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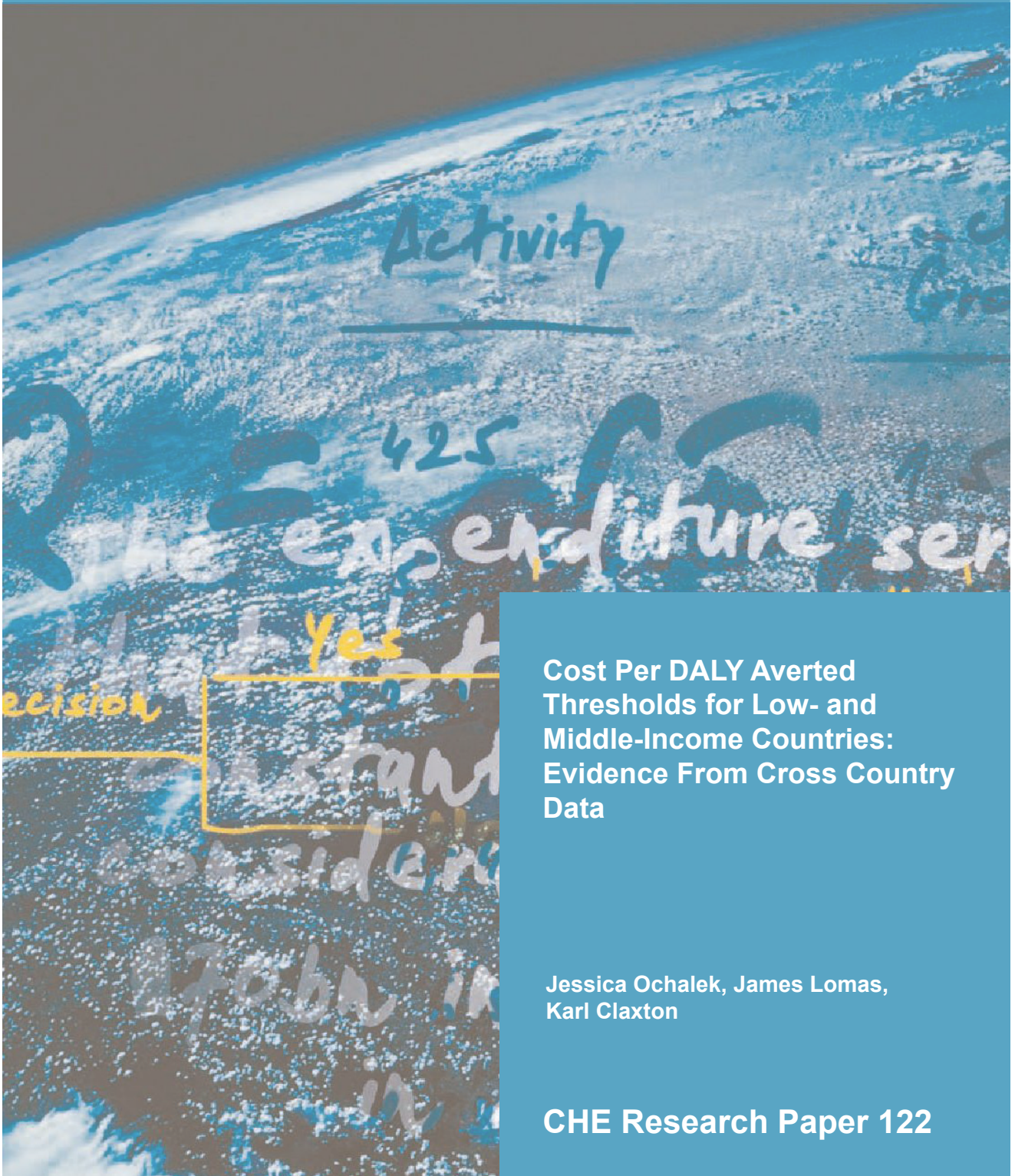
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Centre For Health Economics

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**Cost Per DALY Averted
Thresholds for Low- and
Middle-Income Countries:
Evidence From Cross Country
Data**

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CHE Research Paper 122

Cost per DALY averted thresholds for low- and middle-income countries: evidence from cross country data

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Abstract

Low- and middle-income countries (LMICs) face difficult decisions about which health care interventions are worthwhile given existing constraints on health care expenditure. Decisions require some assessment of the health opportunity costs of proposed investments, i.e., a 'supply side' cost-effectiveness threshold (CET) that represents the likely health effects of changes in health care expenditure.

