8 The value of vaccination

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Introduction

> *You let a doctor take a dainty, helpless baby, and put that stuff from a cow, which has been scratched and had dirt rubbed into her wound, into that child. Even, the Jennerians now admit that infant vaccination spreads disease among children. More mites die from vaccination than from the disease they are supposed to be inoculated against.* (George Bernard Shaw, 1929)

The world has come a long way since George Bernard Shaw fulminated against vaccination in the 1920s. Vaccines are now widely regarded as an effective and cheap tool for improving health. Children in all countries are routinely immunized against major diseases, and the practice has become a central plank of global public health efforts.

Despite these advances, however, immunization coverage remains far from universal, and the developing world in particular remains vulnerable to vaccine-preventable illnesses. For example, global coverage for DTP – the vaccine for diphtheria, tetanus, and pertussis (whooping cough) – had reached 70 per cent in the 1990s, but in Sub-Saharan Africa it stood at just 53 per cent. In Somalia, Nigeria, and Congo, moreover, coverage halved between 1990 and 2000 (WHO, 2002). Vaccination against measles also falls short; the disease caused 660,000 deaths in 2002 (WHO, 2004) In all, 3 million people die each year from vaccine-preventable diseases (Centre for Global Development, 2005).

In the developed world, too, vaccination efforts face obstacles. The rise of a well-organized anti-vaccine movement has persuaded some parents not to immunize their children. Vaccines, the campaigners claim, cause more harm than good: in societies where vaccine-preventable disease prevalence is minimal (ironically as a result of past immunization efforts, although this is rarely acknowledged by campaigners), the side effects of vaccines pose a greater health threat than the diseases themselves. Why, they ask, should everyone be vaccinated in order to protect the relatively small number of people that might contract the disease in the absence of mass immunization?

It is not just populist activists who overlook the positive effects of vaccination. More scientific estimates of the effects of vaccines also tend to underplay the benefits, disregarding the broad economic impacts of immunization in favor of a predominant and narrow focus on the averted costs of medical treatment and health care. With other human capital investments, such as education, economic analysis of the impacts focuses on the effect on earnings. This has not occurred, however, with vaccination, and until recently it did not occur for health in general. Public health specialists generally perceive vaccination as a hugely beneficial investment as it is both cheap and very effective at a population level (the influential 1993 World Development Report, 'Investing in Health', listed the World Health Organization's Expanded Program on Immunization as the first component of "the essential public health package"(World Bank, 1993)). Because of the narrow view of its impacts taken by the rest of the policy-making community, however, policy emphasis on vaccination is weaker than it might be if the full range of benefits were taken into account.

Health economists have long used two well-established tools to evaluate health interventions in economic terms. Both types of analysis are widely used and appropriately respected. Cost-effectiveness analysis (CEA) seeks to determine the cost of an intervention (e.g., vaccination) in relationship to a particular outcome. How much does it cost to save a certain number of lives, or to avert a certain number of illnesses, for example? Averted medical costs (at least those that would be incurred in the short run in the absence of vaccination) are also typically taken into account. Cost-benefit analysis (CBA), by contrast, makes a direct comparison between costs and benefits by monetizing the value of the latter. This technique facilitates comparison of two or more interventions, particularly when there is a range of discrete outcomes.

There are several problems with both types of analysis, as they have been used to date. First, neither type typically takes account of the cost of averted infections that may occur years later. This is understandable, since such infections are hard to predict, but that does not make future cost savings any less important.

Second, both types of analysis take a narrow view of the benefits of vaccination that fails to take account of recent academic work on the effects of health on incomes. The experience of development over the past half-century shows that good health fuels economic growth, just as bad health strangles it. Healthy children perform better at school, and healthy adults are both more productive at work and better able to tend to the health and education of their children. Healthy families are also more likely to save for the future; since they tend to have fewer children, resources spent on them go further, thereby improving their life prospects. Finally, healthier societies may be a stronger magnet for foreign direct investment and tourism than those where disease poses a constant threat.

Third, neither type of analysis factors in the effects that improved health has on triggering lower fertility rates. The combination of lowered mortality rates followed by lowered fertility rates leads to a baby boom generation that, when it reaches working age, can help bring about a significant economic boom (as happened in East Asia). In the case of vaccination, the consequent boost to health can catalyze a change in the age structure of the population (via the lowered fertility rates) that can lead to significant economic benefits.

Our research looks at all CEA and CBA studies listed in Pub. Med. for 2004 and 2005. The wide range of published results emphasizes the difficulties inherent in such work. However, since all of these studies fail to address the broader considerations described in the preceding two paragraphs, they all either overstate the cost of achieving a given beneficial outcome or underestimate the net benefits. It is this insight that spurs the current work.

With the spread of immunization having stalled in many parts of the world, a wider look at its benefits is timely. In this paper, we discuss the value of vaccination from a broad perspective. As well as the health benefits, we examine the cost of vaccine programs and their economic impacts. Vaccination has proved a cost-effective and remarkably efficient way of improving health, and has saved millions of lives. It has the potential, however, to be more effective still, and renewed efforts are needed if the momentum is to be regained.

