Infection

The Health Crisis in the Developing World and What We Should Do About It

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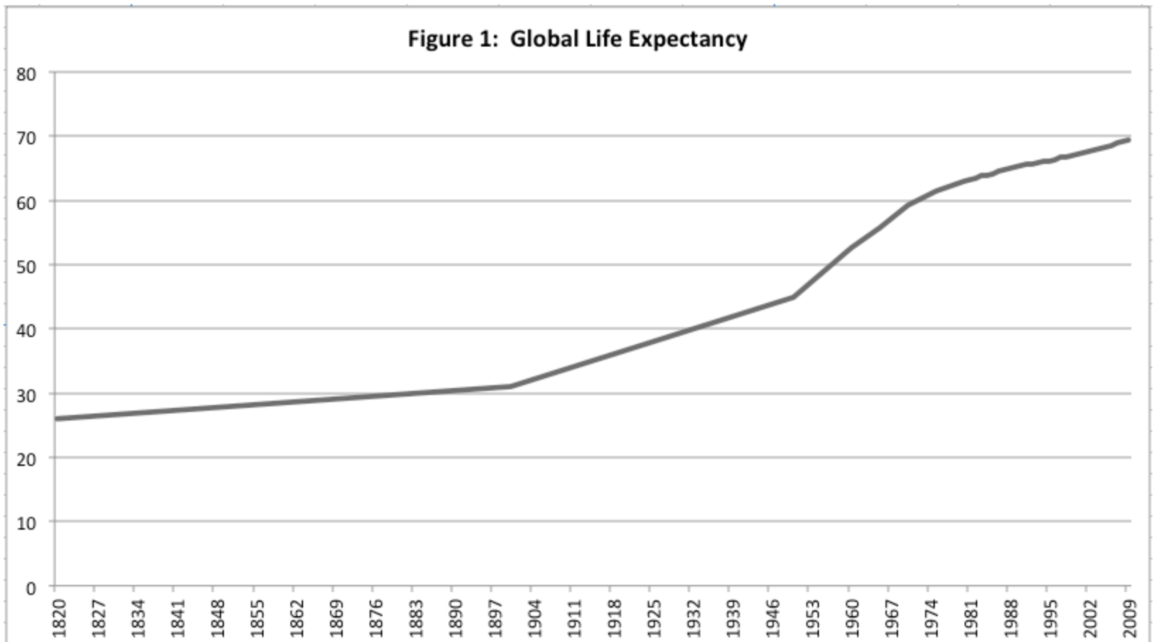
Introduction

By one crucial measure, the earth is becoming a healthier place. Until the nineteenth century, the life expectancy of the average person born on the planet was between 20 and 30 years.[1] As late as 1820, it was approximately 26 years. It then began to increase, first slowly, then rapidly, then more slowly. Today, the number is roughly 70 years and still rising.[2] These trends are captured in the following graph:



Buried in these averages, however, are some persistent disparities. The residents of developed countries continue to live much longer, on average, than the residents of developing countries. For example, in 2012, life expectancy at birth in the United States was

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[1] See 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.

[2] The figures set forth in this paragraph – and in Figure 1, below – were culled from the following sources: 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/. Riley, *Life Expectancy*, Chapter 1.; "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). Where the data supplied by different sources have diverged, we have tried to locate the median, but have given extra weight to sources that seem to us especially reliable.

All of these numbers are potentially misleading in one respect: they presume that health conditions would not change during the person's lifetime. Because health conditions were improving during the nineteenth and twentieth centuries, the average person in fact lived somewhat longer.

Whether we are now approaching an asymptote is contested. Some scientists believe that the human life span cannot be extended indefinitely – and thus that average life expectancy will never rise higher than somewhere between 85 and 100 years. Others believe that scientific advances will continue to raise the ceiling. Because this debate has little to do with the issues addressed in this book, we will not pursue it further.

79 years. Many developed countries had attained even higher levels. In Japan, for instance, in 2012 life expectancy was 84 years. By contrast, in Sierra Leone, it was 46 years. The situation in the rest of sub-Saharan Africa was only modestly better; in most countries in the region, life expectancies were in the 50s. Conditions in Latin America were considerably better, but still substantially worse than in North America or Western Europe. For example, in 2012 life expectancy in Bolivia was 68 years. Many countries in Southeast Asia had similar numbers.[3]

Some of the countries on the lower end of this spectrum have recently experienced improvements – indeed, are closing the gap between themselves and the countries at the top. For example, while life expectancy in the United States has risen by only 4 years since 1990, it Bolivia, it has risen by 10 years; in India by 8 years; in China, by 6 years. [4] Other countries on the lower end, however, are stagnating. Of the 163 nations that in 1990 had life expectancies lower than that in the United States, 43 gained less between 1990 and 2009 than then United States.[5] Indeed, in 14 of those countries, life expectancy declined.[6]

Set forth below is a map, prepared by the World Health Organization (WHO), that compares (using 10-year ranges) the life expectancy in all countries:

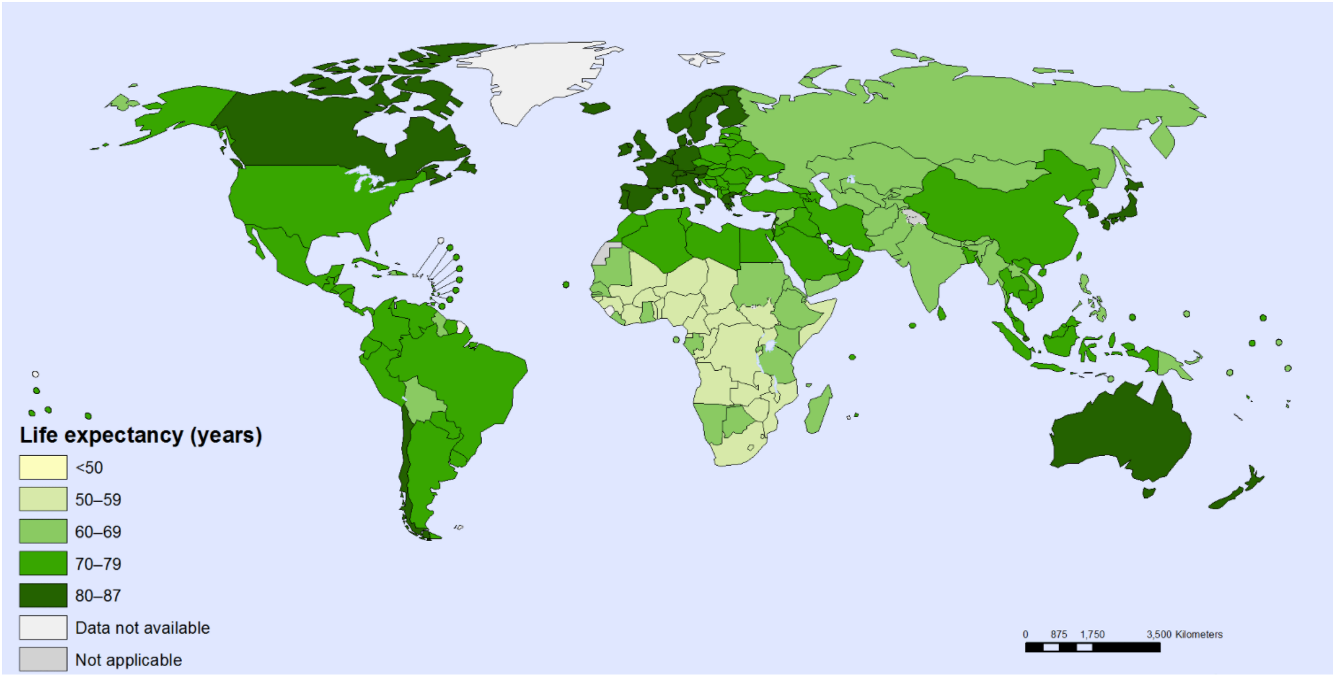
[3] All data are from WHO, "World Health 2014". The numbers provided by the World Bank are slightly lower. Its database reports that 2012 life expectancy in the United States was 79; in Japan, 83; in Sierra Leone, 45; in Bolivia, 67. World_Bank, "Life Expectancy at Birth," http://data.worldbank.org/indicator/SP.DYN.LE00.IN.

