9

Economic Evaluation of the Benefits and Costs of Disease Elimination and Eradication Initiatives

Kimberly M. Thompson and Radboud J. Duintjer Tebbens

Abstract

As health care costs continue to increase, economic evaluations of public health interventions play an increasingly important role in resource allocation decisions. In some cases, opportunities exist to eliminate and eradicate some diseases; such efforts typically require committing significant amounts of financial resources, with eradication also requiring international cooperation and coordination. Are investments in disease elimination or eradication worthwhile? How can we evaluate the economics of elimination and eradication efforts? What methodological issues might warrant special consideration? At a time when global health leaders continue to strive for global eradication of wild polioviruses types 1 and 3 (type 2 eradication occurred in 1999) and guinea worm (dracunculiasis), and to debate other eradication efforts related to measles and malaria, economic analyses can provide important context for the discussions. One of the most significant challenges in conducting economic analyses relates to valuing the direct and indirect benefits of elimination nationally and eradication globally. This chapter discusses the requirements for disease elimination or eradication. It presents the methods and challenges and raises key questions associated with evaluating the economic benefits of disease elimination and eradication.

Introduction

Global spending on health exceeds several trillion US dollars annually (WHO 2007c), and costs continue to increase with the growing global population, development, and improvements in health services and technology. A recent edition of the "State of the World's Vaccines and Immunization" (WHO et al. 2009) highlights the enormous health benefits achieved within the last decade

From "Disease Eradication in the 21st Century: Implications for Global Health," edited by S. L. Cochi and W. R. Dowdle. Strüngmann Forum Report, vol. 7, J. Lupp, series ed. Cambridge, MA: MIT Press. ISBN 978-0-262-01673-5.

from infectious disease prevention due to increased global investment in immunization. As noted in the report, "immunization remains one of the most cost-effective health interventions…[and] by keeping children healthy, immunization helps extend life expectancy and the time spent on productive activity" (WHO et al. 2009:74). Although the well-recognized benefits of vaccines include improving both the quality and length of life, vaccines cost money to produce and distribute; thus the public health community must make investment cases to support public health commitments to and prioritization of expenditures on vaccines. Economic analyses play a critical role with respect to characterizing the benefits and costs of elimination and eradication initiatives.

In some cases, the use of vaccines and/or other interventions (e.g., the isolation of potentially infected patients) can lead to the elimination or eradication of a human disease (for a discussion on definitions, see Cochi and Dowdle, this volume). Following the cessation of transmission of a disease within national or regional borders, people in the area still generally need to continue to use the vaccine or other intervention to maintain high levels of population immunity, to protect themselves from potential importation of the disease from other countries or regions, and to inhibit the reestablishment of transmission. Going beyond national disease control efforts, elimination and eradication initiatives generally require some level of international coordination and cooperation to ensure that the infections cease to circulate in all populations contemporaneously. Control measures (e.g., vaccination) may still be desirable given the possibility of an unintentional (e.g., accidental laboratory release) or intentional (e.g., bioterrorism attack) reintroduction of the infectious agent; thus, economic analyses of elimination and eradication initiatives should explicitly consider the costs and benefits of activities required to maintain the infection-free and/or disease-free state (Miller et al. 2006; Thompson and Duintjer Tebbens 2007). This may prove challenging, because estimating the post-elimination or post-eradication costs and benefits requires making assumptions about future policies and uncertain risks, and modeling the various potential policy options. We expect, however, that such analyses can play a significant role in informing policies, and we recognize that investment cases will need to consider the different values and perspectives that individual nations or regions may bring to international discussions.

Economists typically evaluate health interventions using cost-effectiveness analysis (CEA) and benefit-cost analysis (BCA). In the context of health economics, existing guidelines attempt to standardize the analytical methods used to assess the incremental impacts of potential new health interventions compared to the current intervention using cost-effectiveness methods (e.g., Gold et al. 1996; WHO 2008a). Although traditional CEA tends to provide a static assessment (i.e., to evaluate the economics by taking a snapshot at a fixed point in time), within the last decade analysts have increasingly recognized the importance of taking a dynamic perspective and combining economic models with infection transmission models (Edmunds et al. 1999; Brisson and Edmunds

From "Disease Eradication in the 21st Century: Implications for Global Health," edited by S. L. Cochi and W. R. Dowdle. Strüngmann Forum Report, vol. 7, J. Lupp, series ed. Cambridge, MA: MIT Press. ISBN 978-0-262-01673-5.

