Childhood immunization

Vaccines are one of the true wonders of humanity, having saved more lives than any other medical invention. Where they've been widely embraced, vaccines have essentially eliminated the spread of diseases that once ran rampant. Nevertheless, in low- and lower-middle-income countries, many people, particularly children, still die from vaccine-preventable diseases. Increasing spending on vaccinations can save half a million lives each year and is one of the best investments for the world.

Smallpox: The power of vaccines

Vaccines can be traced to the endeavors of physician Edward Jenner. He is widely considered the founder of immunization, when he in the 18th century helped to bring about the end of smallpox. For thousands of years, smallpox devastated humanity. The virus is believed to have first appeared as long ago as 10,000 BCE. Smallpox skin lesions have been found on the mummy of the pharaoh Ramses V who died more than 3000 years ago. The disease was also reported in ancient China and India. When smallpox cases surged, it could wreak civilization-wide destruction. A large-scale epidemic claiming seven million lives has been linked to the start of the decline of the Roman Empire around 100 CE.

By the Middle Ages, smallpox frequently reached epidemic levels across Europe. In 1241 CE, when smallpox first came to Iceland, 20,000 of the country's 70,000 people died. Spread by European explorers to the New World, the disease wreaked havoc on indigenous populations and played a crucial role in the fall of both the Aztec and Incan Empires.

Smallpox struck every stratum of society, including the most privileged. It claimed the lives of Queen Mary II of England, the last of the Tudors; Tsar Peter II of Russia; and King Louis XV of France.

By the time Jenner was born in 1749, 400,000 people died annually of smallpox in Europe, and the virus was responsible for one-third of cases of blindness on the continent. Jenner noticed that women milking cows most often contracted the relatively mild bovine form of the virus, cowpox, and were then immune to smallpox infection. He wasn't the first to make this observation, but he was the first to take action: Jenner placed a sample of the pustule from a cowpox-infected milkmaid's hand under the skin of a young boy. In the first-known case of inoculation, the young boy became immune to smallpox. Jenner decided to name this new procedure vaccination after the Latin word for cow, *vacca.*

We may think of 'anti-vaccination' movements as a modern-day phenomenon, but there have been skeptics since vaccines' invention. Jenner and those who followed him have long been criticized based on religious, scientific, and political objections. When the Compulsory Vaccination Act of 1853 mandated inoculation of all infants born in England or Wales against smallpox, people objected because they believed it violated their personal liberty. Many concerns have continued to this day.

Skepticism notwithstanding, smallpox was eventually eradicated through widespread vaccination. There have been no new cases anywhere on the planet since 1978. Unfortunately,

smallpox is the only human infectious disease to have been eradicated. Partly, this is because smallpox only infects humans, making it easier to eradicate than most other infectious diseases that also infect animals and can come back later to reinfect humans.

Those who followed in Jenner's footsteps refined the vaccine and even developed a version that could be stored for weeks, making it possible to transport the vaccine to all ends of the earth, regardless of climate or distance from a manufacturer. Once the technology was available, the United Nations generated enough political momentum to roll out a global vaccination program.

Yet, today it is easy to forget what a momentous public health achievement the eradication of smallpox really is. Up until its eradication, in the 20th century alone, the virus managed to kill 300 to 500 million people—many times the number those killed in both World Wars.

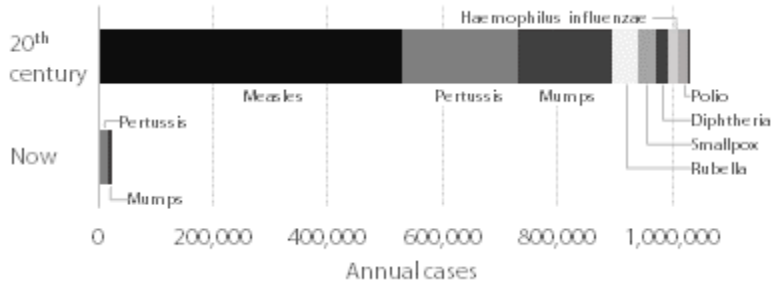
Cheap jabs' big payoff for rich and poor alike