Part 1 of the paper provides a brief summary of the history of vaccination and its impacts on human health. Part 2 looks at the state of play today and at the reasons why progress on vaccine delivery and development has slowed, and part 3 outlines why rate of return analysis and calculations of economic impacts suggest policy makers should direct more resources toward vaccination. Part 4, which reviews both cost-effectiveness analysis and cost-benefit analysis, indicates that a broader view of the long-term benefits of vaccination makes immunization programs much more worthwhile, in terms of their economic consequences, than has been thought in the past. Part 5 details our study on immunization and cognitive development, which has, in turn, been linked to higher earnings. Part 6 estimates the rate of return to one of GAVI's prospective investments, showing that this return is quite high.

A glorious past

The theory behind vaccination was brought to the West from Asia. The Chinese had observed that certain illnesses could only be contracted once, so they experimented with giving healthy individuals doses of diseases such as smallpox that would be too small to make them ill but large enough to stimulate immunity. The process was known as variolation and, in the case of smallpox, usually involved injecting powder from smallpox scabs into the vein. Although some individuals fell ill or died during the process, smallpox rates among communities that had been variolated were significantly lower than elsewhere.

Variolation was introduced to Britain by Lady Mary Wortley Montagu, who had observed the process in Turkey, where her husband was British ambassador, in the early 18th century. Several decades later, Edward Jenner, who had undergone variolation as a child, noticed that people who contracted cowpox after working with cows became immune to smallpox. To test this observation, he injected a small child with cowpox. The child fell ill with cowpox but, when later injected with smallpox, did not contract the latter disease. Jenner published his findings in 1798, and named the process 'vaccination', from the Latin word for cowpox (The Hutchinson Encyclopaedia, 1999).

In 1890, Emil von Behring and Shibasaburo Kitasato gave substance to Jenner's observation when they discovered antibodies. Injecting a small amount of a disease organism into an uninfected individual, they found, stimulated the production of antibodies, which fought off the initial attack and thereby prepared the body to fend off infection later in life. At around this time, vaccines for rabies, cholera, typhoid, and the plague were developed, although it was not until after the World War II that vaccines became a widespread tool for improving health. Today, 26 diseases are vaccine-preventable.

Since World War II, vaccination has had a major impact on global health, as the following list of successes shows:

- Smallpox, which had killed two million people per year until the late 1960s, was wiped out by 1979 after a massive worldwide immunization campaign.
- The number of polio cases fell from over 300,000 per year in the 1980s to just 2,000 in 2002 (Global Alliance for Vaccines and Immunization website, 2002).

- Two-thirds of developing countries have eradicated neonatal tetanus (WHO, 2002)
- Since the launch of the World Health Organization's Expanded Program on Immunization (EPI) in 1974, the number of reported measles deaths has dropped from 6 million to less than 1 million per year.
- Whooping cough cases have fallen from 3 million per year to less than a quarter of a million.
- Diphtheria cases have declined from 80,000 in 1975 to less than 10,000 today (Birmingham & Stein, 2003).
- The haemophilus influenzae B (Hib) vaccine has reduced the incidence of Hib meningitis in Europe by 90 per cent in ten years (Ehreth, 2003).

The EPI includes six vaccines, covering diphtheria, tetanus, whooping cough, measles, polio, and tuberculosis. Before 1974, only 5 per cent of children were vaccinated against these diseases. Today over 70 per cent are vaccinated (WHO, 2002). The program has reduced the share of the six diseases it tackles in the total burden of disease in young children from 23 per cent to less than 10 per cent since the mid-1970s (WHO, 2001). It has been estimated that declines in diphtheria, measles, and whooping cough have averted well over a million deaths in developing countries (Birmingham & Stein, 2003).

In 2000, in an effort to maintain the EPI momentum, the Global Alliance for Vaccines and Immunization was launched. GAVI comprises United Nations agencies, governments, donors, foundations, private companies, and academic institutions. It has six core strategic objectives: GAVI

- Improve access to sustainable immunization services
- Expand the use of all existing safe and cost-effective vaccines, and promote delivery of other appropriate interventions at immunization contacts
- support the national and international accelerated disease control targets for vaccine-preventable diseases

- Accelerate the development and introduction of new vaccines and technologies
- Accelerate research and development efforts for vaccines needed primarily in developing countries
- Make immunization coverage a centerpiece in international development efforts

As we will see part 2 of the paper, such an initiative is urgently needed.

A difficult present

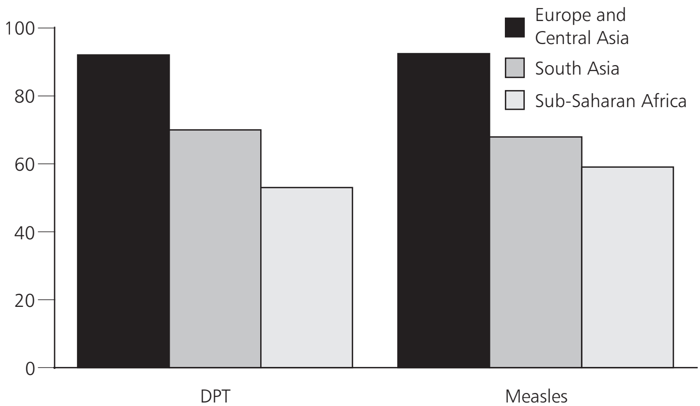
Lost momentum

The rapid progress towards universal vaccination coverage in the 1970s and 1980s has slowed in recent years.

