

Estimating the Avertable Disease Burden and Cost-Effectiveness in Millions Saved Third Edition

Andrew Mirelman, Amanda Glassman, Miriam Temin

Abstract

Millions Saved (2016) is a new edition of detailed case studies on the attributable impact of global health programs at scale. As an input to the book, this paper provides an independent assessment of the cost-effectiveness of a selection of the cases using ex post information from impact evaluations, with the objective of illustrating how economic evaluation can be used in decision making and to provide further evidence on the extent of health gains produced for the funding provided. We reviewed the evidence and calculated the averted disease burden and cost-effectiveness for a selected group of public health successes, finding that large health gains have been achieved in programs that represent good value for money. Since these cases represent known successes, this is to be expected; however, some key issues emerge. In many cases, estimates of cost-effectiveness are not available for programs at scale and thus estimating efficiency losses and scale-up dynamics is only possible with modeling and by making large assumptions. When assessed in reference to the GDP per capita of the country, many of the programs compare favorably, though the GDP per capita threshold may not be the correct figure for making decisions. Health systems and sectoral interventions, such as those that address access to care or provide resources directly (e.g. cash transfers), present difficulties when estimating standard measures of cost-effectiveness. These difficulties can be partially overcome with high quality studies that evaluate implementation or by using alternative measures of efficiency such as those relating to administrative efficiency. The lessons learned from calculating the cost-effectiveness for many scaled-up programs across a range of health areas and country settings provides lessons for future considerations of the value of scaling up effective health interventions in national health programs.

JEL Codes: H5, H43, H51, I1, I10, I12, I13, I14, I18

Keywords: Health, Medical Care, Medico Economic, Cost-Effectiveness, Program Evaluation.

**Estimating the Avertable Disease Burden and Cost-Effectiveness in
Millions Saved Third Edition**

Andrew Mirelman
University of York

Amanda Glassman
Director of Global Health Policy, Center for Global Development

Miriam Temin
Population Council

The authors acknowledge funding received from the Bill & Melinda Gates Foundation and Good Ventures, and thank the anonymous peer reviewers as well as Rachel Nugent, formerly of the Disease Control Priorities Network for her comments and input.

The Center for Global Development is also grateful for contributions from the Bill & Melinda Gates Foundation and Good Ventures in support of this work.

Andrew Mirelman, Amanda Glassman, and Miriam Temin. 2016. "Estimating the Avertable Disease Burden and Cost-Effectiveness in Millions Saved Third Edition." CGD Working Paper 429. Washington, DC: Center for Global Development.
<http://www.cgdev.org/publication/estimating-avertable-disease-burden-and-cost-effectiveness-millions-saved-third-edition>

Center for Global Development
2055 L Street NW
Washington, DC 20036

202.416.4000
(f) 202.416.4050

www.cgdev.org

The Center for Global Development is an independent, nonprofit policy research organization dedicated to reducing global poverty and inequality and to making globalization work for the poor. Use and dissemination of this Working Paper is encouraged; however, reproduced copies may not be used for commercial purposes. Further usage is permitted under the terms of the Creative Commons License.

The views expressed in CGD Working Papers are those of the authors and should not be attributed to the board of directors or funders of the Center for Global Development.

Contents

Introduction.....	1
Methods.....	2
Reviewing the Evidence on Cost-Effectiveness.....	2
Calculating Averted Disease Burden.....	2
Calculating Costs.....	3
Calculating Cost-Effectiveness.....	4
The Cost-Effectiveness Ratio.....	4
Results.....	5
Estimating Disease Burden in DALYs.....	5
Results for Calculating Cost-Effectiveness.....	5
Estimating <i>Ex Post</i> Value for Money in Programs.....	7
Conclusion.....	7
Tables.....	11
Appendix 1 – Detailed Estimation Table.....	13
Appendix 2 – Model Details and Results.....	16
1. Estimating the Disease Burden and Cost-Effectiveness: ART in Botswana.....	16
2. Estimating the Disease Burden and Cost-Effectiveness: MenAfriVac in Chad.....	17
3. Estimating the Disease Burden and Cost-Effectiveness: Hepatitis B in China.....	18
4. Estimating the Disease Burden and Cost-Effectiveness: De-Worming in Kenya.....	20
5. Estimating the Disease Burden and Cost-Effectiveness: Malaria in Zambia.....	21
6. Estimating the Disease Burden and Cost-Effectiveness: Piso Firme in Mexico.....	23
7. Estimating the Disease Burden and Cost-Effectiveness: Motorcycle Helmets in Vietnam.....	25
8. Estimating the Disease Burden and Cost-Effectiveness: Sanitation in Indonesia.....	26
9. Estimating the Disease Burden and Cost-Effectiveness: Tobacco in Thailand.....	28
10. Estimating the Disease Burden and Cost-Effectiveness: Avahan.....	30

Introduction

Over the last decade, there has been a large increase of impact evaluations in health, studies that measure and establish the attributable impact of newly-introduced technologies and interventions on health outcomes in low- and middle-income countries. However, no matter how effective a particular intervention may be, without information on the costs alongside the benefits, it is impossible to establish whether an investment is worth the money. The analysis of benefits net of costs, or cost-effectiveness analysis (CEA), is generally done *ex ante* since a primary goal of such analysis is to inform decisions about intervention adoption. CEA conducted *ex post*, which is generally done for impact evaluation, may provide information about implementation and context that accounts for health system characteristics or political economy.

The third edition of the *Millions Saved* book (MS3) provides detailed case studies of global health successes and a few disappointments at scale [1]. As a part of this book, an independent assessment of cost-effectiveness of a selection of cases was conducted that uses *ex post* information from impact assessment. The objective is to show how economic evaluation can be used in decision making for at-scale programs and provide further evidence as to how successful (or unsuccessful) they were.

To be included in MS3, a case had to meet several criteria that were assessed in consultation with global health experts. One of the selection criteria was whether the case could show attributable impact in terms of improving health outcome. A second criteria for case selection was whether the case is considered good value for money. In general, this was assessed qualitatively by the expert group and a quantitative estimate of the value for money was still deemed useful. Only a subset of MS3's case studies were selected for an original economic evaluation analysis. The specific cases were chosen based reasons of data availability and analytical tractability. Twelve of the 22 total cases that were featured in MS3 were selected. The cases are grouped according to four categories: medicine and technology roll-out, expanding access to health services, targeted cash transfers to improve health, and population-wide behavior change. All of the successful programs in the 'Medicine and Technology Roll-Out' (n=6) and the 'Population-Wide Behavior Change' (n=4) categories were included as they were the most likely to deal with a single health problem and have a tractable attributable impact.

From the other two categories, 'Expanding Access to Health Services' and 'Targeted Cash Transfers to Improve Health', one case from each was selected to estimate the averted burden and cost-effectiveness. These were the *Plan Nacer* program in Argentina and the Orphans and Vulnerable Children Cash Transfer (CT-OVC) program in Kenya. The CT-OVC case was selected because of the availability of health impact estimates that were attributable to the intervention and *Plan Nacer* was selected because there was existing economic evaluation evidence. The selection of only two cases for economic evaluation in these two categories, which feature more complex and non-biomedical interventions shows the limitation of standard methods of economic evaluation for these intervention scenarios.

This work serves as a starting point for understanding the impact and efficiency associated with the selected cases in the MS3 in terms of averted health burden as well as the costs per health impact, but it should be stressed that these are approximate results. Decision-makers who would use such information should conduct or account for further detailed economic evaluations that relate to their specific settings.

Methods

Reviewing the Evidence on Cost-Effectiveness

We reviewed relevant published literature and databases for studies in low and middle-income countries that provide evidence for the cost-effectiveness of the chosen MS3 cases. We attempted to identify all possible relevant evidence on related costs and health outcomes. In many cases, the published evidence that was needed came from different country settings that was translated to the country of interest. The following databases were searched:

- The Disease Control Priorities Project 2nd Edition (DCP2) [2]
- The Cochrane Library [3]
- Tufts CEA Registry [4]
- Google Scholar
- PubMed/Medline

Although our review of the literature was not systematic, additional searching through the citations of relevant papers and consultations with experts were conducted to identify relevant evidence for each case. While some key published evidence will have certainly been missed, we are fairly confident that most key evidence has been considered.

Calculating Averted Disease Burden

The health impact for each case was obtained from the attributable estimate from impact evaluations. This gave us an incremental estimate of the health benefits accounting for a counterfactual situation. The estimates of health benefit were usually provided in natural units such as deaths or cases of illness averted. These were then translated to a single, summary unit of health, the disability adjusted life year (DALY). The DALY was selected because it accounts for both morbidity and mortality and is a summary measure of the total health burden averted across cases. The DALY is the standard measure used to estimate disease burden by the World Health Organization (WHO), the global burden of disease project (GBD), and the Disease Control Priorities Network (DCP)¹ [5-7]

Conceptually, DALYs can be thought of as the shortfall from healthy (disease-free) life. There are several key parameters used for calculating DALYs, which are: maximum lifespan, age-weighting, and discount rate. These parameters can be set by the analyst and recommendations for the value of each has changed over time. For the purposes of MS3, we used the recommended DALY parameters from the latest estimates of disease burden from the World Health Organization [8]. The WHO recommends using no age-weighting, no discounting and a maximum lifespan of 86 years when presenting estimates of disease burden. When the DALYs are entered into calculations for cost-effectiveness analysis, we additionally discount them at a rate of 3%.