The eradication of smallpox points to how a relatively small investment in vaccination efforts can produce incredible returns. Take the doctoral thesis of one of the epidemiologists who worked on the eradication of smallpox, Larry Brilliant. He showed that India suffered about $150 million (in 1978 dollars) in damages each year from smallpox while the disease still ran rampant—one-third of this was treatment costs, and two-thirds the cost of deaths, using standard economic measures. However, the final push to eradicate the disease had only cost India an additional $3.5 million per year. In his calculations, he found the country made its additional investment back every 43 days since then in avoided costs.

Funding vaccination efforts in low- and middle-income countries greatly benefited rich nations too. Prior to smallpox's global eradication, the USA had to continually invest in vaccination programs to prevent the reintroduction of the disease after it had been eliminated domestically. America had to vaccinate 5.6 million every year and revaccinate another 8.6 million. (It was recommended that anyone traveling to areas with smallpox be revaccinated regularly). Not only did people continue to suffer from the virus—more than 200 were hospitalized, nine were killed, and four became permanently disabled—but this carried a high cost of $300 million annually in 1978 dollars both from vaccination costs and from productive time lost.

Compare this to what the USA paid to help eradicate smallpox across the world. In the last decade before global eradication was achieved, the USA spent about $21 million in total. Even disregarding what other countries gained, this means America's investment paid off *every 26 day*s since then in avoided costs. By spending $21 million, it avoided spending $300 million each and every year.

While smallpox understandably has gotten most of the headlines, vaccines have also saved people from all kinds of lethal diseases. Shots have blunted huge killers, including measles, pertussis, mumps, and rubella. The incredible number of avoided disease cases in the USA alone can be seen in Figure 13.1.



Source: https://www.pnas.org/doi/full/10.1073/pnas.1704507114

Figure 13.1 Average annual USA cases of vaccine-preventable diseases over the 20th century and today.

Over the 20th century, on average, more than one million people, mostly children, suffered from vaccine-preventable diseases each year in the USA (most of these cases happened in the first part of the century). Half of those afflicted suffered from measles and one-fifth from pertussis. Today, the caseload has dropped by 98%. This is the power of immunization yet, it has not been felt in many other areas of the world to nearly the same degree.

Despite global promises, we are not doing enough

By the turn of the century, vaccines were already preventing over 10 million deaths annually. One 1998 study estimated that in the absence of immunization, the world would every year experience an additional 5 million deaths from smallpox, 1.7 million from measles, 1.3 million from neonatal tetanus, 1 million from pertussis, half a million from paralytic cases of polio, and almost a million from hepatitis B, diphtheria, and tuberculosis.

But many people still suffered from diseases for which they could have been vaccinated, particularly in low- and lower-middle-income countries. This is why expanding vaccine coverage was a major focus during the Millennium Development Goals (MDGs). A key promise was to cut child mortality by two-thirds. Although the world fell short, 'only' reducing child mortality by half, international efforts still helped cut annual child deaths from 12 million in 1990 to just above 6 million in 2015 (see Figure 2.1)

Much of that decrease was attributable to vaccines. Though smallpox had, of course, been eradicated by the time the MDGs were set forth, there were still many more preventable diseases ravaging the world. The UN estimates that expanded measles vaccinations alone prevented 15.6 million child deaths in the first 13 years of the new millennium. In addition to other efforts, in the same year that the MDGs were signed, the Bill & Melinda Gates Foundation, with other founding partners, started Gavi, the Vaccine Alliance, to accelerate access to vaccines in the world's poorest countries. In the first 17 years of the new century, it alone delivered about half of all development aid for vaccines. One study found that in just the short period from 2000 to 2015, an increase in vaccine coverage avoided more than 2 million annual deaths, delivering a third of the total mortality reduction achieved in the MDGs.