2003; Thompson and Duintjer Tebbens 2006; WHO 2008a). However, the dynamics of disease elimination and eradication differ from those of disease control (Duintjer Tebbens and Thompson 2009). Notably, theoretical analyses show that achieving eradication may prove difficult if prevalence of the disease drives demand for vaccine (Geoffard and Philipson 1997) (or by extension, the demand for elimination- or eradication-related control efforts). In the context of evaluating the economics of polio eradication, we demonstrated that as disease incidence drops due to significant investments in vaccination, this could lead to a perception that further investments are not worthwhile and to public demands to shift resources to other interventions, which ultimately could yield both higher costs and cases (Thompson and Duintjer Tebbens 2007). Part of the reason for this perception stems from the fact that cases of disease prevented defy observation: we cannot easily count events that do not happen, but we can easily add up financial costs. Models can play a critical role by bringing transparency to both the benefit and cost sides of the discussion. We reviewed the historical successful and failed efforts to eradicate endemic diseases and demonstrated the real trade-offs associated with changing perceptions and priorities in the context of managing multiple eradicable diseases competing for resources (Duintjer Tebbens and Thompson 2009). Other studies explored eradication in the context of game theoretic approaches (e.g., Barrett 2003, 2004; Barrett and Hoel 2007; Thompson and Duintjer Tebbens 2008b). A recent article (Beutels et al. 2008) emphasized that traditional economic methods fail when assessing the economics of emerging diseases, which may be eliminated or eradicated, in large part due to their inability (a) to develop appropriate infection transmission models given uncertainty about characteristics of the emerging pathogen, (b) to characterize the costs and effectiveness of potential interventions, and (c) to do so rapidly enough to inform urgent decisions (i.e., delaying actions until completion of analyses may mean missing critical opportunities for prevention).

Requirements for Disease Elimination or Eradication

Before considering the value and valuation of disease elimination or eradication, it is important to provide context related to the life cycle of diseases and prerequisites for disease elimination or eradication. In the context of their impact on global human health, we characterize diseases as occurring in the following phases:

1. emerging (initial detection/outbreak of a new disease),
2. epidemic (subsequent outbreaks and spread to other areas),
3. endemic and not controllable (continuing circulation of infectious agent in the absence of control strategies),

From "Disease Eradication in the 21st Century: Implications for Global Health," edited by S. L. Cochi and W. R. Dowdle. Strüngmann Forum Report, vol. 7, J. Lupp, series ed. Cambridge, MA: MIT Press. ISBN 978-0-262-01673-5.

4. endemic and controllable (continuing circulation of infectious agent in the presence of control strategies),
5. eliminated, and
6. eradicated.

Countries typically go through these phases at different times, which may blur the distinction of these phases globally.

Although our discussion focuses primarily on diseases in the last phases, efforts to eradicate an emerging disease represent important and valuable opportunities to prevent it from becoming endemic. For example, public health officials successfully detected the emergence of severe acute respiratory syndrome (SARS) and quarantined infectious people despite delayed notification of its emergence in the Guangdong province in China. SARS cases occurred in thirty countries around the world, with the disease establishing chains of transmission in six countries (WHO 2003b). As a result of globally coordinated activities, SARS failed to achieve sustained chains of transmission and disappeared. The significant investment in stopping transmission led to a complete disruption of the chains of transmission for SARS. However, this does not meet the definition of eradication of established human diseases (see Cochi and Dowdle, this volume), because SARS never became established and an uncertain nonhuman reservoir may exist which could lead to reemergence at some point. Still, we emphasize the importance of valuing the ability to stop an emerging disease like SARS from becoming established and thus requiring eradication.

In the case of SARS, impacted areas clearly suffered significant economic losses (GAO 2004). Remarkably, however, no studies currently exist that quantify both the costs incurred and benefits generated by the World Health Organization (WHO), U.S. Centers for Disease Control and Prevention (CDC), and other public health and health system authorities whose efforts collectively stopped SARS before it could become established or endemic. An economic analysis of the use of quarantine to stop the outbreak in Toronto reported cost savings (Gupta et al. 2005). We anticipate that analyses for other countries would show similar results, although requirements for international assistance to support efforts in some countries may necessitate transfers of financial, scientific, and health resources. In our initial efforts to assess the costs and benefits retrospectively, we could not find documentation of the costs incurred by the CDC or WHO, which transferred resources in the form of essential supplies for infection control and teams of specialists. Based on the costs incurred in impacted areas and the threat of a pandemic (i.e., rapid spread of an emerging disease throughout a large part of the world), we hypothesize that economic analyses of the efforts implemented to eradicate SARS would most likely suggest that the efforts represented a cost- and life-saving investment. For example, extrapolating the economic impacts experienced by Toronto to major U.S. urban areas provides some indication that prevention of a SARS outbreak in

From "Disease Eradication in the 21st Century: Implications for Global Health," edited by S. L. Cochi and W. R. Dowdle. Strüngmann Forum Report, vol. 7, J. Lupp, series ed. Cambridge, MA: MIT Press. ISBN 978-0-262-01673-5.

the United States led to significant savings. The CDC's contributions to the efforts largely came from reallocation of existing resources, albeit with the reallocation of resources implying real opportunity costs associated with using the resources for SARS instead of their original purposes. In this regard, we suggest the need to ensure the existence of sufficient global resources to eradicate any future emerging diseases rapidly before they become endemic. We should expect that emerging diseases may occur in the future, and appreciate the importance of preparedness in our ability to control, eliminate, or eradicate new diseases as they emerge. We also emphasize that in the context of responding to an outbreak, faster is generally better (Thompson et al. 2006). Thus, global health authorities should seek to ensure that proper incentives exist to motivate early detection, reporting, coordination, and action related to the management of emerging diseases.