Declining funding for immunization has been mirrored in stagnating or falling coverage. UNICEF funding for vaccination fell from $182 million to $51.4 million between 1990 and 1998 (Gauri, 2002). Global coverage of the diphtheria, tetanus, and pertussis (DTP3) vaccine has stalled at around 74 per cent since 1990 (GAVI, 2003). Fifty-seven developing countries have yet to eliminate neonatal tetanus, and 200,000 babies died of the disease in 2000 (WHO, 2002). Yellow fever has made a comeback, despite the availability of an effective vaccine; the number of outbreaks increased sharply after governments curtailed programs in the belief they had vanquished the disease (GAVI, 2001).

Developing countries lag behind the West in terms of vaccination coverage. Measles immunization rates are over 90 per cent in Europe but below 70 per cent in South Asia and below 60 per cent in Sub-Saharan Africa (see figure 1) (World Bank, 2004). Ten developing countries reported cases of polio in June 2005, despite the massive (and largely successful) global effort to eradicate the virus (WHO, 2005). Sixty-two per cent of countries, meanwhile, had still not achieved full routine immunization coverage in 2003, with GAVI estimating that at least 9.2 million additional infants need to be reached to achieve full coverage (GAVI, 2003).

Figure 1 **Disparities in immunization rates**
% of children (12–23 months) immunized



Source: World Bank, 2004

There are several factors behind this loss of momentum. First, although dramatic progress has been made in increasing worldwide vaccination coverage from below 5 per cent to above 70 per cent, the task has inevitably become harder now that the easiest-to-reach populations have been vaccinated. Many of those whom campaigns have not yet reached are either living in inaccessible areas, out of range of clinics and health services, or reluctant to be vaccinated or to vaccinate their children. Because these communities are more elusive, the average cost per vaccination has increased, and it may be that other apparently cheaper health interventions have become more attractive.

Second, there are many practical problems impeding vaccine delivery. Delivering vaccines to patients requires functioning freezers and refrigerators (which in turn require a constant supply of energy); good roads and reliable transport to move the vaccines from port to clinic; clinics with access to people who need to be immunized; parents who know the value of vaccination; trained medical staff to deliver the dose; and sterile syringes.

Many of the poor countries where vaccine coverage has stalled lack all or part of this infrastructure. In Burkina Faso and Niger for example, 23 per cent of refrigerators used for storing vaccines were found to be non-functioning (GAVI, 2003). Only 16 per cent of vaccine-importing countries could guarantee vaccine safety and quality, (WHO, 2002) while a further study of 19 developing countries found that at least half of injections were unsafe (WHO, 2002).

The third factor behind the lack of progress in recent years is political. Political disruptions have affected coverage in some areas. In Somalia and Congo, for example, where vaccination rates have fallen rapidly in the past decade, war and social breakdown have impeded public health campaigns, despite "vaccination days" in Congo that temporarily halted fighting. Gauri et al. have found that the quality of institutions and governance are positively correlated with vaccination coverage (Guari, et al. 2002). Immunization campaigns do not operate in isolation – they are dependent on the prevailing political and social environment. As that environment is altered, immunization may be interrupted.

Politics in the developed world have also played a part. According to a report by the US Institute of Medicine, in 1982 the US vaccine industry was forced to stop offering low-price vaccines to developing countries following congressional hearings that "savaged" the industry for "allegedly subsidizing vaccines for the poor children of the world by charging high costs to US families and taxpayers" (Institute of Medicine, 1997). As the Institute of Medicine points out, this move was based on a flawed premise, as the US vaccines would have been developed anyway to protect American children and travelers.

The fourth reason for the lost momentum relates to public perceptions of vaccination. As coverage spreads through a community, it reaches a point at which those who are unvaccinated are highly unlikely to catch a disease because herd immunity has set in. At this juncture, it may be more rational for an individual to refuse vaccination in order to avoid any risk of side effects. With oral polio vaccine, for example, there is a 1 in 1 million chance of paralysis, and in societies where mass vaccination has eliminated the disease, the risk of paralysis is greater than that of catching polio itself. What had once been a public and private good is now a public good but a private risk. As more and more people choose to avoid this risk, of course, overall coverage rates decline, and the community is once again exposed to the threat of the disease.

Public perceptions have been influenced by vaccine scares. Controversy and the attendant bad publicity about the safety of vaccines has been abetted by incidents such as the withdrawal of half the US supply of flu vaccines in 2004 due to contamination at the manufacturer, Chiron's UK plant (Los Angeles Times, 2005) and by the swine flu vaccine, which led to deaths of some of those immunized (while the flu itself did not arrive).