In the Sustainable Development Goals (SDGs), world leaders declared that they would essentially eradicateeradicate infectious diseases. The third SDG aims to "ensure healthy lives

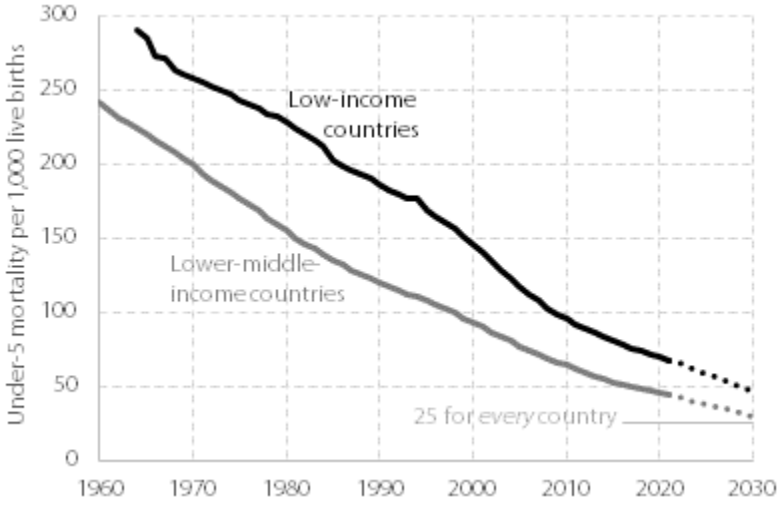
and promote well-being for all at all ages," with an ambitious target in SDG 3.3 on infectious diseases:

> By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases, and combat hepatitis, waterborne diseases and other communicable diseases.

One of the key indicators for these two goals can be found in SDG 3.2 on neonatal and child mortality, which reads:

> By 2030, end preventable deaths of newborns and children under 5 years of age, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1000 live births and under-5 mortality to at least as low as 25 per 1000 live births.

Unfortunately, world leaders are not delivering sufficiently on these promises. As pictured in Figure 13.2, mortality among children under five years old has continued to drop (although slower during Covid). But even assuming that the pace from 2015–19 will be resumed, the average rate across lower-middle-income countries will be above the SDG's target, and low-income countries will be far above.



Source: https://data.worldbank.org/indicator/SH.DYN.MORT?locations=XM-XN Notice that the pre-1990 data are from older versions of the World Bank Development Indicators

Figure 13.1 Under-5 death rate per 1,000 live births 1960–2021, with trend to 2030, based on 2015–19. The SDGs promise that all countries will be below 25 in 2030.

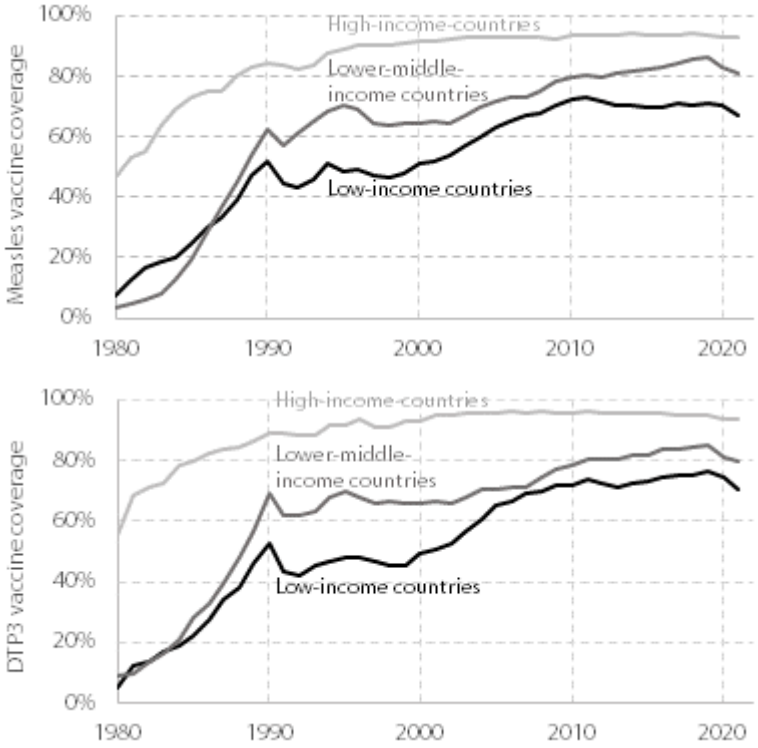
More broadly, we're not on track to meet the third SDG goal of ensuring healthy lives and well-being for all ages. Based on trends from before the outbreak of Covid, these promises would only be achieved in 2090, 60 years late. Disruptions from the coronavirus and lockdowns retarded vaccination trends in 2020 and 2021 and diverted health funds away from immunization coverage, creating 'the perfect storm' for outbreaks of measles and other diseases. Recent years have also seen a rise in anti-vaccine skepticism in some countries, which affected not only the reach of the vaccines against Covid but also other illnesses. This is problematic because even fairly small reductions in childhood vaccines' reach can have pervasive consequences.