Since most human diseases of concern emerged long ago (Shulman 2004), they fall into the middle disease phases (i.e., epidemic, endemic, or eliminated), which are the focus of this book (see Cochi and Dowdle, this volume). Although many developed countries have successfully stopped the transmission of some diseases, the same diseases remain endemic in other countries. Different types of infectious agents require different types of interventions and, notably, some types of interventions exist only for a subset of infectious agents (i.e., vaccines or medications currently exist for some diseases but not others). The development and widespread use of antibiotic, antitoxin, and antiviral medications to combat infections significantly reduced their adverse health outcomes, but also created conditions that select for resistant organisms, thus creating new problems.

The development of vaccines represents one of the most important tools for preventing many viral and bacterial vaccine-preventable diseases. Although intentional infection of humans to protect them from disease began many centuries ago in the form of variolation, the concept of vaccination derives from the development of the use of a vaccine made from cowpox to protect people from smallpox (Jenner 1801; Fenner et al. 1988). Edward Jenner's 1801 prophecy that "the annihilation of smallpox—the most dreadful scourge of the human race—will be the final result of this practice" (Jenner 1801:8) did not become reality until nearly 180 years later, when global smallpox eradication was certified in 1979 (Fenner et al. 1988).

In 1988, the World Health Assembly committed to the "elimination of the indigenous transmission of wild poliomyelitis viruses" (World Health Assembly 1988), which led to the launch of the Global Polio Eradication Initiative (GPEI). Following the development and introduction of poliovirus vaccines in the mid-1950s and early 1960s, countries increasingly adopted them for disease control efforts. Czechoslovakia and Cuba documented the absence of indigenous wild poliovirus transmission in 1960 and 1962, respectively (Slonim et al. 1995; Más Lago 1999). The burden of polio disease in the United States dropped rapidly in the 1960s and 1970s, and the United States successfully

From "Disease Eradication in the 21st Century: Implications for Global Health," edited by S. L. Cochi and W. R. Dowdle. Strüngmann Forum Report, vol. 7, J. Lupp, series ed. Cambridge, MA: MIT Press. ISBN 978-0-262-01673-5.

stopped indigenous circulation of all three types of wild polioviruses in 1979 (Thompson and Duintjer Tebbens 2006; Alexander et al. 2004). In 1985, the Pan American Health Organization (PAHO) resolved to stop indigenous transmission of wild poliovirus in the Americas by 1990, which it achieved in 1991 (Tambini et al. 2006). The GPEI achieved the global eradication of type 2 wild polioviruses shortly before 2000 (WHO 2001c), although the overall eradication initiative seeks to eradicate all three types of wild polioviruses (i.e., polio eradication).

Evaluating the feasibility of elimination or eradication requires consideration of many factors. Countries or regions need to possess the tools required to detect the disease based on a defined classification of identifiable disease symptoms and/or laboratory tests and the tools required to stop the transmission of the disease. For diseases that only involve person-to-person spread (i.e., no vector or other environmental reservoir) this may mean isolation of infected (or potentially infected) individuals, as with SARS. Diseases that involve vectors or environmental media may require activities to control or stop transmission from these sources. This occurs now in the case of the parasitic infection dracunculiasis (guinea worm), which requires isolating humans carrying a worm from water sources. For vaccine-preventable diseases, stopping transmission occurs once a population achieves a sufficiently high level of overall immunity (i.e., herd or population immunity) that stops the transmission of infection. The feasibility of stopping transmission depends on the ability of the vaccine to provide at least partial protection from infection, access to sufficient quantities of the vaccine required, an effective vaccine delivery system, absence of nonhuman reservoirs, and maintaining levels of population immunity to transmission of infections sufficient to stop transmission throughout the nation or region. For diseases that we can potentially stop by using nonvaccine interventions, including pharmaceutical products, feasibility depends on sufficient quantities of the intervention and effective use throughout the nation or region. In general, success depends on a functional health system or a dedicated program that can coordinate and manage national and/or regional resources and continue vigilant disease surveillance as well as any efforts required to avoid importations. Sustained success requires prohibiting any infections that get imported from establishing new chains of transmission by responding quickly and effectively.

The prerequisites for global eradication include the ability to eradicate disease from all countries contemporaneously and a global commitment to coordinate efforts. Eradication initiatives will generally require the establishment and maintenance of a global disease surveillance system, which requires significant investment of resources and may require sharing and transfer of both technologies and other resources.