In addition, alarms over the safety of vaccines such as that for measles, mumps and rubella (MMR), which some believe to cause autism, have further fanned the anti-vaccine movement's flames. In the United States, disputes continue to rage about the scientific basis of such claims, but the preponderance of the evidence, according to the US Centers for Disease Control, says that the MMR vaccine is safe (Kennedy, 2005). In the UK, physician Andrew Wakefield caused alarm over the MMR vaccine for the same reason. Rates of MMR coverage dropped in Britain and elsewhere in the wake of this scare, before Wakefield's case was to a large extent discredited and the journal that had published his research, *The Lancet*, partially retracted the study.

A survey of public reactions to Wakefield's findings showed that 53 per cent of people believed that, because media coverage gave roughly equal space to support and rejection of the autism theory, the scientific evidence base must be similarly balanced (Hargreaves et al., 2003). Only 25 per cent, moreover, were aware that no link between MMR and autism had been found in the overwhelming majority of studies (Lewis & Speers 2003). A similar scare occurred over the hepatitis B vaccine, which in the mid-1990s was briefly believed to cause multiple sclerosis in some who received it. Subsequent cohort and case-control studies found no link between the two (Halsey 2003).

Vaccine scares do not always lack foundation. The Rotashield vaccine for rotavirus, which was approved in the US in 1998, was withdrawn a year later after reports were received of acute intussusception (a potentially serious bowel condition) occurring shortly after delivery of the vaccine. A study later confirmed this relationship – between 1 in 5,000 and 1 in 10,000 infants developed intussusception within two weeks of vaccination (Mulholland & Bjorvatn, 2003). Such events, as well as causing enormous financial losses to the company that developed the vaccine, can have negative effects on public trust in immunization. They also increase pressure on governments to tighten regulation of vaccines, thereby making their production even more costly.[2]

In response to these types of controversies in the United States, the Institute of Medicine has called for independent oversight of vaccine safety studies to ensure the fairness and openness of the Vaccine Safety Datalink program, which is overseen by the CDC.[3]

Imperiled innovation

As well as vaccine coverage, development of new vaccines has also stalled in recent years. The number of major western pharmaceutical companies making vaccines fell from 26 in 1967 to five today, although some of the slack has been taken up by developing-country manufacturers (Washington Times, 2005). As profit margins for rich-world vaccines have outpaced those for vaccines needed by poor countries, drug developers have concentrated ever more on diseases of the developed world.

The profitability deficit for developing-world vaccines is huge. The developing-world vaccine market is estimated at just 10–15 per cent of the world total and less than 0.2 per cent of the entire global pharmaceutical market (Siwolop, 2001). The total volume of all vaccine doses acquired by UNICEF and the Pan American Health Organization (PAHO) for distribution in the developing world, moreover, is 100 times greater than the number of doses of Prevnar (a vaccine for diseases caused by streptococcus pneumoniae) delivered in the US, but brings in less than half the revenue.

Rich and poor countries have different immunization needs. Parents in rich and poor countries alike are concerned with the safety of vaccine delivery; but governments in poor countries are concerned with its cost, too. Products have therefore begun to diverge, even when they tackle the same illness, and the new vaccines that respond to developed-world demands are often too expensive for poor countries. In the 1990s, for example, developed countries began to use the DTaP instead of DTwP vaccine. DTaP (which incorporates an acellular pertussis vaccine) is more expensive and no more effective than DTwP (which contains a whole-cell pertussis vaccine), but it has fewer side effects and has therefore proved more popular with developed-world consumers. Similarly, the oral polio vaccine has been replaced in countries such as the US by inactivated polio vaccine (IPV), which is delivered by injection. Unlike OPV, the IPV vaccine cannot cause paralysis (Batson et al., 2003).

Pharmaceutical companies have found it difficult to persuade shareholders of the value of continuing to develop vaccines for poor countries. The pharmaceutical giant Glaxo SmithKline, for example, reported in 2001 that it was planning to allocate its freeze-drying capacity to haemophilus influenzae B (Hib) vaccine rather than the less profitable meningitis A/C vaccine. Doses of the DTwP vaccine offered to UNICEF, moreover, declined from 600 million in 1998 to 150 million two years later (GAVI, 2001).

Intellectual property rights present a further challenge to vaccine development. Unlike many other drugs, people generally need only one dose of a vaccine or vaccine booster. Manufacturers therefore need to gain a return on their investment from a single use, rather than over a full course of treatment as in the case of antibiotics or over a patient's entire lifetime as in the case of antiretroviral drugs for AIDS. Companies are thus particularly zealous about protecting vaccine patents – monopoly over production of a vaccine is, they believe, the best way to profit from it. Generic drug producers in poor countries, however, threaten these patents and increase the risk that vaccine developers will not gain a satisfactory return on their investment. Compulsory drug licensing, moreover, which some countries have introduced for antiretroviral treatment for AIDS, may deter future investment in drugs for the developing world. If pharmaceutical companies cannot guarantee a return on their research and development costs through the end of the patent period, the attraction of vaccines for developing countries may weaken further.

