After graduating from college, I spent a year teaching high school in a rural area of western Kenya.¹ Six months into the job, I went to Nairobi to purchase textbooks for the school and run some other errands. When I arrived I felt a bit like a country bumpkin, having been living in a house with mud walls and a thatched roof and suddenly being surrounded by skyscrapers. People in western Kenya had told me that Nairobi, situated at some 5,000 feet in altitude, would be very cold. As someone who was used to Kansas winters, I assumed what constituted “cold” in equatorial Nairobi would not affect me, but I did, indeed, find myself getting chills.

As I made my rounds in Nairobi, I felt very lethargic. I would stop into a restaurant, order food, and then realize I couldn't bring myself to eat. I would leave and, feeling weak, go into another restaurant, order food, and again push it away. The next day I would feel better and wonder why I’d been so sluggish, only to again slip into lethargy and weakness a bit later. This went on for several days.

At one point I needed to make a phone call, and sought out the nearest pay phone, which happened to be in a hospital—actually, one of the best private hospitals in Nairobi. While making the call, I realized I was too weak to walk out and had to see a doctor.

It turned out that an anopheles mosquito had gotten past my mosquito net and bitten me, injecting the infective form of the malaria parasite, known as sporozoites, into my blood. The parasites had

¹ The personal experiences related in this Introduction are Michael Kremer's.
moved to my liver, where they changed form and reproduced, giving rise to blood-stage malaria.

As the parasites multiplied, destroying my red blood cells, I began to experience nausea, exhaustion, fever, sweating, and shaking chills. My alternating periods of strength and weakness were characteristic of malaria. If I had been out in the village and not gotten to a doctor, the condition could have led to death through severe anemia, or by stemming blood flow to the brain and other organs.

I checked into the hospital in Nairobi. My memory of what happened thereafter is a blur. I remember waking from strange nightmareish dreams. The type of malaria I had proved resistant to the first-line drug used to fight the disease, but the doctors switched me to alternatives and kept me on them until I recovered. I returned to the village fifteen pounds lighter.

Of course, I was phenomenally lucky to receive first-rate care. Many people in Africa live far from clinics, cannot afford to see a competent doctor, or do not have the money to pay for effective medicine.

I saw this vividly illustrated years later when I returned for a visit to the village where I had lived in Kenya. One of my friends there had malaria. Unlike me, he recognized the symptoms, but he lived several hour’s walk from a hospital, and was not much inclined to go there in any case, knowing that patients regularly have to share a bed. The first-line malaria medicine is readily available over-the-counter in Kenya, and costs less than a dollar. But when I arrived, my friend hadn’t been medicated because he couldn’t afford the pills. While he was unlikely to die from the disease, he was sufficiently sick to be unable to work, and the resulting inability to afford essentials made him even weaker.

Malaria is only one of the diseases that plague low-income countries. Together, malaria, tuberculosis, and the strains of HIV common in Africa kill 5 million people each year. Diseases like schistosomiasis, which many people in higher-income countries have never heard of, also impose a heavy burden on poor countries. Vaccines offer the best hope for conquering these diseases because they are relatively easy to deliver, even in countries with weak health-care infrastructure. Yet re-
search on vaccines for diseases that primarily affect low-income countries remains minimal.

In this book we examine the reasons for this lack of research and propose that foreign aid donors encourage this research by committing in advance to help finance the purchase of suitable vaccines.

We argue that a key reason why pharmaceutical firms have been reluctant to invest in R&D on vaccines for diseases that primarily affect poor countries is that they fear they would not be able to sell the vaccine at prices that would cover their risk-adjusted costs. The low anticipated price reflects not only the poverty of the relevant populations, but also severe distortions in markets for vaccines for these diseases. Intellectual property rights for pharmaceuticals have historically been weak in low-income countries. Most vaccines sold in these countries are priced at pennies per dose, a tiny fraction of their social value—even measured in terms of what people with very low incomes would pay for the protection. Once pharmaceutical companies have invested in the research necessary to develop vaccines, governments often use their powers as regulators, dominant purchasers, and arbiters of intellectual property rights to keep prices low.