[4] These numbers are derived from WHO, "World Health 2014"., pp. 63-68. If we employ the data supplied by the World Bank, the story is slightly different: Life expectancy in the United States rose 3.526 years between 1990 and 2012; in Bolivia, by 8.148 years; in India, by 7.682 years; and in China, by 5.728 years.

[5] [Adjust these numbers for 2012.] These numbers are conservative, because they are derived from the World Bank's data, which, as indicated above, report that the United States gained only 3.526 years in life expectancy between 1990 and 2012. 43 of the 163 nations that lagged behind the United States in 1990 gained less than that. If we employed the WHO's data, the numbers would look even worse.

[6] All of these numbers are derived from the data that can be downloaded from the World Bank's website: http://data.worldbank.org/indicator/SP.DYN.LE00.IN. Cf. Goklany, *The Improving State of the World*, 38. ("Of the 176 entities for which the World Bank's online database had data, 39 had lower life expectancy in 2003 than in 1990. Of those, 25 were in sub-Saharan Africa, 9 were part of the former Soviet Union, 4 were from Latin America and the Caribbean, and 1 was North Korea.")

Figure 2: Life Expectancy at Birth (2012)[7]

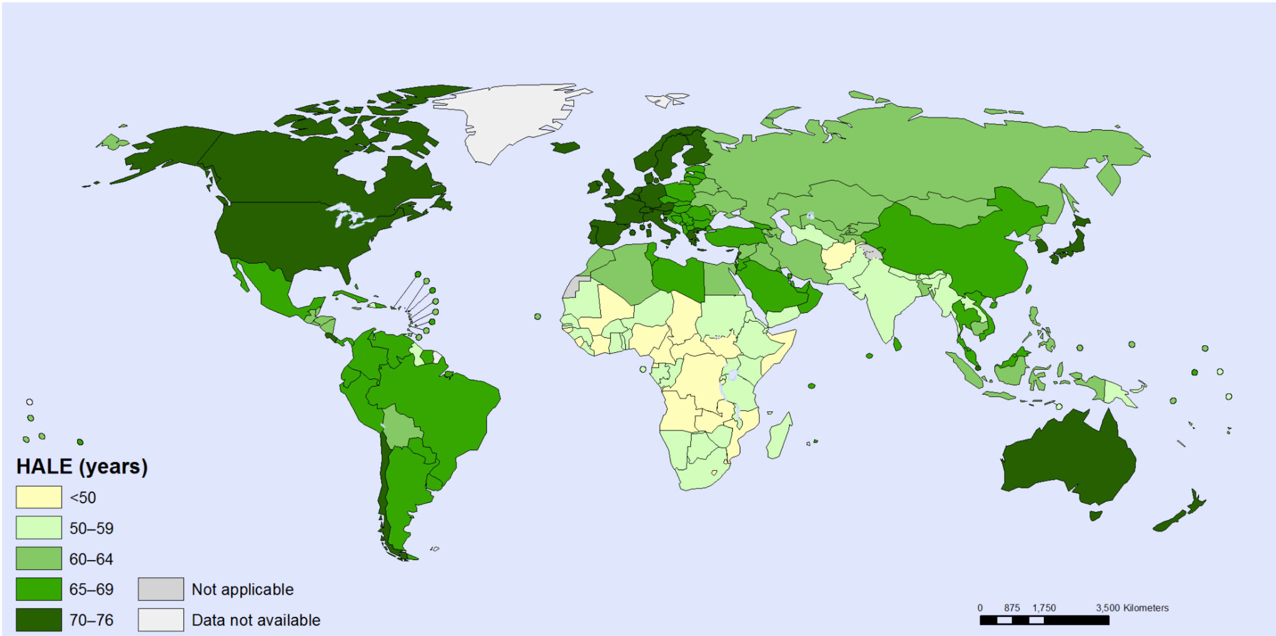


The disparity among regions becomes even sharper when one takes into account, not merely how long the typical resident lives, but also the amount of time he or she is sick. The World Health Organization has developed a metric for comparing countries and regions on this basis. "Healthy Life Expectancy" (HALE) measures life expectancy at birth, adjusted (downward) for time spent in ill health. "It is most easily understood as the equivalent number of years in full health that a newborn can expect to live based on current rates of ill-health and mortality."[8] The map set forth below compares the HALEs of the countries of the world.

[7] Source: http://gamapserver.who.int/mapLibrary/Files/Maps/Global_LifeExpectancy_bothsexes_2012.png. [Replace with custom map using 5-year intervals.]

[8] WHO, "The World Health Report 2004: Changing History," (2004): 96. The Report goes on to explain: "The measurement of time spent in poor health is based on combining condition-specific estimates from the Global Burden of Disease study with estimates of the prevalence of different health states by age and sex derived from the MCSS [Multi-Country Survey Study], and weighted using health state valuations." The methodology that the WHO employs to "weight" – in other words, to compare the severity of – different afflictions is controversial. We will examine the controversy and its implications in Chapter 9. The controversy has little relevance, however, for the gross comparisons with which we are presently concerned.

Figure 3: Healthy Life Expectancy at Birth (2012)[9]



As the map makes clear, the divergence among countries is extreme. As of 2012, HALE in Japan was 75; in the United States, 70. In much of sub-Saharan Africa, it was under 50.[10]

These data demand our attention for two independent reasons. First, radical disparity in access to a condition as fundamental as health should outrage us. Second, the data provide an antidote to fatalism. The high levels of health in some parts of the world make it plain that the low levels in other parts are not inevitable. Collectively, we could do much better – and we should.

The first step in determining how we might change these conditions is, of course, to determine what causes them. Why are conditions so good in some regions and so bad in others? As one might imagine, many factors are at work. For example, countries at war have lower life expectancies than countries at peace.[11] Both suicide and homicide rates vary sharply by country.[12] The prevalence of smoking in each country affects the incidence of

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9 Source: http://gamapserver.who.int/mapLibrary/Files/Maps/Global_HALE_BothSexes_2012.png. [Replace with custom map using 5-year intervals.]

10 For a comprehensive list, see WHO, "World Health 2014"., Table 1.

11 See [United Nations Development Programme], "The Human Impact of War: Life Expectancy in Selected Countries," http://www.undp.org/cpr/content/economic_recovery/Key_data_1.shtml.

12 See World Health Organization, Preventing Suicide: A Global Imperative, http://www.who.int/mental_health/suicide-prevention/en/. A few examples show the disparity: Republic of Korea: 41.7 per 100,000 for males, 18 for females; Japan: 26.9 for males, 10.1 for females; France: 19.3 for males, 6 for females; Peru: 4.4 for males, 2.1 for females. An interactive map showing the rates in each country can be found at http://gamapserver.who.int/gho/interactive_charts/mental_health/suicide_rates/atlas.html. For the equally sharp divergence in homicide rates, see World Bank, Intentional Homicides (per 100,000 people): http://data.worldbank.org/indicator/VC.IHR.PSRC.P5.

lung cancer (and related diseases), which in turn affects life expectancy.[13] The incidence of fatal traffic accidents varies with the number of vehicles per capita, the frequency with which drivers consume alcohol or drugs, the strength of traffic safety regulations, and so forth.[14] But among the many causal factors, one looms largest. The principal determinant of the inequality reflected in Figure 3 is the incidence of communicable diseases.

The easiest way to discern the importance of this variable is to compare the magnitude and causes of morbidity and mortality in different parts of the world. For this purpose (and for many other purposes throughout this book), we will use a metric developed by the World Health Organization, known as Disability Adjusted Life Years (DALYs). That index is designed to measure the losses caused by a particular disease or condition both through premature deaths and through ill health. One DALY "can be thought of as one lost year of 'healthy' life." [15] For reasons we will explore later, this metric is far from perfect, but is the only relevant index for which we currently have good comparative data – and is adequate for present purposes.