From “Disease Eradication in the 21st Century: Implications for Global Health,“ edited by S. L. Cochi and W. R. Dowdle. Strüngmann Forum Report, vol. 7, J. Lupp, series ed. Cambridge, MA: MIT Press. ISBN 978-0-262-01673-5.

Valuation of Disease Elimination and Eradication

Economic analyses for infectious diseases must begin by considering the disease phase and feasibility, as discussed in the previous section. We emphasize that traditional economic methods will encounter significant challenges when assessing the economics of emerging diseases (Beutels et al. 2008), but analysts should seek, whenever possible, to evaluate the specific interventions required to eliminate an emerging disease before it becomes endemic. Economic assessments must identify potential interventions, quantify the costs of the interventions, and estimate the health benefits associated with their implementation. In the context of an emerging disease, for which the nature and ability to transmit represent significant uncertainties, analysts face significant challenges in forecasting the potential burdens of disease (with or without any interventions) and in identifying interventions to evaluate. Adding to these difficulties, national economic evaluations should also attempt to consider the positive externalities for other countries associated with eradication in the context of their national activities (i.e., failure to contain and stop transmission will lead to exportation to other countries that will incur costs to fight it, and many of these countries might be willing to pay significant amounts to prevent importation). Thus, in the context of an economic analysis to stop an emerging disease, the economics of eradication represent a relevant consideration; countries will need to create appropriate mechanisms to transfer all required resources from the countries willing to share available required resources to the countries which need them. This may imply incurring transaction costs associated with the transfer of resources, mobilizing financial resources and supplies, political negotiations for access to impacted areas, and managing issues related to ownership of scientific information and data generated by scientific and operational experts brought in to help. Based on the experience with SARS, some of this occurs already because of existing relationships between national and global health authorities that facilitate transactions and reduce some of these costs. However, the process remains somewhat informal, and consideration of transaction costs may represent an important step. By including the example of SARS, efforts taken to stop transmission of a disease before it becomes established represent a very valuable, important, and often-overlooked form of disease eradication activities. Thus, for an emerging disease, national economic analyses of transmission cessation activities need to be framed to include both the national and global perspectives, given large expected values of some countries (e.g., high-income countries) to invest in global prevention of establishment of the emerging disease.

For established diseases, we anticipate that economists will evaluate interventions to achieve national or regional disease elimination using standard CEA and BCA methods, by comparing the incremental costs and benefits of the elimination interventions to the base case comparator. These analyses require evaluation of both the benefits and costs. A typical CEA focuses on

From "Disease Eradication in the 21st Century: Implications for Global Health," edited by S. L. Cochi and W. R. Dowdle. Strüngmann Forum Report, vol. 7, J. Lupp, series ed. Cambridge, MA: MIT Press. ISBN 978-0-262-01673-5.

estimation of the incremental cost-effectiveness ratio (ICER) in monetary units (e.g., USD) per health outcome of the intervention (*i*) (i.e., the elimination or eradication initiative) compared to the comparator (*c*) (i.e., the base case or status quo):

$$ICER(i,c) = \frac{\sum_{j=t_0}^{t}\left[\left(C_{j,i} - C_{j,c} - \left(H_{j,c} - H_{j,i}\right)T\right)/\left(1+\delta\right)^{i-t_0}\right]}{\sum_{j=t_0}^{t}\left[\left(H_{j,c} - H_{j,i}\right)/\left(1+\delta\right)^{j-t_0}\right]} \quad (9.1)$$

where $C_{j,p}$ represents costs for policy scenario p (with p either i or c) during year j; $H_{j,p}$ is the incidence of health outcome for policy scenario p during year j; T describes the direct treatment costs per unit of health outcome; δ is the discount rate; t_0 represents the starting time of implementation of the intervention; and t signifies the end time of the analytical time horizon (typically chosen such that outcomes beyond time t have little impact on overall outcome due to discounting)

Many interventions impact both mortality and morbidity; thus CEA guidelines focus on reporting the health outcomes in the form of disability- or quality-adjusted life years (i.e., DALYs or QALYs) (WHO 2008a). Estimation of ICERs requires inclusion of the average treatment cost per case (T) to capture the real financial savings associated with not treating the prevented health outcomes. However, interpretation of the ICER and desirability of investing in the intervention require implicit valuation of the health outcomes estimated in the denominator (i.e., the decision maker must judge the cost-effectiveness and acceptability of a certain cost per health outcome determined by the CEA). The use of BCA depends on making the valuation of the denominator explicit (i.e., including an estimate of the monetary value or shadow price associated with the health outcomes saved). Thus, a typical BCA focuses on estimating the incremental net benefits (INB) in dollars associated with implementing the intervention (*i*) compared to the base case comparator (*c*):

$$INB(i,c) = \sum_{j=t_0}^{t}\left[\left(\left(H_{j,c} - H_{j,i}\right)\left(T+W\right) - \left(C_{j,i} - C_{j,c}\right)\right)/\left(1+\delta\right)^{i-t_0}\right] \quad (9.2)$$

where W represents the societal willingness-to-pay per unit of health outcome saved for indirect benefits to society associated with productivity gains, avoided pain and suffering, and other avoided burdens (not including direct treatment costs, T).

