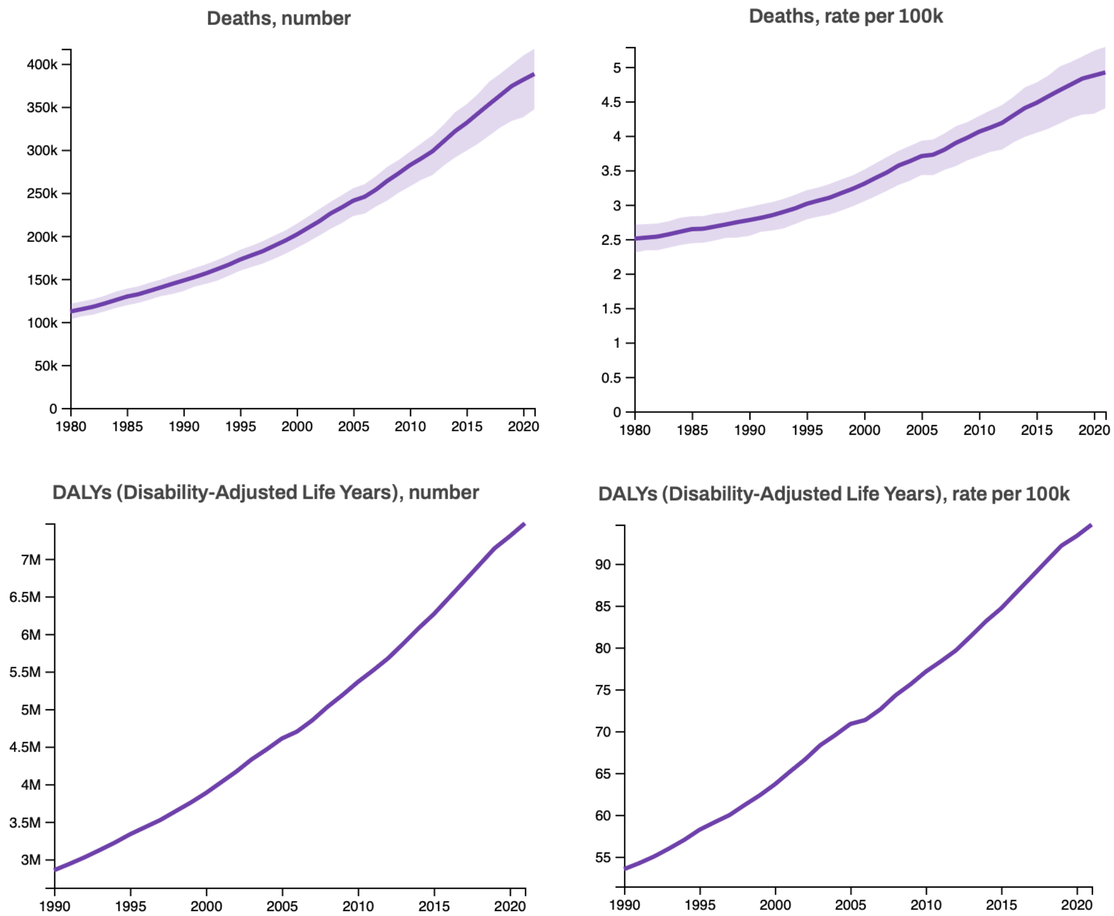
77 See Rami Abd-Rabu et al., "Global, Regional, and National Burden of Colorectal Cancer and Its Risk Factors, 1990–2019: A Systematic Analysis for the Global Burden of Disease Study 2019," *Lancet Gastroenterology & Hepatology* 7, no. 7 (2022); Yue Xi and Pengfei Xu, "Global Colorectal Cancer Burden in 2020 and Projections to 2040," *Translational oncology* 14, no. 10 (2021); WHO, "Colorectal Cancer," (2023). One of the reasons that colorectal cancer is so deadly is that it is typically asymptomatic in its early stages, and only a small percentage of people, globally, are routinely tested. Thus, by the time it is detected, it is often metatastic.

78 Source: Xi and Xu, "Global Colorectal Cancer Burden," 101174.

79 WHO, "Colorectal Cancer."

2016, the number had grown to 6.1 million – a 21% increase in the age-standardized prevalence rate. Annual deaths grew at the same alarming pace, reaching 211,000 globally. And the total number of disability adjusted life years lost per year Parkinson's exceeded 3 million.[80] Since then, as shown below, the numbers have continued to rise.

Global Burdens of Parkinson's Disease[81]



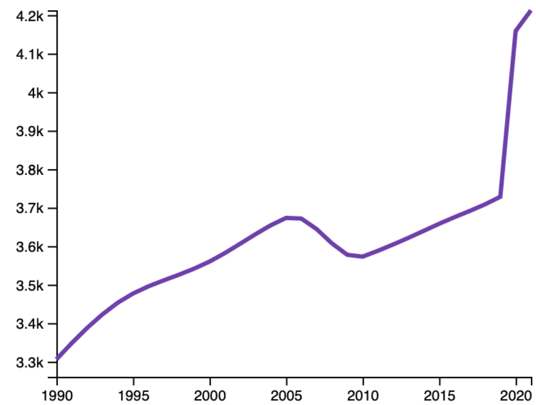
Theories abound concerning the causes of these trends, but no one seems sure.

The prevalence of **depression** also appears to be increasing – both in crude numbers and, more alarmingly, in terms of the age-standardized rate. It's difficult to measure, in part because of variations in how depression is defined, and in part because of the absence of a comprehensive reporting system. But all of the relevant studies indicate that its prevalence is growing. A recent meta-analysis reported an increase in the prevalence of "elevated depressive symptoms among adolescents globally" from 24% in the decade

[80] See E. Ray Dorsey et al., "Global, Regional, and National Burden of Parkinson's Disease, 1990–2016: A Systematic Analysis for the Global Burden of Disease Study 2016," *Lancet neurology* 17, no. 11 (2018).

[81] Source of the data: IMHE.

ending in 2010 to 38% in the decade ending in 2020.[82] Stress, anxiety, and depression then increased sharply during the pandemic.[83] The IMHE's estimates of the recent history of the global prevalence rate (per 100,000 people) for "depressive disorders" are shown below.



In contrast to Parkinson's disease and depression, the age-standardized prevalence of **Alzheimer's disease** and other forms of dementia does not seem to be increasing significantly – but nor is it decreasing. In other words, this war is at a stalemate. Stalemate, however, has a major cost. Because the global population has been both growing and aging, the total number of deaths from dementia has increased sharply – and will continue to do so. Currently, roughly 55 million people are living with dementia; by 2050, the number is expected to be 139 million.[84] The financial costs associated with dementia are staggering: roughly $1.3 trillion per year globally in 2019; projected to be $2.8 trillion by 2030.[85] The human costs are even greater.

To be sure, the global health situation is not all doom and gloom. We are making great progress in some sectors. Perhaps the most important involves cardiovascular disease, which has long been the single largest cause of deaths worldwide. Although the total number of deaths continues to rise, the mortality rate associated with heart disease has been marching steadily downward. Even more dramatic have been the gains in the past 30 years with respect to lower respiratory infections – the most common of which is pneumonia. Here the total number of deaths has dropped sharply, primarily because of success in combatting pneumonia in young children, and the age-standardized mortality rate has plummeted. Breakthroughs in the prevention and treatment of many other diseases continue to occur. The age-standardized rates for several cancers, for example, are going

[82] See Shefaly Shorey, Esperanza Debby Ng, and Celine H. J. Wong, "Global Prevalence of Depression and Elevated Depressive Symptoms among Adolescents: A Systematic Review and Meta-Analysis," *British journal of clinical psychology* 61, no. 2 (2022).

[83] See Damian F. Santomauro et al., "Global Prevalence and Burden of Depressive and Anxiety Disorders in 204 Countries and Territories in 2020 Due to the Covid-19 Pandemic," *The Lancet* 398, no. 10312 (2021).

[84] See Ellis Rubinstein et al., "A Call to Action: The Global Response to Dementia through Policy Innovation," (2015).

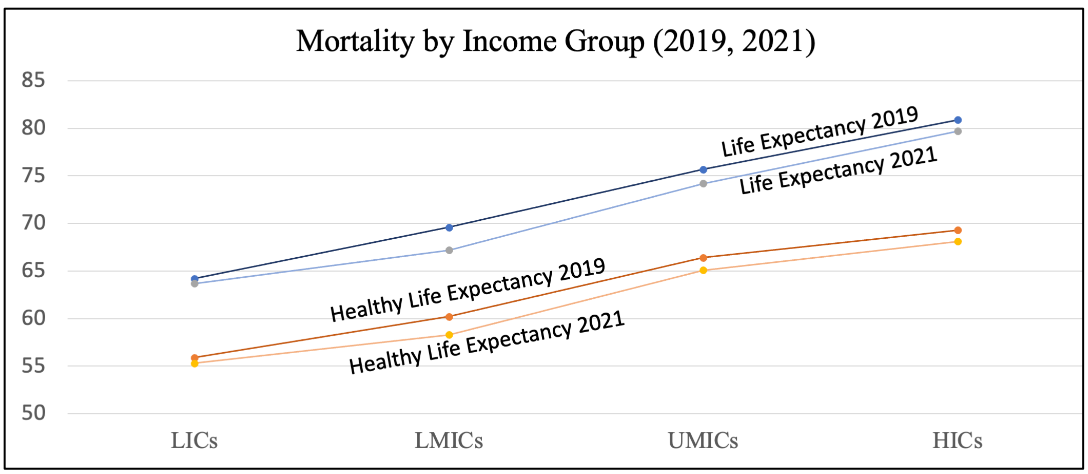
[85] Alzheimer's Disease Internartional, "World Alzheimer Report 2023: Reducing Dementia Risk; Never Too Early, Never Too Late," (2023): 11.

down. But the visibility of such advances and breakthroughs should not blind us to the many sectors where we are not advancing – or indeed are losing ground.