For case studies where there were no readily available figures for the averted natural health outcomes, a mathematical disease model was constructed to estimate the number of averted cases of disease and deaths. The disease models were populated with parameters from the literature review. To the best degree possible, the models were parametrized with

¹DCP3 is a collaborator on the Millions Saved Third Edition project along with CGD.

information from the case country, however, in several cases where data could not be found or did not exist, parameters were obtained from studies in other settings (e.g. neighboring or regional countries) that were plausibly similar.

For each estimate of health impact, whether reported in the literature or calculated in a model, we document the target population and intervention coverage, which can be used to understand the total averted disease burden. We defined the target population as those people in a given geographic area where the intervention or program was implemented who are in the age range of potentially affected by the health condition or who would potentially receive the intervention. For example, in the case of ART in Botswana, the target population is the entire country population over 18 years old as this was the population used in the impact evaluation [9]. When total population estimates were not provided by the case impact evaluations, we modeled the target population using the country population from the closest year as the impact evaluation for appropriate age group from the United Nations Population Division database [10]. When estimates were calculated across multiple years, the analysis followed the target population of a single annual cohort over a given time horizon. For example, in the ART case, the population older than 18 years old in year 1 became the population of 19 year olds in year 2 and no replacement cohort entered as new 18 year olds.

For coverage, we used information from the scale-up of the intervention when it was available to estimate the averted burden. For cases that lacked coverage information, we assumed that the intervention was introduced to the entire target population. In these cases the analysis provides an upper-limit estimate of the averted health burden.

Information on the key parameters used in each case are shown in the first four columns of Table 1. The table shows the time horizon over which the analysis was conducted, the target population and the key health outcomes used. In several interventions with lifelong protection, such as the prevention of Hepatitis B in China, lifetime sequelae from the illness were also counted in the DALYs. The latter columns of Table 1 are discussed subsequently in the Results section.

Calculating Costs

The costs represent the value of resources that are required to carry out a given activity. We adopted a standard approach of presenting the costs of the activities related to the intervention from the perspective of a health system. Cost data for each case were found in different formats. In several cases, the total budget figures for the program were known, in which case a total program cost could be estimated. In other cases where total costs were not reported, unit costs from the literature were identified. Using these costs, the implied reference case is the ‘status quo’ when for the cost-effectiveness analysis. This assumes that the program’s costs – like the approach to benefits described above – are assumed to be incremental to a ‘do nothing’ scenario. This is unlikely to be accurate in the real-world and the costs of relevant alternative programs, as well as the opportunity costs, should be incorporated when conducting these analysis for decision makers.

To standardize costs, we converted them to a common currency unit and year (2014 United States dollars). As did not estimate costs from averting future illness or the time cost to patients and caregivers, the costs only represents the financial costs, not the economic costs, of the program. The costs here should be understood as the best estimate of resources used to implement the intervention.

Calculating Cost-Effectiveness

A basic cost-effectiveness analysis was also conducted for several of the cases. The cost-effectiveness analysis used the parameters listed in Box 1 in each analysis.

Box 1. Key Cost-Effectiveness Parameters

Parameter	Description
1. Perspective	Provider or health system, generally public provider/government
2. Target Population	Population at risk for having the illness and for which the intervention is relevant (e.g. under-fives, school age, etc.)
3. Time Horizon	Length of the case-study program. For several illnesses, long-term outcomes past the length of the program were also modeled
4. Base case scenario	No intervention. Here, the recommendations from the WHO's generalized cost-effectiveness analysis guidelines are used [11]
5. Sensitivity Analysis	None provided in this report

The Cost-Effectiveness Ratio

A cost-effectiveness ratio can either be presented as an average ratio, which looks at the value of the total costs divided by the total effects of the program or intervention, or as an incremental value of the costs and effects compared to another scenario. Average ratios provide information for understanding the general level of value for money of a given intervention, while incremental ratios are best for making decisions about introducing a new intervention in comparison to other intervention options [11]. Our estimates use the averted disease burden and the resource costs from the perspective of the health system (or government) of the program to provide an approximate incremental cost-effectiveness ratio, however, since we use only a comparison to the status quo, or 'no intervention', scenario, further decisions should attempt to include all relevant comparator interventions.

For determining whether an intervention is cost-effective or not, the cost-effectiveness ratio is assessed against a threshold value. There is, however, debate about what this threshold value should represent [12]. A commonly employed threshold is a range of one to three times a country's gross domestic product (GDP) per capita. In this case, any intervention with a cost-effectiveness ratio (in terms of dollars/DALY averted) less than this figure is deemed 'very cost-effective' and any estimate less than three times the GDP per capita is deemed 'cost-effective' [13]. Other threshold values may take account of the opportunity costs for health, which in a health budget represents the inverse of the marginal productivity

of health spending [14]. These have been used in several high income countries but have not yet been implemented in low and middle income countries [15]. For this reason, we note what the GDP per capita of the country setting is as a reference point, however we recommend that implementation considerations be made based on further evidence of real opportunity costs.

Results

Estimating Disease Burden in DALYs

The fifth and sixth columns of Table 1 give estimates of the averted deaths and DALYs from the different programs. There were 513,481 total deaths averted from the 12 programs. The total averted deaths were driven by several programs that had high impacts on averted deaths. The top two were the Avahan program in India, which averted 202,000 deaths and implementation of ART in Botswana, which averted 143,637 deaths. This highlights the severity of HIV/AIDS in terms of mortality and its harmful impact on population-wide mortality in Sub-Saharan Africa. The Hepatitis B vaccination program in China also averted a large number of deaths, 93,200, followed by programs for malaria prevention in Zambia (29,900), tobacco control in Thailand (29,357) and the Menafrivac program in Chad (12,469). While we do not draw comparisons across cases, these figures do give a sense of which programs will have large impacts on mortality and which will have benefits that mainly come from reductions in morbidity. They also highlight that for some programs, deriving attributable estimates of averted burden is difficult. For example, for the CT-OVC program in Kenya, no estimate of averted deaths was found in the literature.

The total DALYs averted for the programs was found to be 18,921,455. The estimates vary predictably across cases, though again the importance of averting HIV/AIDS mortality is seen to provide some of the largest estimates, with over 8 million DALYs averted for the ART program in Botswana and over 3 million DALYs averted for the Avahan program in India. All of the programs averted DALYs that were at the least in the tens of thousands. The importance of averting morbidity is also captured with the DALY estimates and programs that had relatively few deaths averted, such as the deworming program in Kenya and *Plan Nacer* in Argentina averted large numbers of DALYs, 99,568 and 72,800 respectively.

In an extended table in the Appendix, the DALY estimates are compared to estimates from the WHO's Global Health Estimates (GHE) effort [16]. Note that the GHE estimates do not align perfectly with the program estimates since they are presented for the entire disease burden in the closest possible year to program implementation.

Results for Calculating Cost-Effectiveness

The last column of Table 1 shows results for the cost-effectiveness for each case study. For the 'Medicine and Technology Roll-out' category, the cost-effectiveness ratios in terms of dollars per DALY averted for all cases was less than or equal to USD \$100 per DALY. This result highlights that low price biomedical interventions with proven impact shown to be attractive investments when introduced successfully at scale. This finding should be understood in the context that the cases were selected because they were considered "cost-effective". *Piso Firme* was the one case in the 'Medicine and Technology Roll-out' category where a cost-effectiveness ratio could not be calculated. The authors of the impact

evaluation, however, found that for a single Mexican state, *Piso Firme* cost about \$150 per household and this compares favorably with the cost for achieving similar education outcomes in Latin American cash transfer programs [17].

In the ‘Expanding Access to Health Services’ category, the case of Argentina’s *Plan Nacer* had an original cost-effectiveness estimate calculated as part of the impact evaluation. We used these results for our study because the impact evaluation was conducted during the project scale-up. The study is notable because it is one of the only studies to estimate the cost-effectiveness of a structural health systems intervention. This has rarely been done even in developed countries [18]. It is important to keep in mind, however, the question of ‘what is cost-effective?’ when considering *Plan Nacer* and that this depends on how the program compares with alternative investments. For example, the cost-effectiveness of a performance incentive program could be compared with a similar increase in funds that does not have performance elements. Likewise, the cost-effectiveness could be assessed for an increase in expenditure *in addition* to adding performance incentives if the program.

Calculating the cost-effectiveness in terms of health outcomes of the cash transfer programs included in the ‘Targeted Cash Transfers to Improve Health’ section is similarly problematic because of the multiple development objectives underlying these interventions. In this case, efficiency is measured in terms of the cost-transfer ratio (CTR), which is a measure of administrative efficiency (cost of the program divided by the amount of the transfer). Here, the CTR value below one means that the program is cheaper than the amount of monetary benefit disbursed. In comparison with the CTR of other cash transfer programs, the CTR of the Kenya CT-OVC falls within the range that is generally seen of 0.1 to 0.5 [19]. The CTR, however, is an aggregated measure, pooled across the entire program, and needs to be considered in terms of when in the program life it is calculated. For example, at the start of program, the CTR will be much higher due to fixed capital and other start-up costs [20].