There is a lively and important debate regarding the costs of drug development and how they should be assessed. The pharmaceutical industry has long claimed that the enormous costs of development are only sustainable by the prices charged for the subset of drugs that are finally approved. Critics have argued that the development costs are overstated, with Relman and Angell (Relman & Angell, 2002) pointedly stating that "… research and development (R&D) constitutes a relatively small part of the budgets of the large drug companies. Their marketing and advertising expenditures are much greater than their investment in R&D." In addition, they argue that the pharmaceutical companies are not as innovative as generally assumed – and that much of the spending on truly new drugs is taxpayer-supported. DiMasi et al. respond to some of the drug industry's critics, (DiMasi et al., 2004) carefully critiquing their methodology, and offer new estimates of drug development costs (Di Masi et al., 2003). (Relman and Angell also critique DiMasi et al.)

As Relman and Angel note, not all investment in vaccines comes from the private sector. Government research agencies and academic institutions are responsible for much investment in basic scientific research. A widely promoted means of filling the gap between the needs of developing countries and the demands of pharmaceutical firms' shareholders is for public organizations to step in and guarantee a market for vaccines once private companies have developed them. GAVI is currently coordinating this effort internationally but, as the downfall of an earlier initiative shows, encouraging diverse organizations to work together to achieve a common goal is a task riven with complexities.

William Muraskin has detailed the demise of the Children's Vaccine Initiative (CVI), which was launched by the World Health Organization in 1990 in response to the slowdown in development of new vaccines and poor distribution of existing ones (Muraskin, 1998). The CVI's efforts to bring together public and private sector scientists and organizations to work towards solutions were unsuccessful. As Muraskin explains, there was a "great gulf of distrust, often bordering on contempt," between public and private sectors. Public sector scientists saw their private sector counterparts as being purely driven by profit, while the latter saw the public sector as a wasteful and untrustworthy partner. The WHO closed the CVI down in 1999. Such experience reinvigorates the question of government's responsibility for ensuring the timely development and production of vaccines – both for old diseases and new. One alternative is that governments themselves could create greater vaccine development and production capacities. Another option is for governments to offer major financial incentives to pharmaceutical corporations in exchange for guaranteed increases in development efforts and actual construction of vaccine production facilities. Under this latter scenario, a government could promote competition among companies for contracts of this type. The case of avian flu, which could soon burst onto the world scene on a terrifying scale, brings this discussion into sharp focus: governments must assess whether they can rely on the private sector to take the initiative in guaranteeing public health when the steps needed to make such guarantees currently look unprofitable.

Developing and delivering vaccines, then, are by no means straightforward tasks. The progress in eliminating smallpox and drastically reducing cases of polio shows that with will and effort immunization campaigns can be successful, but the momentum for mass immunization has stalled in recent years. In the next section we examine the case for a renewed global effort to extend vaccination coverage, focusing on the economic impacts of vaccine programs.

An uncertain future

The narrow perspective

Assessment of the benefits of vaccines has traditionally focused on a specific range of health-related impacts. Cost-effectiveness and cost-benefit analyses of the numbers of averted illnesses, hospitalizations and deaths; disability-adjusted life years (DALYs) gained; and medical costs avoided are the most common assessment methods. Cost-effectiveness analysis looks at the cost of a health intervention per life saved (or per DALY gained, etc.); cost-benefit analysis takes into account the value of each life saved or the extra years of healthy life gained, and compares the total value of those benefits to the cost of the intervention.

The World Health Organization, for example, has estimated that polio eradication will save governments $1.5 billion per year in vaccine, treatment, and rehabilitation costs. The elimination of smallpox is thought to have saved $275 million per year in direct health care costs (GAVI, 2003); Barrett estimates that the $100 million invested in eradicating the disease in the ten years after 1967 "saved the world about $1.35 billion a year" (Barrett, 2004). And the US Institute of Medicine reports that for every dollar spent on the MMR vaccine, $21 is saved (Institute of Medicine, 1997).

Other cost-effectiveness studies have also found that vaccination campaigns lead to substantial savings in medical costs,[4] but a recent review of 60 studies on the effectiveness, cost, and cost-effectiveness of immunization programs in developing countries concluded that the literature base on cost-effectiveness was flimsy. Only three of the studies addressed cost-effectiveness, and most studies were riddled with weaknesses. Few provided confidence intervals for their findings, follow-up was limited, data sources were not clearly defined, and there was little discussion of confounding variables. Studies on costs, moreover, found wide variations depending on the setting in which a vaccine was being delivered, making estimates of cost-effectiveness difficult to generalize (Pegurri et al., 2005).

The available literature on DALYs suggests immunization is a highly cost-effective intervention. The total cost of the EPI vaccine package is less than $1 (Gauri et al., 2002). According to GAVI, most vaccination campaigns cost less than $50 per year of healthy life gained. By contrast, treatment for diseases such as hypertension in the US costs between $4,340 and $87,940 for each DALY gained (GAVI, 2003). Jamison et al. estimated that the EPI vaccine program costs $14–20 per year of healthy life gained in low-income countries (Jamison et al., 1993). Miller and McCann show a similar cost for the Hib vaccine in Africa, and that Hepatitis B immunization in low-income, high-prevalence countries costs just $8–11 per DALY gained (Miller & McCann, 2000).