C. Inequality

Not only are the threats presented by these and other diseases increasingly serious, the burdens that many of them impose – and are likely to impose in the future – are distributed highly unequally. There are several dimensions on which that inequality might be measured, and we will address many in due course. But, because this is a book about global policy, our primary focus will be on inequality in health outcomes across countries. We'll begin our analysis with a rough cut – juxtaposing health outcomes and disease burdens in the four major groups of countries as defined by the World Bank. We'll then slice the onion more finely – comparing outcomes and burdens across individual countries.

The following chart compares the four major groups in terms of average life expectancy at birth and average healthy life expectancy, using data provided by the World Health Organization. The four circles on the dark blue and dark orange lines show the relevant numbers for each group in 2019, just before the start of the COVID pandemic. The points on the lighter blue and lighter orange lines show the numbers in 2021, the most recent year for which comparative data is available.



Notice that every indicator in every group of countries declined between 2019 and 2021 – confirmation of the extraordinary impact of COVID-19. For present purposes, however, we are more concerned with the differences among the four groups – represented graphically by the slopes of the four lines.

In 2019, those differences were large. The difference in life expectancy between high-income and low-income countries was 16.7 years, and the difference in healthy life expectancy between high-income and low-income countries was 13.4 years. LMICs and UMICs were spaced reasonably evenly between the poles.

Somewhat surprisingly, COVID reduced the gaps slightly. By 2021, the difference in life expectancy between high-income and low-income countries had declined from 16.7 to 16.0 years, and the difference in healthy life expectancy had declined from 13.4 to 12.8

years. This is one (among many) indication that the pandemic had more severe impacts on rich countries than on poor countries. We'll consider why in due course.

As we've seen, the pandemic is now fading. We know from many sources that the modest reduction in global inequality it caused was short-lived. Unfortunately, comprehensive post-pandemic data is not yet available. Accordingly, to explore the causes of the chronic inequality among the groups of countries (i.e., inequality undistorted by COVID), we will have to make do for the time being with the 2019 numbers. (By the time this book is ready for publication, we may have access to a post-pandemic dataset.)

Set forth below are two tables, both containing data from 2019. The first focuses on mortality; the second on the combination of mortality and morbidity.

Table X: Mortality by Income Group (2019)

	A	B	C	D	E	F
1		**Low Income Countries**	**Lower Middle-Income Countries**	**Upper Middle-Income Countries**	**High Income Countries**	**All countries**
2	Population (thousands)	660,718 (8.5%)	2,927,475 (37.5%)	2,794,430 (35.8%)	1,361,044 (17.5%)	7,796,280
3	Average Life expectancy	64.2	69.6	75.7	80.9	73.1
4	Infectious and Parasitic Diseases (deaths; crude mortality per 100,000)	1,209,688 183.1	2,994,398 102.3	721,595 25.8	260,243 19.1	5,196,351 66.7
5	Respiratory Infections (deaths; crude mortality per 100,000)	434,513 65.8	1,117,900 38.2	639,997 22.9	439,037 32.3	2,650,960 34.0
6	Maternal Conditions (deaths; crude mortality per 100,000)	84,745 12.8	134,260 4.6	18,522 0.7	1,605 0.1	240,068 30.8
7	Neonatal Conditions (deaths; crude mortality per 100,000)	544,646 82.4	1,267,170 43.3	210,515 7.5	32,092 2.36	2,060,130 26.4
8	Nutritional Deficiencies (deaths; crude mortality per 100,000)	64,303 9.7	78,844 2.7	73,327 2.6	38,354 2.82	255,767 3.3
9	Noncommunicable Conditions (deaths; crude mortality per 100,000)	1,915,033 289.8	11,847,851 404.7	16,968,295 607.2	10,993,735 807.7	42,009,746 538.8
10	Injuries (deaths; crude mortality per 100,000)	556,256 84.2	1,770,622 60.5	1,465,986 52.5	711,700 52.3	4,545,979 58.3
11	*All Causes (deaths; crude mortality per 100,000)*	*4,809,183* *727.9*	*19,211,045* *656.2*	*20,098,236* *719.2*	*12,476,766* *916.7*	*56,959,000* *730.6*

Table Y: Mortality and Morbidity by Income Group (2019)[86]

	A	B	C	D	E	F
1		**Low Income Countries**	**Lower Middle Income Countries**	**Upper Middle Income Countries**	**High Income Countries**	**All countries**
2	Population	660,718 (8.5%)	2,927,475 (37.5%)	2,794,430 (35.8%)	1,361,044 (17.5%)	7,796,280
3	Average HALE	55.9	60.2	66.4	69.3	63.5
4	Infectious and Parasitic Diseases (DALYs)	82989 (26.7%) 12415	182400 (58.6%) 6260	40117 (12.9%) 1382	5812 (1.9%) 475	311318 4039
5	Respiratory Infections (DALYs)	27212 (23.8%) 4071	60336 (52.7%) 2071	20058 (17.5%) 691	6825 (6.0%) 558	114431 2200
6	Maternal Conditions (DALYs)	4333 (34.3%) 648	6903 (54.6%) 237	1276 (10.1%) 44	137 (0.1%) 11	12649 164
7	Neonatal Conditions (DALYs)	48277 (23.9%) 7222	123036 (60.1%) 4223	26134 (12.9%) 900	4374 (2.2%) 357	201821 2618
8	Nutritional Deficiencies (DALYs)	9351 (19.4%) 1399	28883 (60.0%) 991	7979 (16.6%) 275	1912 (4.0%) 156	48125 624
9	Noncommunicable Conditions (DALYs)	105219 (6.6%) 15741	559850 (35.4%) 19215	622356 (39.3%) 21442	295231 (18.7%) 24126	1582657 20532
10	Injuries (DALYs)	34034 (13.1%) 5091	105188 (40.3%) 3610	88065 (33.8%) 3034	33423 (12.8%) 2731	260710 3382
11	*All Causes (DALYs)*	*311416* *(12.3%)* *46587*	*1066596* *(42.1%)* *36608*	*805985* *(31.8%)* *27768*	*347714* *(13.7%)* *28414*	*2531710* *32844*

These tables are complex and merit some explanation. In both, the numbers in Row 2 indicate the number of persons and the percentage of the global population that lives in each group of countries identified by the World Bank. In Table X, the numbers in Row 3 indicate the average life expectancy at birth in each group. The remaining rows then show the number of people in each group who died as a result of each major cause and the associated crude mortality rate. (Unfortunately, the corresponding age-standardized rates are not available at this level of granularity.)

In Table Y, the numbers in Row 3 indicate the average Healthy Life Expectancy of each group. In all of the cells in Rows 4 through 10, the first number indicates (in thousands) the total number of DALYs forfeited annually in that region by the disease or condition of the type at issue, the second number shows the percentage borne by countries in that group of the total number of DALYs caused by that type of disease or condition

[86] All data are derived from WHO, "Global Health Estimates 2019: Dalys by Age, Sex and Cause," (Geneva2020). A description of the methods and data sources used by the WHO in assembling this data is available at http://terrance.who.int/mediacentre/data/ghe/GlobalCOD_method_2000_2016.pdf?ua=1.

globally, and the third number indicates the number of DALYs per 100,000 population suffered annually in that group as a result of the disease or condition. So, for example, cell E10 informs us that, in 2019, injuries (both intentional and unintentional) resulted in a loss of 33,423,000 DALYs in high-income countries (which represented 12.8% of the global DALY burden from injuries) and those same injuries caused a loss of 2731 DALYs for every 100,000 people in high-income countries.

As both tables makes clear, most of the sources of mortality and morbidity are distributed highly unequally among the four income-based categories of countries. For example, Rows 6 and 7 in both tables confirm the common expectation that losses due to maternal and neonatal conditions are much higher in poor countries than in rich countries. And Row 8 in both tables confirms that people starve or are malnourished in poor countries much more often than in rich countries.

Some nuances lurk elsewhere in the tables. For example, a comparison of Row 10 in Table Y with the same row in Table X reveals that, while the loss of <u>DALYs</u> due to injuries is much higher in richer countries than in poorer countries, <u>deaths</u> due to injuries are not quite so unequally distributed.

But all of the aforementioned comparisons pale when we turn our attention to Row 4. The maldistribution of infectious diseases, it quickly becomes apparent, is extreme. The mortality rate associated with those diseases is low-income countries is almost 10 times the rate in high-income countries. Even more striking is the corresponding comparison in Table Y. When mortality is combined with morbidity, the losses per year in low-income countries is 26 times the rate in high-income countries. The rates in lower-middle-income and upper-middle-income countries are spaced reasonably evenly between those poles.

Equally dramatic is the sheer amount of suffering. The total number of DALYs forfeited in poor countries through the prevalence of infectious diseases is enormous: 83 million per year in low-income countries and 182 million in lower-middle-income countries.