Challenges arise with respect to estimating all components of these equations. Estimating costs typically requires extrapolation from limited data for the intervention and the comparator, and estimating benefits typically requires disease modeling and extrapolation. All aspects of the valuation present difficult questions, with selection of the discount rate, time horizon, perspective, and framing recognized as important choices. Despite decades of recognition

From "Disease Eradication in the 21st Century: Implications for Global Health," edited by S. L. Cochi and W. R. Dowdle. Strüngmann Forum Report, vol. 7, J. Lupp, series ed. Cambridge, MA: MIT Press. ISBN 978-0-262-01673-5.

of the limited data for valuation (e.g., Creese and Henderson 1980; Cutting 1980), these critical inputs for economic analyses remain highly uncertain. Challenges arise with respect to characterizing both the direct and the indirect benefits. Direct benefits include reductions in mortality and morbidity, which we typically estimate using both data and models, and the associated saved treatment costs, which must be monetized. Indirect benefits include "intangibles" like avoided pain, suffering, and fear, productivity gains associated with family members no longer needing to provide care, and other positive externalities (e.g., reduced disruption of the health care system from disease outbreaks no longer occurring). One method for capturing the indirect benefits uses a value for willingness-to-pay per DALY saved on the order of the average annual gross national income as a best estimate, assuming this captures the real human capital costs associated with losses in productivity due to disability (Hutubessy et al. 2003; WHO 2001b, 2008a). This approach recognizes the large differences that exist in values, preferences, and abilities to spend resources in countries of different income levels. Given that valuation inputs remain highly uncertain and difficult to quantify and that this approach only captures the real productivity losses and not the intangible components of the willingness-to-pay, analysts typically consider a wide range of potential values in sensitivity analyses, with upper bounds of up to three times the average annual gross national income per DALY (WHO 2001b).

Challenges also arise with respect to the time horizon and other framing assumptions that determine the scope of the model (e.g., the choice of t_0, t, and δ in Eqs. 9.1, 9.2), which analysts similarly explore in sensitivity analyses. We demonstrated that choices related to framing significantly influence the economic estimates of historical polio control and elimination activities in the United States (Thompson and Duintjer Tebbens 2006). The discount rate (or rate of time preference) represents an area of ongoing discussion and debate in economics (Gravelle and Smith 2001; Parsonage and Neuburger 1992; van Hout 1998). Although existing guidelines suggest the use of a relatively low discount rate (e.g., 3%) for both future monetary and health outcomes (WHO 2008a; Gold et al. 1996), the choice of the discount rate can significantly impact economic results (WHO 2008a). These issues represent important considerations in economic assessments for elimination and eradication initiatives. Since interventions often continue due to importation risks, we expect an even greater impact in the context of evaluating global eradication efforts, which may consider cessation of the interventions given the absence of any globally circulating infections or disease.

Valuation of Global Eradication

Remarkably, relatively little literature exists related to the economic evaluation of global disease eradication successes. Barrett (2006) and Miller et al.

From "Disease Eradication in the 21st Century: Implications for Global Health," edited by S. L. Cochi and W. R. Dowdle. Strüngmann Forum Report, vol. 7, J. Lupp, series ed. Cambridge, MA: MIT Press. ISBN 978-0-262-01673-5.

(2006) present highly favorable economics of the 1967 Intensified Smallpox Eradication Programme, based on historical data (Fenner et al. 1988) and the economic benefits received by the entire world compared to the costs paid by the developed countries that provided international funding. Including the costs paid by the endemic countries (i.e., 31 countries, representing the nearly one billion people that were still reporting cases of smallpox in 1967) decreases the estimated benefit/cost ratio by approximately a factor of 3 (Miller et al. 2006). Even with these costs, the Intensified Smallpox Eradication Programme remains a good global investment based on the benefit/cost ratio, with the endemic countries experiencing a significantly larger proportion of the benefits. We could not find any published economic analyses related to smallpox eradication that follow current guidelines for economic analysis or consider other parts of (or the entire) time horizon between Jenner's vision of smallpox eradication and the actual achievement nearly 180 years later. We also could not find any analyses that quantified the global economics of cessation of transmission of an emerging disease, like for SARS. We found no economic analysis of the global eradication of wild poliovirus type 2, which occurred as part of the GPEI's effort to eradicate all three types of wild polioviruses.

We recently completed an economic analysis of the costs and benefits of the GPEI (Duintjer Tebbens et al. 2011) based on the current status of the program and consideration of post-eradication risk management policies (Thompson et al. 2008; Duintjer Tebbens et al. 2008). Although polio eradication, defined as the complete global disruption of transmission of all three types of wild polioviruses, remains an ongoing effort, the analysis suggests significant benefits associated with the GPEI. Several challenges and insights emerge from that analysis.