In 2021, this resulted in an estimated 25 million children under the age of one missing all basic vaccines for diseases like measles. This is the highest number since 2009, up almost 6 million from 2019. The time is ripe to step up progress.

Vaccines can save many more at low cost

A number of vaccine-treatable diseases have been eradicated mainly in rich nations but remain prevalent in poorer countries. There is a tremendous opportunity to save lives by expanding inoculation to these areas of the world.

One such infectious disease is measles. As you can see in Figure 13.3, wealthy nations were largely inoculated against it by 2000, but coverage remains lower in both low- and lower-middle-income countries. More measles inoculations could save tens of thousands of lives. In 1990, when we had the first relatively accurate global estimates, the world saw about 800,000 annual measles deaths—today, that has been reduced 10-fold to 83,000.



Sources: *https://data.worldbank.org/indicator/SH.IMM.IDPT?locations=XM-XN-XD, https://data.worldbank.org/indicator/SH.IMM.MEAS?locations=XM-XN-XD*

Figure 13.2 Vaccine rates for measles and DTP3 1980–2021.

There is similar potential with the DTP3 vaccine, which covers diphtheria, tetanus, and pertussis, that in 2019 still killed 155,000, almost all in low- and lower-middle-income countries. Diphtheria can lead to difficulty breathing, heart failure, paralysis, and death. It was once a major cause of illness and death in children, claiming more than 15,000 lives in the USA in 1921. Now, it is unheard of in wealthy countries but remains devastating in less-well-off ones. Tetanus, which causes the painful stiffening of muscles and can lead to serious health problems, enters the

body through cuts and wounds. Pertussis, also known as "whooping cough," can cause violent coughing and is extremely dangerous for babies and young children who contract it.

The DTP3 vaccine data show more than just the potential of one type of inoculation. Rates of DTP3 use are often considered a proxy for the basic vaccines recommended in childhood and are a signal of how well countries promote routine immunization services overall. Places where DTP3 inoculation rates are low likely also have low immunization rates for most other vaccines.

More childhood immunization could save millions

The question is, how many more lives can be saved, and at what cost? The researchers for the paper on which this chapter is based use a vaccine economics model to estimate just that. Their model estimates the number of deaths that vaccination avoided in the past and could avoid up through 2030.