What then are the infectious diseases whose incidence has given rise to these disparities? There are many, it turns out, of which 28 did most of the damage. Eight of them were discussed in the previous section. The full list, the clusters in which they are conventionally organized, and the data concerning their impacts are set forth in the chart presented on the opposite page.[87]

[87] The two reports from which these data are gleaned are: ibid.; WHO, "Global Health Estimates 2019: Estimated Deaths by Age, Sex, and Cause," (Geneva2020).

Table Z: Infectious Diseases (2019)

	Global Deaths (thousands)	Global DALYs (thousands)
HIV/AIDS	715	44,590
Tuberculosis*	1,327	59,109
Malaria*	578	49,830
STDs (excluding HIV/AIDS)		
Syphilis	60	5,519
Chlamydia	1	160
Gonorrhoea	0	72
Trichomoniasis	0	266
Genital herpes	0	253
Other STDs	4	506
Diarrhoeal Diseases	1,324	74,699
Childhood Diseases		
Pertussis ("whooping cough")	132	11828
Diphtheria	5	392
Measles	132	11553
Tetanus	23	1506
Meningitis	221	15579
Encephalitis	82	4632
Hepatitis		
A	33	2229
B	42	2202
C	19	643
E	4	254
Parasitic and vector diseases (excluding Malaria)		
Trypanosomiasis*	1	66
Chagas*	7	208
Schistosomiasis	14	1934
Leishmaniasis*	6	869
Lymphatic filariasis (elephantiasis)	0	1375
Onchocerciasis (river blindness)	0	1285
Cysticercosis	8	1071
Echinococcosis	9	505
Dengue	26	1907
Trachoma (infectious blindness)	0	134
Yellow fever	7	489
Rabies	48	2833
Intestinal nematode infections		
Ascariasis	4	715
Trichuriasis	0	194
Hookworm	0	593
Food-bourne trematodes	0	887
Leprosy	0	29
Other infectious diseases	365	20556
Totals	**5,196**	**321,476**

Before we go on, a note about terminology: The WHO has, influentially, classified diseases as Type I, Type II, and Type III, corresponding to global, developing-country, and neglected diseases.[88] All of the diseases included in Table Z fall into the second category, meaning that the burdens associated with them are borne overwhelmingly by developing countries.[89] All except HIV/AIDS (and, perhaps, TB) are also "neglected diseases,"[90] so called for reasons that will become increasingly obvious. Finally, the diseases marked with asterisks were identified by a joint roundtable of the WHO and the International Federation of Pharmaceutical Manufacturers Associations (IFMPA) as the ailments most in need of additional research – and consequently have come to be known as "priority diseases."[91] We will try to use these labels consistently in the book.

The most striking number in Figure Y is the total number of deaths. Together, infectious diseases killed roughly 5.1 million people in 2019 – 82% of them in low-income or lower-middle-income countries. But that number, horrific as it is, seriously understates the problem. Several of these diseases – Chlamydia, Gonorrhoea, Diphtheria, Lymphatic filariasis, Onchocerciasis, and all of the intestinal infections – kill few people, but cause the loss of large numbers of DALYs. When those figures are added to the DALY losses associated with the major killers, the total is staggering: the equivalent, annually, of 321 million years of lost human life – 85% of them in low-income or lower-middle-income countries.

The global losses due to respiratory infections are distributed almost as unequally. Included in this category are the common cold, bronchitis, and pneumonia. As row 5 in Figure Y shows, the number of DALYs per capita caused by those ailments in low-income countries is seven times the corresponding number in high-income countries.

Turning finally to noncommunicable conditions (for which we will use the conventional abbreviation NCDs), Row 9 of both tables makes clear that the diseases in this category now cause by far the largest number of deaths and of lost DALYs throughout the world. At first glance, however, they do not seem to contribute to global health

[88] WHO, Investing in Health for Economic Development – Report of the Commission on Macroeconomics and Health 78 (2001) ("*Type I diseases* are incident in both rich and poor countries"; "*Type II diseases* are incident in both rich and poor countries, but with a substantial proportion of the cases in the poor countries [...] HIV/AIDS and tuberculosis are examples"; "*Type III diseases* are those that are overwhelmingly or exclusively incident in the developing countries.").

[89] See Lanjouw & Cockburn 1999, defining "developing country diseases" in similar terms.

[90] Among the sources using these terms – although not always identically – are Medecins Sans Frontieres, *Fatal Imbalance: The Crisis in Research and Development for Drugs for Neglected Diseases* (2001); Patrice Trouiller et al., *Drug Development for Neglected Diseases: A Deficient Market and a Public-Health Policy Failure*, 359 LANCET 2188 (2002); WHO, World Health Report 2003; and EFPIA, *infra*, note 91.

[91] Cited in European Federation of Pharmaceutical Industries and Associations, *Research & Development (R&D) and Diseases Prevalent in Developing Countries*, available at http://www.efpia.org/4_pos/access/RDdevecountries.pdf. The criteria used to determine which diseases were in greatest need of further R&D included the toll taken by the disease, the adequacy of currently available treatments, the presence of scientifically tractable targets, and whether or not substantial R&D was already underway. A similar list of diseases has been devised by the Medecins Sans Frontieres Campaign for Access to Essential Medicines; *see* http://www.accessmed-msf.org/ (identifying the Campaign's "Target Diseases" as HIV/AIDS, tuberculosis, malaria, leishmaniasis, trypanosomiasis, trachoma and meningitis, the last of which, while technically not a developing-country disease, does have roughly 90% of its global deaths and DALYs toll occur in the developing world).

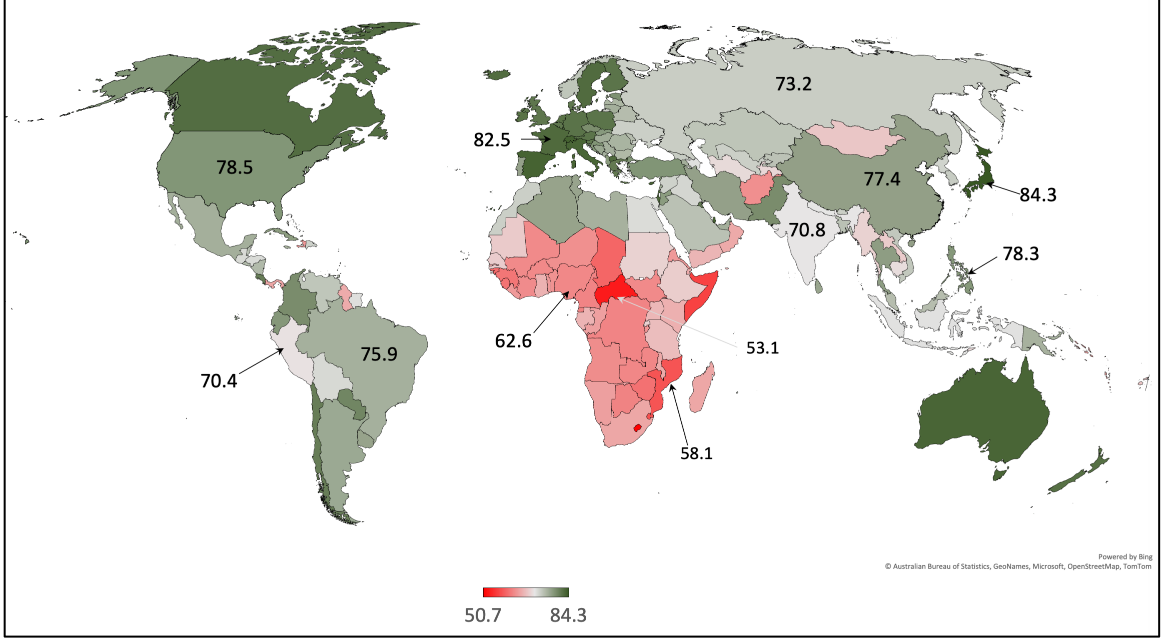
inequality. Indeed, the losses per person from NCDs are lower in poorer countries than in richer countries. Figure X thus seems to confirm the common view that, the more wealthy a country, the more likely are its residents to suffer from heart disease, cancer, and so forth. (We will return to this issue shortly.)

The data we have deployed thus far, rough as they are, should be sufficient to establish two propositions: (1) Global inequality in health outcomes is severe. (2) The inequality is due in substantial part to unequal burdens from infectious diseases, broadly defined. Those propositions, in turn, are sufficient to motivate the project of this book.