This paper provides a framework for generating country-level CETs using existing published estimates of the mortality effect of health expenditure. Two different estimation strategies are used (Bokhari et al (2007) and Moreno-Serra and Smith (2015)) and, where possible, estimation is extended to include other measures of mortality, survival and disability outcomes, reflecting the demographic and other characteristics of each LMIC.

The results suggest that CETs representing likely health opportunity costs tend to be below the lower bound suggested by WHO of 1x GDP per capita. Hence, many previous and existing recommendations about which interventions are cost-effective that are based on the WHO threshold are likely to do more harm than good.

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List of abbreviations

CEA	Cost effectiveness analysis
CET	Cost effectiveness threshold
CLE	Conditional life expectancy
DALY	Disability adjusted life year
GBD	Global Burden of Disease
GDP	Gross domestic product
HIC	High-income country
HITAP	Health Intervention and Technology Assessment Program
HRQoL	Health-related quality of life
ICER	Incremental cost effectiveness ratio
IV	Instrumental variable
LIC	Low-income country
LMIC	Low- and middle-income country
MCH	Macroeconomic Commission on Health
MIC	Middle-income country
NICE	National Institute for Health and Clinical Excellence
PPP	Purchasing power parity
QALY	Quality adjusted life year
YLD	Year of life disabled
YLL	Year of life lost
VSL	Value of a statistical life
WHO	World Health Organization
WHO-CHOICE	WHOosing Interventions that are Cost-Effective
WTP	Willingness to pay

1. Introduction

1.1 Policy context

Policy-makers in low- and middle-income countries (LMICs), just as in high-income countries (HICs), face difficult decisions about how to use the available health care resources to achieve the greatest improvement in agreed social objectives in a way that is accountable.¹ An important objective of health care is to improve health itself, which includes improvements in survival and reductions in morbidity. This requires an assessment of whether the improvement in health outcomes offered by investing additional resources in a health intervention (which may be a technology, service or a whole programme of care) exceeds the improvement in health that would have been possible if the additional resources required had, instead, been made available for other health care activities. Therefore, some assessment of the health opportunity costs of additional health care expenditure is unavoidable if the best use is to be made of available resources.

Incremental cost-effectiveness ratios (ICERs) provide a useful summary of the additional costs of a proposed intervention and the additional health benefit it offers. However, to decide whether the intervention will improve health outcomes overall (so can be regarded as cost-effective and should be approved, reimbursed or included in a benefits package) a comparison is required with an assessment of the likely health opportunity costs, commonly described as a cost-effectiveness threshold (CET) (Drummond et al. 2015). To date much effort has been devoted to assessing the incremental costs and effects of proposed interventions but there remains much confusion about what a cost-effectiveness threshold ought to represent and what type of evidence might inform its assessment. The values recommend or cited by decision making and advisory bodies (both national and supra national) have not been evidence based and reflect a lack of conceptual clarity (Revill et al. 2014).

Research in the UK has demonstrated that an empirical assessment of the expected health opportunity costs is possible, based on an estimate of the health effects of changes in health care expenditure (Claxton, Martin, et al. 2015). A similar approach is possible based on existing estimates of the effect of different levels of (and changes in) health care expenditure on mortality outcomes using cross country level data. We demonstrate how these estimates can be extended to include the likely impact on length and quality of life (measured by Disability Adjusted Life Years, DALYs), reflecting a country's demography, epidemiology, level of health care expenditure, income and other characteristics (Salomon et al. 2012). Any estimates will rest on whether the health effects of changes in health expenditure can be identified from aggregate cross-country level data. Despite the challenges, we are able to provide a range of estimates of a cost per DALY threshold for up to 89 low- and middle-income countries. This demonstrates that some empirical assessment of cost per DALY thresholds for particular countries is possible using published evidence and other data currently available. Importantly, it is now possible to make what was previously an abstract and confused concept real. Its assessment can help inform decision making within low- and middle-income countries and influence how other supra national bodies make recommendations and investment and purchasing decisions.