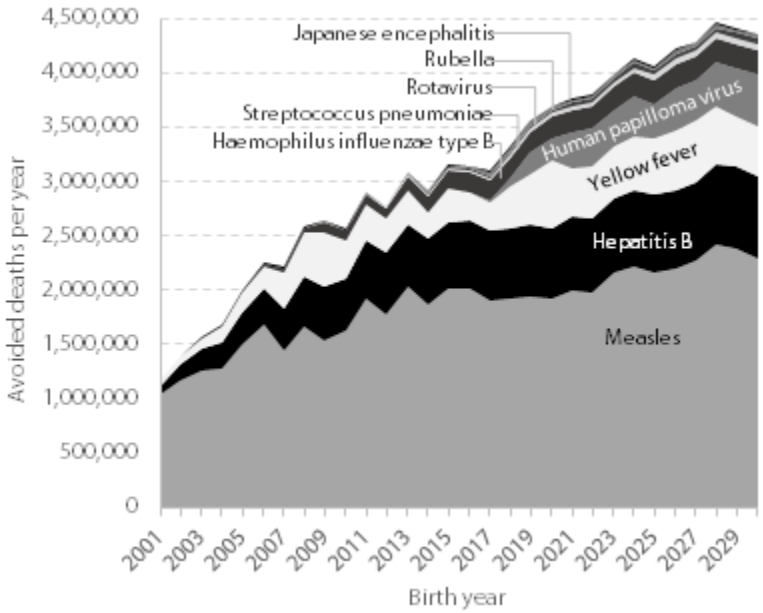


Figure 13.3 Number of lives in low- and lower-middle-income countries saved for each birth year, across their lives, compared to a world without vaccinations.

Figure 13.4 shows that our current vaccination efforts will save 3.8 million of the children born in 2022, compared to a world where no one was vaccinated. Almost 2 million of these children will be saved in their first few years of life from dying of measles—the largest opportunity to prevent deaths by inoculation. The second-largest impact comes from vaccinating against hepatitis B, which becomes lethal as a person reaches old age, and chronic infection can progress to liver cancer. Inoculation can save 683,000 of the children born in 2022 from eventually dying of that condition.

Yellow fever is next. Still endemic in 47 countries in Africa, Central America, and South America, the disease would have killed an additional 477,000 children born in 2022 had they not been inoculated. Another 670,000 will be saved from a few other vaccines, including 350,000 vaccinated against HPV, which eventually can cause cervical cancer in women.

For the birth years 2023 and onwards, Figure 13.5 shows how ever more vaccine coverage will result in more lives saved. The authors compare this scenario to a world in which we do not increase immunization rates but keep vaccination rates at 2022 levels for the rest of the decade, which would mean no rise in avoided deaths.

This comparison shows that many additional lives can be saved by increasing vaccination rates. The difference in deaths between this projection and the estimation, if we keep vaccination rates around 2022 levels for the rest of the decade, is the hatched area in Figure 13.5. Most of the lives that could be saved are of very young children.

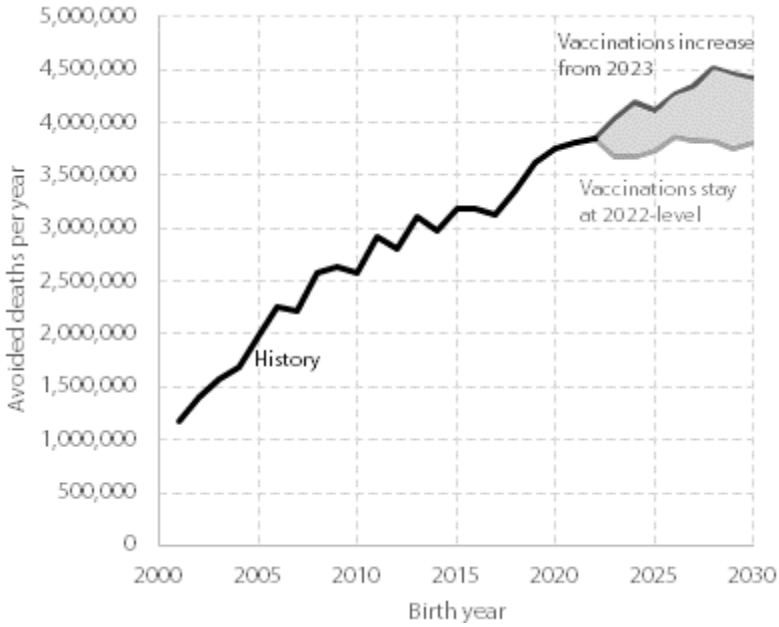


Figure 13.4 Annual avoided deaths by birth year, 2000–2030, with and without additional vaccinations from 2023.

In total, over the rest of the SDG period (effectively 2023–30), an additional vaccine investment can avoid some 4.1 million deaths. When using standard evaluations across time and growth in income, the benefits are worth a little over a trillion dollars in today's money.