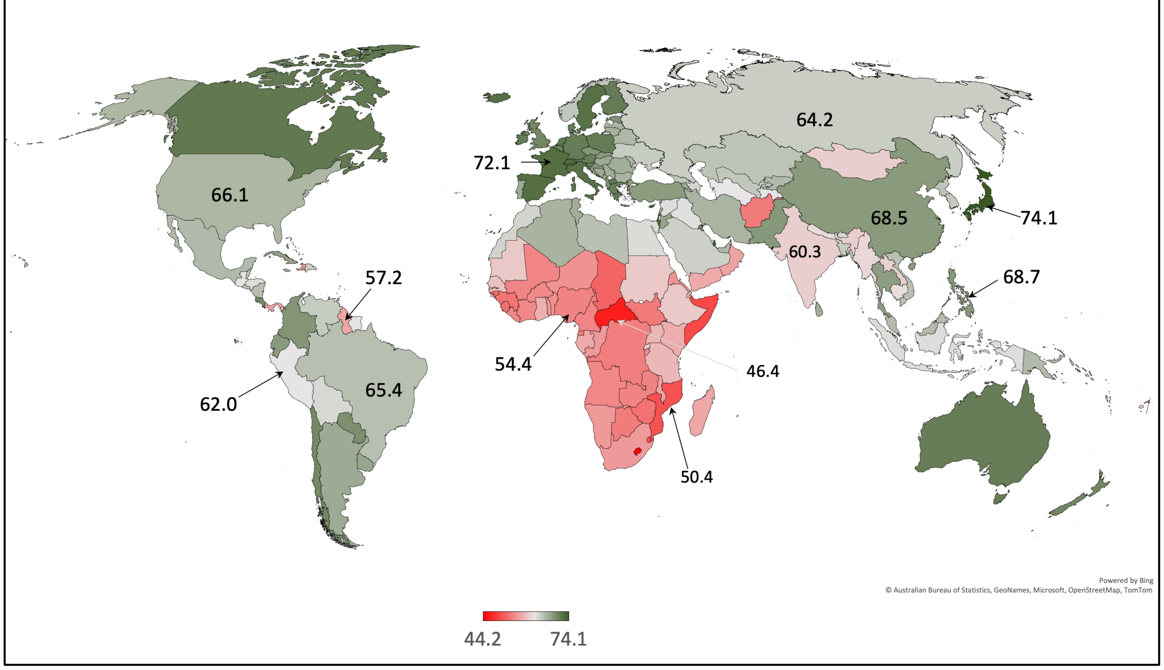
But we can refine the analysis in two ways – by breaking down the World Bank's categories into individual countries, and then by examining how each country fared with respect to each of the 14 diseases in our sample. These refinements will reinforce our central points, but also expose subtleties that will prove useful when, in subsequent chapters, we begin to explore solutions to the crisis.

Presenting the dense country-level data using tables would be unhelpful; the blizzard of numbers would obscure both the overall trends and the subtleties. Instead, we will use maps. The first two maps, below, show life expectancy and healthy life expectancy (again, as of 2019) for each country.

Life Expectancy at Birth (2019)



Healthy Life Expectancy (HALE) at Birth (2019)

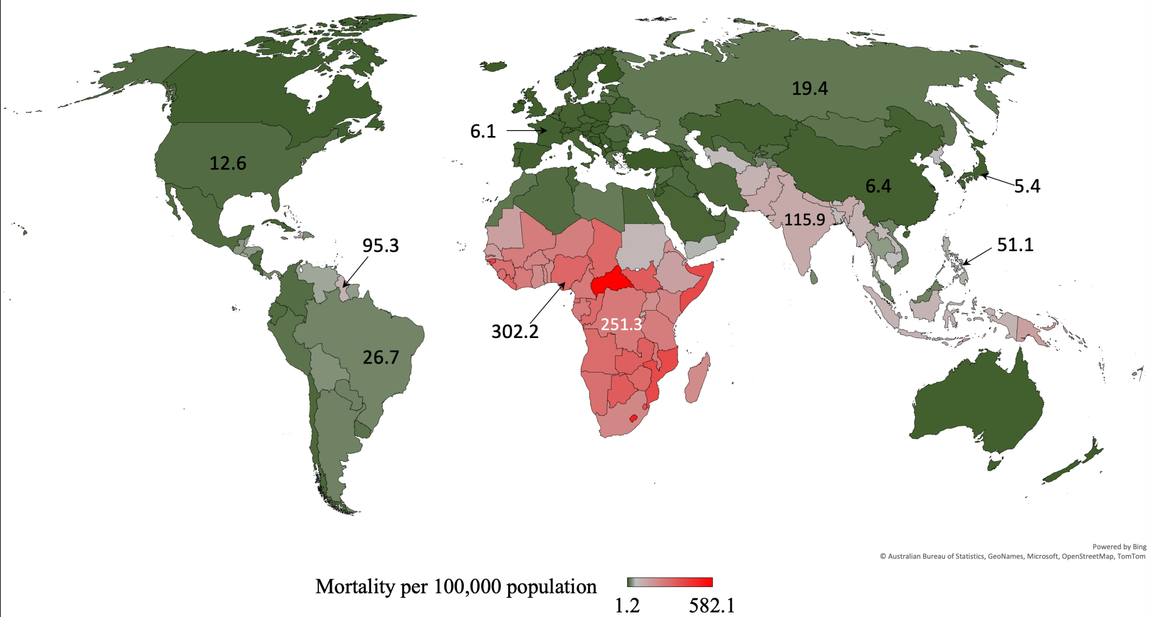


Many things are striking about these maps. For example, readers may be surprised to see that the populations of China, the United States, Brazil, and the Soviet Union are remarkably similar in terms of both life expectancy and healthy life expectancy – and that all four fall well below the countries of western Europe. Also noteworthy are the substantial variations in health outcomes among the countries in several regions: Latin America, South Asia, and above all Africa.

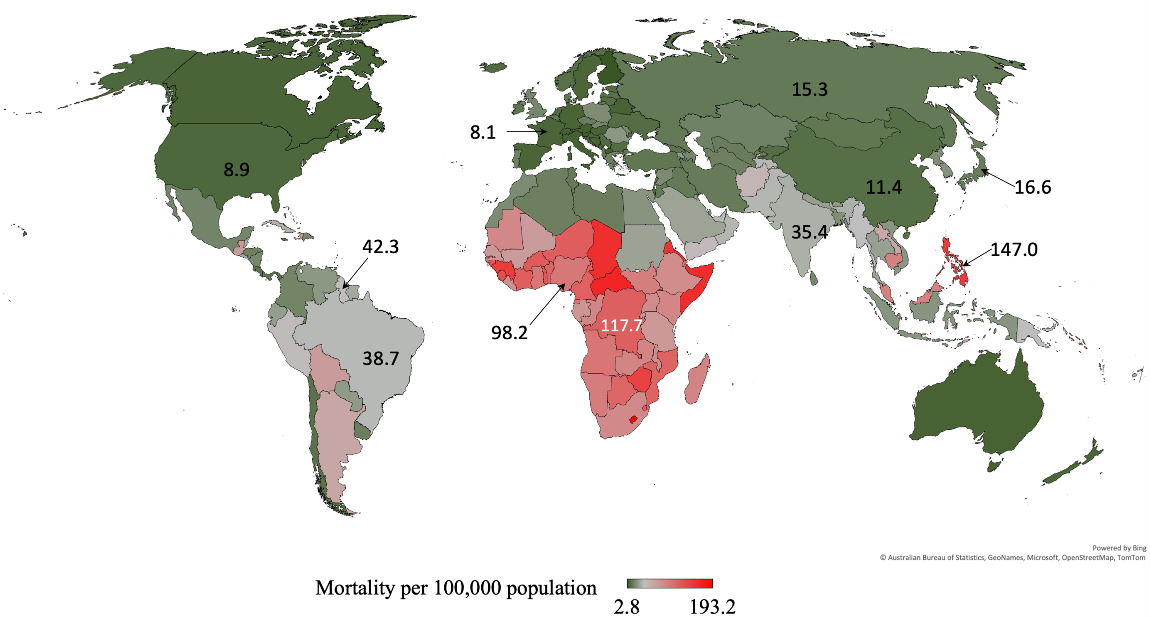
But the most important and germane of the messages conveyed by these two maps is the magnitude of the inequality among countries. In terms of life expectancy, the gap between the most hospitable country (Japan) and the least (Lesotho) is 26.3 years. In terms of healthy life expectancy, the gap is 29.9 years.

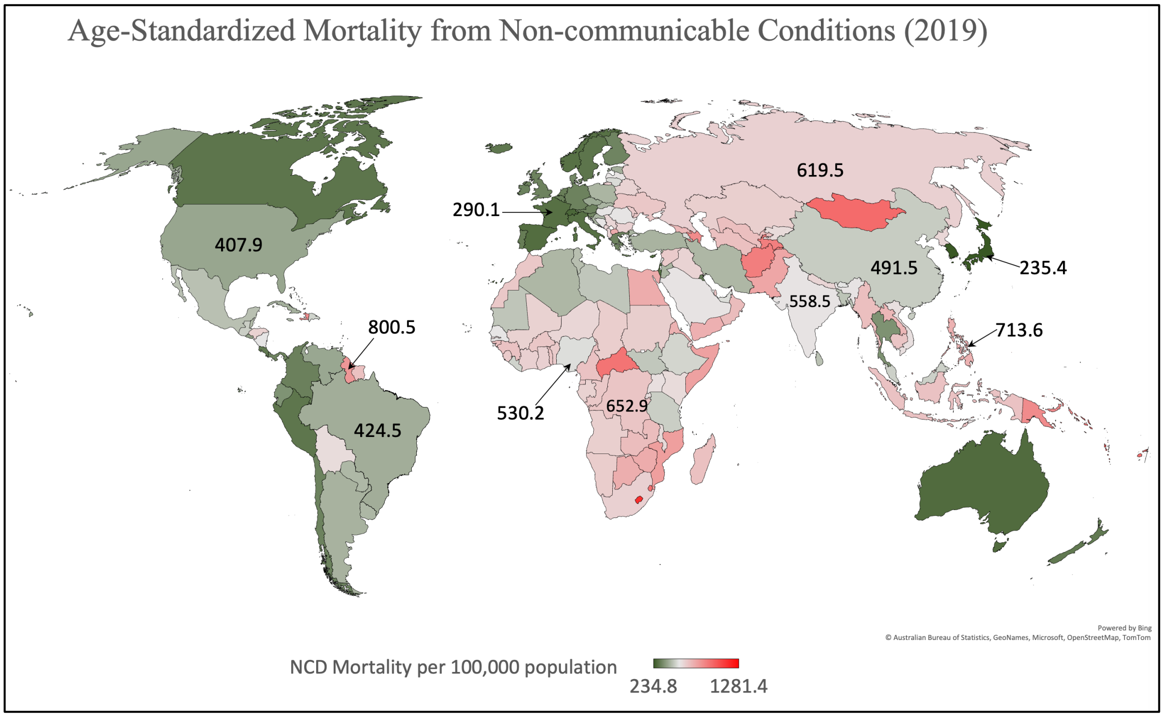
When looking for explanations – both for these huge overall disparities and for the more complex pattern patterns revealed by the maps – we would do well to consider the same three families of disease that loomed largest when we considered the differences among the World-Bank groups: infectious diseases, respiratory infections, and noncommunicable conditions. We might use any of several metrics to determine their relative impacts on a country-by-country level. For the time being we will focus on one: age-standardized mortality rates. The following three maps display the relevant data.