In the ‘Population-Wide Behavior Change’ category, all of the interventions appeared relatively cost-effective. The cases of tobacco control in Thailand and Avahan in India fell under USD \$100 per DALY while sanitation in Indonesia was \$213 per DALY and helmets were around \$1,200 per DALY. These results were similar to those estimates found in the literature, although our estimate of the cost-effectiveness of helmets was higher than those seen in other studies. This may be due to underestimation of the health impacts, which are difficult to measure. For this helmet intervention, we used data for averted deaths from police data, that are typically known to be under-reported [21].

Finally, for all programs we note that the cost-effectiveness ratios appear to be favorable in terms of the broad comparison to the GDP per capita of each country, with most interventions falling well under one times the GDP per capita. Only in the case of helmets for Vietnam was the ratio even close to the GDP per capita. While this is promising, and in some sense expected, the GDP per capita threshold is also criticized as a threshold measure for making cost-effectiveness conclusions [22]. Estimating a true cost-effectiveness threshold for health budgets in low and middle-income countries is difficult and is rarely explicit even in high income countries. An exception is the threshold calculated in the United Kingdom and used by the National Institutes of Clinical Excellence (NICE) when deciding which interventions to fund through the National Health Service [23]. That being said, the use of a GDP per capita threshold is used widely in global health and does represent an estimate that incorporates a broad willingness to pay (WTP) perspective.

Estimating Ex Post Value for Money in Programs

A finding of this work is that estimating the cost-effectiveness of programs *ex post*, is a difficult task that is not usually undertaken. This is highlighted by the fact that we could not find cost-effectiveness estimates for many of the programs that were conducted at scale, with the one exception being *Plan Nacer* in Argentina. In each case, we estimated the disease burden and the costs according to available data or with simplifying assumptions.

Understanding the value in terms of health benefits per dollar of a program is critical for policymakers and for achieving the most efficiency in terms of available resources. In most cases, cost-effectiveness is assessed prior to an intervention or very early on in a program's life, if at all. In these pilot phase projects, the constraints to the program's effectiveness may be different than it would be during the scale up and wider roll-out. It is possible that as it is scaled up, the program would become more inefficient as leakages are magnified due to the larger scale. On the other hand, the program could become even more efficient over time as program learning reduces the level of leakage and economies of scale are realized [24].

The issue of how effectiveness may decline in larger programs has already been documented in some education programs where external validity of an impact evaluation of a development program at small scale disappears when it is scaled up [25]. There is no reason why this impact should not be seen for health programs as well as for education.

Generally, all of the programs are deemed cost-effective according to the literature that was found in our search, but there could also be further considerations of costs and benefits that refine or provide insights into the cost-effectiveness of these programs. Difficult to measure costs, such as the cost of policy irreversibility, might be included if the programs are modeled using different approaches that account for options value [26].

In terms of quantifying impacts, there may be benefits that may not be captured by scaled policies such as cross-sector benefits and spillovers (either positive or negative). This is especially the case for interventions that are designed to address cross-sector issues (e.g. cash transfers). Certain health issues may also have relatively large spillovers, which is typically not accounted for in impact evaluations. In the example of deworming in Kenya, the issue of spillovers is considered to be quite important due to the infectious nature of the pathogen and the potential for protection from herd immunity. Spillover benefits have also been seen to be quite important in the case of smoking. For some issues, such as non-communicable diseases or road traffic injuries (e.g. Vietnam helmets), the benefits are mainly internalized, so we could be more confident in excluding them from the cost-effectiveness estimation. Putting the costs and effects together, it is also not as straightforward to compare a scaled program to other programs incrementally as is done for biomedical interventions [27]. For this reason, our results may not provide a clear picture of how efficient the program is with regards to other potential interventions. Future work might also look at how the cost-effectiveness of each program is also related to a well-functioning health system. Specifically, this may have implications for the cost of implementation if a country needs to invest in human resources, infrastructure and other indirect program costs.

Conclusion

We reviewed the evidence and calculated the averted disease burden and cost-effectiveness for a selected group of public health successes. The results show that large health gains have been achieved in programs that represent good value for money. Since these cases represent known successes, this is to be expected; however, some relevant issues emerge. In many

cases, estimates of cost-effectiveness are not available for programs at scale and thus estimating efficiency losses and scale-up dynamics is only possible with modeling and by making large assumptions. When assessed in reference to the GDP per capita of the country, many of the programs compare favorably, though the GDP per capita threshold may not be the correct figure for making decisions. Health systems and sectoral interventions, such as those that address access to care or provide resources directly (e.g. cash transfers), present difficulties when estimating standard measures of cost-effectiveness. These difficulties can partially be overcome with high quality studies that evaluate implementation or by using alternative measures of efficiency such as those relating to administrative efficiency. The lessons learned from calculating the cost-effectiveness for many scaled-up programs across a range of health areas and country settings provides lessons for future considerations of the value of scaling up effective health interventions in national health programs.

References

1. Glassman, A. and M. Temin, *Millions Saved: New Cases of Proven Success in Global Health*. 3rd ed. 2016, Washington, DC: Center for Global Development. 300.
2. Laxminarayan, R., J. Chow, and S.A. Shahid-Salles, *Intervention Cost-Effectiveness: Overview of Main Messages*, in *Disease Control Priorities in Developing Countries*, D.T. Jamison, et al., Editors. 2006: Washington (DC).
3. Cochrane, *The Cochrane Library: The Cochrane Collaboration*. 2014, Wiley: Chichester.
4. *Cost-Effectiveness Analysis Registry*. 2014: Tufts University.
5. DCPN, in *Disease Control Priorities in Developing Countries*, D.T. Jamison, et al., Editors. 2006: Washington (DC).
6. Murray, C.J., A.D. Lopez, and D.T. Jamison, *The global burden of disease in 1990: summary results, sensitivity analysis and future directions*. Bull World Health Organ, 1994. 72(3): p. 495-509.
7. WHO, *The Global Burden of Disease: 2004 Update*. 2008, World Health Organization: Geneva.
8. WHO, *WHO methods and data sources for global burden of disease estimates 2000-2011* 2013, The World Health Organization: Geneva.
9. Farahani, M., et al., *Outcomes of the Botswana national HIV/AIDS treatment programme from 2002 to 2010: a longitudinal analysis*. Lancet Glob Health, 2014. 2(1): p. e44-50.
10. United Nations, *World Population Prospects: The 2012 Revision*, D.o.E.a.S.A. United Nations, Population Division, Editor. 2013.
11. Hutubessy, R., D. Chisholm, and T.T. Edejer, *Generalized cost-effectiveness analysis for national-level priority-setting in the health sector*. Cost Eff Resour Alloc, 2003. 1(1): p. 8.
12. Marseille, E., et al., *Thresholds for the cost-effectiveness of interventions: alternative approaches*. Bull World Health Organ, 2015. 93(2): p. 118-24.
13. CMH, *Macroeconomics and health: investing in health for economic development*. 2001, The Commission on Macroeconomics in Health; The World Health Organization: Geneva.
14. Claxton, K., et al., *Methods for the Estimation of the NICE Cost Effectiveness Threshold*, in *Centre for Health Economics Research Paper*. 2013: York, UK. p. 119.
15. Schwarzer, R., et al., *Systematic overview of cost-effectiveness thresholds in ten countries across four continents*. J Comp Eff Res, 2015. 4(5): p. 485-504.
16. WHO. *Global Health Estimates*. 2014 September, 3 2014]; Available from: http://www.who.int/healthinfo/global_burden_disease/en/.
17. Sorace, C. *China's Vision for Developing Sichuan's Post-Earthquake Countryside: Turning Unruly Peasants into Grateful Urban Citizens*. 2014 June 2014// [cited 0; 218: [404-27].
18. Jia, P. *Employment and Working Hour Effects of Minimum Wage Increase: Evidence from China*. 2014 March-April 2014// [cited 22; 2: [61-80].