Figure 4, below, compares the numbers of DALYs incurred in different parts of the world by each of the principal causes of death or disability.

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[13] See Samuel H. Preston, Dana A. Glei, and John R. Wilmoth, "Contribution of Smoking to International Differences in Life Expectancy," in *International Differences in Mortality at Older Ages: Dimensions and Sources*, ed. Eileen M. Crimmins, Samuel H. Preston, and Barney Cohen(Washington, D.C.: National Academies Press, 2010).

[14] See, for example, J. R. M. Ameen and J. A. Naji, "Causal Models for Road Accident Fatalities in Yemen," *Accident Analysis and Prevention* 33, no. 4 (2001); Siem Oppe, "The Development of Traffic and Traffic Safety in Six Developed Countries," ibid.23, no. 5 (1991).

[15] WORLD HEALTH ORGANIZATION, THE WORLD HEALTH REPORT at 137 (2003).

Figure 4[16]

	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 (in thousands)	846,348 (12%)	2,506,068 (35.4%)	2,429,453 (34.3%)	1,293,593 (18.3%)	7,075,456
3	Infectious and Parasitic Diseases	153,294 (35.4%) .181	213,576 (49.4%) .085	53,902 (12.5%) 0.22	11,676 (2.7%) .009	432448 .061
4	Respiratory Infections	47,865 (31%) .057	77,189 (50%) .031	21,561 (14%) .009	7,554 (5%) .006	154,169 .022
5	Maternal Conditions	8352 (42%) .010	9708 (48%) .004	1799 (9%) .0007	233 (1%) .0002	20092 .003
6	Neonatal Conditions	65465 (27%) .077	136527 (58%) .054	30443 (13%) .013	4502 (2%) .002	236938 .033
7	Nutritional Deficiencies	26415 (32%) .031	41486 (51%) .017	11677 (14%) .005	2504 (3%) .002	82082 .012
8	Noncommunicable Conditions	155,429 (10.3%) .184	530,318 (35.1%) .212	504,353 (33.3%) .208	322,478 (21.3%) .249	1512578 .214
9	Injuries	50,808 (16.6%) .060	130,045 (42.6%) .052	84,977 (27.8%) .035	39,721 (13.0%) .031	305,552 .043
10	**All Causes**	**507,628 (18.5%) .600**	**1,138,851 (41.5%) .454**	**708,712 (25.8%) .292**	**388,668 (14.2%) .300**	**2,743,857 .388**

The numbers in the cells in Row 2 indicate the number of persons and the percentage of the global population that lives in each region. In all of the other cells in the table, the first number indicates (in thousands) the total number of DALYs caused in that region by diseases or conditions of the type at issue, the second number shows the percentage borne by countries in that region of the number of DALYs caused by that disease or condition globally, and the third number indicates the number of DALYs per person suffered in that region as a result of the disease or condition. So, for example, cell E9 informs us that, in 2012, injuries (both intentional and unintentional) resulted in a loss of 39,721,000 DALYs in high-income countries (which represented 13% of the global DALY

[16] All data are derived from WHO, "World Health 2014". The four income groups used in this chart were derived (by the WHO) from the World Bank's classification of countries for the fiscal year 2014. See http://data.worldbank.org/about/country-and-lending-groups.

burden from injuries) and that injuries in high-income countries caused a loss of .031 DALYs per person.

Some of the conclusions that can be derived from this table are unsurprising. For example, by comparing E9 to the other cells in Row 9, we learn that losses per person due to injuries are higher in poorer countries. Indeed, that rate is roughly twice as high in law-income countries as in high-income countries. Rows 5 and 6 confirm the common expectation that losses due to maternal and neonatal conditions are also much higher in poor countries that in rich countries.

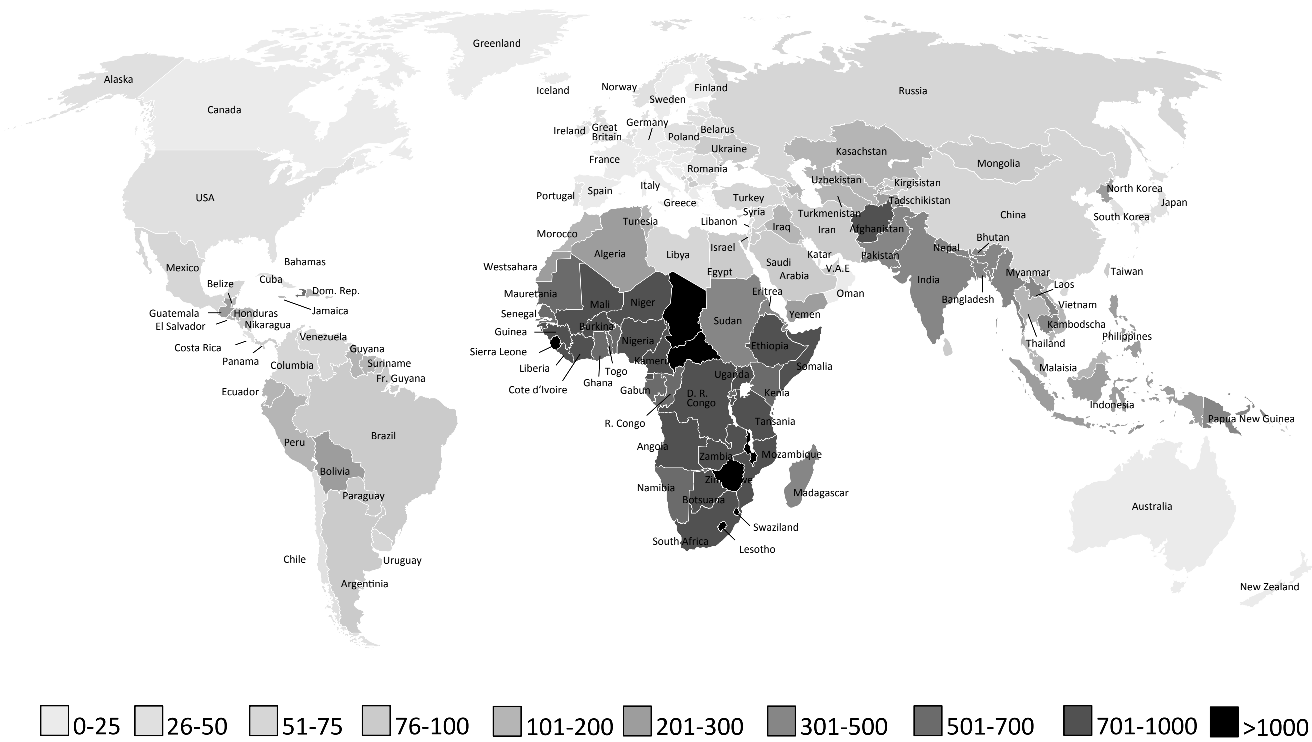
Other conclusions are more intriguing. For example, we learn from Row 8 that noncommunicable diseases now cause by far the largest number of lost DALYs throughout the world. (Within this group, the most burdensome subcategories are, in order, cardiovascular disease [including heart disease and stroke], cancer, mental and behavioral disorders, respiratory diseases, and musculoskeletal diseases [arthritis, back pain, and so forth].) However, the losses per person from such ailments are somewhat lower in poorer countries than in richer countries.

Most striking of all are the numbers in Row 3. Infectious and parasitic diseases, we can see, are vastly more common in low-income and lower-middle-income countries than in the upper tiers. The number of DALYs lost per person from these causes in low-income countries is triple the global average and 20 times the rate in high-income countries. The number of DALYs lost per person in lower-middle-income countries is 1.4 times the global average and 9.4 times the rate in high-income countries. Equally important, the total number of DALYs forfeited in poor countries through the prevalence of such diseases is enormous: 153 million per year in low-income countries and 213 million in lower-middle-income countries – much larger numbers than result from any other cause except noncommunicable diseases. When one recalls that those noncommunicable diseases are less burdensome in poor countries than in rich countries, it becomes apparent that the principal cause of the global health disparity is inequality in the prevalence of infectious diseases.