Age-Standardized Mortality from Infectious Diseases (2019)



Age-Standardized Mortality from Respiratory Infections (2019)





If there were any doubt concerning the inequality of the burdens associated with infectious diseases, these maps would dispel it. The ranges in the first map (1.2 to 582) and the second (2.8 to 193) are simply astonishing, and the patterns in those two maps align to a distressingly high degree with the patterns of life expectancy and healthy life expectancy.

More surprising is the pattern of the third map, which shows age-standardized mortality for NCDs. The rough numbers discussed above seemed to support the conventional view that NCDs bear more heavily on rich countries than on poor countries. Here, when the data have been broken down by country – and, most importantly, have been adjusted to control for the fact that the residents of rich countries are, on average, older than the residents of poor countries – a different picture emerges. Even with respect to NCDs, it appears that poor countries fare worse. To be sure, the correlation between wealth and burdens is not as strong as with respect to infectious diseases, and the range of burdens is not as big (234 to 1281). But the standard pattern emerges yet again: the residents of Japan, Western Europe, Australia, New Zealand, and (to some extent) North America are less likely to die at any given age from an NCD than are the residents of Africa, Asia, and some portions of Latin America.

Indeed, as overall life expectancy in poor countries gradually improves, the incidence and prevalence of NCDs in those countries has been increasing (and likely will continue to increase) more rapidly than in richer countries. This of course will exacerbate overall health inequality.

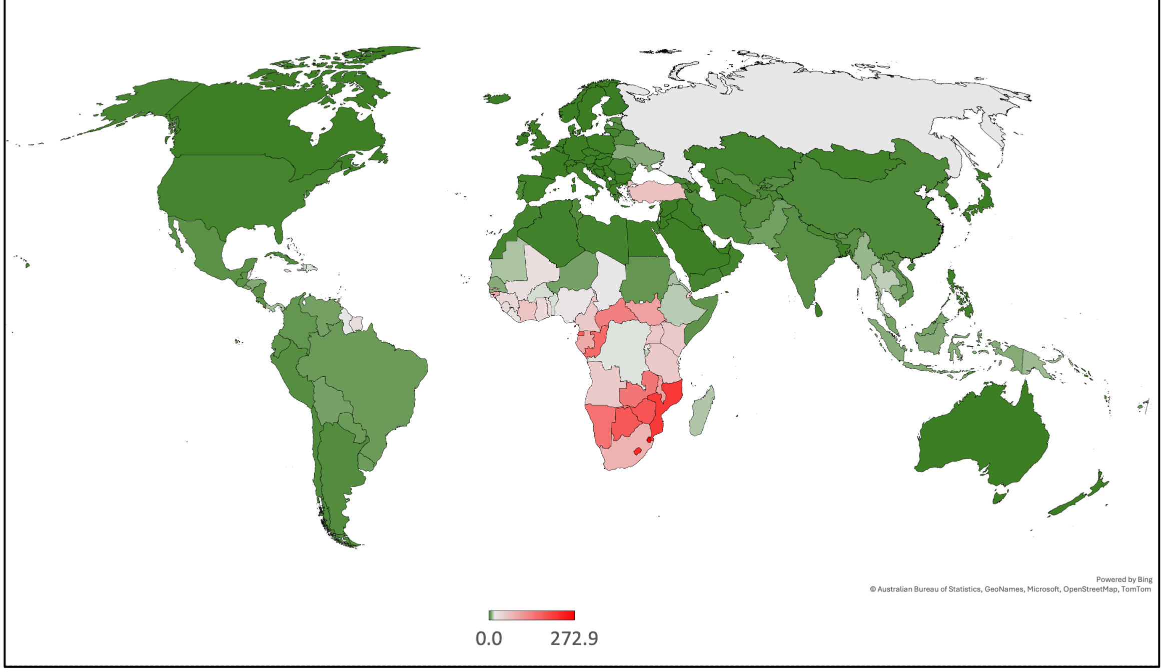
One other point lurks in the first of the three maps. As some members of the audiences to which we have presented drafts of this book have pointed out, most low-income and lower-middle-income countries are located reasonably close to the equator, and some of the pathogens and vectors (such a mosquitos) that, in combination, cause infectious diseases are more common in warm climates than in temperate zones. It is thus unsurprising, they have suggested, that the burdens of infectious diseases are heavier in poor countries than in rich countries. Typically left unsaid is the implication that eliminating that disparity altogether is likely to be impossible.

There is a good deal of force to this point, but its limits are suggested by the large differences in infectious-disease burdens within sets of countries that are geographically proximate. For example, the age-standardized mortality rate (per 100,000 people) associated with infectious diseases in South Korea (a HIC) in 2019 was 10.1, while in North Korea (a LIC) it was 64.3. The corresponding burden in Singapore (a HIC) was 3.9, while in Malaysia and Indonesia (which surround Singapore) (both UMICs), it was 25.5 and 115.9, respectively. In short, climate matters, but not as much as is sometimes supposed.

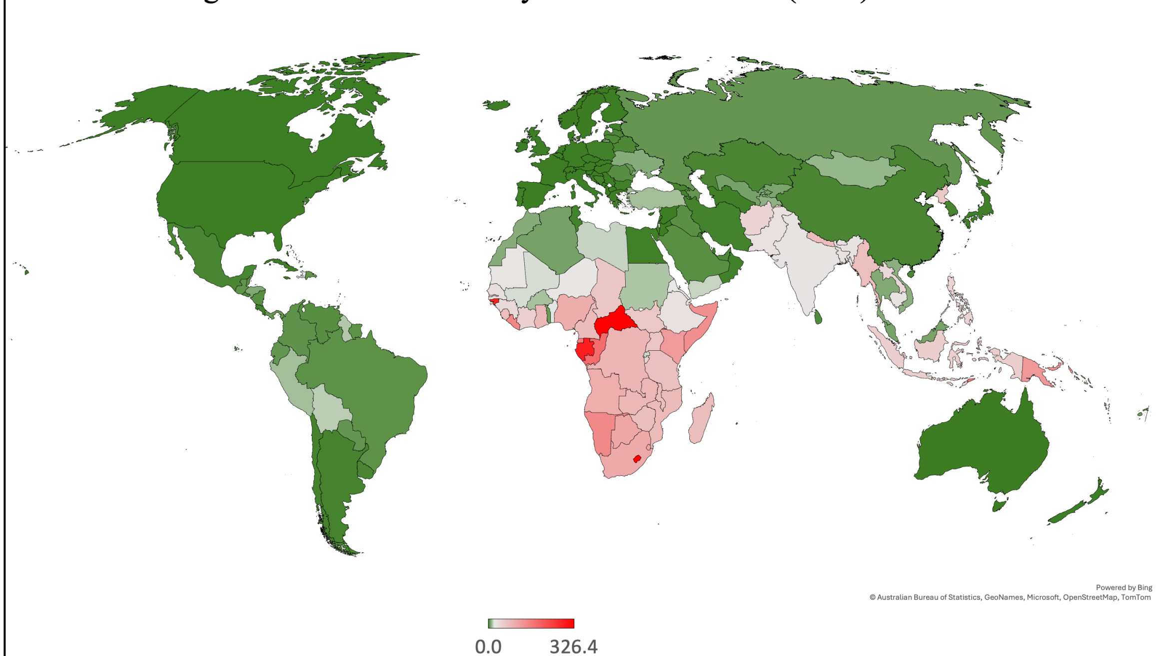
We will close by displaying a final set of maps that show (in terms of age-standardized mortality) country-by-country burdens associated with the diseases chronicled above that we have selected as illustrative of the current crisis. Because these maps show the footprints of individual diseases, we no longer need to rely upon the 2019 data in order to avoid the distortions associated with the inclusion of COVID-19 in the mix. Accordingly, we will use the most recent available dataset, which is from 2021. (Again, by the time this book is ready for publication, we hope to have access to even more recent data.)

These final maps are not essential to the argument of this chapter. We include them, nevertheless, for two reasons. First, they provide foundations for some specific reform proposals advanced in chapters 5 through 10. Second, they help corrode the impression (which some of the preceding maps may have left) that the problem of infectious diseases is exclusively an “Africa problem.” As will soon become apparent, some of the infectious diseases bear equally heavily on low-income and lower-middle-income countries outside Africa.