First, evaluating the economics of global eradication depends on estimating the number of endemic countries at the time the global eradication initiative starts and appropriately attributing the costs and benefits based on the state of the world at the outset of the initiative. For example, both global smallpox eradication and global polio eradication began following substantial reductions in the incidence of smallpox and polio diseases globally, although the amount of reduction varied considerably: 31 countries with less than 1 billion people living in these countries endemic for the one serotype of smallpox at the launch of the Intensified Smallpox Eradication Programme compared to more than 125 countries with more than 4.5 billion people living in these countries endemic for the three serotypes of wild polioviruses at the launch of the GPEI. With respect to current discussions of measles eradication, we note that significant progress toward elimination and eradication by many nations and WHO regions based on current goals may mean that a relatively small fraction of countries will ultimately directly benefit from a global eradication initiative, although ensuring effective coordination to achieve eradication may require its creation. Nevertheless, the indirect benefits may extend to all countries if global eradication leads to a significant reduction in importation outbreaks or

From "Disease Eradication in the 21st Century: Implications for Global Health," edited by S. L. Cochi and W. R. Dowdle. Strüngmann Forum Report, vol. 7, J. Lupp, series ed. Cambridge, MA: MIT Press. ISBN 978-0-262-01673-5.

enables eventual cessation of vaccination. The different relative starting points mean that we cannot compare the economics of different eradication efforts directly, although estimates of the net benefits from BCAs for any eradication effort should suffice to indicate the value of the initiative. Based on our modeling, performing CEAs for global eradication initiatives does not make sense given the large differences in the valuation and costs that exist for countries of different income levels. This occurs because analysts often can only provide appropriate estimates of ICERs for individual countries or countries grouped in a similar income level. Providing an "average" ICER for a global eradication effort aggregated at the global level will yield a result that national leaders will find difficult to evaluate, because they will most likely want to compare it to the ICERs for interventions that they undertake nationally. In our analyses of global policies, for which some readers might expect to see global ICERs (Thompson et al. 2008; Duintjer Tebbens et al. 2011), we reported ICERs stratified by income level to provide some indication of the large variability in estimates; we intentionally did not report a global ICER since it could mislead some decision makers by making them see either a significantly smaller or larger ICER than would in fact represent their country. We emphasize that income-level averaged ICERs may suffice to provide an indication of the variability for global analyses, but analysts would need to report national ICERs to support discussion of national and possibly also regional policy discussions. Given the highly variable values and preferences that occur over income levels, national leaders should compare an ICER in $/DALY to their national GNI or GDP per capita (WHO 2008a). However, this means that they need ICERs that reflect the appropriate costs for their country. BCA does not run into these issues because the valuation should occur explicitly as part of the process. Consequently, we believe that economic analyses of eradication initiatives should focus on providing BCA results. Any global eradication analysis will need to address the framing issue of determining the level of stratification required to communicate effectively to decision makers and key stakeholders.

Second, economic analyses must consider the dynamic nature of the eradication process, because countries may disrupt transmission at different times and those that stopped transmission must maintain disruption until all countries contemporaneously disrupt transmission. Models considering the dynamics of disease eradication suggest that the economically optimal path toward eradication involves strong coordination and rapid achievement of this goal (Barrett and Hoel 2007; Duintjer Tebbens and Thompson 2009). However, the economics of stopping transmission may only appear attractive in some countries initially (e.g., those with high health care expenditures and conditions that do not favor transmission of the infectious agent). For example, the costs of the intervention may decrease with time due to economies of scale associated with increased adoption and optimization of production processes. In addition, global eradication may become economically preferable to merely controlling the disease in countries experiencing continued transmission after a critical

From "Disease Eradication in the 21st Century: Implications for Global Health," edited by S. L. Cochi and W. R. Dowdle. Strüngmann Forum Report, vol. 7, J. Lupp, series ed. Cambridge, MA: MIT Press. ISBN 978-0-262-01673-5.

number of countries control or stop their transmission. This occurs because the risks of importation and the expected time until global eradication decrease, which implies fewer years of intensive efforts required to achieve and maintain national activities (Barrett and Hoel 2007). Failing to consider the dynamics of the process and the costs of delays may lead to an underestimation of the costs of global eradication. This can easily occur because estimating the costs of global eradication depends on making assumptions about national and global activities. We note that developing the types of integrated models needed to support policy considerations (e.g., Thompson et al. 2008; Duintjer Tebbens et al. 2008) may require consideration of many factors and careful documentation of the options (e.g., Sangrujee et al. 2003), risks (e.g., Duintjer Tebbens et al. 2006a), costs (e.g., Duintjer Tebbens et al. 2006b), and dynamics (e.g., Duintjer Tebbens et al. 2005). Experience shows that such forecast activities may not always go as planned. For example, in spite of the global commitment to eradicate wild polioviruses in 1988, some large countries and regions did not begin the necessary vaccination and surveillance efforts until very shortly before the year 2000 (Aylward et al. 2003). Characterizing the costs as a function of time also requires addressing the reality that all countries will need to pay costs associated with achieving global eradication until it occurs, which generally implies relatively large costs for the "last mile" or final stages. We emphasize that an important mismatch may occur during the final stages of global eradication, because costs tend to be relatively high while the number of visible cases is relatively low. During this time communication efforts will need to emphasize that the investment of the high costs means the prevention of a large number of cases.