If we put morbidity to one side and focus exclusively on mortality data, the picture changes slightly, but not fundamentally. Indeed, the disparity between the death rate from infectious diseases in poor regions and the death rate from those diseases in richer regions is at least as sharp as the corresponding disparity in aggregate disease burdens. The map in Figure 5, below, shows the relevant numbers as of 2008. [17]

[17] All of the data embodied in this map have been derived from "World Health Statistics 2011," http://www.who.int/gho/publications/world_health_statistics/EN_WHS2011_Full.pdf. The number for the Western Sahara (not a member of the World Health Organization) has been interpolated. [Update with WHO data for 2012. Consider inserting regression analysis, assessing correlation of contagious-disease mortality rates and life expectancy data – both for latest year available: 2012.]

Figure 5: Age-Standardized Mortality for Contagious Diseases, 2008
(per 100,000 population)



Four years later, the picture was much the same. For example, in 2012 the age-adjusted mortality rate[18] for communicable diseases was 31 per 100,000 in the United States, 1,327 in Sierra Leone. In the former, 80% of years of life lost were caused by noncommunicable diseases, 12% by injuries, and 8% by communicable diseases. In the latter, 19% of years of life lost were caused by noncommunicable diseases, 8% by injuries, and 73% by communicable diseases.[19]

Data of these various sorts converge on one conclusion: people in developing countries die sooner and suffer more than their counterparts in developed countries – in large part because of the higher prevalence in developing countries of communicable diseases. How the prevalence of those diseases might be reduced – and the lives of the residents of the developing world correspondingly improved – is the focus of this book.

We do not mean to suggest, of course, that noncommunicable diseases do not represent a serious problem in developing countries. Heart disease, cancer, diabetes and the

[18] The way in which age adjustment of mortality rates works is well explained in http://www.health.ny.gov/diseases/chronic/ageadj.htm.

[19] All numbers derived from WHO, "World Health 2014".

like are just as deadly in sub-Saharan Africa as they are in North America and Western Europe. Indeed, as one might expect, in the subset of developing countries where people are living longer, noncommunicable diseases are becoming more common, not less.[20] Nor should a focus on communicable diseases deflect attention from the problem of mental illness in the developing world. The misery associated with depression certainly rivals that associated with most physical ailments, and depression is distressingly common everywhere.[21]

For three reasons, however, we will concentrate on communicable diseases. First, as indicated above, the disparity in the incidence of those diseases is the principal cause of the health gap between the developed and the developing world.[22] Second, and related, the fact that the prevalence of communicable diseases is so low in the developed world gives us confidence that there is no insurmountable technological impediment to reducing their prevalence in the developing world. In other words, the problem is tractable. Finally, as will soon become apparent, solving the problems associated with communicable diseases is hard enough; we leave to others the different challenges presented by noncommunicable diseases, injuries, and mental disorders.

We pause for a moment to consider a common objection to the second of these three reasons. Many participants in the various lectures and seminars in which we have discussed the arguments that appear in this book have suggested that the unequal distribution of communicable diseases may be more resistant to change than we think. In particular, they contend that such diseases thrive in warm climates. It is no accident, they suggest, that the dark-colored countries in Figure 5 are clustered around the equator. At least until climate change fundamentally alters global temperatures, they argue, inequality among regions is inevitable. Perhaps, but other data cast doubt on this pessimism. For example, Singapore, which straddles the equator, has a communicable-disease mortality rate of 68 – comparable to that of many European countries and roughly half of the rate associated with Malaysia, to which Singapore is attached.[23] Even within Sub-Saharan Africa, the mortality rates associated with communicable diseases vary widely. The number

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20 See "The Global Burden of Disease: 2004 Update," http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_full.pdf. 47-48.; "Noncommunicable Diseases: Country Profiles, 2011," (2011), http://whqlibdoc.who.int/publications/2011/9789241502283_eng.pdf.; Sheri Fink and Rebecca Rabinowitz, "The Un's Battle with Ncds," *Foreign Affairs*.

21 See Steve Hyman et al., "Mental Disorders," in *Disease Control Priorities in Developing Countries*, ed. Dean Jamison(New York: Oxford University Press, 2006); Vikram Patel et al., "Depression in Developing Countries: Lessons from Zimbabwe," *BMJ* 322; WHO, "Depression," http://www.who.int/mental_health/management/depression/definition/en/.("Depression is the leading cause of disability as measured by YLDs and the 4th leading contributor to the global burden of disease (DALYs) in 2000. By the year 2020, depression is projected to reach 2nd place of the ranking of DALYs calcuated for all ages, both sexes.")

22 By contrast, the incidence of mental disorders in general is not substantially higher in the developing world than in the developed world. Depression, by far the most common of those disorders, causes the loss of 9,054 DALYs per year per million population in high-income countries – slightly above the global average of 8,431. The corresponding numbers for developing regions are 4,905 in Sub-Saharan Africa; 9,919 in Latin American and the Caribbean; 6,544 in the Middle East and North Africa; 8,944 in Europe and Central Asia; 10,507 in South Asia; and 7,594 in East Asia and the Pacific. Hyman et al., "Mental Disorders," 606.

23 See WHO, "World Health 2014"., pp. 80, 82.

associated with Sierra Leone, already mentioned, is 1,327; by contrast, the rates in several other countries in the region with similar climates are less than half that. The contrast between the two countries on the Korean peninsula provides another illustration of the limited significance of climate. The contagious-disease mortality rate in South Korea is 34 (almost identical to the United States); in North Korea, it's 117.[24] In short, climate may matter, but not as much as is often supposed.

For these reasons, most of our attention from here on will be devoted to communicable illnesses. What, then, are those illnesses? There are many, it turns out, but the 28 most important are set forth in the chart below. The list, the clusters in which they are organized, and the data concerning their impacts are all taken from the most recent report by the World Health Organization.[25]

[24] Id. at 72, 80.

[25] The two reports from which these data are gleaned are: ""Summary: Deaths by cause and by World Bank Group (2014) and "Summary: DALYs by cause and by World Bank income group" (2014).

Figure 6: Infectious Diseases (2012)

	Global Deaths (thousands)	Global DALYs (thousands)
HIV/AIDS	1,534	91,907
Tuberculosis*	935	43,650
Malaria*	618	55,111
Diarrhoeal Diseases	1,498	99,728
Meningitis	395	30,182
Encephalitis	78	5,418
Hepatitis		
B	149	6,416
C	39	1,270
Dengue	29	1,445
Tropical Diseases		
Trypanosomiasis*	18	1,264
Chagas*	8	528
Schistosomiasis	22	4,026
Leishmaniasis*	48	3,374
Lymphatic filariasis (elephantiasis)	0	2,839
Onchocerciasis (river blindness)	0	598
STDs (excluding HIV/AIDS)		
Syphilis	79	7,039
Chlamydia	1	1,430
Gonorrhoea	1	545
Childhood Diseases		
Pertussis ("whooping cough")	67	6,142
Diphtheria	3	223
Measles	130	11,531
Tetanus	66	5,656
Leprosy	8	257
Trachoma (infectious blindness)	0	299
Rabies	35	2,265
Intestinal nematode infections		
Ascariasis	3	1,355
Trichuriasis	0	666
Hookworm	0	3,246
Totals	**5,764**	**388,410**[26]

[26] An attentive reader will notice that this number is less than number (432,448) listed in Figure 4 as the total number of DALYs associated with infectious diseases throughout the world. The reason is that Figure 6 focuses on the most burdensome of the diseases (which will occupy our attention throughout the remainder of this book) and thus excludes a large number of diseases that cause relatively few harms. In particular, included in Figure 4 but excluded from Figure 6 are: trichomoniasis (173,000 DALYs), sexually transmitted diseases other than syphilis, chlamydia, and gonorrhoea (734,000 DALYs), and a variety of aliments that the WHO classifies as "other infectious diseases" (which collectively cause a loss of 43,131,000 DALYs).