1.2 What should the cost-effectiveness threshold represent?

The confusion about what a CET ought to represent is evident in the values recommended or cited by decision making and advisory bodies. In particular, there has been a failure to clearly distinguish the 'demand side' (what the value of health and health care expenditure should be) and the 'supply sides' (what improvement in health is possible given existing resources).

¹ For consistency, we define LMICs by the World Bank's classifications of countries by income in 2000.

The ‘demand side’ notion of the threshold has been expressed in two subtly different ways: i) aspirational values, which represent a particular view of what value *ought* to be placed on improvements in health (Revill et al. 2014); and ii) those founded on evidence from willingness to pay and value of a statistical life studies (using stated or revealed preferences) (Ryen & Svensson 2014; Viscusi & Aldy 2003), which represent the value that individuals are *thought* to place on health improvement. Both imply what health care expenditure *ought* to be. Therefore, they are a ‘demand side’ concept, which rests on disputed questions of social value, rather than being founded on the health effects of the resources currently devoted to health (a supply side concept, which is an empirical question) (Drummond et al. 2015). There is a real danger that demand side values, and especially aspirational ones might be substantially higher than an assessment of what the health opportunity costs actually are (the supply side). As a consequence their use is likely to reduce overall population health and exacerbate healthcare inequalities. They also fail to identify the real (and potentially much greater) value of devoting more resources to health care. For this reason they don’t contribute to greater accountability in low- and middle-, as well as in high-income countries, for the health care and other expenditure decisions made at a local, national and supra national level (Revill et al. 2014).

Thresholds that are cited are often a statement of ‘what should be’ or ‘norms’ that are not founded on the empirical question posed by the supply side notion of health opportunity cost. HICs such as the US and UK have applied values of US\$50,000-\$100,000 and GB£20,000-30,000 per quality adjusted life year (QALY), respectively, with the latter being used as a key criteria in decisions made by the National Institute for Health and Clinical Excellence (NICE) in the UK (Neumann et al. 2014; Grosse 2008). This explicit threshold range has been used by NICE since 2004 (National Institute for Clinical Excellence 2004), and is based on the values implied by the decisions it made between 1999 and 2003 (Rawlins & Culyer 2004). As such it has become an established norm, which, at best, represents how NICE makes decisions (current evidence suggests that the thresholds implied by its decisions are, in fact, much higher (Dakin et al. 2014; Devlin & Parkin 2004)) rather than an empirical assessment of either the demand or supply side (Claxton, Sculpher, et al. 2015).

The “WHO-CHOICE threshold” of 1-3x GDP per capita has been widely cited as criteria for cost-effectiveness in LMIC settings. Based on a 2001 report by the Macroeconomic Commission on Health (MCH), it relies on estimates of the value of a statistical life (WHO 2001; Jamison et al. 2013). These were adopted by the World Health Organization (WHO) in 2005 to serve as a guide alongside WHO-CHOICE (WHO 2015). They have been used as generic and internationally applicable criteria to classify interventions being evaluated as highly cost-effective (less than 1x GDP per capita), cost-effective (less than 3x GDP per capita) or not cost-effective (3x GDP per capita or higher) (Marseille et al. 2015). The problem is that these widely cited criteria are aspirational ones, which reflect a particular view of what the ‘demand-side’ ought to be. Importantly, they don’t account for the ‘supply-side’ opportunity costs of the interventions under consideration.

Despite the widely recognised shortcomings of the 1-3x GDP norms (Newall et al. 2014; Marseille et al. 2015), they have been commonly used as criteria in LMIC settings of which few (or even HICs for that matter) have their own country-specific CET estimates. One exception is the Health Intervention and Technology Assessment Program (HITAP) in Thailand, which uses a CET based on estimates of willingness to pay derived from stated preference methods (Thavorncharoensap et al. 2013; Nimdet & Ngorsuraches 2015; The Subcommittee for Development of the National List of Essential Medicines 2007; Jirawattanapaisal et al. 2009). It represents a “social valuation” of health relative to other consumption opportunities, so it is an estimate of a possible ‘demand-side’, which although empirically derived, does not necessarily represent what the ‘supply-side’ currently delivers.