Research on vaccines is an “international public good” because the benefits of scientific and technological advances spill over to many nations. Hence, none of the many small countries that would benefit from a malaria, tuberculosis, or HIV vaccine has an incentive to encourage research by unilaterally offering to pay higher prices. And accordingly, private developers lack incentives to pursue socially valuable research on diseases primarily affecting low-income countries.

Incentive systems to encourage development of new products can be broadly classified as push programs, which subsidize research inputs, or pull programs, which reward developers for actually creating the desired product. Government-directed push programs are well suited for basic research. But for the later, applied stages of research, pull programs are also needed. With pull programs, money changes hands only after a successful product is developed. This approach of rewarding results gives researchers strong incentives to self-select
projects that have the best chance of success. Pull programs also create incentives for researchers to focus on developing a vaccine, rather than pursuing ancillary goals, such as publishing journal articles. Moreover, appropriately designed pull programs can help ensure that, if new vaccines are developed, they will reach those people who need them. Several historical precedents, such as the Orphan Drug Act, suggest pull-like mechanisms can be effective tools for spurring product development.

The most attractive form of pull program is generally a commitment to fully or partially finance vaccine purchases for poor countries. Alternative pull approaches have significant disadvantages. Extending patents on other pharmaceuticals to reward developers of new products, for example, would place the entire burden of financing new products on the people who buy these other pharmaceuticals. Purchasing and distributing existing vaccines which are not being fully utilized would be a cost-effective way to save lives, but simply increasing prices for existing vaccines without explicit incentives for developing new ones would be an expensive and ineffective way to spur research on new vaccines.

For vaccine commitments to increase research activity, developers must believe that the sponsor will not renege once desired products have been developed and research costs sunk. If structured appropriately, these commitments can be legally binding contracts, as evidenced by legal precedents. The credibility of vaccine commitments can be further enhanced by specifying in advance the rules that govern the eligibility and pricing of vaccines, as well as by insulating the arbiters of these rules from political pressure.

Requiring candidate products to meet basic technical requirements, including approval by a competent national regulatory agency such as the U.S. Food and Drug Administration, would ensure that funds were spent only on effective vaccines. Requiring low-income countries to agree before a qualifying vaccine is used, and perhaps requiring them or other donors to contribute part of the production and distribution cost—would help ensure that products purchased by the program would be useful under actual field conditions.

One way to structure a vaccine commitment would be to guarantee
a price of, say, $15–$20 per person for the first 200–250 million people immunized, in exchange for a commitment from the developer to subsequently drop the price in the poorest countries to a modest markup over manufacturing cost. A commitment of this size would offer firms an opportunity for sales comparable to those available in commercial markets. It would be extremely cost-effective, saving more lives than virtually any imaginable comparable health expenditure.

Vaccine commitments could be undertaken by international organizations such as the World Bank, by national governments, by private foundations such as the Bill & Melinda Gates Foundation, or by a combination of these groups. If a commitment to purchase vaccines failed to produce an effective vaccine, no donor funds would be spent; if it succeeded, tens of millions of lives would be saved at remarkably low cost.

This book lays out the rationale for a vaccine commitment and discusses how it could be designed. Chapter 2 reviews the disease environments in low-income countries and chapter 3 discusses the low level of research on diseases primarily affecting low income countries. (Readers familiar with health issues in developing countries may wish to skip these chapters.) In chapter 4 we discuss the market distortions that limit research in general and particularly limit research on vaccines against diseases that primarily affect poor countries. Chapters 5 and 6 outline the potential roles push and pull programs can play in addressing market failures in R&D. Chapter 7 reviews various types of pull programs and argues that commitments to help finance vaccine purchases would be most attractive. Chapters 8, 9, and 10 discuss how pull programs could be structured: how a candidate vaccine’s eligibility for such a program could be determined, how much to pay for a vaccine, and how payments should be structured, for example to divide the reward between multiple providers. Chapter 11 explains how a similar approach might be used to induce R&D on other products, such as other medical technologies and technologies that could improve agricultural productivity in the tropics. Finally, chapter 12 discusses the political economy of a vaccine commitment and how it could be designed to meet the needs of possible sponsors.