A note about terminology: The WHO has, influentially, classified diseases as Type I, II, and III, corresponding to global, developing-country and neglected diseases.[27] All of the diseases included in this chart fall into the second category, meaning that the burdens associated with them are borne overwhelmingly by developing countries.[28] All except HIV/AIDS (and, perhaps, TB) are also "neglected diseases," [29] so called for reasons that should be obvious and will become more so in the remainder of this book. 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."[30] We will try to use these labels consistently in the book.

The most striking number in Figure 5 is of course the total number of deaths. Together, these diseases kill roughly 6 million people per year -- 98% of them in developing countries.[31] 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 388 million years of lost human life.

How might we reduce these numbers? A natural place to start when looking for answers would be a survey of the techniques that developed countries have already employed to cut sharply the incidence of infectious diseases in their territories. For these purposes, the United States is representative. Beginning in the late nineteenth century, three main strategies enabled the United States to lower dramatically both mortality and morbidity associated with such diseases.

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[27] 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.").

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

[29] 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 30.

[30] 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).

[31] [Recheck the 98% number, using 2012 data. Subdivide the numbers by low-income countries and lower-middle-income countries.]

The first of those strategies consisted of improvements in sanitation and hygiene. The principal initiatives were: cleaning up food-supply systems (for example, the widespread adoption of milk pasteurization and meat inspections); improvements in consumer behavior (for example, habits of personal hygiene, care in food preparation, and breast feeding); and improvements in the water supply (principally through filtration and chlorination).[32] The impact of the last of these innovations was especially large. Between 1900 and 1937, the infectious-disease mortality rate in the United States fell from 797 per 100,000 population (a number roughly comparable to the rate in sub-Saharan Africa today) to 283 – an average decline of 2.8% per year.[33] Almost half of that reduction can be traced to the deployment of municipal water-supply systems.[34]

The science used to justify these public-health initiatives evolved in a halting, complicated way. In the early nineteenth century, diseases were commonly thought to be caused by "miasmas," poisonous vapors that emanated from contaminated water and filth. By the early twentieth century, that belief had been largely displaced (in the United States) by what came to be known as germ theory, the heart of which is recognition of the crucial roles played by microorganisms in contagious diseases. The stages in this transition were intricate.[35] But fortunately, most of the theories deployed during this trajectory pointed toward a common set of precautions and innovations.

Germ theory also provided an important catalyst for the second of the strategies: immunization. Whereas the public-health initiatives of the first third of the century reduced the exposure of people to pathogens, either by killing those pathogens or by blocking their transmission to humans, immunization altered people's bodies so they did not contract infectious diseases (or were protected against the toxins they produced) even when they were exposed to the pathogens.[36]

The first important vaccine was for smallpox. Developed in 1798, it was used increasingly widely in the United States in the early nineteenth century – and eventually succeeded in eradicating the disease altogether.[37] The next major wave of vaccine

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32 See John W. Sanders et al., "The Epidemiological Transition: The Current Status of Infectious Diseases in the Developed Versus the Developing World," *Science Progress* 9, no. 1 (2008): 7-8.

33 See Gregory L. Armstrong, Laura A. Conn, and Robert W. Pinner, "Trends in Infectious Disease Mortality in the United States During the 20th Century," *Journal of the American Medical Association* 281, no. 1 (1999): 63.

34 See D. Cutler and G. Miller, "The Role of Public Health Improvements in Health Advances: The Twentieth-Century United States," *Demography* 42(2005).

35 See Howard D. Kramer, "The Germ Theory and the Early Public Health Program in the United States," *Bulletin of the History of Medicine* 22, no. 3 (1948); Nancy J. Tomes, "American Attitudes toward the Germ Theory of Disease: Phyllis Allen Richmond Revisited," *Journal of the History of Medicine and Allied Sciences* 61, no. 3 (1997); "The Private Side of Health: Sanitary Science, Domestic Hygiene, and the Germ Theory, 1870-1900," *Bulletin of the History of Medicine* 64, no. 4 (1990); Riley, *Life Expectancy*, 60-68; Andrea Patterson, "Germs and Jim Crow: The Impact of Microbiology on Public Health Policies in Progressive Era American South," *Journal of the History of Biology* 42(2009).

36 For a detailed explanation of the ways in which different types of vaccines work, see Anita M. Loughlin and Steffanie A. Strathdee, "Vaccines: Past, Present, and Future," in *Infectious Disease Epidemiology: Theory and Practice*, ed. Kenrad E. Nelson and Carolyn F. Masters(Boston: Jones and Bartlett, 2007).

37 See F. Fenner et al., *Vaccines*(Philadephia: W.B. Saunders Company, 1994); Loughlin and Strathdee, "Vaccines," 374-77.

development began in the 1920s. Soon thereafter, federally funded vaccination programs made these innovations available to almost all children in the United States. The key innovations and the pace at which they were disseminated are illustrated by the following chart:

Figure 7: First-Generation Vaccines in the United States

Disease	First Vaccine	Developed	First widely distributed in US
Tuberculosis	Bacillus Calmette-Guerin (BCG) vaccine[38]	1921	1949
Diptheria	toxoid (inactivated toxin) vaccine[39]	1923	mid-1940s
Pertussis ("Whooping Cough")	Whole-cell vaccine[40]	1926	mid-1940s
Tetanus	toxoid (inactivated toxin) vaccine[41]	1927	mid-1940s
Yellow Fever	17D vaccine[42]	1932	1941
Polio	Salk inactivated vaccine[43]	1952	late-1950s
Measles	Edmonston B strain live vaccine[44]	1964	1974
Mumps	"Jeryl Lynn" strain[45]	1967	1977
Rubella	Live non-human attenuated vaccines[46]	1969	1970
Hepatitis B	Heptavax vaccine[47]	1981	1980s
Varicella-zoster ("chicken pox")	Varivax	1984	1989
Haemophilus Influenza type b	Bacterium capsular polysaccharide Hib vaccine	1985	1985
Rotavirus	Rotashield	1998	1998

In several cases, these first-generation vaccines proved imperfect, either because their effectiveness was limited or because they had bad side-effects, but they were soon

[38] See Jaqueline S. Coberly and Richard E. Chaisson, "Tuberculosis," in *Infectious Disease Epidemiology*, ed. Kenrad E. Nelson and Carolyn F. Masters(Boston: Jones and Bartlett, 2007), 683-85.

[39] See http://www.immunizationinfo.org/vaccines/diphtheria#history-of-the-vaccine.

[40] See http://www.immunizationinfo.org/vaccines/pertussis-whooping-cough#history-of-the-vaccine.

[41] See http://www.immunizationinfo.org/vaccines/tetanus.

[42] See J. Gordon Frierson, "The Yellow Fever Vaccine: A History," *Yale Journal of Biology and Medicine* 83, no. 2 (2010).

[43] See Bonnie A. Maybury Okonek and Linda Morganstein, "Development of Polio Vaccines," http://www.accessexcellence.org/AE/AEC/CC/polio.php.

[44] See Loughlin and Strathdee, "Vaccines," 370-71.

[45] See "Measles, Mumps, Rubella: History of the Vaccine," National Network for Immunization Information, April 22, 2010: http://www.immunizationinfo.org/vaccines/mumps#history-of-the-vaccine.

[46] See Stanley A. Plotkin, "The History of Rubella and Rubella Vaccination Leading to Elimination," *Clinical Infectious Diseases* 43(2006).