19. Li, S. *Poverty Reduction and Effects of Pro-poor Policies in Rural China*. 2014 March-April 2014// [cited 22; 2: [22-41].
20. Bosch, M. and R.M. Campos-Vazquez. *The Trade-Offs of Welfare Policies in Labor Markets with Informal Jobs: The Case of the "Seguro Popular" Program in Mexico*. 2014 November 2014// [cited 6; 4: [71-99].
21. Rizov, I. and E. Rodriguez-Cerezo. *The European Coexistence Bureau: Five Years' Experience*. 2014 2014// [cited 17; 1: [22-27].
22. Kaletski, E. and N. Prakash. *Does Political Reservation for Minorities Affect Child Labor? Evidence from India*. 2014 2014//; pages].
23. Cummins, J. *On the Use and Misuse of Child Height-for-Age Z-score in the Demographic and Health Surveys*. 2013 2013//; Pages].
24. Wu, B. *Mismeasurement in Pay-for-Performance: Evidence from an Intervention to Reduce Health Care Spending in China*. 2014 2014//; pages].
25. Bate, R., et al. *Poor Quality Drugs and Global Trade: A Pilot Study*. 2014 2014//.
26. Kueng, L. and E. Yakovlev. *How Persistent Are Consumption Habits? Micro-Evidence from Russia's Alcohol Market*. 2014 2014//.
27. Fischer, G., et al. *To Charge or Not to Charge: Evidence from a Health Products Experiment in Uganda*. 2014 2014//.
28. Granich, R., et al., *Expanding ART for treatment and prevention of HIV in South Africa: estimated cost and cost-effectiveness 2011-2050*. PLoS One, 2012. 7(2): p. e30216.
29. Kahn, J.G., et al., *Cost-effectiveness of antiretroviral therapy for prevention*. Curr HIV Res, 2011. 9(6): p. 405-15.
30. Bovier, P.A., K. Wyss, and H.J. Au, *A cost-effectiveness analysis of vaccination strategies against N. meningitidis meningitis in sub-Saharan African countries*. Soc Sci Med, 1999. 48(9): p. 1205-20.
31. LaForce, F.M. and J.M. Okwo-Bele, *Eliminating epidemic Group A meningococcal meningitis in Africa through a new vaccine*. Health Aff (Millwood), 2011. 30(6): p. 1049-57.
32. Griffiths, U.K., G. Hutton, and E. Das Dores Pascoal, *The cost-effectiveness of introducing hepatitis B vaccine into infant immunization services in Mozambique*. Health Policy Plan, 2005. 20(1): p. 50-9.
33. Brooker, S., et al., *Cost and cost-effectiveness of nationwide school-based helminth control in Uganda: intra-country variation and effects of scaling-up*. Health Policy Plan, 2008. 23(1): p. 24-35.
34. Sinick, J. *Cost-Effectiveness in \$/DALY for Deworming Interventions*. 2014 [cited 2014 8/19/2014]; Available from: <http://www.givewell.org/print/1579>.
35. J-PAL, *Deworming: A Best Buy for Development*. 2012, Abdul Latif Jameel Poverty Action Lab.
36. van Vugt, M., et al., *Malaria treatment and prophylaxis in endemic and nonendemic countries: evidence on strategies and their cost-effectiveness*. Future Microbiol, 2011. 6(12): p. 1485-500.
37. White, M.T., et al., *Costs and cost-effectiveness of malaria control interventions--a systematic review*. Malar J, 2011. 10: p. 337.
38. Jha, P., et al., *Tobacco Addiction*, in *Disease Control Priorities in Developing Countries*, D.T. Jamison, et al., Editors. 2006: Washington (DC).
39. Salomon, J.A., et al., *Common values in assessing health outcomes from disease and injury: disability weights measurement study for the Global Burden of Disease Study 2010*. Lancet, 2012. 380(9859): p. 2129-43.
40. GoB, G.o.B., *The Models of Care Project: An Analysis of the National Antiretroviral Treatment Programme, Masa, 2007-2011*. 2012. p. 1-43.
41. Daugla, D.M., et al., *Effect of a serogroup A meningococcal conjugate vaccine (PsA-TT) on serogroup A meningococcal meningitis and carriage in Chad: a community study [corrected]*. Lancet, 2014. 383(9911): p. 40-7.

42. Suraratdecha, C., C. Levin, and F.M. LaForce, *Disease Burden from Group A Neisseria meningitidis Meningitis in Hyperendemic Countries of the African Meningitis Belt*. Handbook of Disease Burdens and Quality of Life Measures, 2010: p. 1313-1322.
43. Hadler, S.C., et al., *The impact of hepatitis B vaccine in China and in the China GAVI Project*. Vaccine, 2013. 31 Suppl 9: p. J66-72.
44. Mwandawiro, C.S., et al., *Monitoring and evaluating the impact of national school-based deworming in Kenya: study design and baseline results*. Parasit Vectors, 2013. 6: p. 198.
45. Miguel, E. and M. Kremer, *Worms: Identifying Impacts on Education and Health in the Presence of Treatment Externalities*. Econometrica, 2004. 72(1): p. 159-217.
46. Eisele, T.P., et al., *Estimates of child deaths prevented from malaria prevention scale-up in Africa 2001-2010*. Malar J, 2012. 11: p. 93.
47. WHO, *World Malaria Report 2012*. 2012, World Health Organization: Geneva. p. 1-288.
48. PSI, *DALY Calculation for Malaria PPT (ACT) & Rapid Diagnostic Kit (RDK)*. Population Services International.
49. Cattaneo, M.D., et al., *Housing, Health, and Happiness*. American Economic Journal: Economic Policy, 2009. 1(1): p. 75-105.
50. Velazquez, F.R., et al., *Diarrhea morbidity and mortality in Mexican children: impact of rotavirus disease*. Pediatr Infect Dis J, 2004. 23(10 Suppl): p. S149-55.
51. Lamberti, L.M., C.L. Fischer Walker, and R.E. Black, *Systematic review of diarrhea duration and severity in children and adults in low- and middle-income countries*. BMC Public Health, 2012. 12: p. 276.
52. Passmore, J.W., et al., *The formulation and implementation of a national helmet law: a case study from Viet Nam*. Bull World Health Organ, 2010. 88(10): p. 783-7.
53. Olson, Z., et al., *Helmet regulation in Vietnam: impact on health, equity and medical impoverishment*. Inj Prev, 2016.
54. Ngo, A.D., et al., *Road traffic related mortality in Vietnam: evidence for policy from a national sample mortality surveillance system*. BMC Public Health, 2012. 12: p. 561.
55. Bishai, D.M. and A.A. Hyder, *Modeling the cost effectiveness of injury interventions in lower and middle income countries: opportunities and challenges*. Cost Eff Resour Alloc, 2006. 4: p. 2.
56. Hung, D.V., M.R. Stevenson, and R.Q. Ivers, *Prevalence of helmet use among motorcycle riders in Vietnam*. Inj Prev, 2006. 12(6): p. 409-13.
57. ILO, *ILO Global Wage Database*, I.L. Organization, Editor. 2012.
58. Cameron, L., M. Shah, and S. Olivia, *Impact Evaluation of a Large-Scale Rural Sanitation Project in Indonesia*, in *Policy Research Working Paper*. 2013, The World Bank: Washington, DC. p. 1-57.
59. Kosek, M., C. Bern, and R.L. Guerrant, *The global burden of diarrhoeal disease, as estimated from studies published between 1992 and 2000*. Bull World Health Organ, 2003. 81(3): p. 197-204.
60. Amin, S., A. Rangarajan, and E. Borkum, *Improving Sanitation at Scale: Lessons from TSSM Implementation in East Java, Indonesia*. 2011, Mathematica Policy Research Inc.
61. Levy, D.T., et al., *The role of tobacco control policies in reducing smoking and deaths in a middle income nation: results from the Thailand SimSmoke simulation model*. Tob Control, 2008. 17(1): p. 53-9.
62. GBD, *The Global Burden of Disease*, I.f.H.M.a. Evaluation, Editor. 2013.
63. Ranson, M.K., et al., *Global and regional estimates of the effectiveness and cost-effectiveness of price increases and other tobacco control policies*. Nicotine Tob Res, 2002. 4(3): p. 311-9.
64. Vassall, A., et al., *Cost-effectiveness of HIV prevention for high-risk groups at scale: an economic evaluation of the Avahan programme in south India*. Lancet Glob Health, 2014. 2(9): p. e531-40.

Tables

Table 1. Estimated Health Impacts and Economic Evaluation

Program	Time Horizon	Target Population	Key Health Outcomes	Deaths Averted	DALYs Averted	Cost-Effectiveness Ratio (USD\$/DALY)
MEDICINE AND TECHNOLOGY ROLL-OUT						
ART in Botswana	2002-2010	Over-18 population of Botswana	Morbidity and Mortality from AIDS	143,637	8,116,079	475
MenAfriVac in Chad	2011 - 2013	Under-30 population of Chad	Morbidity and Mortality from acute meningitis	12,469	875,844	96.36
HepB vaccine in China	2003 – 2009	Western and Middle Provinces of China, under-fives	Morbidity and Mortality from Hepatocellular Carcinoma, Cirrhosis, acute infection	93,200	3,100,000	3.33
De-worming in Kenya	2012 (year of scale up)	All school-age children in Kenya	Morbidity from soil-transmitted helminths and schistosomiasis	NA	99,568	56.63
Malaria Control in Zambia	2001-2010	Under-fives in Zambia	Morbidity and Mortality from acute Malaria	29,900	2,500,000	13.50
Piso Firme in Mexico	2007-2013	Mexican households with dirt floors, population under 6 years old	Diarrhea morbidity and mortality, Anaemia morbidity	408	34,248	NA
EXPANDING ACCESS TO HEALTH SERVICES						
<i>Plan Nacer</i> Argentina	2005-2008	Newborn population in 7 provinces in northern Argentina	Neonatal mortality and low birth weight morbidity	733	72,800	\$814