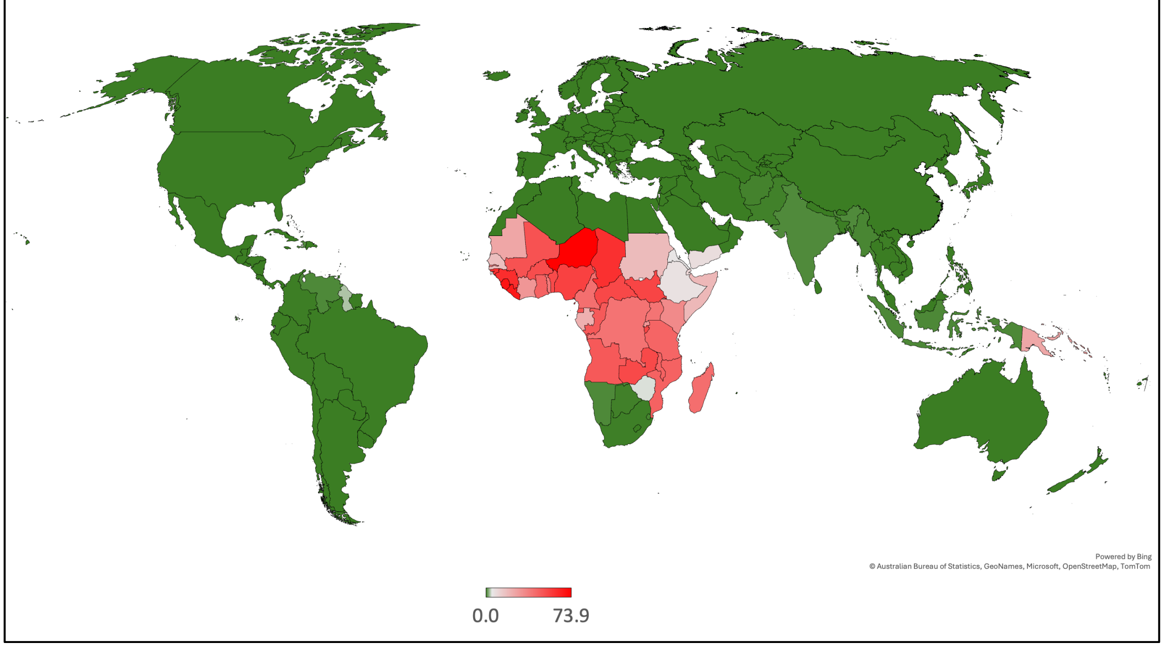
Age-Standardized Mortality from HIV/AIDS (2021)



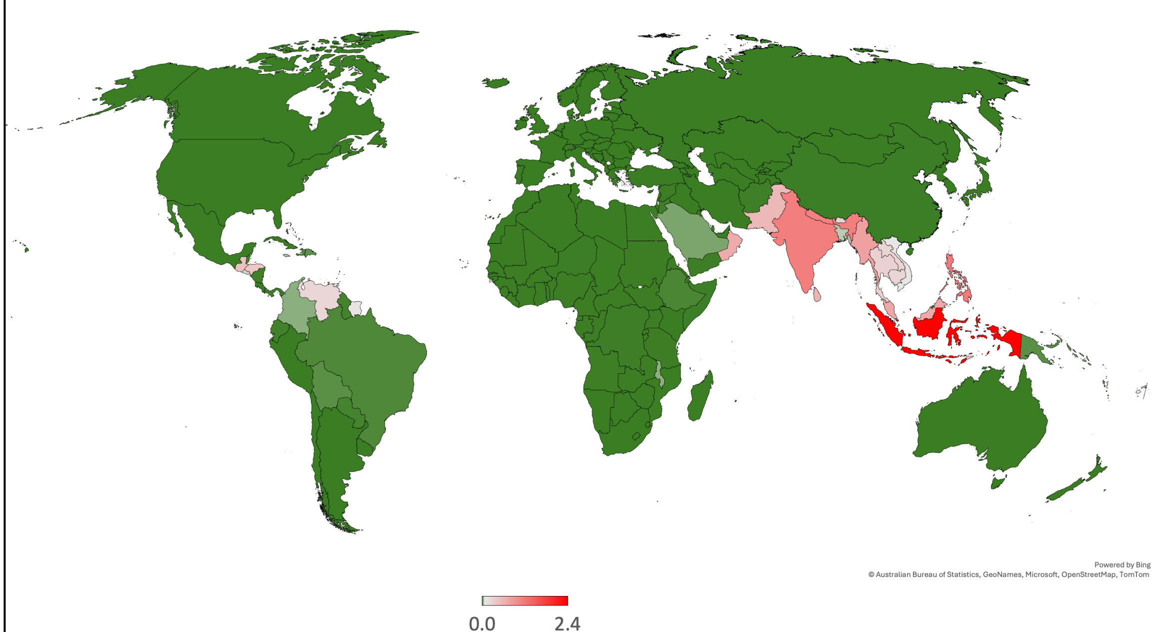
Age-Standardized Mortality from Tuberculosis (2021)



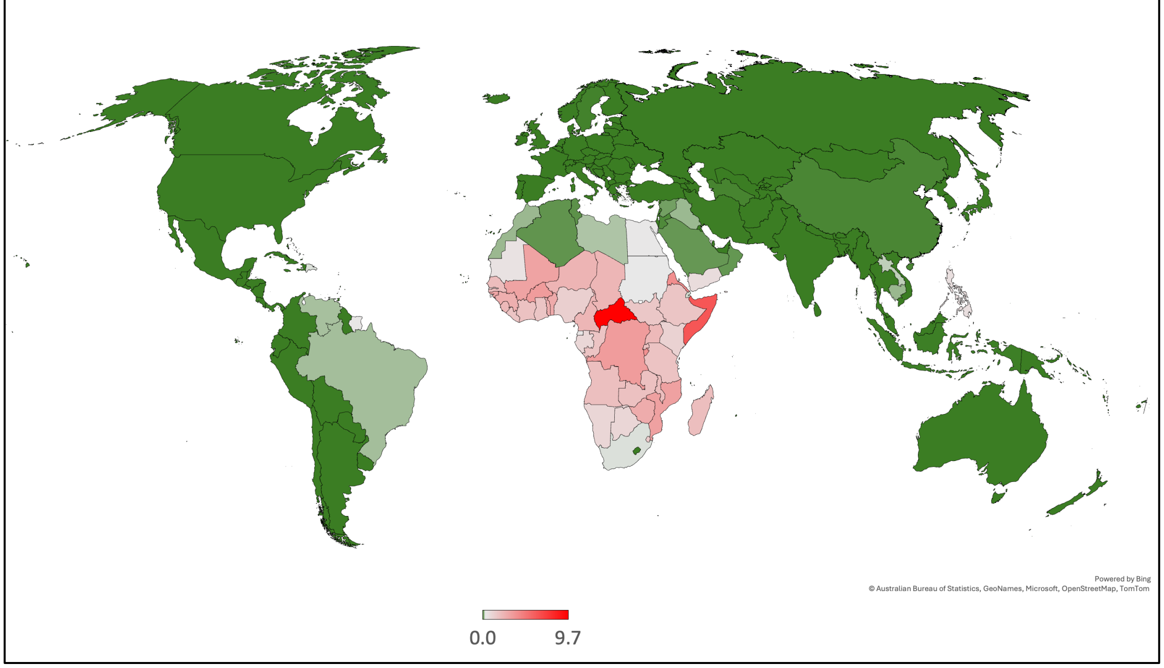
Age-Standardized Mortality from Malaria (2021)



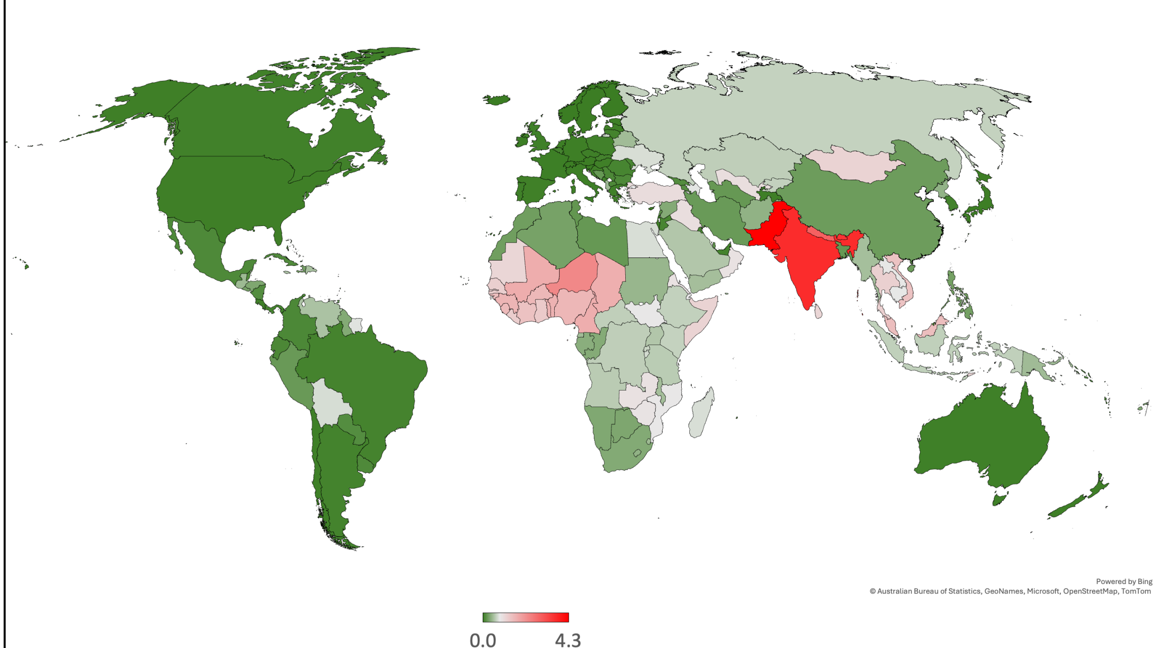
Age-Standardized Mortality from Dengue (2021)



