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Review

Valuing vaccines: Deficiencies and remedies☆

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ABSTRACT

Current evaluation models for the value of vaccines typically account for a small subset of the full social and economic benefits of vaccination. Health investments yield positive economic benefits via several channels at the household, community, and national levels. Underestimating, or worse, not considering these benefits can lead to ill-founded recommendations regarding the introduction of vaccines into immunization programs. The clear and strong links between health and wealth suggest the need to redesign valuation frameworks for vaccination so that the full costs may be properly weighed against the full benefits of vaccines.

1. Introduction

Conducting economic analyses of medical interventions such as vaccination is not a routine exercise for many in the public health field and may even seem suspect. However, an economic lens is sensible, promising, and practical for evaluating strategies to reduce disease through the development and delivery of effective vaccines. Vaccination is costly, but evidence from a growing body of research suggests that the costs of failing to vaccinate are even higher.

This article summarizes recent research that focuses on identifying and estimating the full economic and social benefits of vaccine-driven health improvements. Looking at vaccination with an economic lens is meaningful because it communicates in the language of decision makers who have the power of the purse: ministers of finance, ministers of planning, central bank governors, economic advisers to prime ministers and presidents, investors, and CEOs.

Three points are critical to understanding this emerging approach to health impact measurement. First, the theory- and evidence-based proposition that "healthier means wealthier" provides a key intellectual foundation for conceptualizing the value of health interventions including medical devices, drugs, and vaccines. Second, vaccination can promote improvements in economic wellbeing through various channels. Third, health economists have an important role to play in operationalizing these ideas.

Until recently, economists failed to recognize the full economic benefits of health. As a result, they unwittingly undervalued many health interventions – including vaccination. Undervaluation translates into underinvestment – both in the development and the delivery of vaccines. This undervaluation seems to be substantial. Thus far the low cost of many prominent vaccines, like those for diphtheria, tetanus, and pertussis (DTP); measles; and polio [1], have mitigated the practical consequences of this bias. However, continued undervaluation is much more perilous with respect to a new generation of more costly vaccines, such as those against rotavirus, human papilloma virus, pneumococcal disease, and meningococcal B. Additional vaccine breakthroughs are currently on the horizon, most notably against Ebola and dengue, and the net social benefits of these and other vaccines are easily misjudged in the face of high costs and undervalued benefits.

Correcting these under-valuations will keep health economists very busy in the coming years as they review and revise long-held assumptions and pursue research inquiries that capture the full benefits of vaccination—vaccine by vaccine, and country by country.

2. Links between health and wealth

Scholars of economic development have long recognized that high-income populations are generally healthier populations. This pattern holds for different income measures, different health measures, and at different time points. For decades, macroeconomists adhered to the view that the positive cross-country association between income and health reflected causality running from

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income to health. This is a logical presumption given that when people have more money, they tend to have better nutrition and access to safe water, sanitation, more and better health care, and better psychosocial resources like community recreation facilities.

However, about 15 years ago some macroeconomists began to wonder whether improved health could be a significant driver of economic growth. That proposition is also plausible: a healthier workforce tends to be more and better educated, energetic, and productive with better fertility control and a stronger propensity to save money for the future. This kind of workforce is attractive to foreign investors.

Macroeconomists were lamentably slow in exploring the directionality of the health-income relationship; however, microeconomists have long understood the connections between health and economic growth. For example, in 1962, Selma Mushkin published an article entitled "Health as an investment" in a top economics journal [2]. She presented numerous ideas about the economic benefits of health, which spawned a considerable body of research that treated health as a form of human capital, akin to knowledge and skill.

The reverse link from health to income has been the subject of much rigorous statistical and econometric analysis, especially over the last decade. That research supports the finding that health is an exceedingly robust and powerful predictor of income growth and also of poverty alleviation. For example, a 10-year gain in life expectancy translates into as much as 1 additional percentage point of annual growth in income per capita [3], which when compared with the average 2–3% annual growth per capita in a world economy is quite significant.

Further, a 1-percentage point gain is meaningful because a 10-year increase in life expectancy is well within the grasp of many countries. It is only half of the increase in life expectancy the world has enjoyed during the past 50 years [4], and it is also half of the life expectancy improvement that several leading European demographers are projecting for many wealthy industrial countries during this century. Additionally, a 1-percentage point change is noteworthy because of compound interest, which magnifies the effect of that 1-percent boost when maintained over time.

Taken as a whole, these ideas and evidence of the potent synergy between health and income help explain the strong presence of health in ongoing discussions about the post-Millennium Development Goals agenda. They also figure prominently in the much-heralded final report of *The Lancet* Commission on Investing in Health entitled "Global Health 2035: A World Converging within a Generation" [5]. These concepts elevate health to the same importance as basic education as a fundamental instrument of economic growth and development.