Third, the costs of post-eradication activities may represent a significant consideration. For example, in the context of polio eradication, some countries may choose to continue to use or switch to using the more expensive inactivated poliovirus vaccine for routine vaccination to lower their risks of outbreaks from potential failures of containment or due to circulating live oral poliovirus vaccine viruses (Thompson et al. 2008). Although the cessation of vaccination and/or other disease control efforts may represent major economic dividends of an eradication initiative, we emphasize that economists must carefully assess post-eradication activities and consider different scenarios in the face of different potential future policies (Thompson et al. 2008; Barrett 2010).

Fourth, for any incremental economic analysis for disease eradication, analysts must compare at least one hypothetical scenario. For example, in the context of evaluating the benefits of polio eradication, we compared the actual GPEI to a scenario representing the alternative world with only routine vaccination (Duintjer Tebbens et al. 2011). Selection of the appropriate comparator for analysis can significantly influence the results and the insights associated with the analysis. One of the most challenging aspects of comparator forecasts relates to assumptions about the intervention over time. For example, what

From "Disease Eradication in the 21st Century: Implications for Global Health," edited by S. L. Cochi and W. R. Dowdle. Strüngmann Forum Report, vol. 7, J. Lupp, series ed. Cambridge, MA: MIT Press. ISBN 978-0-262-01673-5.

assumptions make sense for routine immunization rates: will they go up, go down, or stay constant over time?

Fifth, many of the choices related to the time horizon, time preferences, and framing can significantly impact the analysis and results (e.g., the choice of t_0, t, and δ in Eqs. 9.1, 9.2, with the modification that t_0 = starting time of implementation of the global eradication effort). Consideration of the discount rate for eradication initiatives raises interesting issues. Without discounting, the prevention of future cases extends to all future generations, which could theoretically imply infinite benefits and the need for an infinite time horizon (or a time horizon that theoretically goes until the uncertain time when the last human being on Earth dies). With discounting, the benefits to future generations disappear at some point in the analysis. The main issue this raises relates to intergenerational considerations, because some of the people who benefit from elimination or eradication initiatives undertaken now will not incur costs of the initiatives, although they benefit and they might be willing to pay such costs. Future generations might strongly prefer for current generations to address eradication instead of extending the burden of disease into the future, but they cannot express their preferences. We expect that economists will continue to perform baseline analyses using relatively low discount rates and present the results for a range of discount rates in sensitivity analyses, but that discussion about this issue will continue.

Finally, methods to estimate the indirect benefits continue to require development and need greater application with respect to disease elimination and eradication initiatives. Quantifying the benefits of a healthier population with respect to productivity and human capital represent significant challenges, and a large part of the value that societies place on health may depend on whether people perceive preventable cases of disease and disability as the norm (i.e., acceptable by default) or not. Disease elimination and eradication initiatives can fundamentally change expectations about health, because once people recognize the possibility of controlling or stopping a disease, this can lead to demands for public disease prevention initiatives. The value of preventing disease and disability in individuals impacts society, because societal resources used for treatment become available for other uses. For example, with effective measles vaccination efforts, the space required for measles wards in hospitals becomes available for treating patients with other diseases. Widespread vaccination for polio quickly led to the end of large rooms filled with iron lungs in hospitals. Thus, polio vaccination meant not only savings of treatment costs for the individual patients, but also big savings for the overall health system. Healthier children also mean more productive families, because caring for disabled family members takes people out of the workforce and uses family resources. Although economists attempt to capture indirect benefits using willingness-to-pay estimates, more current and future research will need to develop these methods further and ensure that they capture all of the benefits, including those that span generations.

From "Disease Eradication in the 21st Century: Implications for Global Health," edited by S. L. Cochi and W. R. Dowdle. Strüngmann Forum Report, vol. 7, J. Lupp, series ed. Cambridge, MA: MIT Press. ISBN 978-0-262-01673-5.

Discussion

Although economic analyses provide important information for disease elimination and eradication decisions, analysts encounter challenges preparing them and decision makers face challenges using their results. Economic analyses also represent only one consideration. The option to stop a disease from causing adverse health outcomes permanently into the future implies the opportunity to prevent any future human suffering caused by the disease, and this raises ethical and other considerations (Emerson, this volume; Emerson and Singer 2010).