TARGETED CASH TRANSFERS TO IMPROVE HEALTH						
CT-OVC in Kenya	2007-2009	Households with an orphan or vulnerable child	Delayed sexual debut, reduced likelihood of multiple sexual partners and early pregnancy among girls, and improved mental health among boys	NA	NA	CTR of 0.34
POPULATION-WIDE BEHAVIOR CHANGE						
Helmets in Vietnam	2008 (single year)	Entire country, all ages	Injuries and Deaths from traffic accidents	1,557	90,582	1,248
Sanitation in Indonesia	2007 - 2010	East Java Indonesia, population under 5	Diarrhea morbidity and mortality	220	18,666	213
Tobacco Control in Thailand	1991-2006	Entire Thailand population, ages 15 and over	Deaths and morbidity averted from COPD, Lung Cancer and Cardiovascular Disease	29,357	541,695	75.40
Avahan HIV in India	2004-2008	Entire Avahan area, 83 districts	Morbidity and Mortality from AIDS	202,000	3,471,973	46.00

Note: The cost-effectiveness of *Plan Nacer* was conducted by the researchers who also conducted the impact analysis, Gertler et al. 2014. CTR is the cash-transfer ratio. NA means that no significant health impact measure

Appendix 1 – Detailed Estimation Table

Table EXT.1. Detail: Estimates of Deaths and DALYs averted

Program	Time Horizon	Target Population	Key Health Outcomes	Deaths Averted	DALYs Averted	Putting DALYs into context	Cost/[unit] (USD)	Cost per DALY ratio (\$financial/DALY)	Putting ICER into Context
Medicine and Technology Roll-Out									
ART in Botswana (2012 GDP per capita: USD \$7,255)	2002-2010	Over-18 population of Botswana	Morbidity and Mortality from AIDS	143,637	8,116,079	WHO GHE estimates 1,078,100 DALYs from AIDS in 2000 and 324,600 DALYs from AIDS in 2012 in Botswana [16].	\$813 million	\$475	Laxminarayan 2006 (DCP2): \$350/DALY - \$1494/DALY [2]. Granich 2012 in ZA find anywhere from cost-saving to \$1400/DALY [28]. Kahn 2011 find \$200/DALY in ZA [29].
MenAfriVac in Chad (2012 GDP per capita: USD \$1,053)	2011 - 2013	Under-30 population of Chad	Morbidity and Mortality from acute meningitis	12,469	875,844	WHO GHE estimates 456,700 DALYs from Acute Meningitis in Chad population <30 in 2012 [16].	Budget: \$70 million for MVP creation and to develop vaccine \$1.40 per vaccinated person (LaForce 2011)	96.36	Bovier 1999 et al. Finds routine polysaccharide vaccination is about \$50/QALY and about \$1200 per fatal case in SSA [30]. Laforce and Okwo-Bele – Evidence that switching to conjugate vaccine is cost-saving because of improved duration of effect over polysaccharide vaccine [31].
HepB vaccine in China (2012 GDP per capita: USD \$6,092)	2003 – 2009	Western and Middle Provinces of China, under-fives	Morbidity and Mortality from Hepatocellular Carcinoma, Cirrhosis, acute infection	93,200	3,100,000	WHO GHE estimates 1,479,400 DALYs from acute HepB in all ages in 2000. 9,757,700 DALYs from Liver Ca in 2000 in all ages and 4,587,500 DALYs from Cirrhosis in all ages in 2000 [16].	\$10,345,200 Budget: Initial 5 year estimated project cost = \$76 million	\$3.33	DCP2: \$23,520/DALY (table 2.B.2, from deaths averted only) [2]. Griffiths 2005: \$36/DALY (undiscounted DALY); \$47/DALY (discounted DALY) [32].
De-worming in Kenya (2012 GDP per capita: USD \$1,165)	2012 (year of scale up)	All school-age children in Kenya	Morbidity from soil-transmitted helminths and schistosemiasis	NA	99,568	WHO GHE estimates 154,934 DALYs in 2000 in children ages 5-14. This declines to 40,267 DALYs in 2012 in children ages 5-14 [16].	NA	\$56.63	DCP2: \$3/DALY with range \$2/DALY - \$9/DALY (albendazole, a. trichuris & hookworm); \$336/DALY - \$692/DALY (praziquantel only, schisto); \$8/DALY - \$19/DALY (albendazole + praziquantel) [2]. Brooker 2008 et al. US\$3.19/case anaemia averted (Uganda) [33]. GiveWell: \$28.19-\$70.48/DALY (schisto); \$82.54/DALY (STH) [34]. J-PAL: US\$4.55/DALY [35].

Malaria in Zambia (2012 GDP per capita: USD \$1,771)	2001-2010	All newborns in Zambia	Morbidity and Mortality from acute Malaria	29,900	2,500,000	WHO GHE 760,100 DALYs from malaria in 2000 in Zambia in all ages (697,800 of these are in 0-4 years). [16].	Budget: Total budget of \$60 million, including in-kind contributions and \$25 million from MOH	\$13.5	DCP2: ITN: \$11/DALY, range \$5/DALY - \$17/DALY; IRS: \$17/DALY, range \$9/DALY - \$24/DALY; IPTT: \$19/DALY, range \$13/DALY - \$24/DALY (with sulfadoxine pyrimethamine, with other drug \$2-\$11/DALY; ACT: <\$150/DALY (change from choloquine, will get worse over time though) [2]. Van Vugt 2011 et al. (review): IPTT: \$2.90-\$39.63/DALY (Conteh); IPTp: \$1/DALY (Mbonye, Sicuri) [36]. White 2011 et al (review): ITN: \$27/DALY (8.15-110), IRS: \$143/DALY (135-150), IPT: \$24/DALY (1.08-44.24), (note: all CE ratios are provider perspective) [37].
Piso Firme in Mexico (2012 GDP per capita: USD \$9,817)	2007-2013	Mexican households with dirt floors, population under 6 years old	Diarrhea morbidity and mortality	408	34,248	WHO GHE estimates 178,100 DALYs from diarrheal disease in Mexico in 2012 [16].	NA	NA	NA
Expanding Access to Health Services									
<i>Plan Nacer</i> Argentina (2012 GDP per capita: USD \$13,693)	2005-2008	Newborn population in 7 provinces in northern Argentina	Neonatal mortality and low birth weight morbidity	733	72,800	WHO GHE estimates 237,800 DALYs from neonatal conditions in 0-4 years in 2000 (all, not specific for deaths) [16].	NA	\$814/DALY, range \$442-5,086/DALY	NA
Targeted Cash Transfers to Improve Health									
CT-OVC in Kenya (2012 GDP per capita: USD \$1,165)	2007-2009	Households with an orphan or vulnerable child	Delayed sexual debut, reduced likelihood of multiple sexual partners and early pregnancy among girls, and improved mental health among boys	NA	NA	NA	Budget: 776,677,119 KSH for 2006-2009 pilot	CTR of 0.34	NA

Population-wide Behavior Change									
Helmets in Vietnam (2012 GDP per capita: USD \$1,755)	2008 (single year)	Entire country, all ages	Injuries and Deaths from traffic accidents	1,557	90,582	WHO GHE estimates 1,270,400 DALYs from road injury in all ages in Vietnam in 2012 [16].	NA	1,248	\$467/DALY (Thailand) [2].
Sanitation in Indonesia (2012 GDP per capita: USD \$3,551)	2007 - 2010	East Java Indonesia, population under 5	Diarrhea morbidity and mortality	220	18,666	WHO GHE estimates 930,100 DALYs from Diarrhea in 0-4 year in Indonesia in 2012 [16].	\$13,989,000	213	\$4,185/DALY, range \$1,974-\$6,390/DALY (Improved infrastructure for at least 5 years). \$141/DALY, range \$11-\$270/DALY, low cost latrines where needed [2].
Tobacco in Thailand (2012 GDP per capita: USD \$5,479)	1991-2006	Entire Thailand population, ages 15 and over	Deaths and morbidity averted from COPD, Lung Cancer and Cardiovascular Disease	29,357	541,695	WHO GHE 2000: lung cancers - 340,000 DALYs. COPD - 675,000 DALYs. CVD - 2,738,000 DALYs [16]. WHO GHE 2012: lung cancers - 467,000 DALYs. COPD - 739,000 DALYs. CVD - 3,151,000 DALYs [16].	NA	75.40	Price interventions: \$22/DALY, range \$13-195/DALY globally. (range, \$3-\$142/DALY in LMIC). Non-Price interventions: \$353/DALY (non-price e.g. advertising bans, smoking restrictions, supply reduction, health information).NRT: \$396/DALY, range \$54-\$674/DALY [38].
Avahan – India (2012 GDP per capita: USD \$1,503)	2004-2008	Entire Avahan area, 83 districts	Morbidity and mortality from AIDS	202,000 HIV infections averted	3,471,973	WHO GHE 2000: HIV/AIDS 6,377,000 DALYs [16]. WHO GHE 2012: HIV/AIDS 8,041,000 DALYs [16].	\$158,570,000 Vassall 2014: \$327/person reached in the 4 years of the program.	46	DCP2: VTC: \$14-\$261/DALY; Peer education for high-risk groups (SWs and IDUs): \$1-\$74/DALY; Social marketing condoms: \$19-\$205/DALY; PMTCT with nevirapine: \$192/DALY range \$7-\$377/DALY; STI treatment: \$57/DALY range \$9-\$105/DALY; ART treatment: \$10-\$500/DALY; Home care: \$673/DALY; ART in low adherence: \$922/DALY range \$350-\$1494/DALY; Treat opportunistic infection: \$156/DALY range \$3-\$310/DALY; Chandrashekar 2012 et al (ppt) \$18-329/DALY[2].