The parallel between health and education offers some useful insights. Education was severely neglected as a public investment prior to the publication of studies on its costs and benefits. The costs of education encompass tuition and fees as well as the opportunity cost of foregoing an income while attending school. The benefits are mainly the higher productivity and income of students after they leave school and enter the workforce.

A key figure in this line of research was George Psacharopoulos, a University of Chicago–trained economist working at the World Bank. He made a career of collecting and synthesizing studies on the return on investment in education for different countries, different demographic groups, and different timeframes. Psacharopoulos noticed that these studies uniformly suggested that education offered a return on investment that was high by any reasonable financial standard. He helped leverage this compelling observation into a colossal boost in education lending, grant funding, and spending policy at the World Bank and in many countries.

Development economists have started to focus on the investment value of health spending just as they previously came to focus on the investment value of education spending. Leveling the playing field between health spending and other social priorities raises the prospect of significant expansions of the health sector.

One noteworthy benefit of such potential expansions is the possibility of virtuous spirals in which improvements in health lead to improvements in income, which lead to further improvements in health and so on. In other words, through a process of cumulative causality, interventions that promote health can serve as fuel for economic growth and development. By the same token, a costly and vicious downward spiral can also gain momentum through adverse health and income shocks that are met with complacency.

Gro Brundtland, former Prime Minister of Norway and former head of the World Health Organization (WHO), summarizes the basic points well. In launching the report of the WHO Commission on Macroeconomics and Health in late 2001, Brundtland stated, "During the 1980s, investments in health were increasingly seen by economists as an add-on that developing countries could only afford after having reached a middle-income level. I was convinced this was wrong: you need a two-pillar approach. A healthy population is a prerequisite for growth as much as a result of it" [6]. Increased and improved research on the full benefits of vaccination thus offers policymakers the foundation necessary to leverage health interventions as sustainable and indispensable components of development strategies.

3. Vaccination as a driver of both health and wealth

Given the rigorous evidence that health promotes wealth, economic evaluations of health interventions should consider and account for the full set of economic benefits that follow from those interventions. Doing so is nothing more than proper accounting, which is the prudent and responsible way to allocate funds to promote public wellbeing.

My research on the value of vaccination began 10 years ago while David Canning and I were attempting to explore, at the request of Tore Godal, the economic case for including vaccination as the pilot for Gordon Brown's International Finance Facility—an innovative mechanism for financing development. We scoured the literature and found it to be replete with books and articles that focused heavily on two benefits: avoided medical care costs and avoided income loss associated with parental absenteeism from work. Economists routinely mention and analyze health gains associated with vaccination, but they rarely attempt to monetize them.

Avoided costs of care and lost income are indisputable benefits of a vaccination program. The problem is that these are just two components of a much wider set of overall benefits that vaccination can confer on vaccinated children, their parents, and their communities—a set of benefits that are rarely addressed in the economic literature.

For example, healthy children have better school attendance. They also attend school for more years and learn more each year they are enrolled. Vaccinated children also tend to avoid the long-term sequelae associated with certain childhood diseases, such as neurological impairments, hearing loss, and various other physical disabilities [7]. This suggests higher productivity and earnings as adults. The health gains also suggest utilitarian value, above and beyond their implications for productivity and earnings.

With respect to older family members, parents and grandparents tend to be healthier themselves if their children and grandchildren are healthy. They also have lower rates of absenteeism and fewer episodes of low productivity related to illness, fatigue, and the mental burden of caring for sick children.

Society also derives benefits from vaccinated, healthy kids. These benefits relate to herd effects, reduced usage of antibiotics and slower development of antibiotic resistance, reduced

health anxiety, reduced risk of future disease lessens the need to insure against ill health, and the fertility reduction that tends to accompany improvements in child survival—also known as the demographic dividend [7].

Failing to account for these broader benefits at family, community, and national levels can result in substantial underestimation of the value of vaccines. The results of this underestimation could be very significant because low rates of return naturally discourage the allocation of resources to the development and delivery of vaccines. Insofar as our failure to conceptualize and measure the full benefits has, and will increasingly, prevent us from realizing the potential of vaccination to protect and promote human health and economic wellbeing, the stakes are potentially quite high.

4. Evidence to operationalize the conceptual value of vaccination framework

The evidence to support a broad-based value of vaccination framework is compelling. Economists rely on two methods to evaluate the desirability of a health intervention like vaccination. The first is benefit–cost analysis (BCA), which is closely akin to return on investment, and the second is cost-effectiveness analysis (CEA).

Of these, BCA is better suited to the economic evaluation of vaccination programs for two reasons. First, it can account for a diverse set of health and non-health outcomes; and second, it can be used to compare health and non-health interventions. It does so by translating diverse benefits into monetary measures that can be combined. In contrast, CEA is limited by its inability to handle more than one outcome at a time and cannot be used to compare health and non-health interventions.