A threshold representing the health opportunity cost (or the shadow price of the resource constraint) is consistent with an objective of maximising health within a constrained optimisation problem (Epstein et al.; Stinnett & Paltiel 1996; Weinstein & Zeckhauser 1973). As health care systems in all countries face some restrictions on the growth in health care expenditure, the CET should reflect these supply side health opportunity costs². As well as having a well worked and sound theoretical foundation, recent research has sought to inform its assessment by estimating the health effects of changes in health expenditure. Such estimates represent health opportunity costs (of marginal changes³) either when an intervention is funded from additional resources (the health effects of other things likely to be done if the resources were made available for other health care uses), or when the resources required must be found from existing commitments (the health effects of those things that are likely to be given up).

Therefore, the problem of estimating a CET that represents health opportunity cost is the same as estimating the relationship between changes in health care expenditure and health outcome (typically measured as QALYs gained or DALYs averted⁴). This is the approach that was taken in research conducted in the United Kingdom, which used national data on expenditure and outcomes in different areas of disease (programme budget categories) reported at a local level (Martin et al. 2008; Claxton, Martin, et al. 2015). By exploiting the variation in expenditure and mortality outcomes, the relationship between changes in spending and mortality was estimated while accounting for sources of endogeneity⁵. With additional information about age and gender of the patient population these mortality effects can be expressed as a cost per life-year threshold (£25,241 per life year). By using the effect of expenditure on the mortality and life-year burden of disease as a surrogate for the effects on a more complete measure of health burden (one that also includes morbidity burden), a cost per QALY threshold that reflects the likely impact of expenditure on both mortality and morbidity was estimated (£12,936 per QALY).

The data demands of this type of within country analysis may be excessive for many other countries and particularly in LMICs. As a result the rapid replication of this study design may not be possible in most LMICs. It does however pose the question of ‘what does the evidence that is available suggest about the scale of health opportunity costs in other countries?’ For example, (Woods et al., 2015) uses the UK estimate and extrapolates to other countries based on the existing evidence of the income elasticity of the value of health (Hammit & Robinson 2011; Milligan et al. 2014; Getzen 2000) and purchasing power parity. They show that adjusting the UK estimate with what is currently known about the income elasticity, CETs based on opportunity costs may be much lower than the 1-3xGDP per capita norms.

This paper represents a next logical step, by asking what do existing estimates of the effect of different levels of (and changes in) health care expenditure on mortality outcomes using cross country level data suggest about the scale of health opportunity costs in LMICs. To do so we extend existing estimates to include the likely impact on length and quality of life (measured by Disability

² Even when there are no restrictions on the growth in health care expenditure, reimbursing or covering a higher-cost intervention will increase the costs of private insurance and/or out-of-pocket expenditure. Therefore, opportunity costs will fall on both consumption (those who are able and willing to pay the higher costs) and indirectly on health as well (those unable or unwilling to pay).

³ If changes are large relative to total resources (non marginal) then health opportunity costs are likely to be underestimated when resources need to be found from existing commitments, i.e., the threshold is likely to be lower for larger budget impacts (more health is likely to be given up). Equally, the health gains from non marginal increases in resources are likely to be lower.

⁴ Units of health are typically measured as QALYs or DALYs. Note that a gain in health is an increase in QALYs, but is referred to as a decrease in DALYs.

⁵ Most importantly simultaneity where health outcomes both determine and are determined by expenditure e.g., poorer outcomes in one disease area might lead to more spending in that area but more spending will also improve outcomes (see section 1.3 below).

Adjusted Life Years, DALYs (Salomon et al. 2012)), reflecting a country's demography, epidemiology, level of health care expenditure, income and other characteristics.

1.3 Estimating the health effects of changes in health care expenditure

The extent to which health outcomes are affected by health care expenditure is a fundamental question that has been investigated over many years. Whilst, intuitively, health expenditure ought to be a positive input into health production, the challenges involved in identifying this effect have meant that empirical work has produced mixed results. Whether work is being conducted over time or across countries, researchers have often struggled to control for all possible external factors that may affect health.

The challenges include the important differences between countries (heterogeneity), much of which cannot be fully captured and controlled for using existing data, even if it is assumed that systematically unbiased measurements are available. An early example in the literature of a macro-level study employing a conventional regression analysis is Cochrane et al. (1978). The authors examined the relationship between mortality rates, gross national product and consumption of inputs including health care provision among 18 developed countries. Their analysis was unable to find a strong and robust relationship between greater quantities of health care and reduced mortality. More recently, Or (2001), analysing data across 21 OECD countries between 1970 and 1995 with similar methods, found a substantial reduction in mortality associated with increasing doctor numbers. Looking at 15 countries in the EU between 1980 and 1995, Nixon & Ulmann (2006) performed a regression analysis with health outcomes (life expectancy at birth for males and females and infant mortality) as the dependent variable and many health and health care independent variables including per capita health care expenditure. Whilst they conclude that health care inputs have a significant impact upon infant mortality, they result in only modest improvements in life expectancy.

