POLICY WISDOM

Can improved cost and impact analyses foster broader and faster vaccine adoption?

By: Ana Rita Gonzalez, ScD, CPH
President & CEO, Policy Wisdom, LLC

Abstract

Vaccination cost-effectively improves health and prevents disability and death. Still, potential exists for wider use of both traditional vaccines (e.g., polio) and ones new to the market (e.g., HPV). Increasingly, policy decisions to adopt vaccines and/or enlarge programs are made primarily, often exclusively, on relatively straightforward cost analyses and projections; nonetheless, current cost models are insufficient to correctly attribute value to vaccines. Improved outcome measures, defined threshold guidelines, and consideration of the intangible benefits of vaccinations are needed; no one factor, especially cost, should determine their availability. Casting these evaluations as "vaccine value and impact analysis" more fully portrays the far-reaching health and societal benefits of immunization. Evidence drawn from thoughtfully crafted analyses will better inform policy makers and support stronger and sustained commitments from governments to expand vaccination budgets.

Keywords: *vaccine adoption criteria; cost effectiveness analyses; formulary decision making; public health policy*

.....

Introduction

Immunization is one of history's most successful public health interventions; every country has benefited from life-saving vaccines. Morbidity and mortality have decreased and diseases have been reduced and eradicated. Vaccines now have stronger immunogenicity, are safer for the very young, elderly, and immune-compromised, and easier to store; their value is unquestionable.

Routine childhood immunizations against diphtheria, tetanus, pertussis, and measles prevent 2.5 million deaths worldwide annually. Smallpox was eradicated in 1979; worldwide measles mortality has declined by 78%; polio incidence has been reduced by 99%, making polio the next candidate for eradication.[1] Vaccines thus are among the most cost-effective public health interventions available. The control of polio, for example, is estimated to save $1.5 billion annually globally.[2] An analysis of the 7 routine childhood vaccinations used in 2001 in the U.S. found they provided a net savings of almost $10 billion in direct costs, four times that spent.[3]

POLICY WISDOM

Vaccine-preventable diseases (e.g., meningitis) can result in both mental and physical disabilities, devastating health expenses, and stresses on both family and trained healthcare providers; these can lead to short- and long-term illnesses, loss of income, and sometimes death. Good health is widely recognized as necessary for economic growth, while poor health slows economic development. Investments in health are among the most efficient ways of alleviating poverty,[4] and vaccination yields economically significant gains.[5] Immunizations are proven to save healthcare costs; their broader benefits include poverty reduction, economic development, smaller family size, and herd immunity.

A recent cost analysis by Harvard School of Public Health researchers specifically considered these broader economic benefits. Bloom and colleagues studied the economic impact of the Global Alliance for Vaccines and Immunization's (GAVI) vaccination campaign, projected to aid 75 low-income countries with a combined population of 3.8 billion.[4] Once the cohort of vaccinated children reaches working age, the total annual income will rise from $410 million in 2005 to $1.34 billion by 2020. After calculating such variables as cost per death averted, and increases in annual earnings and life expectancy, the authors concluded that the internal rate of return to the program would be 12% in 2005 and reach 18% in 2020 (the rate of return for education ranges from 11-19% for various countries). The authors note that even these figures are conservative because they do not consider averted medical costs and the value of survivors' reduced pain and suffering, among other factors.[4]

Increasing access to existing and future vaccines in the poorest countries is the cornerstone of these successes: More than 6 million deaths and 400 million cases of illness can be averted in the next 10 years by increasing routine vaccinations in these countries, with a total savings of over $6 billion in treatment costs and $145 billion in productivity losses.[6] However, extending immunizations to more people can only be achieved with strong, sustained commitments from national governments, expressed by expanding immunization budgets and supported by global partnerships.

Expanding vaccine use is likely to have implications for manufacturers' interest in further vaccine research and development. Recently, American philanthropist Bill Gates noted that vaccines once thought unprofitable in fact have become important revenue generators for pharmaceutical companies and, consequently, for funding research and development.[7]

This paper outlines some challenges and possible solutions to globally expanding immunization coverage, focusing on issues related to vaccine value beyond simple cost evaluations. The "cost" benefits of immunizations must be expressed in terms that take both a broad and long view of impacts on society beyond effects on the patient, family, and healthcare system. No one measure, especially cost, should determine vaccines' availability.