[47] See Hepatitis B Foundation, "Hepatitis B Vaccine History," October 21, 2009: http://www.hepb.org/professionals/hepatitis_b_vaccine.htm.

followed by improved versions. Widespread administration of these vaccines quickly resulted in precipitous declines in all of the diseases at issue.[48]

The third strategy overlapped the second. During the same period in which vaccines were being developed and deployed, other researchers were developing new medicines that could cure people who had become infected. The most revolutionary of them were antibiotics. Of those, the most famous were penicillin and streptomycin, both developed in the early 1940s. They were followed by a host of other more specialized antimicrobials. These proved to have seemingly miraculous powers in suppressing previously uncontrollable infections: pneumonia, meningitis, tuberculosis, malaria, and fungal infections. More recently, the same strategy has led to drugs that can suppress viral infections, such as HIV.[49]

The effect of the second and third strategies, in combination, was an even more dramatic drop in infectious-disease mortality rates. Between 1937 and 1952, the rate declined from 283 to 75 – an average reduction of 8.2% per year. Between 1953 and 1980, it kept dropping, but more slowly – specifically, at an average rate of 2.3%. By 1980, the number was 36 – less than 5% of the number in 1900. These trends stand out sharply in the following graph.

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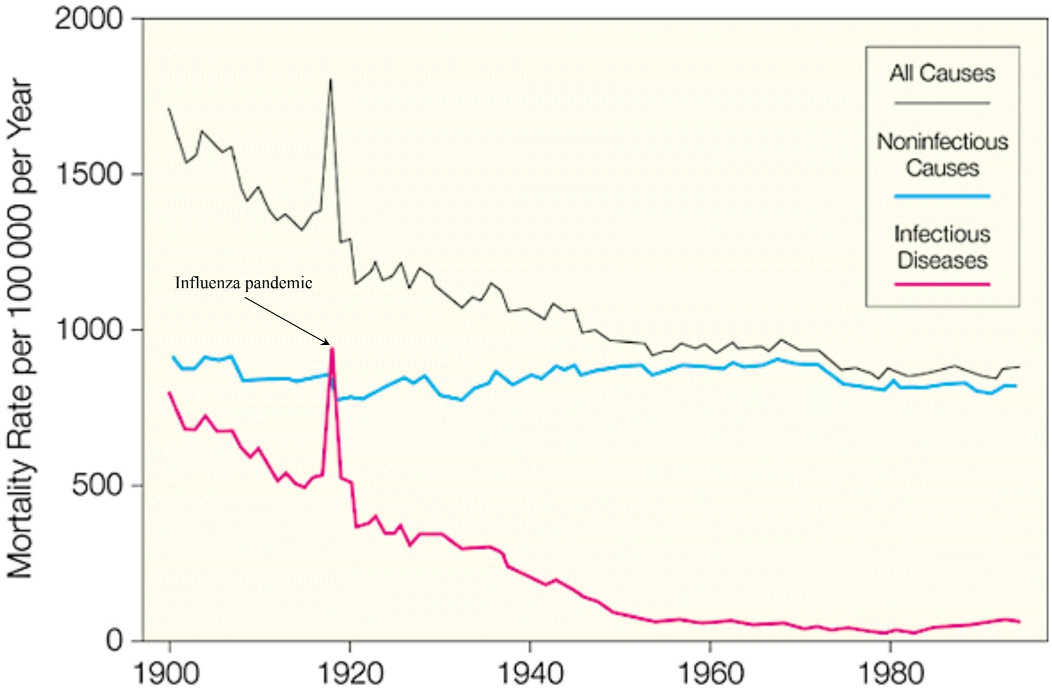
[48] See Sanders et al., "Epidemiological Transition," 9-10. For graphs showing the declines in selected diseases, see: Loughlin and Strathdee, "Vaccines," 369-70, 71, 73.(polio, measles, and Haemophilus influenza type b); http://www.healthsentinel.com/joomla/images/stories/graphs/us-diphtheria-1900-1967.jpg (diphtheria); http://www.healthsentinel.com/joomla/images/stories/graphs/us-pertussis-1900-1967.jpg (pertussis); http://www.healthsentinel.com/joomla/images/stories/graphs/us-measles.jpg (measles).

[49] See Sanders et al., "Epidemiological Transition," 10.

Figure 8: U.S. Mortality Rates, 1900-1996



adapted from Armstrong et al., "Trends in Infectious Diseases," Journal of the American Medical Association 281 (1999): 61.

Notice (among other things) the tight linkage between the mortality rate for infectious diseases and the overall mortality rate. The huge drop in the latter during the twentieth century (and the corresponding increase in life expectancy in the United States) is largely attributable to the progress we have made in controlling infectious diseases.[50] These remarkable gains, to repeat, were due primarily to the success of the three interlocking initiatives: public-health programs, which limit Americans' exposure to bacteria and viruses; immunization programs; and medicines capable of curing people of the diseases we fail to prevent.[51]

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50 Note that these are "raw" mortality rates, not age-adjusted mortality rates. That makes a difference when interpreting the stability over time of the mortality rate associated with noninfectious causes. One should not infer from its constancy that we have made no progress in controlling heart disease, cancer, industrial accidents, and so forth. On the contrary, we have made considerable progress – the main effect of which is that these things are catching up to us at later ages.

51 For the most part, these three strategies were complementary. In particular, the public-health initiatives reduced the need for vaccines and medicines, by limiting the set of pathogens to which people were exposed. But occasionally the effect was reversed. The most important case involved polio. Prior to the installation of modern water and sanitation systems, infants were often exposed to the three polio viruses. However -- either because they were receiving antibodies from their mothers through breast milk or because the receptors necessary for an infection to pass from the gastrointestinal tract to neurons are not expressed until later in childhood – the babies rarely contracted the paralytic form of polio, but instead developed their own antibodies, which then protected them throughout their lives. The public health initiatives, by reducing the frequency with which infants were exposed to the viruses, increased the incidence of the disease and intensified the need for a vaccine. See Okonek and Morganstein, "Development of Polio Vaccines".; Loughlin and Strathdee, "Vaccines," 369.

When combating infectious diseases in developing countries, we can and should rely on the same three approaches. The first of the three initiatives is already well underway. In recent years, developing countries have gone far to institute the same public-health reforms that proved so important in the United States. 69% of the population in low-income countries now use what the WHO classifies as "improved drinking water sources" (up from 52% in 1990), and 37% of the populations in those countries now use "improved sanitation" (up from 19% in 1990).[52] The health benefits of these initiatives have been large, and we should certainly complete the process.

Unfortunately, it is already apparent that these public-health initiatives will not, by themselves, solve the problem. Indeed, they appear to be less efficacious in curbing infectious diseases than they were in the United States – in part because most of the diseases that currently ravage developing countries are less dependent upon drinking water for transmission than were the major killers in the United States. For example, in Zimbabwe, 80% of the population uses clean sources of drinking water, but the contagious-disease mortality rate is 711 (per 100,000), 23 times the rate in the United States. In Lesotho, 81% uses clean water, but the corresponding mortality rate is 1,110, 36 times the rate in the United States. Even in Sierra Leone, which currently has the highest contagious-disease mortality rate in the world, 60% of the population uses clean water.[53]

Other comparative data make clear that public-health initiatives, although surely important, are not sufficient (and perhaps not always essential) to suppress infectious diseases. For example, in Peru, the percentage of residents who use clean water is 87%, not much higher than Lesotho, but the contagious-disease mortality rate is only 121 (per 100,000), 9% of the level in Lesotho. In Madagascar, only 50% of the residents use clean drinking water (well below the percentages in Sierra Leone, Zimbabwe, and Lesotho), but the contagious-disease mortality rate is 430 – substantially better than the rates in those countries.[54]

Effectively curbing infectious diseases in the developing world thus requires us also to deploy the second and third strategies – just as we did in the United States. We need to immunize residents (preferably while they are children) against the diseases that are transmitted in ways we can't block, and we need to provide infected people with medicines that will save their lives or at least make their lives bearable.