It is perhaps unsurprising that there is no consistent finding amongst the above studies, since a conventional regression analysis requires assuming that many of the independent variables considered are exogenous, which is unlikely to be a plausible assumption in this context owing to issues of simultaneity⁶ and omitted variable bias (Gravelle & Backhouse 1987). In addition, Gravelle and Backhouse (1987) note that the effects of health care on health outcomes are likely to be lagged and not contemporaneous. In recent years, more sophisticated statistical methods that recognise these challenges and attempt to overcome them have been applied to cross-country data to address this research question where certain variables are allowed to be endogenous. The key contribution of these methods is that variables are allowed to be endogenous by identifying instrumental variables (IV), which should determine the level of the endogenous independent variable, but not affect the dependent variable other than indirectly through the impact of the endogenous independent variable (Cawley 2015). The IV approach provides identification through random variation in the endogenous variable under consideration.

Bokhari et al. (2007) applies this method to cross-sectional data and models both public expenditure on health and a country's GDP as endogenous variables. In addition, donor funding (external funds), which represents a significant proportion of health care financing in LMICs, is explicitly incorporated into the model. Bokhari et al. (2007) find a statistically and economically significant effect of public expenditure on health reducing three mortality outcomes. An IV approach has also been applied to panel data in a number of cases *inter alia* Filmer & Pritchett (1999), Wagstaff & Claeson (2004) and Moreno-Serra & Smith (2015). Among these, Moreno-Serra and Smith (2015) employ an innovative

⁶ Poor health outcomes might prompt more health expenditure, but more health expenditure will also improve outcomes, i.e., health outcomes both determine and are determined by expenditure.

approach where reverse causality is explicitly modeled by employing a method described in Brückner (2013). This method requires an IV for health rather than health care expenditure, and the reverse causality effect of health on health care expenditure is first modeled before finding the causal effect of health care expenditure on health. Other potential causes of endogeneity are mitigated by the inclusion of fixed effects and differential effects of health care expenditure on health are allowed for through an LMIC interaction term. In contrast with Filmer and Pritchett (1999) and Wagstaff and Claeson (2004), Moreno-Serra and Smith (2015) are able to identify a statistically and economically significant reduction in mortality due to increases in different types of health care expenditures.

The framework of analysis set out in this paper can be applied to the results of any econometric study thought to identify plausible effects on mortality of changes or differences in health expenditure (regardless of statistical significance). The selected studies Bokhari et al. (2007) and Moreno-Serra and Smith (2015) are chosen because they find plausible and statistically significant effects of expenditure and represent the most sophisticated and coherent modeling strategies given the econometric challenges of the research questions. They also provide an opportunity to demonstrate how survival effects can be derived when mortality effects are estimated as elasticities or as absolute effects, while reflecting the epidemiology and demographics of specific countries. In addition, they enable the evaluation of how direct estimation of survival and morbidity effects can be used to adjust mortality based estimates and examine the plausibility of the assumptions that might otherwise be required.

1.4 Aims and objectives

The purpose of this paper is to show how these cross-country econometric models, using Bokhari et al. (2007) and Moreno-Serra and Smith (2015) as examples of two different approaches, can be used as an input for calculating country-specific CETs through analysis of other health outcomes, use of additional data and explicitly made modeling assumptions.

1.5 Report structure

Chapter 1 of this report has sought to clarify why an estimate of health opportunity costs is a key assessment and introduce the literature relevant to estimating appropriate CETs for LMICs. It has emphasized the need for further research making best use of currently available evidence and data, to which this paper contributes. Chapters 2 and 3 answer four successive questions that allow us to estimate a cost per DALY averted CET:

1. What are the mortality effects of changes in expenditure?
2. What are the survival effects of changes in expenditure?
3. What are the morbidity effects of changes in expenditure?
4. What are the combined survival and morbidity effects of changes in expenditure?