POLICY WISDOM

Challenges to Increasing Access

Several factors inhibit increasing access to immunizations. In developed nations where vaccination coverage is high, the main obstacle is general public complacency. Substantial immunization rates have successfully lowered disease prevalence; as this declines, so does awareness of the disease and its effects. Earlier fears of disease (a child's dying of measles) are replaced by fear of vaccines themselves, undermining vaccine acceptance and immunization programs.[8]

In developing and transitional countries, the principal challenge is expanding coverage of already existing and comparatively low-cost vaccines and introducing new ones whose costs have not yet been amortized by years of use. Though external factors combine to prevent successful and consistent increase of coverage, a more common limiting factor is cost. Introducing new vaccines to immunization schedules can be a lengthy, resource-consuming process. Countries need funds to purchase vaccines, an infrastructure capable of delivering them, and a system that encourages compliance with immunization schedules—all of which demand that governments expand national budgets.

A joint 2010 World Health Organization (WHO) and United Nations Children's Fund (UNICEF) report catalogued past trends in immunization financing by WHO Member States.[9] The global average of total vaccine expenditures financed by national governments increased slowly since 2000 (from 74% to 77%). In Europe and the Americas, more than 90% of vaccine costs are funded by national governments. Predictably, low-income countries had the least government support (around 30%), confirming their dependence on external funding.[9] Cost will become even more critical as some donors reduce funding, other health priorities (e.g., HIV/AIDS) compete for limited resources, and countries try to increase coverage and add new and less well amortized vaccines to routine schedules.[10] The meager increases in government funding reported by WHO/UNICEF are insufficient to withstand these challenges; governments must substantially increase vaccine budgets.

To ensure that vaccines most needed in developing countries are created and available, incentives for pharmaceutical companies are needed. Pressuring industry to continually lower prices is short sighted, especially as multi-dollar vaccines enter the market. Due to differences in development (research and development [R&D], manufacturing, distribution, etc.), vaccines' costs will always vary. For example, high volumes of the live attenuated oral polio vaccine can be produced with low costs, making mass vaccination feasible. More complex vaccines require more time and resources for production and quality control, thus yields are lower.[11]

Pharmaceuticals have begun to consider vaccine development an economically satisfactory pursuit (even in contrast to other drugs that are more profitable to sell but have much smaller demand). Lowering vaccine prices is often promoted as a solution to greater adoption, but will likely have serious economic ramifications, including fewer companies investing in development. In spite of the emerging trend to view vaccines as good income, major manufacturers have left the market because of price commoditization, reduced research funding, high cost of production facilities, and narrow profit margins (see Barder, 2011, on more consequences of forcing lower prices).[12]

Strategies for overcoming cost barriers on the producer side certainly make vaccines more affordable for consumers. For example, offering tax credits to industry to reduce R&D expenses and implementing regulatory reciprocity among different countries can lower purchase costs. Providing long-term contracts for vaccine purchase of the type GAVI has successfully applied, decreasing liability risks**,** improving technology transfers, and developing innovative financing mechanisms are prime examples of public policies that can increase vaccine affordability. However, reliance on charities such as GAVI and incentives to compensate for limited government funding is necessarily time limited. As Rappuoli suggested, the future of vaccines depends on creating a self-sustaining system; long-term sustainability can only be achieved by ascribing an economic value to vaccines that truly reflects the long-term benefits of a healthy population.[13]

Issues with Cost Analysis

Economic evaluations, mainly cost-effectiveness analysis (CEA) and cost-benefit analysis (CBA), can be helpful resources for health policy decisions and budgetary restrictions. However, a cautionary view is needed. A purely economic approach to immunizations falls far short of cataloging other critical benefits. Changes in health are so complex and far reaching that benefits and costs to society can be miscalculated. For example, averted medical costs and loss of productivity are easily assessed, while measuring herd immunity, cost of future averted infections/diseases, and the overall economic growth of a country is considerably more complex.