For example, BCA can be used to examine the impact of a particular health intervention on both duration of inpatient care and incremental employment and earnings. But CEA can only handle these outcomes one at a time, which does not allow for a holistic assessment.

In addition, BCA can be used to compare the benefits of allocating resources to a health intervention with the benefits of allocating those same resources to a non-health intervention, such as a school lunch program. By contrast, CEA utterly and totally fails with respect to such a comparison.

However, CEA is useful under some circumstances, for example, when a health minister is trying to set spending priorities given a designated budget. But it is not useful for a finance minister who is trying to decide between health and non-health spending priorities. Also, the greater power of BCA comes at a price, because it often requires the imposition of strong and not uncontroversial assumptions, such as placing a monetary value on life itself. Nevertheless, in comparison with benefit–cost analysis, cost-effectiveness analysis is much more limited in its virtues and applications.

Teams around the world have worked for several years to expand the evidence base for the value of vaccination by researching and reviewing the broader economic benefits of vaccination through original research [8–13] and comprehensive systematic reviews [14–19]. Deogaonkar and colleagues searched the literature for studies on the broader impact of vaccines in low- and middle-income settings and found 26 studies published between 1990 and 2011 that discussed benefits beyond the traditionally accounted for “narrow” ones [16]. In these articles, community health externalities (i.e., herd effects) were the most common benefit category included; outcome-related productivity gains were accounted for in eight studies; and no study included behavior-related productivity gains or community level economic externalities.

In a similar synthesis, Ozawa and colleagues explored the types of benefits reported in economic evaluations of vaccines in low- and middle-income countries [20]. Ozawa’s search yielded 23 studies, of which nine included community health externalities, five captured outcome-related productivity gains, three captured community economic externalities in the form of outbreak prevention savings, and two accounted for behavior-related productivity gains.

My colleagues and I have conducted research on the full economic impact of vaccination, which began with a study focused on a proposal from Gavi, the Vaccine Alliance, to extend the use of a variety of childhood vaccines to 75 low-income countries during 2005–2020 [13]. At a cost of US $13 billion the proposal sought to expand coverage of the traditional basic childhood vaccination package (DTP, tuberculosis, polio, and measles vaccines totaling about US$20 per package); increase coverage of the underused haemophilus influenzae type b (Hib), hepatitis B (Hep B), and yellow fever vaccines; and help finance the introduction of vaccines covering meningococcus, pneumococcus, and rotavirus. In principle, the proposed Gavi initiative would save lives, reduce medical care costs, and ultimately encourage higher labor force productivity by supporting the physical and mental development of children. That is precisely what the calculations documented, as we conservatively estimated the rate of return on investment in the Gavi immunization program to be 12% by 2005, rising to 18% by 2020 [13].

Those numbers put immunization in the same class as basic education as an instrument for promoting economic wellbeing. Education is commonly regarded as having the highest impact of all developmental interventions [21], and if vaccination is a close comparison, the potential for increased investment in vaccine development and delivery is much greater.

Further research used data from the Philippines to examine children’s cognitive development and its association with receiving the standard expanded program for immunization (EPI) vaccines in the first two years of life. Cognitive ability, as measured by test scores, can affect wages earned as an adult, thereby allowing a comparison of costly vaccines early in life with higher wages later in life. Using propensity score analysis to account for the nonrandom distribution of vaccination coverage, we found that vaccinated kids achieved significantly higher test scores [12]. Translating those gains into adult earnings yielded another striking result: a 21% rate of return on the vaccine spending, even higher than the Gavi study.

These results inspired further study of the full value of Hib vaccination [11]. Here we explored the option of delivering the Hib vaccine in pentavalent form with DTP and Hep B, which significantly reduces its incremental delivery cost. Indeed, delivering the Hib vaccine in pentavalent form requires less cold-chain storage and less waste disposal, and health workers do not have to undergo additional training to administer and track a separate vaccine product. This study adjusted estimates reported in the literature to account in part for the full benefits of the Hib vaccine above and beyond avoided medical care costs and the loss of parental work time. Based on these calculations, the benefit–cost ratio was significantly elevated for all studies and went from less than one to well above one for several studies [11]. In economic terms, this represents a reversal of recommendations against investing in the vaccine to recommendations in favor. It may also explain why just 52% of children worldwide received the full three-dose course of Hib vaccine in 2013 [22].

Each vaccine differs in its efficacy, coverage, and administration logistics, all of which affect cost. In general, no standard template exists for applying these ideas. Analyses must be tailored specifically to the alterations that vaccines cause in the incidence and profile of each disease and to their country-specific economic implications. This requires taking the general benefits framework and customizing each category of benefit to the relevant clinical endpoints and their epidemiological and economic sequelae.