Chapter 2 answers each of these questions in turn using Bokhari et al's (2007) model and dataset alongside additional data from the World Bank and the Global Burden of Disease (GBD). The assumptions necessary to get from estimates of the effect of changes in health expenditure on mortality to survival, morbidity and both combined are outlined and discussed (see sections 2.1 to 2.4). Chapter 3 is similarly structured, but uses key input parameters from the Moreno-Serra and Smith (2015) model (see sections 3.1 to 3.4). The results from the two sources of estimated parameters are presented in 2.5 and 3.5 respectively. Finally, Chapter 4 concludes by comparing results to those generated in related papers in the literature before drawing out some implications for policy and future research. A full table of country-specific CETs generated in this paper can be found in the Appendix.

2. Estimates based on cross sectional data

Bokhari et al. (2007) uses a cross-section of 127 countries from the year 2000 and focuses on the effect of public expenditure on health on under-5 mortality and maternal mortality. They consider that both a country's GDP and public expenditure on health – along with a number of interactions of public expenditure on health and other covariates – are endogenous, and use several IVs including economic and political variables as well as the military expenditures of neighbouring countries. Their results indicate that the mean elasticity of public expenditure under-5 mortality is -0.33 and the corresponding maternal mortality mean elasticity over countries is -0.50.

Given that the dataset used by Bokhari et al (2007) is a cross-section, we are able to expand their dataset to also estimate other outcomes of interest using data from GBD that are not available in panel form, but exist for the year 2000, as well as additional data from the World Bank. This means we can employ the Bokhari et al (2007) model, exactly as in the published paper, but substitute the mortality outcomes for country-level adult aged 15-60 male and female mortality, YLL per capita, YLD per capita and DALY per capita outcomes.⁷ By doing this we are able to directly answer the questions that we would like to address: 'what are the survival effects of changes in expenditure?' and 'what are the morbidity effects of changes in expenditure?' This is one of the key ways in which Chapter 2 differs from Chapter 3, where fewer outcomes are estimated since the Moreno-Serra and Smith (2015) model is estimated using a panel data structure and thus values for YLL, YLD and DALY per capita are not available on a year-by-year basis. Given the range of outcomes we can estimate in the current section, we are ultimately able to calculate DALYs averted in four different ways.

2.1 What are the mortality effects of changes in expenditure?

Bokhari et al. (2007) estimate the effect of public expenditure on health on under-5 and maternal mortality. These estimates, while interesting in their own right, do not provide enough information about how mortality among the full population is affected by changes in expenditure. (This would require, for example, extrapolating from maternal or under-5 mortality to the full adult population). We were able to use their data and model to better determine the effect of changes in expenditure on mortality across the full population by running their model on additional mortality outcomes: adult male and adult female mortality, which are also available from the World Bank. Although adult male and female mortality only cover individuals ages 15-60, using these variables alongside under-5 mortality gives us the greatest coverage of the population available in existing cross-country data. As mortality rates are reported annually under-5, adult male and adult female mortality are also estimated using the Moreno-Serra and Smith estimation strategy in Chapter 3.

In the model employed by Bokhari et al. (2007), all variables are log transformed prior to estimation of the model, and the resulting regression coefficients are therefore interpreted as elasticities. When the under-5 mortality elasticity of public expenditure on health is -0.33, this should be interpreted as saying that a 1% increase in public expenditure on health causes a 0.33% reduction in under-5 mortality. Assuming a constant elasticity between health expenditure and health is consistent with a Cobb-Douglas health production function where there may be diminishing marginal returns to health expenditure. Bokhari et al. (2007) also allow the outcome elasticity of public expenditure on health to vary by country through the use of interaction terms. In so doing their model assumes a direct effect of public expenditure on health which is "mitigated or enhanced" depending on two factors: the level of deviation of donor funding pledged in 1998 (assumed to be dispersed in the year 2000) from the historical average level of donor funding (measured as the average level pledged between 1993 and 1997); and the level of infrastructure (as

⁷ The authors would like to thank Farasat Bokhari for the generous provision of the data and Stata code used in Bokhari et al. (2007). In doing this, data was not available for Dominica, St. Kitts and Nevis, St. Lucia and St. Vincent and the Grenadines. As a consequence, no results are presented for these countries in this section.

captured by using paved roads per unit area). Since the levels of these two factors vary between countries, the resulting elasticities also vary between countries.⁸