Again, substantial progress on these fronts has been made in recent years. All of the vaccines listed in Figure 6 – which were originally developed to combat diseases endemic in the United States and Europe – are now (or will soon be) available in developing countries. For example, thanks in large part to the WHO's Expanded Programme on Immunization, 80% of one-year-old children in low-income countries have now received the MDG4 measles vaccine (up from 56% in 1990). 80% have received the DTP3 (diphtheria, tetanus, and pertussis) vaccine; 76% have received the HepB3 (Hepatitis B) vaccine, and 74% have

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52 WHO, "World Health 2014" 126. The corresponding current numbers for lower-middle-income countries are 88% and 48%; for upper-middle-income countries, 93% and 74%; and for high-income countries, 99% and 96%. Id.

53 Ibid., Tables 2 & 5.

54 Ibid.

received the Hib3 influenza vaccine.[55] (In Sierra Leone and Zimbabwe, these numbers are even higher.[56]) The latest good news on this front is that, recently, GlaxoSmithKline, the holder of the patent on Rotarix, a new vaccine for rotavirus,[57] announced that it will make the vaccine available (through UNICEF) in developing countries for a price 95% less than the price at which it is sold in developed countries.[58] To be sure, much work remains to be done. Roughly 23 million infants in the developing world still do not receive the benefits of routine immunization.[59] But the progress to date has been impressive.

But what of the infectious diseases that do not have counterparts in developed countries? Here is where the real trouble starts. Effective vaccines for these diseases simply are not available. There exists no vaccine for malaria or HIV – which together kill over two million people per year. For tuberculosis, the third member of the "big three," there does exist a vaccine: the venerable BCG vaccine, originally developed from the cousin of the TB bacterium that afflicts cattle. BCG remains effective against some forms of TB – specifically, tuberculous meningitis and miliary tuberculosis – as well as against some unrelated diseases, such as leprosy. But in tropical climates (particularly rural areas), it has little power to prevent pulmonary tuberculosis among adults.[60] No vaccine of any sort is available for any of the "tropical diseases" – Trypanosomiasis,[61] Chagas,[62] Schistosomiasis,[63] Leishmaniasis,[64] Lymphatic filariasis, and Onchocerciasis. The same is true for Trachoma,[65] Dengue,[66] Ascariasis,[67] Trichuriasis,[68] and Hookworm.[69]

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55 See ibid., 114.

56 See ibid., 112.; WHO-UNICEF Estimates of Immunization Coverage: the Republic of Zimbabwe, http://apps.who.int/immunization_monitoring/en/globalsummary/timeseries/TSWUcoverageByCountry.cfm?country=ZWE.

57 The dynamic that led to the development in 2006 of Rotarix (as well as RotaTeq, another safe and effective rotavirus vaccine) will be described in detail in Chapter 1. For now, it suffices to observe that rotavirus causes roughly 50,000 hospitalizations per year in the United States. See http://www.rotavirusvaccine.org/documents/RotaQA_Jan06.pdf.

58 "GSK to Offer Steep Discount of Rotarix to Developing Countries," Pharmapodia (June 6, 2011), http://blog.pharmapodia.com/2011/06/gsk-to-offer-steep-discount-of-rotarix.html.

59 See "Global Routine Vaccination Coverage," Centers for Disease Control and Prevention (October 29, 2010), http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5942a3.htm. [Update.]

60 See Frank Shann, "Bcg Vaccination in Developing Countries," *BMJ* 340. Additional details concerning the limitations of the BCG vaccine are provided in Chapter 1.

61 See S Magez et al., "Current Status of Vaccination against African Trypanosomiasis," *Parasitology* 137, no. 14 (2010).

62 See Mary Ann Roser, "Baylor Doctor Working on Chagas Vaccine," *Statesman*, October 7, 2011.

63 http://www.who.int/vaccine_research/diseases/soa_parasitic/en/index5.html.

64 See Lukasz Kedzierski, "Leismaniasis Vaccine: Where Are We Today?," *Journal of Infectious Diseases* 2(2010).

65 See http://www.medindia.net/news/Experimental-Trachoma-Vaccine-Protects-Monkeys-91825-1.htm.

66 "Planning for the Introduction of Dengue Vaccines," Hanoi, April 19, 2011, http://www.denguevaccines.org/sites/default/files/APDPBReport_Hanoi_April2011_Highlights.pdf.

67 See http://www.bvgh.org/Biopharmaceutical-Solutions/Global-Health-Primer/Diseases/cid/ViewDetails/ItemID/20.aspx.

68 See http://www.bvgh.org/Biopharmaceutical-Solutions/Global-Health-Primer/Diseases/cid/ViewDetails/ItemID/20.aspx.

69 See http://www.sabin.org/vaccine-development/vaccines/hookworm.

Why? Are these diseases that much more difficult to understand and combat? In a few cases, yes. HIV is the clear example. But in most cases, no. Indeed, for the majority of the neglected diseases, promising avenues for the development of vaccines were identified long ago. But we have not, as yet, invested in these projects the resources necessary to generate and test the vaccines we need.

What about medicines? Do we at least have ways of controlling the diseases once people have contracted them? The answer varies. For a few of the diseases, there are no cures. Dengue, for example, infects roughly 40 million people a year, 18,000 of whom die. The only treatments for the disease are symptomatic.[70] For most of the diseases, therapies do exist, but many are outdated, limited in their effectiveness, or poorly adapted for use in developing countries. For example, the available treatments for Chagas disease (which currently afflicts roughly 10 million people) are almost always effective if initiated during the very early stages of the disease, but are much less potent if (as is common) they are not applied until the chronic stage.[71] The recent development of nifurtimox-eflornithine combination therapy (NECT) has sharply increased the effectiveness of responses to late-stage sleeping sickness, but detection is still difficult (requiring a lumbar puncture), and the treatment "remains labour-intensive, requiring 7 days of infusions of eflornithine twice a day, plus 10 days of oral nifurtimox tablets 3 times a day, … a minimum of 4 nurses, … and a doctor, to prescribe treatment and manage potential adverse events."[72] The area of most dramatic recent progress concerns treatments for HIV/AIDS. The development of anti-retroviral therapies (ARTs) has sharply reduced the mortality rate associated with the disease, not just in developed countries, but also in the developing world.[73] However, ARTs suppress the infection; they do not cure it. And they often become less effective over time, forcing patients to move from first-generation to second-generation to third-generation drugs.[74] In short, some medicines capable of curing or ameliorating developing-country diseases certainly do exist, but they are far from ideal.

The last and most galling piece of the puzzle: The medicines that are available often cost more than can be afforded by most of the people who need them. A few examples:

- Roughly 3.5% of the 9 million new cases of active tuberculosis reported each year involve variants of the disease that are resistant to the standard course of antibiotics. Patients who contract those variants require special treatments – so-called DR-TB drugs. Whereas the costs of the standard TB treatments are now modest, the cost of a DR-TB regimen is not – typically, between $4,400 and

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70 See WHO, Neglected Tropical Diseases, (2009), http://whqlibdoc.who.int/publications/2009/9789241598705_eng.pdf. 33.

71 See ibid., 18.

72 See Jacqueline Tong et al., "Challenges of Controlling Sleeping Sickness in Areas of Violent Conflict: Experience in the Democratic Republic of Congo," *Conflict and Health* 5, no. 7 (2011).

73 See Hillary Rodham Clinton, "Creating and AIDS-Free Generation," November 8, 2011, available at http://www.state.gov/secretary/rm/2011/11/176810.htm; USAID, "HIV/AIDS Health Profile: Sub-Saharan Africa," March 2011, available at http://www.usaid.gov/our_work/global_health/aids/Countries/africa/hiv_summary_africa.pdf. [Update.]

74 See MSF, "Hiv/Aids Treatment in Developing Countries: The Battle for Long-Term Survival Has Just Begun," (2009), http://www.doctorswithoutborders.org/publications/reports/2009/msf_hiv-aids-treatment_battle-for-long-term-survival.pdf.