Although cost-effectiveness provides a robust demonstration of the extent to which vaccines reduce medical costs, it does not take account of the wider range of benefits that are covered by cost-benefit analysis. The latter also has the advantage of being comparable with investments that take place outside the health sector.

Many cost-benefit analyses of vaccination have shown positive effects. In South Africa, a study of the mass measles immunization campaign of 1996 and 1997 found a benefit-cost ratio of 2.27 in the province of Mpumalanga (Uzicanin et al., 2004). In Japan, the benefit-cost ratio of subsidized influenza vaccinations for the elderly was estimated at 22.9 (Ohkusa, 2005). Purdy et al. found that most of the costs related to pertussis are due to lost productivity at work and that the benefit-cost ratio of the immunization of 10 to 19 year olds is strongly positive (Purdy et al., 2004).

Some studies, on the other hand, have shown higher costs than benefits. In the study of measles immunization in South Africa, the benefit-cost ratio in the Western Cape province was 0.89 (Uzicanin, 2004). And a study to assess the incorporation of the pneumoccocal 7-valent conjugated vaccine into the routine immunization program in Spain found a benefit-cost ratio of only 0.59 (Navas et al., 2005).

A wider view

Neither cost-effectiveness nor cost-benefit analysis has so far taken full account of the broader economic impacts of immunization. These impacts stem from the fact that immunization protects individuals not only against getting an illness per se, but also against the long-term effects of that illness on their physical, emotional, and cognitive development. For example, by stunting physical growth, childhood diseases can curtail opportunities for carrying out manual labor during adulthood. In developing countries, where manual work is frequently the only option, physical handicaps are particularly damaging. Cognitive development may also be affected by vaccine-preventable disease. Measles, for example, can cause brain damage or impair learning abilities, with severe impacts on a child's life prospects.

The importance of these effects is borne out by recent work demonstrating the link from improved health to economic growth. This research has made clear the importance of health interventions for achieving growth and suggests that cost-effectiveness analyses, as currently conducted, are likely to underestimate the benefits of vaccination.

There are several channels through which health improves wealth. The first is through its impact on education. Healthy children are better able to attend school and to learn effectively while in class. Studies have found that health interventions such as de-worming programs and iron supplementation reduce absenteeism from school (Miguel et al., 2004). Curing whipworm infection, meanwhile, has been found to lead to improved test scores (Nokes et al., 1992).

The second channel is through health's impact on productivity. Like schoolchildren, healthier workers have better attendance rates and are more energetic and mentally robust. Workers in healthy communities, moreover, need to take less time off to care for sick relatives. Body size, which is greatly influenced by one's health during childhood, has been found to have large impacts on long-term productivity (Fogel, 1991). Bloom et al. have calculated that a one-year increase in life expectancy improves labor productivity by 4 per cent (Bloom et al., 1998).

The third means by which health improves wealth is through its effect on savings and investment. Healthier people expect to live longer, so they have a greater incentive to save for retirement. They are also able to work productively for longer, giving them more time to save. Workers and entrepreneurs therefore have a larger capital base to draw on for investment, leading to greater job creation and higher incomes. The savings booms in the East Asian "tiger" economies in the last quarter of the 20th century were largely driven by rising life expectancy and greater savings for retirement.

Finally, health can boost economies via a demographic dividend. The transition from high to low rates of mortality in many developing countries has been rapid. Largely brought about by medical and dietary improvements, the transition has contributed to falls in fertility as parents realize they need fewer children to attain their ideal family size. The boom in young dependents that occurs when mortality falls is therefore followed by a decline in fertility. At this stage, parents can concentrate their resources in nurturing fewer children, thus increasing the latter's prospects of receiving a good education and effective health care. As the boom generation reaches working age, and provided it encounters a policy environment that is favorable to job creation, it can give a large boost to an economy by swelling the ratio of workers to dependents. It has been estimated that the demographic dividend accounted for as much as one third of East Asia's "economic miracle" (Bloom et al., 1998).

A more thorough investigation of the impacts of vaccination, then, should look not just at direct medical cost savings and averted illness, but also at the effects on cognitive development, educational attainment, labor productivity, income, savings, investment, and fertility.

The benefits of vaccination – new evidence

The effect of GAVI

We have carried out calculations for two vaccination campaigns, taking into account the broader economic impacts of immunization. The first study assesses GAVI's program to extend the use of the traditional basic childhood vaccination package; increase coverage of the underused Hib, hepatitis B, and yellow fever vaccines; and help finance the introduction of anticipated vaccines covering pneumococcal disease, rotavirus, and meningococcal A/C conjugate. This program will operate in 75 low-income countries with a combined population of 3.8 billion from 2005–2020, and will cost $13 billion. We examine the likely effect of the program on worker productivity at the individual level. The second study covers efforts in the Philippines to immunize children with DTP, TB, polio, and measles vaccines. It measures vaccines' effects on children's cognitive development, an important determinant of adult earnings.