Table 1. Summary statistics for estimated elasticities among LMICs

	Under-5 mortality	Adult male mortality	Adult female mortality
Min	-0.36	-0.20	-0.20
Max	-0.25	-0.08	-0.10
Mean	-0.33	-0.18	-0.18

We can move from estimates of the effect of hypothetical changes in expenditure on mortality to obtain cost per DALY averted thresholds through a series of steps similar to those undertaken by Claxton et al (2015).⁹ To begin, the estimated country-specific elasticities can be used to calculate the number of deaths averted by changes in expenditure in a given country using that country's baseline mortality rates for different age and gender categories, by subtracting the number of deaths after the change in expenditure from the number of deaths before the change in expenditure.

The available mortality rates are not crude mortality rates (i.e., deaths per 1,000 population), but instead cumulative mortality rates. We cannot simply multiply this mortality rate by the population to obtain the absolute number of deaths in a given country. The under-5 mortality rate is the cumulative probability of death by age 5, and the adult mortality rates are the cumulative probability of death by age 60 conditional on being alive at age 15. Thus a three-step process is necessary to determine the absolute number of deaths by age and gender in a country from the World Bank mortality rates.

Equations 1-7 show how to obtain deaths averted for each group g adult males or adult females. First, the annual rate given the cumulative rate provided by World Bank mortality rate for males or females $MR_{pre_{ig}}$ must be calculated. Assuming here, but relaxed later, a constant rate over time, and using the 45 year mortality probability (i.e. from ages 15 to 60), the annual adult male and female mortality rates prior to the change in expenditure for a given country i are calculated as:

$$(1) \quad AMR_{pre_{ig}} = -\ln((1 - MR_{pre_{ig}})/1000)/45$$

We divide by 1,000 to account for the fact the mortality rate is expressed in multiples of 1,000. As the risk of death is not constant between ages 15 and 60 and increases with age, multiplying the constant annual mortality rate from (1) by population in each age category would give an inaccurate number of absolute baseline deaths. Thus a second step is required whereby the constant mortality rates calculated in (1) are weighted by known mortality rates. This enables us to obtain more accurate mortality rates and thus more accurate calculations of absolute deaths. The Global Burden of Disease (GBD) provides mortality rates by five-year age category (and split into separate categories for 0-1 and 1-4 year olds) for each country and we use these to weight the constant rates obtained from equation (1) for each five-year age category from 15 to 60. The gender specific weight for each five-year age category is calculated as

$$(2) \quad MRweight_{ijg} = GBDP_{ijg}/GBDP_{ig}$$

⁸ A table including all the elasticities is provided in Appendix 1.

⁹ Similar to the main results from Claxton et al (2015), our results are also presented in terms of cost per undiscounted health benefits.

where $GBDP_{ijg}$ is the GBD probability of death for the given age category j in country i . And \overline{GBDP}_{ig} is the average mortality rate among ages 15-60 for males or females in country i . Weighting by mortality rates by five-year age category (as opposed to annual age-specific mortality rates, which are not available) implicitly assumes that the mortality rate is constant across those five years and that the population within that five-year age category is divided evenly across each age that makes up the category.¹⁰ This is, however, a less stringent assumption than assuming that mortality rates are constant across all ages between 15 and 60. The third and final step is to calculate total absolute baseline deaths.

$$(3) \quad absdeaths_{pre_{ig}} = \sum_{j=1}^9 (AMR_{pre_{ijg}} * MRweight_{ijg} * population_{ijg})$$

In order to calculate the number of deaths averted by the change in expenditure, we need to calculate absolute deaths after the hypothetical change in expenditure. Once the mortality rate after the change in expenditure is calculated, this process mirrors equations (1) – (3) above. The mortality rate after the change in expenditure $MR_{post_{ig}}$ for group g of males or females from the estimated country specific elasticity:

$$(4) \quad MR_{post_{ig}} = MR_{pre_{ig}} - (MR_{pre_{ig}} * (-1 * adult\ MR\ elasticity_{ig}))$$

From this, the annual mortality rate after the change in expenditure $AMR_{post_{ig}}$ for males or females is:

$$(5) \quad AMR_{post_{ig}} = -\ln((1 - MR_{post_{ig}})/1000)/45$$

The same gender specific weights as calculated in equation (2) for each age group are used, and the number of deaths in each age category after the change in expenditure is calculated as:

$$(6) \quad absdeaths_{post_{ig}} = \sum_{j=1}^9 (AMR_{post_{ijg}} * MRweight_{ijg} * population_{ijg})$$