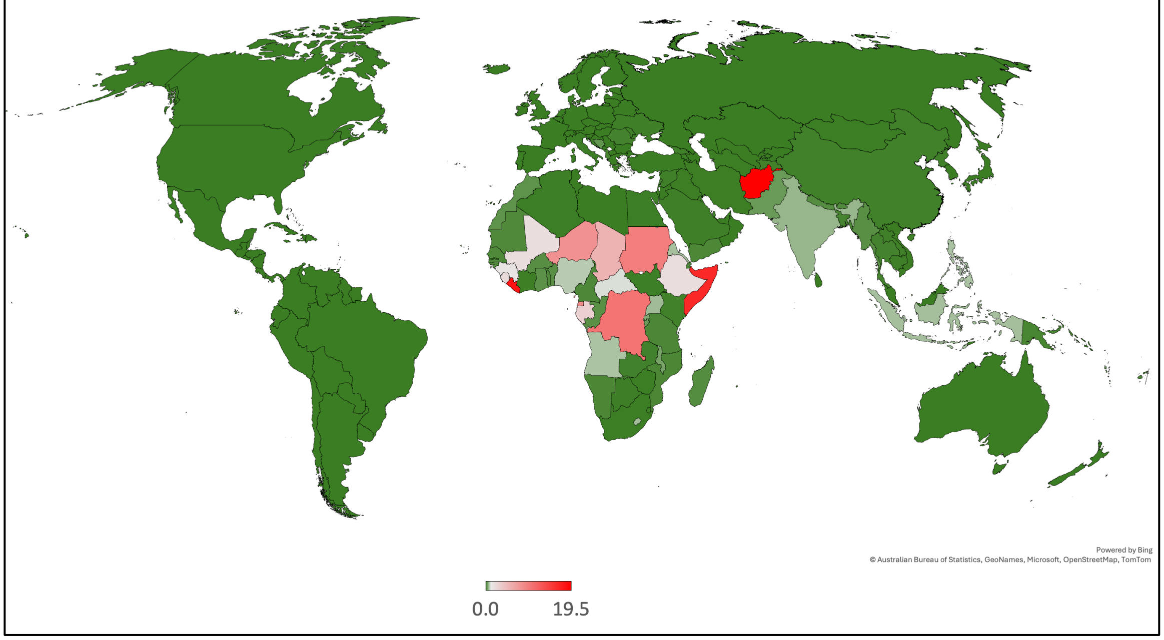
Age-Standardized Mortality from Schistosomiasis (2021)



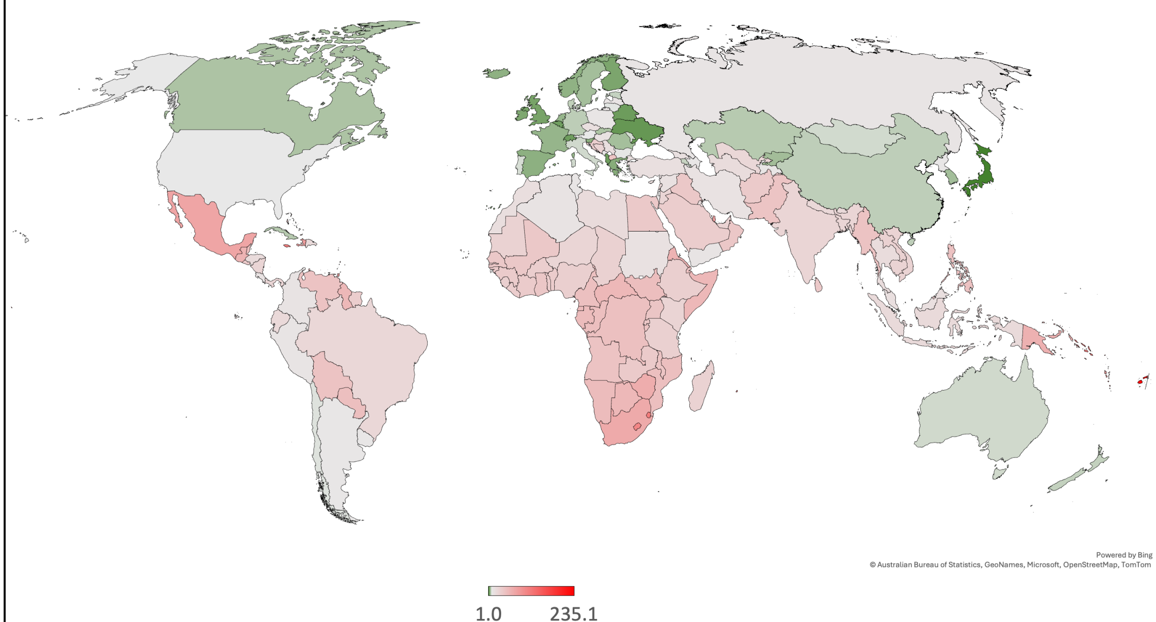
Age-Standardized Mortality from Encephalitis (2021)



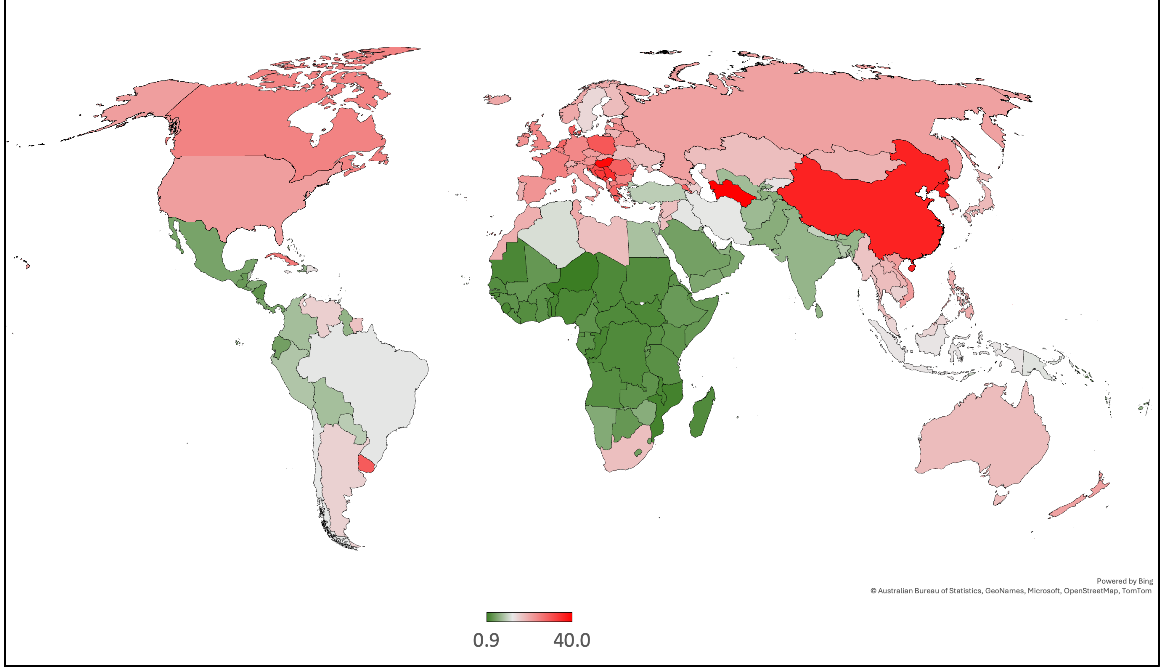
Age-Standardized Mortality from Measles (2021)