To some extent, the use of economic evaluations depends on the country and culture and, inevitably, on economic resources and how costs will shape healthcare policies and systems. Developed nations tend to add a new vaccine to routine schedules if it's safer and/or more effective than previous ones or targets a disease for which no vaccine has been available. Americans, for example, place particular importance on innovation and are more willing to pay higher prices for something new, even if it is only marginally better than an older version.[14] Conversely, the United Kingdom (U.K.), deemphasizes innovation and concentrates on extending healthcare coverage to the greatest amount of people even if

the tradeoff is what some refer to as "rationing health care." Sampat and Drummond explain that this approach in the U.K., along with the increased use of health technology assessments (HTAs), has led to the exclusion of several technologies from the national healthcare plan because they exceed a certain price threshold.[14] Unfortunately, vaccines may be similarly limited by costs if cost assessments are not based on a broad number of sensitively assessed variables.

Cost analysis studies must factor for both the cost benefits of doing something and NOT doing something, which can create complex metrics. Herd immunity, loss of parental work time, and prevention of morbidity (and their opposites) are merely a few criteria considered when evaluating the economic impact of immunizations. For example, in 1994, medical costs in the U.S. were determined to be too high for a routine varicella vaccination program to save costs to the healthcare system.[15] Yet examined from a societal perspective that included medical and lost-work costs, varicella immunization resulted in a net savings of more than $5 for every dollar invested. A similar situation arose with the first rotavirus vaccine, where a universal immunization program at $20 per dose would produce a net loss ($107 million) to the healthcare system but a net savings ($296 million) to society.[16]

A more complex example is the heptavalent pneumococcal conjugate vaccine (PCV7). A CEA in 2000 projected that a single dose would cost $80,000 per life-year saved (LY) and would only achieve cost savings if the purchase list price were lowered.[15] Because this is a 4-dose series, the cost would actually be closer to $110,000 per LY saved.[17] However, the real-life benefits of PCV7 were much greater than calculated because it induced herd immunity and more people were protected than just the number vaccinated. In fact, the indirect benefits surpassed the direct benefits of in 2003, with more than twice as many cases prevented indirectly than directly.[18]

Unfortunately, economic evaluations have too often overlooked these broader vaccination-related benefits. A review of cost analysis studies published from 2004 - 2005 in PubMed found that they failed to account for such factors as the cost of averted infections that can occur later in life and smaller family size, both of which inevitably change the structure of the population.[4] Even proven and accepted principles such as the effects of health on income (good health drives economic growth and vice versa) were not included. Furthermore, they "…all either overstate the cost of achieving a given beneficial outcome or underestimate the net benefits" (p18).[4]

The value of vaccination should not be underestimated, even when cost-related benefits are difficult to decipher or calculate. Intangible health outcomes like reducing health risks, pain, and suffering, are major considerations when it comes to immunizations and they often cannot be measured with CEAs and CBAs. Currently, vaccines are seen as cost

effective if their cost is lower than the various collective costs due to treatment, working days lost, and other factors. For example, the diphtheria, tetanus, and pertussis (DTP) vaccine saves $6.21 and the measles, mumps, and rubella (MMR) vaccine saves $16.34 in direct medical costs for every dollar spent.[13]

However, when other variables are considered in addition to direct costs of purchase against direct costs of treatment, policy makers better understand the true value of vaccines, especially those new to the market. For example, other variables to be considered could include costs of transportation to and from treatment, the need for additional medical and/or public health staff should an epidemic occur, the long-term costs of caring for people who develop serious sequellae (mental and/or physical deficits, infertility, and risk for other infections), and myriad other issues.

Once the criteria for analysis are selected, we must determine what we are comparing the new vaccine to: a placebo, another similar intervention, or an older intervention. Clearly, comparative effectiveness is the most relevant. Compared to older vaccines, newer interventions might be seen as more or equally cost effective while older ones can be re-evaluated and eliminated if no longer necessary. This is also a better way of determining both the cost and effectiveness differences between two similar vaccines, as was the case for replacing the live oral poliovirus vaccine with the inactivated injected vaccine. Though the inactivated vaccine is costlier to administer, the Advisory Committee on Immunization Practices (ACIP) decided to replace the live vaccine because it eliminates the small risk of vaccine-associated paralytic poliomyelitis.[19]