Note: CTR: cash-transfer ratio, is the ratio of resources to the total amount of the transfer.

Appendix 2 – Model Details and Results

The following 10 sections in this appendix provide more details about the modeling approaches, assumptions made and key references for the calculation of disease burden and costs that went into the consideration of cost-effectiveness. Estimates for the case of *Plan Nacer* in Argentina and the case of cash transfers for orphans and vulnerable children in Kenya are not included here as estimates were taken directly from other sources.

1. Estimating the Disease Burden and Cost-Effectiveness: ART in Botswana

I. Model Details

Disease burden

We began by taking the 2002 population in Botswana over the age of 18. We used population estimates from the UN Population Division and apportioned the 5 year age groups equally into single year age groups. We followed the initial 2002 cohort until the year 2010 and also assumed that future cohorts were the same in terms of population size [10].

The population that was positive for HIV/AIDS was estimated using a prevalence rate of 25%. We assume that this prevalence remains constant for the remainder of the time period, which is a plausible assumption when looking at the data from UNAIDS for Botswana. In a situation where Masa is not implemented, we use a case-fatality rate (CFR) of 12.8% for the HIV/AIDS positive population [9]. To find the avertable deaths, a CFR of 2.7% was used in the scenario where ART is available in Botswana. Years of life lost were calculated from the age of death and a maximum life span of 86 years. Years of life with disability (YLD) were calculated using a disability weight of 0.547 for HIV/AIDS patients not on ART. We find that this is reduced to 0.053 when patients are on ART [39].

Box 1.1

Model Parameters Perspective: Provider

- Modeling approach: Simulated cohort of 2002 population
- Timeframe: 2002-2010
- Target population: Botswana population >18 years
- Health outcomes: HIV morbidity and mortality
- Currency unit: US\$
- Summary health measure: Disability-adjusted life year (DALY)

Key Assumptions

- All HIV/AIDS positive people were eligible for the Masa program.
- Masa is scaled up in the first year (2002) and maintains full coverage for the entire period.

Costs of the Program

The Masa program costs \$357 per patient for the government in 2011 [40]. This unit cost was multiplied by the projected patients who receive ART. This is 238,000 people in 2002 representing 2.28 million patient-years for the period 2002-2011. Using the \$357 unit costs gives a total program cost of \$813 million.

II. Results

The total deaths averted for the Botswana HIV/AIDS population is 143,637 which gives 8,116,079 DALYs averted. Taking the total costs into account gives a cost-effectiveness ratio of \$100.29 per DALY averted.

Table 1.1

Infections Averted	Deaths Averted	DALYs Averted	Cost/[unit] ([currency])	ICER (\$/DALY)
NA	143,637	8,116,079	\$813 million	100.29

2. Estimating the Disease Burden and Cost-Effectiveness: MenAfriVac in Chad

I. Model Details

Disease burden

The burden of disease attributable to meningitis A prior to vaccine introduction and after introduction was calculated using the incidence of meningitis A reported by Daugla and colleagues [41]. Pre-vaccine incidence was 43.8 per 100,000 population and post-vaccine incidence was 2.48 per 100,000 population. Population estimates for Chad in 2010 were taken from the UN Population Division database [10].

In each situation of pre and post-vaccine, the case-fatality rate (CFR) of 11.6% was used to calculate the total number of deaths [42]. The estimate of CFR has a high level of uncertainty and is expected to vary by age group as well as access to medical care [30].

Costs

While there are no available canned estimates for the provider costs for MenAfriVac in Chad, the vaccine is cheap, at around \$0.40 per dose, which increases to \$1.40 per dose with the addition of injection material as well as operational and infrastructure costs [31].

Box 2.1**Model Parameters**

- Perspective: Provider
- Modeling approach: Simulated cohort
- Timeframe: 2011-2013
- Target population: Population under 30 in Chad.
- Health outcomes: Acute meningitis A morbidity and mortality.
- Currency unit: US\$
- Summary health measure: Disability-adjusted life year (DALY)

Key Assumptions

- Scale-up of the MenAfriVac vaccine in Chad in 2011 was nearly instantaneous.
- The CFR of meningitis A does not vary with the incidence of disease.

II. Results

Results from this modeling exercise are provided in the following table.

Table 2.1

Deaths Averted	DALYs Averted	Cost/[unit] ([currency])	ICER (\$/DALY)
12,469	875,844	NA	96.36

3. Estimating the Disease Burden and Cost-Effectiveness: Hepatitis B in China

I. Model Details

Disease burden

The number of deaths averted from the China GAVI Project (CGP) was taken from a study that assessed the impact over the years 2003 to 2009 [43]. This study provided an estimate of the total Hepatitis B related deaths averted in the CGP provinces from all vaccination activities as well as an estimate of the averted Hepatitis B deaths that are attributed to the CGP program. The total estimated averted burden was 680,000 deaths and CGP-attributable averted burden was 93,200 for the years 2003-2009 [43].

The causes of the averted deaths were estimated according to the cause-specific distribution of deaths [43]. The three causes of death that represent the majority of the mortality attributed to Hepatitis B are: Hepatocellular carcinoma (HCC), Cirrhosis and Fulminant infection.

The years of life lived in disability (YLD) were calculated for each of the three causes of mortality according to estimates in the literature of the duration of illness and the associated disability weight [32, 39].

The years of life lost (YLL) were calculated by taking the difference between a maximum assumed life span of 86 years and subtracting that by the average age of death for each cause and multiplying it by the number of deaths in each cause.

Costs

Hadler et al. also include estimates of cost of the Hepatitis B program [43]. They estimate that program cost \$76 million in program costs for the years 2002-2007 and that the undiscounted cost per future infection averted and future death averted is \$28.7 and \$160. These are estimated using the total number of averted deaths and not just the incremental averted deaths for the program. Our calculation of the results finds that with a simple division, the total cost per future averted death is \$111 (\$76 million divided by 680,000 deaths) and the total cost per averted DALY is \$3.36 (\$76 million divided by 22.64 million DALYs). We use the total deaths averted instead of the incremental deaths averted due to the difficulty of establishing an estimate for the incremental cost.

Box 3.1

Model Parameters and Assumptions

- Perspective: Provider
- Modeling approach: Convert averted deaths according to disease timeline
- Timeframe: 2003-2009
- Target population: Underfives in Western and Middle Provinces of China
- Health outcomes: Morbidity and mortality from Hepatocellular Carcinoma, Cirrhosis and fulminant infection.
- Currency unit: US\$
- Summary measure of effect: Disability-adjusted life year (DALY)

Key Assumptions

- The three causes of death: HCC, Cirrhosis and fulminant infection reflect the total mortality envelope related to Hepatitis B infection.
- The proportion of causes of death for the incremental averted mortality from Hepatitis B are the same as the proportion for the total mortality from Hepatitis B.
- Co-morbidity between causes of death are negligible.

II. Results

Results from this modeling exercise are provided in the following table.

Table 3.1

Deaths Averted	DALYs Averted	Cost/HepB death averted ([currency])	ICER (\$/DALY)
93,200	3,100,000	\$111	\$3.33

4. Estimating the Disease Burden and Cost-Effectiveness: De-Worming in Kenya

I. Model Details

Disease burden

To estimate the disease burden from deworming, we begin with the estimates for the total number of children treated for soil-transmitted helminthes (STH) (hookworm, whipworm and roundworm) and for schistosomiasis. We assumed that if a child was treated for either of these parasites, then they were infected.

Since we did not know how many children were infected by each of the three types of STH, we apportioned them to a parasite according to published estimates by Mwandawiro and colleagues [44]. For the fourth parasite, schistosomiasis, we simply used the total number treated.

DALYs are calculated for each of the four parasites by using an average DALY per person estimate used by Miguel and Kremer [45]. These are presented in Table 4.1.

Table 4.1

Parasite	DALY/person
1. Schistosomiasis	0.097
2. Hookworm	0.0013
3. Whipworm (<i>T. trichuria</i>)	0.0005
4. Roundworm (<i>A. lumbricoides</i>)	0.0004

Costs and Costs-effectiveness

There has been a vibrant debate about the cost-effectiveness estimates for deworming. In general, these have shown that deworming is a great value with a cost-effectiveness ratio of less than \$100 per DALY averted. The non-profit GiveWell has estimated that the cost-effectiveness ratio is between \$29 to \$70 per DALY averted for schistosomiasis and the estimate for soil-transmitted helminthes is \$82.54 per DALY averted. We used costs that were provided by GiveWell of \$0.37 per child treated per year for schistosomiasis and \$0.085 per child treated per year for soil transmitted helminths [34].