The countries involved in the GAVI immunization program suffer from high rates of child mortality. In countries that are not covered by the program, there are fewer than 10 child deaths per thousand live births. In the GAVI countries, there are over 65 deaths per thousand. GAVI estimates that its program will reduce child mortality by 4 deaths per thousand live births in 2005, rising to 12 per thousand by 2020 as the campaign expands.

We used a life table to translate averted deaths into increased probability of adult survival (the proportion of 15 year olds who reach age 60), and found that the GAVI program will increase the adult survival rate by 5 per 1,000 initially and by 16 per 1,000 by 2020 (life expectancy will increase by half a year initially and by one and a half years by the end of the program).

To translate the latter into growth of wages and income per capita, we used estimates in the economics literature from Shastry and Weil (2003) and Weil (2005) (Shastry & Weil 2002) that show the link between health and wages in individuals.[5] This analysis shows that for a group of 1000 adults, for each additional person surviving from age 15 to 60, average wages rise by 0.179 per cent. Based on the assumption that labor productivity and wages account for two-thirds of national income (Hall & Jones, 1999), we calculate that each extra surviving adult in a group of 1000 boosts income per capita by 0.119 per cent.

From this figure, we calculate that the average percentage increase in income for the children whose immunization coverage increases through the GAVI program will rise from 0.78 per cent in

2005 to 2.39 per cent by 2020. This equates to an increase in annual earnings per child of $14 by 2020 (see table 1). The total increase in income per year once the vaccinated cohort of children start earning will rise from $410 million in 2005 to $1.34 billion by 2020 (at a cost of $638 million in 2005 and $748 million in 2020).

We estimate the internal rate of return to the program by calculating the interest rate that would make the net present value of the flow of future benefits equal the initial costs. The rate of return amounts to 12.4 per cent in 2005, rising to 18 per cent in 2020 as vaccine costs decline. These are conservative estimates, since they do not take account of averted medical costs, the value of reduced pain and suffering among survivors, welfare benefits associated with averted deaths, or demographic dividend effects.

If these additional benefits of vaccination had been included, it is likely that the rate of return would be higher still, and possibly much higher, but even these conservative estimates compare favorably with the average rates of return to schooling. A review of 98 country studies from 1960 to 1997 showed that the average returns for primary, secondary and higher education were 19 per cent, 13 per cent and 11 per cent respectively (Psacharopoulos & Patrinos, 2002). This finding suggests that the benefits of vaccination have been greatly underestimated and amounts to a strong argument for increased immunization in developing countries.

Immunization and cognitive development – evidence from the Philippines

In the Philippines study, we examined the effect of immunization on productivity by looking at its impact on test scores that measure the cognitive ability of ten year olds. There is robust evidence that childhood illness can impair cognitive development, and that the latter affects adult productivity and earnings. Since our data cover children born in 1983–1984 and thus do not offer information on wages, we take scores in cognitive tests at the age of ten as an indicator of likely productivity in adulthood.

Our study involves a sample of 1975 children from the Cebu

Longitudinal Health and Nutrition Survey (CLHNS). CLHNS is part of a longitudinal survey of Filipino women and their children born in the year following 1 May 1983. The women lived in 33 districts of the metropolitan Cebu area. Bi-monthly interviews carried out over two years allow us to track immunization activities in the first two years of a child's life, while a follow-up study conducted between October 1994 and October 1995 provides us with scores on language, mathematics, and IQ tests.

We compared the test score results of children who had received the basic six vaccines (DTP, polio, measles, and TB) in the first two years of life with those who had had no vaccinations. It is important to recognize, of course, that children who are immunized have other advantages that make them more likely to succeed in cognitive tests. For example, they may receive a better education or hail from families that place a great emphasis on health in general, meaning they would score well whether or not they were immunized. In order to eliminate these effects, we used a propensity score matching method that matches each child in the treatment group with a similar control group. We matched children on the probability that they would be vaccinated given their characteristics – that is, their "propensity scores". Groups of children with a certain propensity score were matched with control groups whose propensity scores are close to their own, with the closest-matched groups given more weight (Canning & Seiguer, 2005).

After controlling for these observed characteristics we found that immunization was associated with significantly improved scores in IQ, language, and mathematics tests. The effect was stronger (significant at the 5 per cent confidence level) for IQ and language scores than for mathematics (where the effect was significant at the 10 per cent level). Childhood vaccination appears to have positive and long-term health impacts that translate into increased cognitive ability in ten year olds, which in turn is associated with higher earnings in adulthood.

In both our studies, then, we found significant positive impacts of vaccination programs. As well as improving health, vaccines have long-term effects on the development of an individual. These individual effects, which are produced at a remarkably low cost, are likely to translate into lasting impacts on economies.