Thresholds used to compare monetary values further complicate the accuracy of economic studies. LY and quality-adjusted life years (QALY) are among the most common outcome measures. Though many organizations use these thresholds to make decisions, there are no official national or international guidelines. The WHO recommends a value of three times the gross domestic product per capita. However, the U.S. commonly uses a much lower $50,000-$100,000 per QALY.[19] In the U.K., the National Institute for Health and Clinical Excellence (NICE) will generally not accept interventions above £20,000 per QALY.[20]

Establishing official guidelines for economic evaluation and their thresholds would improve the benefits of cost studies because different analyses currently are not directly comparable. Differences in analytical criteria and assumptions are largely established by varying national recommendations and the authors' preferences, which predictably affect the results. Some differing factors include whether costs are valued from a societal or healthcare perspective, discount rates for costs and benefits, assumptions about the quality of life of caregivers, and children who do not use health services.[21] Because the basic

framework varies, the threshold at which an intervention is considered cost effective differs among different studies.

When RotaTeq® and Rotarix® arrived on the market, several European countries conducted economic evaluations to determine whether to include rotavirus vaccine. A Finnish study found it to be cost effective; another in Belgium found it to be cost effective from a societal perspective but not a healthcare-provider perspective; France and the U.K. found it to not be cost effective. Further analyses reached different conclusions. Belgium and Finland recommended routine vaccination, while the other countries recommended against it.[22] Lack of uniform vaccine coverage is risky with the current global increase in trade and travel and can easily lead to costly international outbreaks. For example, a measles outbreak in California resulted when an unvaccinated child contracted the disease in Switzerland and spread it to hundreds of people upon returning home, including infants too young to receive their first immunizations.[23]

Overcoming the Cost Barrier

Improving outcome measures, implementing threshold guidelines, and considering intangible benefits will produce economic evaluations that can inform policy makers and aid in vaccine funding and introduction. The WHO already provides an extensive guide on conducting and interpreting economic evaluations on immunizations. The handbook considers how to frame an evaluation, what costs should be included, the value of different outcome measures, and, importantly, the inherent uncertainty in economic evaluations. Also included is a comprehensive checklist useful for assessing the quality of cost analysis, an excerpt of which is provided below to highlight the uncertainty factor (the document is available at the URL for reference 24). [24]

POLICY WISDOM

Table 1. Excerpt of WHO checklist for appraising the quality of economic evaluations of immunization programs.[24]

Uncertainty (Chapter 8)	The costs and effects should be presented for all alternatives as well as the incremental costs and effects between alternatives.	Have the costs and effects been presented for all alternatives?
	Those interventions that are dominated, i.e. both more costly and less effective than alternative options, should be excluded first.	Have dominated interventions been identified and excluded?
	As a minimum, one-way sensitivity analyses should be conducted of the following variables: discount rate, vaccination effectiveness (where unknown or uncertain), incidence of disease (including complication rates where relevant), case fatality rates and vaccine price.	Has sensitivity analysis been conducted to assess the robustness of the findings to changes in the value of key parameters? Has the choice of parameters and the ranges over which they have been subjected to sensitivity analysis, been stated and justified?
	Analysis of extremes should be conducted in order to assess the robustness of the findings to changes in the value of multiple parameters at the same time. Where a best or worst case scenario changes the conclusions, a probabilistic sensitivity analysis should be conducted and a CEAC used to represent the uncertainty.	Has analysis of extremes been conducted? Where a best or worst case scenario changes the conclusions, has a probabilistic sensitivity analysis been conducted and a CEAC been used to represent the uncertainty?
	If there is a national CE threshold, analysts should use it. Otherwise, the recommendation made by CMH, and endorsed by WHO, should be used, and the results of their evaluation be classified according to the per capita national GDP of the country in question: less than one classifies a vaccine as 'highly cost-effective'; between 1 and 3 times classifies an intervention as 'cost-effective'; and more than 3 times classifies an intervention as 'cost-ineffective'.	Has the national CE threshold been used, if one exists? If there is no national CE threshold, have the results of the evaluation been classified according to the per capita national GDP of the country in question?
	Findings should be placed in broader context by comparing them to other economic evaluations that have been undertaken in the same or neighbouring countries, after adjusting for inflation.	Have the findings been compared to other economic evaluations undertaken in the same or neighbouring countries?