With respect to the use of economic analysis results, we note that many discussions focus on opportunity costs, because some real resources used for one effort cannot be used for another. The need to pay relatively high costs for a short period of time to achieve eradication and receive long-term benefits often leads to discussions about the opportunity costs associated with the use of the resources during the "last mile" and to suggestions for potential better short-term purposes. We emphasize that opportunity costs require careful consideration for all potential uses. Clearly if a better opportunity exists, based on a rigorous analysis, and no means exist for mobilizing additional resources, then societies must make difficult choices. However, arguments about better opportunities need to show that the alternative use of the resources truly leads to an improvement (i.e., lower costs and lower DALYs lost overall in the short and long term). Thus, consideration of opportunity costs should include not only the potential alternative uses of the resources in the short term, but also the implications of failing to eradicate a disease, and thus incurring ongoing costs for disease control into the long term, because countries will continue to incur such costs. Ignoring these opportunity costs does not make them go away.

The dynamics of optimizing the management of multiple diseases represents an important area for modeling (Duintjer Tebbens and Thompson 2009), particularly because intuition about opportunities may become biased by focusing on cases occurring instead of on the cost-effectiveness of options. Arguments that eradication initiatives represent unreasonable expenses in an absolute sense (e.g., we cannot afford to spend billions of dollars to eradicate a disease) need to consider the context of how such global health projects fit into the context of other major societal projects (Thompson and Duintjer Tebbens 2008b), for which their absolute costs and performance seem favorable. More importantly, we suggest that from an economic perspective, the focus should remain on whether the effort provides net benefits. For a vaccine-preventable disease, the notion that we can invest significantly in building up population immunity as part of an eradication effort and then stop investing prior to achieving eradication without losing any ground represents a logical fallacy. Such an argument fails to appreciate that the true value of an eradication effort derives from the population immunity provided by the vaccine, which protects people from the disease. This protection represents a real value. In all cases,

From "Disease Eradication in the 21st Century: Implications for Global Health," edited by S. L. Cochi and W. R. Dowdle. Strüngmann Forum Report, vol. 7, J. Lupp, series ed. Cambridge, MA: MIT Press. ISBN 978-0-262-01673-5.

efforts to validate analyses and evaluate progress should provide feedback as to whether resource uses represented cost-effective investments that yield net benefits. We also note that those who suggest better opportunities for elimination or eradication funds should recognize that some of the resources might not exist were it not for the goal of disease eradication (i.e., some sources of funding might provide resources to support some types of goals, but not others, and not all funding is fungible).

One of our main insights from reviewing the economics of disease elimination and eradication initiatives relates to the issue that, in the context of global health, eradication initiatives may represent an activity for which an increase in societal investments could lead to significantly more benefits. One interpretation of the concept that we could potentially eradicate multiple diseases, but that we lack resources to do so, is that global health leaders may not appreciate the significant economic benefits of eradication. Notably, the issue of insufficient financial resources threatened smallpox eradication and continues to threaten polio eradication. Unlike other major projects to develop public goods that typically involve public financing, disease eradication initiatives currently depend on raising all of the funds required up front. Part of the challenge for disease eradication may derive from the difficulty that arises in health systems and the public recognizing the savings associated with not incurring disease and not paying the associated treatment costs. Economic and disease modeling can play an important role in helping to make these more clear, and this may be particularly critical when public perceptions focus on the small number of eradication intervention-related adverse events in the absence of large amounts of disease incidence. Another interpretation of the lack of resources to eradicate diseases is that economic analyses need to provide more assessments with respect to making the investment case for disease control, elimination, and eradication efforts. We suggest that investment cases can and should play a much greater role.

Conclusion

Economic analyses can offer important insights related to disease elimination and eradication initiatives. However, analysts must address a number of challenges before the estimates they provide will truly assist decision makers. The valuation of direct and indirect benefits represents an important area for additional research, particularly related to framing the analysis. Selection of the time horizon, the starting point with respect to the scale of the elimination or eradication initiative, and time preference values may significantly impact the results of the analysis. Sensitivity analyses should provide a strategy for analysts to explore the impacts of different possible choices. Additional research may help analysts better quantify time and intergenerational preferences for all economic analyses of elimination and eradication initiatives. For specific

From "Disease Eradication in the 21st Century: Implications for Global Health," edited by S. L. Cochi and W. R. Dowdle. Strüngmann Forum Report, vol. 7, J. Lupp, series ed. Cambridge, MA: MIT Press. ISBN 978-0-262-01673-5.

eradication investment cases, we expect that analysts will need to invest in obtaining the best available estimates of the willingness-to-pay for indirect benefits as they move more toward a BCA approach. Finally, global eradication initiatives will need to address the reality of large differences in the economics for different countries.

From "Disease Eradication in the 21st Century: Implications for Global Health," edited by S. L. Cochi and W. R. Dowdle. Strüngmann Forum Report, vol. 7, J. Lupp, series ed. Cambridge, MA: MIT Press. ISBN 978-0-262-01673-5.