$9,000 in most developing countries. Partly as a result, only a minority of the affected patients get them.[75]

- A combination of legal reforms and philanthropic initiatives (discussed in Chapter 1) has led recently to significant reductions in the prices of the ARTs for HIV/AIDS, especially in low-income countries. That, in turn, has made possible a sharp increase in the number of infected people able to get the medicines. Unfortunately, the price reductions have been largest with respect to first-generation therapies. Second-generation ARTs are substantially more expensive, and the prices of third-generation drugs are higher still.[76] For instance, Tibotec's drug, darunavir, costs over $6000 per person per year in Brazil and over $1000 per patient per year in Africa; the cost of its new drug, rilpivirine, is likely to be at least as high.[77] Similarly, Abbott's drug, Kaletra, costs between $400 and $4000 per person per year in developing countries.[78] The net effect: despite the sharp reduction of the costs of the older ARTs, roughly half of the people in subSaharan Africa infected with HIV still are not receiving them. And those who do start the therapy gradually develop resistance to the first and second-generation drugs, forcing them eventually to turn to the newest versions – which they discover are far beyond their means.[79]
- It is not merely in the high-profile contexts of TB and AIDS that one finds prohibitively high drug prices. In many other settings, run-of-the-mill drugs, long free of patent protection, still cost more than most people can afford. A simple course of antibiotics, for example, can cost a resident of the developing world more than a month's wages.[80]

This final dimension of the health crisis in the developing world is what we will refer to in this book as the "access problem." In brief, we already possess at least some of the drugs necessary to resolve the crisis – "possess" in the senses that we know how to produce those drugs, have confirmed their efficacy, and could manufacture them cheaply. The residents of the developing world desperately need them. But we are unable or unwilling to make the drugs available at prices they could pay. As a result, people die, needlessly. How many? In 2004, the World Health Organization estimated the number to be 10 million per

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75 See "Dr-Tb Drugs under the Microscope," (2011), http://www.msfaccess.org/sites/default/files/MSF_assets/TB/Docs/TB_report_UndertheMicro_ENG_2011.pdf.

76 See "Hiv/Aids Treatment in Developing Countries: The Battle for Long-Term Survival Has Just Begun".

77 See MSF, "Access to Medicines: Johnson & Johnson / Tibotec AIDS Drug Licenses Exclude Too Many Patients," January 28, 2011, available at http://www.doctorswithoutborders.org/press/release.cfm?id=5002&cat=press-release.

78 See Robert Weissman, "AIDS Treatment Revolution: Expand Generic Competition," December 1, 2011, available at http://www.dailykos.com/story/2011/12/01/1041604/-AIDS-Treatment-Revolution:-Expand-Generic-Competition.

79 See Ellen 't Hoen et al., "Driving a Decade of Change: Hiv/Aids, Patents and Access to Medicine for All," *Journal of the International AIDS Society* 14, no. 15 (2011).

80 See WHO, "Equitable Access to Essential Medicines: A Framework for Collective Action," (2004), http://whqlibdoc.who.int/hq/2004/WHO_EDM_2004.4.pdf. Cf. Dilara Inan et al., "Daily Antibiotic Cost of Nosocomial Infections in a Turkish University Hospital," *BMC Infectious Diseases* 5, no. 5 (2005).

year.[81] That figure is probably too high, at least today, but it suggests the severity of the issue.

The access problem is notorious, not just because of its scale, but because it is easily grasped. It calls to mind the most memorable scene in *The Grapes of Wrath*, Steinbeck's widely read depiction of the Great Depression in the United States. As Steinbeck tells the tale, starving migrants from the drought-stricken center of the country have arrived in California, desperate for both work and food. Fruit is abundant there, in part because of the success of scientists in developing fecund and blight-resistant plant varieties. But to give the fruit to the migrants would corrode the market for it. So the fruit is burned – to the dismay both of the scientists whose work and genius made it possible and of the people who are eager to consume it.[82] The handling of pharmaceutical products in developing countries today is similar.

But the visibility and gravity of the access problem should not blind us to what we will call the "incentive problem." In brief, we have thus far failed to stimulate the development of an arsenal of drugs that would enable us to cure or treat the diseases that are ravaging the developing world. Even more serious, we have failed to produce the vaccines that would eradicate those diseases or shield people against them.

Not only is the incentive problem at least as important as the access problem, many of the current proposals for dealing with the latter would exacerbate the former. If we persuade or compel the firms to make the existing drugs available cheaply in developing countries, they will have even less reason in the future to pursue research projects aimed at that market.

The objective of this book is to identify ways in which we might address these two, linked problems simultaneously. More specifically, our goal is to determine how the laws and institutions that we have historically employed to foster the creation of new pharmaceutical products and then to channel the distribution of those products might be adjusted so as both to generate more vaccines and drugs that address neglected diseases and then to make those vaccines and drugs available to the people who need them.

In undertaking this task, we are surely not writing on a blank slate. Much excellent work has already been done on these issues – by economists, physicians, legal scholars, and public-health activists. Our ambition is to distill the best ideas from the existing literature,

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[81] See WHO, "Equitable Access to Essential Medicines: A Framework for Collective Action".

[82] See John Steinbeck, *The Grapes of Wrath* (1930), chapter 25. The key passage merits quotation:

> Men who can graft the trees and make the seed fertile and big can find no way to let the hungry people eat their produce. Men who have created new fruits in the world cannot create a system whereby their fruits may be eaten. And the failure hangs over the State like a great sorrow. The works of the roots of the vines, of the trees, must be destroyed to keep up the price, and this is the saddest, bitterest thing of all. Carloads of oranges dumped on the ground. The people came for miles to take the fruit, but this could not be. How would they buy oranges at twenty cents a dozen if they could drive out and pick them up? And men with hoses squirt kerosene on the oranges, and they are angry at the crime, angry at the people who have come to take the fruit. A million people hungry, needing the fruit – and kerosene sprayed over the golden mountains.

add some new proposals of our own, and then bind them into a coherent whole that has a realistic chance of adoption in the foreseeable future.

Our argument will proceed in the following stages: Part I lays the foundation for the analysis. It begins with a chapter that examines in more detail the infectious diseases that are currently rampant in developing countries and surveys the various ways in which those diseases might be controlled. Chapter 2 then considers the technologies and business practices that currently undergird the process of drug development and the complex roles that governments in developed countries currently play in determining the pace and direction of drug development and deployment.

The heart of the book is Part II, which reviews a wide variety of strategies that might be used reduce the scourge of infectious diseases in the developing world. Our thesis is that no one approach is likely, on its own, to do the job. Rather, a cocktail of interdependent initiatives would be both most effective and most politically palatable. Somewhat more specifically, we advocate a combination of: more extensive and sophisticated use of conditional grants (of money, drugs, or intellectual property) by governments, foundations, pharmaceutical firms, and universities (Chapter 3); legal and political reforms that would facilitate the ability of pharmaceutical firms to engage in price discrimination and then discipline their exercise of that power (Chapter 4); prize systems deployed both by governments and by NGOs that would provide optional alternatives to the patent system as incentives for the creation of kinds of drugs we need (Chapter 5); a new regulatory system that would require all pharmaceutical firms selling drugs in the United States to achieve each year a minimum ratio between the number of DALYs saved through the administration of their products and their revenues (Chapter 6); and finally a set of related adjustments of patent law – some of them involving the national patent systems of developing countries, others involving the treaties that circumscribe the patent laws of both developing and developed countries (Chapter 7).

Adoption of the set of reforms advocated in Part II of the book would cost the residents of developed countries some money. Some of those costs would take the form of increased taxes, others of increased prices for drugs or increased insurance premiums. The financial burdens would not be overwhelming, but they would not be trivial either. In view of the skepticism many Americans (and, to a lesser extent, many Europeans) harbor toward foreign aid of any sort, the imposition of those burdens requires justification. Part III of the book takes up that task. Chapter 8 identifies an overlapping set of moral arguments that support the assumption by residents of developed countries of duties to their counterparts in the developing world. Chapter 9 rebuts some common objections to those arguments.

The conclusion summarizes our recommendations.

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