Summary

Clearly there is scope for more research to be conducted on the diverse benefits of vaccination. The Miller and McCann study cited above shows that rates of return differ by country and by income group. It is likely they also differ by the type of vaccine delivered. Further research is needed to calculate the value of vaccination for different countries and at different stages of development. However, immunization does appear to be an important tool for improving survival and strengthening economies. By boosting cognitive abilities, it improves children's prospects of success when reaching working age. And it does so in an extremely cost-beneficial way. Immunization provides a large return on a small investment – higher than most other health interventions, and at least as high as non-health development interventions such as education.

There is a strong case, therefore, for a renewed international commitment to vaccination. The impressive progress towards universal basic vaccine coverage in the 1970s and 1980s has stalled in the past decade, and several damaging childhood illnesses have begun to return as a result. A revived commitment to vaccination requires action on several fronts. First, the public health establishment must communicate clearer and more compelling messages about the value of vaccination. The targets of such communication should include governments in developed and developing countries, as well as donors that fund vaccination in the latter. Second, these messages should move beyond explanation of the effect of immunization on health and on medical costs to address the broader impacts on economies. Vaccination is not purely a health sector issue – it has resonance for wider economic planning and for long-term economic progress. Apprising finance ministries of its importance is vital for cementing its position in development policy.

The third area where renewed action is needed relates to leadership. At an international level, GAVI has begun to increase awareness of the value of vaccination and to push multiple partners toward expanding its breadth and scope. At the national level, politicians' commitment is important in driving immunization campaigns forward. Traditionally, individuals have submitted to state encouragement to vaccinate because they have trusted government to act in their best interests. Recent problems with vaccines, along with efforts (valid or not) of those who continue to argue that vaccines are unsafe, are weakening this trust. Politicians are not elected on vaccination platforms, so there is no pressure on them to champion vaccines once in power. However, the confusion caused by British Prime Minister Tony Blair's refusal to reveal whether his own son had received the MMR vaccine at the height of the MMR scare highlights the dangers of equivocal leadership on such sensitive issues. Blair's lack of clarity, which was the subject of extensive media coverage, may have increased uncertainty over the vaccine (Lewis & Speers 2003) Public complacency, as measles outbreaks that have followed declines in vaccination coverage in the developed world show, can quickly imperil health, and governments and donors that recognize the benefits of immunization must continually hammer the point home.

Traditionally, governments and donors have only considered the health impacts of vaccine-preventable illnesses, and their effect on overall welfare has been underestimated. However, new evidence on the importance of health as a driver of economic development and poverty reduction suggests the need for a re-think. Vaccines in particular, as the evidence presented in this paper shows, are an inexpensive and extremely effective means of improving health and overall welfare. Their impacts, moreover, are much greater than previously thought.

Making the push to complete worldwide vaccination coverage will be a difficult task, and finding ways of ensuring the continued development of effective vaccines in the future potentially more complex still. Vaccines should be seen not as a cost that swells

Table 1 **Projected costs and economic benefits of the expanded GAVI immunization program**

	2005	*2006*	*2007*	*2008*	*2009*	*2010*	*2011*	*2012*	*2013*	*2014*	*2015*	*2016*	*2017*	*2018*	*2019*	*2020*
Total cost ($million)																
	638	652	583	659	790	862	761	762	1,023	1,051	1,059	994	896	769	727	748
Deaths averted																
	732,673	855,998	923,529	993,247	1,052,696	1,125,275	1,229,883	1,349,584	1,608,999	1,741,284	1,913,958	1,955,902	1,973,229	1,990,757	2,002,458	2,014,390
$ cost per death averted																
	871	761	632	663	750	766	619	565	636	604	553	508	454	386	363	371
Reduction in under 5 mortality rate (per 1000)																
	4.10	4.89	5.43	6.00	6.45	7.11	7.82	8.60	10.20	11.08	12.24	12.43	12.49	12.54	12.56	12.57
Total increase in adult survival rate (per 1000)																
	6.61	7.87	8.74	9.64	10.37	11.43	12.56	13.81	16.38	17.80	19.65	19.97	20.06	20.14	20.17	20.19
Increase in life expectancy (years)																
	0.58	0.69	0.77	0.85	0.91	1.00	1.10	1.21	1.44	1.56	1.73	1.76	1.76	1.77	1.77	1.78
Average percentage increase in income for all children in that cohort																
	0.78	0.93	1.03	1.14	1.23	1.35	1.48	1.63	1.93	2.10	2.32	2.36	2.37	2.38	2.38	2.39
Increased annual earnings per child in the cohort																
	4.61	5.49	6.10	6.73	7.24	7.98	8.77	9.64	11.43	12.43	13.72	13.94	14.00	14.06	14.08	14.10
Increase in total cohort income per year, once earning starts ($millions)																
	410	492	550	610	661	732	809	895	1068	1168	1297	1326	1340	1355	1365	1376
Internal rate of return																
	12.4%	13.2%	14.4%	14.3%	13.8%	13.8%	15.0%	15.5%	14.9%	15.2%	15.8%	16.2%	16.9%	17.8%	18.2%	18.0%

public health budget requirements, but as an investment with enduring and large-scale impacts. The benefits of a push for increased immunization are likely to heavily outweigh the costs, and policy makers who neglect immunization will be missing a great opportunity for promoting development.