Box 4.1

Model Parameters

- Perspective: Provider
- Modeling approach: Single-year cross-sectional prevalence
- Timeframe: April 2013 – March 2014
- Target population: School-age children in Kenya
- Health outcomes: Morbidity from soil-transmitted helminth and schistosomiasis.
- Currency unit: US\$
- Effect unit: Disability-adjusted life year (DALY)

Key Assumptions

- All children treated for STH and schistosomiasis were infected.
- Assume no overlap in infections between soil-transmitted helminthes (STH) parasites.

II. Results

Results from this modeling exercise are provided in the following table.

Table 4.2

Deaths Averted	DALYs Averted	Cost/[unit] ([currency])	ICER (\$/DALY)
NA	99,568	\$0.37 per child per year (schistosomiasis), \$0.085 per child per year (STH)	56.63

5. Estimating the Disease Burden and Cost-Effectiveness: Malaria in Zambia

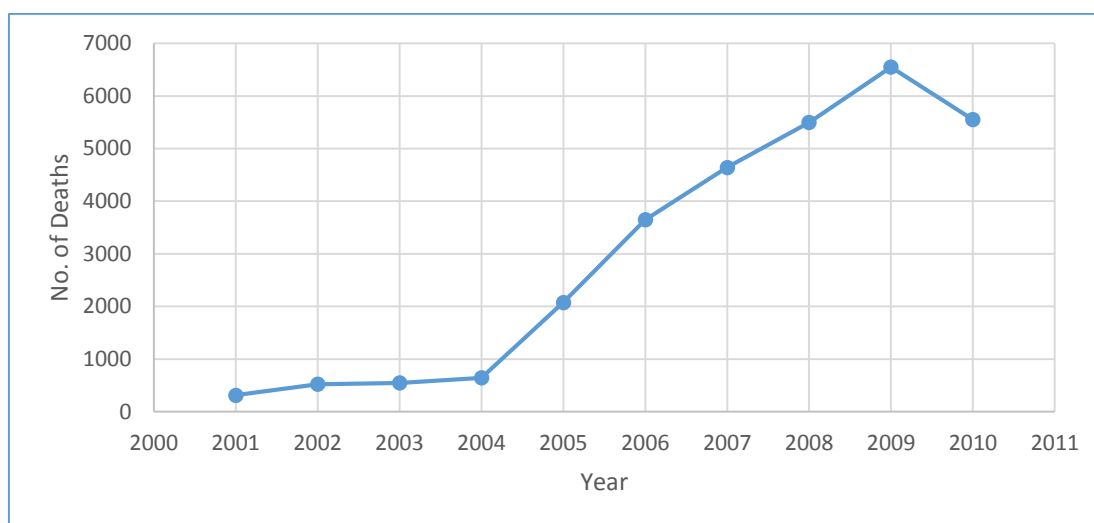
I. Background

The past decade's massive scale-up of malaria activities in Zambia has led to large health gains. We modeled the DALYs and costs for this scale up in terms of health benefits to under five year olds in Zambia from 2001-2010.

II. Methods

With Scale-up from 2001-2010, there were an estimated 29,990 deaths averted from malaria in Zambia [46]. The year by year estimates of these deaths is seen in Figure 5.1. Of these, 96.1% came from vector control and 3.9% came from prevention at pregnancy. DALYs were estimated using the GBD 2010 disability weight, an average estimate of duration and an average age of death of 1.8 [39, 47, 48]. Costs were measured using mean costs from the literature for ITN for vector control and IPT for pregnancy interventions [37].

Figure 5.1 Modeled Deaths Averted in Children in Zambia: 2001 - 2010



Box 5.1

Model Parameters

- Modeling approach: Year on year mortality envelope model
- Timeframe: 2001 - 2010
- Target population: Under five year olds in Zambia
- Health outcomes: Morbidity and mortality from acute malaria
- Currency unit: US\$
- Effect unit: Disability-adjusted life year (DALY)

Key Assumptions

- All health impacts are encompassed through averted mortality. Additional impacts from morbidity of those who do not die is not captured.

Source: [46]

III. Results

Results from this modeling exercise are provided in the following table.

Table 5.1

Deaths Averted	DALYs Averted	Cost/[unit] ([currency])	ICER (\$/DALY)
29,900	2,525,579	\$2.20 for ITN per person per year; \$2.06 IPT per pregnant woman per year	\$13.50

6. Estimating the Disease Burden and Cost-Effectiveness: Piso Firme in Mexico

I. Model Details

Piso Firme was originally introduced in 2000 in one state in Mexico, Coahuila, and was later adopted in more states in 2003. Our model looks at the Mexican population determined to be in need of the Piso Firme program and calculates the estimated health effects in terms of deaths and DALYs averted from the scaled up program.

Disease burden

We begin by taking the estimate of the number Mexican households in need of Piso Firme. This figure is 3 million in 2000 according to Cattaneo et al., which represents 13.5% of the total households in the year 2000 [49]. We then apply this percentage to the total population to determine the total number of people who are eligible for receiving Piso Firme.

We next modeled the total burden of diarrhea for the Piso Firme target population using information from Velasquez et al. [50]. Here the incidence of diarrhea in a single year was 4,588 per 100,000 under five and the mortality from diarrhea in a given year was 23.2 per 100,000 children under five. We made several strong assumptions at this point that population, the force of infection and the force of mortality for diarrhea would remain unchanged by age and over time.

To calculate YLDs for diarrhea, the cases were divided into whether they were mild, moderate or severe. Lamberti et al. 2012 provides estimates for the distribution of mild, moderate and severe cases as well as for

the duration of each type of case [51]. The associated disability weights for each type of diarrhea were taken from the Global Burden of Disease 2010 update [39].

The YLLs were calculated by applying the yearly mortality rate of diarrhea obtained from Velasquez et al. 2004 to the susceptible population. We assumed a maximum lifespan of 86 when calculating the total YLLs.

To then move to the avertable burden of diarrhea realized with Piso Firme, we introduced the effect estimate from Cattaneo et al. [49]. This represented a 1.8% reduction in the incidence rate and mortality rate of diarrhea. Because of our strong assumptions that the population and epidemiology do not vary from year to year, the averted diarrhea disease burden is linear in time.

Cost-effectiveness

Calculating the cost-effectiveness for this program is beyond the scope of this exercise. Given the many benefits of the Piso Firme program, it would require a large effort to accurately quantify the total benefits. We have focused on the diarrhea disease burden because it is readily estimated with an effect estimate (reduction in incidence) and background data to support modeling diarrhea in Mexican children over time.

We can, however, estimate that Piso Firme cost (Mexican peso) \$16,253 million for the years 2007 to 2013. In 2007 USD this is more than \$1.2 billion.

Box 6.1

Model Parameters

- Perspective: Provider
- Modeling approach: Simulated cohort
- Timeframe: 2007-2013
- Target population: Mexican households with dirt floors and associated population under 6 years.
- Health outcomes: Diarrhea morbidity and mortality
- Currency unit: US\$
- Effect unit: Disability-adjusted life year (DALY)

Key Assumptions

- Assume that household composition is the same for all households. Specifically, if the household composition for those who are eligible for Piso Firme and for those who aren't varies, then our estimates will be off. There is a good chance that they do vary so this would be a point for further investigation.
- The population will remain unchanged over time. The population in 2000 was used as a baseline.
- The force of infection and mortality for diarrhea remains unchanged over time.

II. Results

Results from this modeling exercise are provided in the following table.

Table 6.1

Deaths Averted	DALYs Averted	Cost/[unit] ([currency])	ICER (\$/DALY)
408	32,248	NA	NA

7. Estimating the Disease Burden and Cost-Effectiveness: Motorcycle Helmets in Vietnam

I. Background

Recent enforcement of a helmet law in Vietnam has led to an attributable decline in deaths and serious injuries [52]. At the time of this analysis, a cost-effectiveness study had not been conducted, although a recent estimate has shown that the law has prevented a large amount of acute care costs and averted high levels of income loss [53].

II. Methods

We took the aggregate figures for death and serious injury from the impact evaluation for the year 2008 and used this to calculate DALYs. To do so, we apportioned deaths and serious injuries according to the age distribution found in a study of road traffic deaths in Vietnam [54]. The disability weight for long-term disability was used when calculating morbidity effects [39].

To estimate the cost of the policy, we used an approach based on that of Bishai et al. [55]. We assumed there would be infractions for 1% of motorcycle riders, police officers were able to issue 2,500 citations per year and that the cost of the helmet was \$2.00 [55-57].

Box 7.1

Model Parameters

- Perspective: Provider
- Modeling approach: Mortality envelope model
- Timeframe: 2008
- Target population: Entire population of Vietnam
- Health outcomes: Injury and death from road traffic accidents
- Currency unit: US\$
- Effect unit: Disability-adjusted life year (DALY)

Key Assumptions

- The age distribution for deaths applies to serious injuries as well.
- Estimates of deaths and serious injury are independent, at least in terms of DALY calculation.