Part of this increase will focus on the already very widely distributed vaccines, like measles and DTP3, that reach 80% or more in the poorer half of the world. Another part focuses on vaccines that are less commonly used but still have a large opportunity to reduce deaths and disease.

These include the Human Papillomavirus Vaccine (HPV), the pneumococcal vaccine (PCV), and the rotavirus vaccine. HPV is the most common viral infection of the reproductive tract across the globe and can cause cervical cancer in women, as well as other types of cancer and genital

warts in both men and women. Its global coverage in 2020 was just 13%. PCV is important because the bacteria that cause Pneumococcal infections can lead to more severe conditions like pneumonia, blood infections, and bacterial meningitis. And rotaviruses are the most common cause of severe diarrheal disease in young children throughout the world. Although well-administered hydration can save children even with severe diarrhea, many don't get treated, and every year it kills about half a million children under 5. In 2020, less than half of the world got the final dose of the rotavirus vaccine.

Because we have presumably vaccinated in the countries with easier access and vaccinated the children who are easier to reach, increasing coverage of both will get harder. Introducing the less common vaccines of HPV, PCV, and rotavirus in new countries will likely lead to higher costs per child because of additional costs for introduction and startup costs as well as recurrent costs.

Similarly, further increasing vaccination of common vaccines like measles and DTP3 means reaching more marginal and hard-to-reach communities. This will likely be more difficult and hence be more costly per child. This could be because of higher doctor or nurse costs in far-away places, higher costs to distribute and keep the vaccines refrigerated, or perhaps higher costs to convince the as-of-yet unvaccinated. One typical way to convince mothers to take their children to get vaccinated is seen in India, where the government sets up immunization camps where mothers are offered a bag of lentils or a hot meal as an incentive for vaccinating their children. The higher costs similarly reflect that harder-to-reach groups likely will have to take longer trips to get their children vaccinated, losing out on wages or spare time.

To account for these likely cost increases, the authors project substantially higher costs for the additional number of children to be vaccinated. In total, their cost estimate more than doubles compared to a constant cost assumption. The authors warn that the higher costs are uncertain and may actually be exaggerated. This means it's possible that the paper's benefit-cost ratio is too small.

Table 13.1 Costs and benefits in million dollars, and BCR of achieving a more ambitious vaccination policy compared to remaining at 2022-levels, annual averages across 2023–30.

	Additional vaccinations	Vaccination program at 2022-levels
Benefit	$167	$1,070
Cost	$1.7	$3.7
BCR	101	286

Note: Costs and benefits disounted at 8% per year.

Nevertheless, even assuming these relatively high cost increases, increased childhood immunization turns out to be an excellent investment. The researchers find that expanding vaccination across the rest of the decade will, on average, cost $1.66 billion more per year but return benefits worth $167 billion. Therefore, the plan would return a truly remarkable benefit of 101 times the cost, as can be seen in Table 13.1.[1]

[1] The study also gives an interesting estimate of the benefits and costs of the *current* level of vaccines in low- and lower-middle-income countries compared to a world with *no vaccines*. Currently, vaccinations are already saving nearly four million lives each

Conclusion

Since time immemorial, infectious diseases have caused immense heartbreak, taking countless lives, particularly of young children. With vaccines, humanity has a miraculous tool to turn the tide. One of the most successful public health interventions ever, immunization saves millions of lives each year.

Yet, we can do even better. Vaccination rates have faltered amid disruptions from Covid and lockdowns, anti-vaccination concerns, and general funding scarcity. With only a relatively small increased investment of $1.7 billion annually, world leaders can save half a million lives per year—mainly of children—from highly infectious and deadly diseases. It's one of the best possible investments that we can make.

The academic paper is entitled "Benefit-cost analysis using methods from the Decade of Vaccine Economics (DOVE)." It is authored by

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year (see Figure 13.4). The costs of vaccines already used today are lower than for the proposed, more ambitious vaccine policy because we are vaccinating more accessible, easier-to-reach populations. This shows that the current policy is enormously efficient, and backsliding would surrender huge social benefits.