Strict adherence to WHO's guidelines would strengthen current economic evaluations and yield valuable results. In addition to ensuring that evaluations meet a certain standard, reframing the way we refer to and thus think about these studies is critical. Government agencies, policy makers, and pharmaceutical companies are already uncomfortable using current cost-analysis models to influence vaccine availability, concerned that cost will limit access to vaccines. A "vaccine value and impact analysis" would more accurately portray the far-reaching benefits of immunization.

Immunizations are being introduced into new markets faster than ever and vaccine value and impact analyses can support this effort. GAVI has been instrumental in joining governments and companies to introduce vaccines in developing countries soon after these become available in industrialized countries. Faster adoption has been achieved through disease-specific initiatives that concentrated on generating and communicating epidemiological evidence of the disease and the effectiveness of associated vaccines.[4] Including cost issues in these initiatives will be crucial as newer multi-dollar vaccines become available.

For example, GlaxoSmithKline's (GSK) new rotavirus vaccine was primarily introduced in Latin America where countries like Mexico have a high burden of disease. GSK realized better sales than initially expected in a market often considered less profitable than wealthier countries. In fact, profits from sales are estimated to recoup R&D costs within a few years of incorporation into national immunization schedules.[25] In-country research on safety, efficacy, and cost-effectiveness was more valuable to vaccine introduction than external studies. Similarly, area-specific value and impact analysis can help in the overall acceptance of a vaccine. Policy makers can clearly grasp the benefits of a new vaccine, why a country needs it, how much and where money will be spent, and how and when an immunization program will recover initial expenses.

Increased awareness and concrete figures on the value and impact of vaccination will likewise aid policy makers in lobbying for increasing national immunization budgets, which is critically needed in middle- and low-income countries, where governments do not fund most vaccine expenses.[9] Creating a specific national budget line for vaccine purchasing also helps increase awareness, signal long-term commitment, and allow for transparency in budgetary decisions.[26] Research also suggests that countries with a line item for vaccine purchase had a slight increase in the percentage of government funding.[9] Though budget lines and economic analysis cannot guarantee larger immunization budgets, they can be powerful motivators for change.

Conclusion

Immunizations' broadest social and economic benefits are difficult to accurately assess, but incorporating these calculations into cost analyses is critical to fully gauging the true value of a vaccine. A comprehensive vaccine value and impact analysis can show that effective vaccines outweigh their costs in benefits such as a better-educated and more productive population, smaller family sizes, and overall economic growth. Such results will inevitably encourage policy makers to improve immunization programs by increasing health budgets and allowing for the increase in number and types of vaccines available.

POLICY WISDOM

REFERENCES

1. WHO (2011) 10 facts on immunization. WHO, http://www.who.int/features/factfiles/immunization/facts/en/index.html, accessed 19 September 2011.

2. Satcher, D. (1998) Testimony on eradication of polio and control or elimination of measles. Assistant Secretary for Legislation, Department of Health and Human Services, 23 September, http://www.hhs.gov/asl/testify/t980923a.html, accessed 19 September 2011.

3. Fangjun, Z., Santoli, J., Messonnier, M., et al. (2005) Economic evaluation of the 7-vaccine routine childhood immunization schedule in the United States, 2001. *Archives of Pediatrics & Adolescent Medicine* 159(12): 1136-44.

4. Bloom, D., Canning, D., and Weston, M. (2005) The value of vaccination. *World Economics* 6(3): 15-40.

5. Levine, O., Bloom, D., Cherian, T., et al. (2011) The future of immunization policy, implementation, and financing. *The Lancet* 378(9789): 439-448.

6. Stack, M., Ozawa, S., Bishai, D., et al. (2011) Estimated economic benefits during the 'decade of vaccines' include treatment savings, gains in labor productivity. *Health Affairs* 30(6): 1021-1028.

7. Herper, M. (2011) With vaccines, Bill Gates changes the world again. *Forbes*, 11 February, http://www.forbes.com/sites/matthewherper/2011/11/02/the-second-coming-of-bill-gates/, accessed 02 February 2012.

8. Larson, H., Cooper, L., Eskola, J., et al. (2011) Addressing the vaccine confidence gap. *The Lancet* 378(9790): 526-535.