III. Results

Results from this modeling exercise are provided in the following table.

Table 7.1

8.	Severe Injury Averted	Deaths Averted	DALYs Averted	Cost/[unit] ([currency])	ICER (\$/DALY)
	2,495	1,557	90,582	\$2.00 per helmet; \$1,027 salary for police officer in 2008.	\$1,248

Estimating the Disease Burden and Cost-Effectiveness: Sanitation in Indonesia

I. Background

The Total Sanitation and Sanitation Marketing (TSSM) project is an effort in Indonesia to improve sanitation and hygiene behavior. The program has been successful at increasing the access to toilets and reducing the prevalence of diarrhea in children [58].

II. Methods

Disease burden

The sanitation project has the potential to influence outcomes of diarrhea, helminth infection and acute respiratory infection. In their study of the program, Cameron colleagues only find a significant impact on outcomes for diarrhea between a treatment and control group. For this reason, only the averted burden from diarrhea is modeled for burden and cost-effectiveness.

We use population estimates from the UN Population division to obtain the under five population for Indonesia in 2010 [10]. Since we could only find the East Java population for 2010, we assume that it is subject to the same population growth rate as the country as a whole and reduce the population to a 2007 estimate in order to obtain the 3 year effect of the sanitation program. We also assume that the proportion of under fives to the population as a whole in 2007 is the same as that for 2010. The 2007 population estimate for East Java is 35,965,040 with 10.4%, or 3,746,837 under fives.

There is a reported 4.6% prevalence of diarrhea in under fives for a control group, which is reduced to 3.3% for under fives where sanitation was implemented [58]. To obtain years of life with disability (YLDs) from diarrhea, we divide the diarrhea cases into mild, moderate and severe cases according to the percentages used by Lamberti et al. [51]. This study also presents durations for each type of diarrhea and disease weights from the global burden of disease project [39]. We present this information in Table 8.1.

Table 8.1

Type of Diarrhea	Percent of Cases*	Duration (days)*	Disease Weight**
1. Mild	64.8%	4.3	0.061
2. Moderate	34.7%	6.4	0.202
3. Severe	0.5%	8.4	0.281

Source:*[51], **[39]

Finally, we use a case-fatality rate of 0.15% for all cases of diarrhea, which is obtained from a study by Kosek and colleagues to obtain the number of deaths in each situation of pre and post-sanitation intervention [59]. We use a maximum life expectancy of 86 years to obtain the averted years of life lost (YLLs) and do not discount future YLLs gained.

Our four year estimate for deaths averted in under fives in East Java due to the sanitation program is 220, which is equal to approximately 18,666 DALYs in the same period from diarrhea morbidity and life years gained.

Cost-effectiveness

We find that the 4 year cost for the sanitation program was \$13,989,000, or \$78 per latrine) with 72% of this figure coming from households, 21% coming from the program budget and a further 7% coming from the government [60]. When dividing this estimate by the 4 year total DALYs averted, we arrive at a cost-effectiveness ratio of \$749 per DALY averted. If we subtract out the household contributions of \$10,000,000, then the cost-effectiveness ration drops further to \$213 per DALY averted.

Our estimates of cost-effectiveness for the sanitation program may be biased upward since there are most likely non-diarrhea health benefits that occur as well. We also only model the cross-sectional cost-effectiveness, that is, the costs and effects only realized in the 4 year program period, though there are likely to be effects of the program that last well into the future.

Box 8.1

Model Parameters and Assumptions

- Perspective: Provider
- Modeling approach: Simulated cohort
- Timeframe: 2007-2010
- Target population: East Java Indonesia, population under 5
- Health outcomes: Diarrhea morbidity and mortality
- Currency unit: US\$
- Effect unit: Disability-adjusted life year (DALY)

Key Assumptions

- Case-fatality rate does not change for a change in diarrhea prevalence.
- The population in East Java grows at the same rate as that of the whole country and has the same proportion of children under five.

III. Results

Results from this modeling exercise are provided in the following table.

Table 8.2

Deaths Averted	DALYs Averted	Cost/[unit] ([currency])	ICER (\$/DALY)
220	18,666	\$78 per latrine	213

9. Estimating the Disease Burden and Cost-Effectiveness: Tobacco in Thailand

I. Background

Using a modeling approach and the SimSmoke model applied in Thailand, Levy and colleagues find that tobacco policies have potentially prevented many tobacco-related deaths [61].

II. Methods

Disease Burden

We began by taking the information for smoking related deaths from the GBD project for Thailand in 1990, 1995, 2000 and 2005. This included deaths from: 1) tracheus and lung cancer, 2) COPD and 3) cardiovascular and circulatory disease [62]. The amount of deaths that each of these contributed to overall smoking deaths was then taking as a yearly proportion in each of the time periods and a linear trend was used to interpolate estimates between years.

The total deaths that we find in our model is different from the reported deaths in Levy et al. by 2,510 [61]. Given that this represents a low percentage of the total deaths, we are confident that our model is relatively accurate.

Costs

Estimating the costs of fiscal policies such as taxation are difficult. We take an estimate from Ransom et al. that a tax policy is likely to cost 0.005% of GDP [63]. We thus apply this percentage to the GDP for Thailand from 1991-2006. This leads to a total cost of \$24,995,000 over the time period for the tax policy.

Box 9.1

Model Parameters

- Perspective: Provider
- Modeling approach: Cohort model
- Timeframe: 1991-2006
- Target population: Entire Thai population, ages 15 and over
- Health outcomes: Mortality and morbidity from COPD, Lung Cancer, and Cardiovascular Disease
- Currency unit: US\$
- Effect unit: Disability-adjusted life year (DALY)

III. Results

Results from this modeling exercise are provided in the following table.

Table 9.1

Deaths Averted	DALYs Averted	Cost/[unit] ([currency])	ICER (\$/DALY)
29,357	541,695	0.005% of GDP	75.40

10. Estimating the Disease Burden and Cost-Effectiveness: Avahan

I. Background

Avahan is an HIV prevention program that has been introduced in 83 districts in Southern India. The program has an *in situ* economic component where researchers have published the realized health impact and resource usage of the program. The costs, health impacts effects and cost-effectiveness have been estimated and published in a study in the *Lancet Global Health* in 2014 [64].

II. Methods

We relied heavily on the published estimates of averted burden and cost-effectiveness in the analysis of total averted burden and cost-effectiveness for the *Millions Saved* report.

Disease burden

An estimate of the averted disease burden in terms of disability adjusted life years (DALYs) was reported for 22 Avahan districts for the years 2004-2008. Using the total DALYs averted for the 22 districts $D_{T,22}$ and the total infections averted for the 22 districts $I_{T,22}$ we derived an average number of DALYs averted per infection D_i :

$$D_i = D_{T,22} \div I_{T,22} \quad (1)$$

We then used the average DALY per infection to estimate the total DALYs averted for all 83 districts $D_{T,83}$ using the extrapolated estimate of total infections averted for all 83 districts $I_{T,83}$ in the following equation:

$$D_{T,83} = D_i \times I_{T,83} \quad (2)$$

Cost-effectiveness

The cost of resource use was also provided in the published work by Vassall et al. [64]. The total cost per averted infection C_i was used from Table 10.1 of this article as the best estimate of the cost for the fully scaled program. The cost-effectiveness ratio (CER) was calculated as the total cost per averted infection divided by the total averted DALYs according to the following equation.

$$ICER_{83} = (I_{T,83} \times C_i) \div D_{T,83} \quad (3)$$

Given that each term in the numerator and the denominator is an incremental measure (they are “averted”), they implicitly account a counterfactual scenario where no Avahan program is implemented and thus the CER is labeled an incremental CER (ICER) in equation 3. Specific details on the scope of the modeling approach are described in Box 10.1.

Box 10.1**Model Parameters**

- Perspective: Provider
- Modeling approach: Linear extrapolation
- Timeframe: 2004-2008
- Target population: Entire population in Avahan program area in 83 Indian districts
- Health outcomes: HIV infections
- Currency unit: 2011 US\$
- Effect unit: Disability-adjusted life year (DALY)

Key Assumptions

- The efficiency of the Avahan programme in the sampled districts can be extrapolated to non-sampled districts as well.

III. Results

The reported estimate of 202,000 infections averted yielded an average estimate of 17.19 DALYs per averted infection and 3,471,973 total DALYs averted for the years 2004-2008 for the scaled-up Avahan program in 83 districts. The total cost per averted infection was reported as \$785 (2011 US\$), which gives a \$46/DALY averted (all shown in Table 10.1). This estimate is the same as that reported by Vassall et al. as their base case estimate using total provider costs. This is the expected result given the simple linear extrapolation approach used [64].

Table 10.1

Infections Averted	Deaths Averted	DALYs Averted	Cost/HIV infection averted (2011 US\$)	ICER (\$/DALY)
202,000	NA	3,471,973	\$785	46