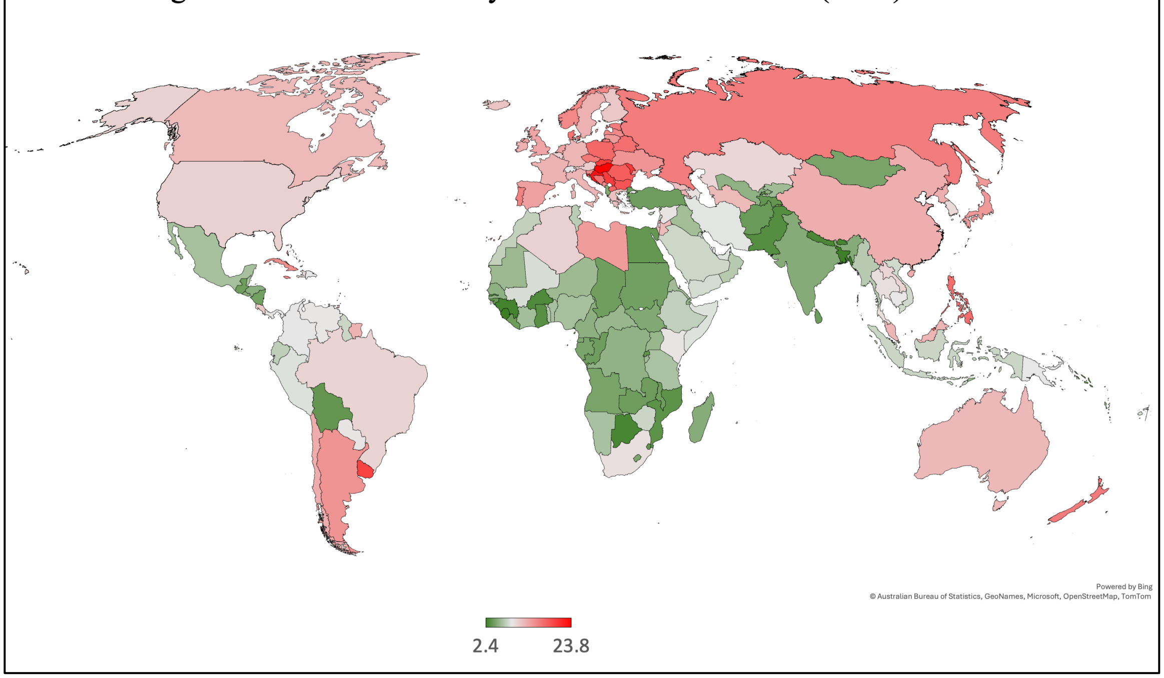
Age-Standardized Mortality from Diabetes (2021)



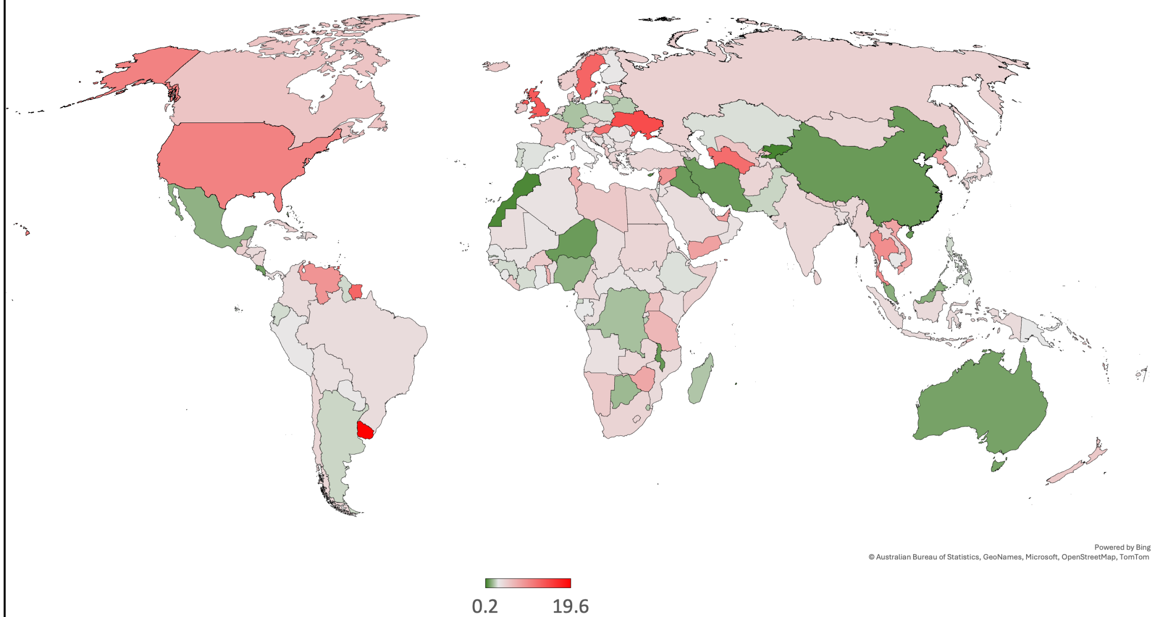
Age-Standardized Mortality from Lung Cancer (2021)



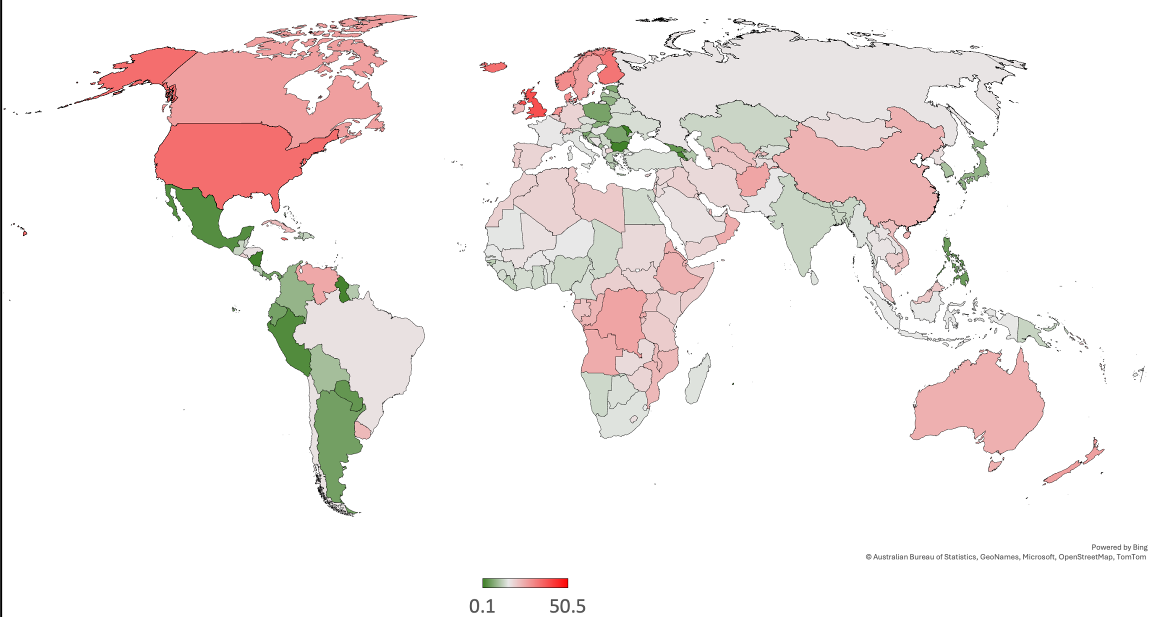
Age-Standardized Mortality from Colorectal Cancer (2021)

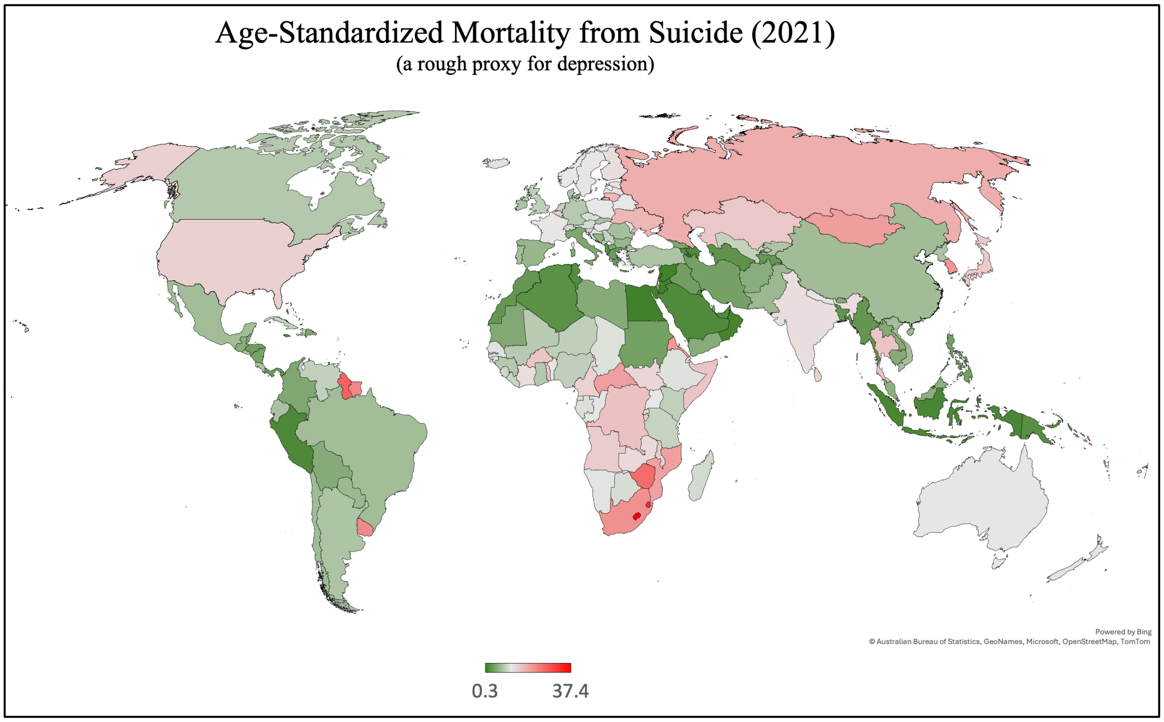


Age-Standardized Mortality from Parkinson's Disease (2021)



Age-Standardized Mortality from Dementia (2021)




Age-Standardized Mortality from Suicide (2021)
(a rough proxy for depression)
Powered by Bing
© Australian Bureau of Statistics, GeoNames, Microsoft, OpenStreetMap, TomTom
0.3
37.4

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