9. WHO (2010) Immunization financing indicators. WHO, http://www.who.int/immunization_financing/analyses/jrf_analysis/en/index.html, accessed 24 September 2011.

10. World Health Organization (WHO) (2005) Economics of immunization: a guide to the literature and other resources. WHO, http://www.who.int/vaccines-documents/DocsPDF05/769_update.pdf, accessed 19 September 2011.

11. Smith, J., Lipsitch, M., and Almond, J. (2011) Vaccine production, distribution, access, and uptake. *The Lancet* 378(9789): 428-438.

12. Barder, O. (2011) Should we pay less for vaccines? Center for Global Development, Global Health Policy, 21 June, http://blogs.cgdev.org/globalhealth/2011/06/should-we-pay-less-for-vaccines.php?utm_source=feedburner&utm_medium=feed&utm_campaign=Feed%3A+cgdev%2Fglobalhealth+%28Global+Health+Policy%29, accessed 19 September 2011.

13. Rappuoli, R., Miller, H., and Falkow, S. (2002) The intangible value of vaccination. *Science* 297(5583): 937-939.

14. Sampat, B. and Drummond, M. (2011) Another special relationship? Interactions between health technology policies and health care systems in the United States and the United Kingdom. *Journal of Health Politics, Policy and Law* 36(1).

15. Lieu, T., Cocchi, S., Black, S., et al. (1994) Cost-effectiveness of a routine varicella vaccination program for US children. *The Journal of the American Medical Association* 271(5): 375-381.

16. Tucker, A., Haddix, A., Bresee, J., Holman, R., et al.(1998) Cost-effectiveness analysis of a rotavirus immunization program for the United States. *The Journal of the American Medical Association* 279(17): 1371-1376.

17. Prosser, L., Ray, G., O'Brien, M., Kleinman, K., et al. (2004) Preferences and willingness to pay for health states prevented by pneumococcal conjugate vaccine. *Pediatrics* 113(2): 283-290.

18. Centers for Disease Control and Prevention (CDC) (2005) Direct and indirect effects of routine vaccination of children with 7-valent pneumococcal conjugate vaccine on incidence of invasive pneumococcal disease, US, 1998-2003. *Morbidity and Mortality Weekly Report* 54: 893-897.

19. Gross, S., Teutsch, S., and Haddix, A. (2007) Lessons from cost-effectiveness research for United States public health policy. *Annual Review of Public Health* 28: 365-391.

20. Culyer, A., McCabe, C., Briggs, A., et al. (2007) Searching for a threshold, not setting one: the role of the National Institute for Health and Clinical Excellence [NICE]. *Journal of Health Services Research & Policy* 12(1): 56–58.

21. Beutels, P., Scuffham, P., and MacIntyre, C. (2008) Funding of drugs: do vaccines warrant a different approach? *The Lancet Infectious Diseases* **8(11)**: 727–733.

22. Jit, M., Bilcke, J., Mangen, M., et al. (2009) The cost-effectiveness of rotavirus vaccination: Comparative analyses for five European countries and transferability in Europe. *Vaccine* 27(44): 6121-6128.

23. CDC (2008) Outbreak of measles – San Diego, California, January-February 2008. *Morbidity and Mortality Weekly Report* 57(8): 203-206.

24. WHO (2008) WHO guide for standardization of economic evaluations of immunization programs. WHO, www.who.int/entity/**immunization**.../tools/who_ivb_08_14_en.pdf, accessed 24 September 2011.

25. Walsh, J. and Mitu, A. (2006) The critical path for vaccine introduction: an analysis based upon the rapid introduction of rotavirus vaccines into Mexico and Brazil. Albert B. Sabin Vaccine Institute, http://www.sabin.org/news-resources/publication/critical-path-vaccine-introduction-analysis-based-upon-rapid-introduction, accessed 19 September 2011.

26. Global Alliance for Vaccines and Immunizations (GAVI) (2001) Preliminary note on budget line item for immunization. GAVI Financing Task Force, 6 September, fr.gavialliance.org/resources/line_item.pdf, accessed 24 September 2011.

9981 SW 143 Street, Miami, Florida 33176
+1.305.964.5784
www.policywisdom.com