Dengue provides a good illustration of the need for this customization. Clearly a vaccine against dengue would yield multiple economic benefits, including those associated with direct medical care costs for ambulatory and hospitalized cases; direct nonmedical care costs such as out-of-pocket expenses for transport, lodging, food, and other expenses incurred by those suffering from dengue and in pursuit of treatment (including related caretaker expenses); and indirect costs in terms of lost work or schooling due to care seeking or care taking. In addition to these standard sources of benefit (i.e., avoided costs), a proper economic evaluation of a dengue vaccine requires accounting for outbreak control costs and the impact of threatened or actual dengue outbreaks on foreign direct investment and tourist flows. Crude data analyses suggest that the full benefits of a dengue vaccine in Brazil could be more than double the standard sources of benefit, with the main difference being the avoided negative impacts of dengue on tourism and foreign direct investment [9,23]. Twice the benefit essentially means twice the return on investment and twice the benefit–cost ratio of a dengue vaccine. That could make all the difference in a decision about whether or not to incorporate a new dengue vaccine in a national immunization plan.

The HPV vaccine is another example that highlights the need to treat each vaccine differently when it comes to measuring its particular benefits. In particular, HPV affects women differently than men and at different ages. Valuing the vaccine against HPV requires a focus on the productivity losses – both in and outside the household – that a woman with cervical cancer might encounter. It also requires focusing on other clinical outcomes such as genital warts and penile and anal cancers.

Additional theory and evidence suggests that many vaccines may confer health benefits disproportionately beyond their intended target group. For example, it is reasonable to infer that childhood immunization against pneumococcal disease will confer secondary protection on elderly people who are not actually vaccinated (i.e., herd immunity). Spillover benefits like these should be included in the valuation of vaccines as they clearly affect broader health outcomes at the community level and are often overlooked in current evaluation models.

5. Data limitations

Traditionally, vaccination-related costs have included the cost of the immunizing agent, the cost of mass-producing and administering that agent, the value of time associated with getting a child to a medical practitioner, and any associated transportation costs. These costs are well understood and quantified and therefore not a focal point for this exploration of the valuation of vaccines.

Considerable doubt exists about benefit–cost ratios associated with particular vaccination programs, mainly due to a lack of information about the scale of potential benefits. A lack of meaningful, accurate, and reliable data on the social and economic impacts of vaccines makes fair and robust evaluations especially challenging. The potential magnitude of the difference between narrow and full benefits seems to justify the collection of more and better data, which has been the biggest continuing frustration in pursuing this line of research for the past decade.

Randomized control trials represent a potential data collection strategy. The traditional role these studies play in measuring vaccine safety, immunogenicity, and efficacy endpoints can be adapted and expanded to capture long-term vaccination impacts. These include the educational, economic, and social outcomes that manifest over time. Follow-up studies in the trial populations to assess impacts on broad outcomes could produce a compelling body of new evidence and guard against the current undervaluation bias.

6. The price spectrum

Pricing of vaccines can be very contentious. At the risk of oversimplification, two extreme positions exist. One school of thought holds that vaccines should be priced only to cover costs of production, delivery, and administration, and the other believes vaccines should be priced based on their full benefits to society. Often a large range arises between these two endpoints.

The crux of the vaccine-pricing debate is to find the range of prices between the two ends of this spectrum. Vaccine prices cannot sustainably fall outside this range. They should not fall below their resource costs or exceed their full social benefits. Where prices actually fall along the spectrum will presumably depend on the interplay of market forces and institutional regulations.

By clearly defining the range of acceptable prices, stakeholders can potentially engage in more productive pricing conversations, ideally resulting in increased coverage and uptake of high-quality vaccines. The contribution of the research presented is to define the nature and measure the location of the upper-bound more clearly.

This research might make the challenge of vaccine pricing more difficult by indicating greater social benefits and thereby raising the upper bound. Conversely, by eliminating uncertainty as to the nature and location of the upper bound, this research might suggest ways toward less contentious pricing approaches. Whether better alignment on the framework for assessing the costs and benefits of vaccines will indeed simplify and expedite the resolution of pricing disputes remains to be seen.

7. Conclusion

Existing data sources and evaluation models do not fully measure the broad social and economic benefits of vaccination, to the detriment of global development strategies and the peril of human health and wellbeing. Concerted efforts are urgently needed to (a) identify existing datasets that hold promise for estimating the full benefits of vaccination programs, and (b) define new approaches to data collection that are appropriate to the challenges at hand.

We are clear on the questions and their importance. We are in good command of the methods needed to generate compelling answers to those questions. What we need are reliable and appropriate data to power the research needed to enjoy gains in public health that are more transformational than incremental.

Conflict of interest statement

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