Equations (1) through (6) are calculated separately for females and males using the different baseline mortality rates and elasticities for each gender. Subtracting deaths post-change from deaths pre-change gives deaths averted:

$$(7) \quad adult\ deaths\ averted_i = \sum_{g=1}^2 (absdeaths_{pre_{ig}} - absdeaths_{post_{ig}})$$

The same strategy is used to determine the annual mortality rate among children under-5 in a given country.¹¹ We first determine the pre-change annual mortality rate among children under 5 $Au5MR_{pre_i}$ again assuming – at first – that the rate is constant over time. A 5 year mortality probability (i.e. from ages 0 to 5) is used, and we divide by 1,000 as before to account for the fact the mortality rate expressed in multiples of 1,000.

$$(8) \quad Au5MR_{pre_i} = -\ln((1 - u5MR_{pre_i})/1000)/5$$

¹⁰ We believe this is a reasonable assumption to make given that the conditional life expectancy information available also only breaks down into five-year age categories, and as a result, the value of having more granular information at this stage would be lost at the next stage where years of life lost averted are calculated.

¹¹ Data on under-5 mortality rate by gender was not available.

where uMR_{pre_i} is under 5 mortality rate from the World bank. To accurately calculate the baseline number of absolute deaths in this age group GBD mortality rates for 0-1 and 1-4 year olds for each country are used to weight the constant annual rates obtained from equation (8). These weights are calculated for only two age categories j : 0-1 year olds and 1-4 year olds.

$$(9) \quad u5MRweight_{ij} = GBDP_{ij} / \overline{GBDP_{i,u5}}$$

Baseline absolute deaths are calculated as:

$$(10) \quad u5deaths_{pre_i} = \sum_{j=1}^2 (u5MR_{pre_i} * u5MRweight_{ij} * population_{ij})$$

Once again, the absolute deaths after the hypothetical change in expenditure must be calculated based upon the change in under-5 mortality rate resulting from the hypothetical change in expenditure. The annual under-5 mortality rate after the change in expenditure $Au5MR_{post_i}$ can be obtained using the estimated country specific elasticity:

$$(11) \quad u5MR_{post_i} = u5MR_{pre_i} - (u5MR_{pre_i} * (-1 * u5MR elasticity_i))$$

Thus the post-change constant annual mortality rate is then calculated as:

$$(12) \quad Au5MR_{post_i} = -\ln((1 - u5MR_{post_i})/1000)/5$$

These are again weighted so that the number of deaths in each age category after the change in expenditure is calculated as:

$$(13) \quad u5deaths_{post_i} = (\sum_{j=1}^2 Au5MR_{post_{ij}} * u5MRweight_{ij} * population_{ij})$$

Subtracting deaths post-change from deaths pre-change in the 0-1 and 1-4 age categories gives lives saved in each, and summing across these two age categories gives total lives saved.

$$(14) \quad u5deaths_{averted_i} = u5deaths_{pre_i} - u5deaths_{post_i}$$

Total lives saved (i.e., deaths averted) by the change in expenditure among 0-5 and 15-60 year olds are thus:

$$(15) \quad lives\ saved\ 0 - 5 \ \& \ 15 - 60_i = u5deaths_{averted_i} + adult\ deaths_{averted_i}$$

Equations (1) through (15) are calculated for each country i . Thus the number of deaths averted in each country depends upon the countries' mortality elasticities of public expenditure on health, baseline mortality rates and the age and gender structures of each country's population. For example, Bolivia and Sierra Leone have very similar elasticities (-0.177 for adult female mortality and -0.180 for adult male mortality in both countries and 0.507 for under-5 mortality for Bolivia and -0.506 for under-5 mortality for Sierra Leone). However, Sierra Leone's baseline mortality rates are more than double those of Bolivia for all three age categories, so more lives are saved among 0-5 and 15-60 year olds in Sierra Leone. Cost per life saved depends not only on how many lives saved, but also upon baseline public expenditure on health per capita. Bolivia spends more than 5 times as much on health than Sierra Leone per capita, and as such a 1% change in spending constitutes a far greater amount in Bolivia than in Sierra Leone. This furthers the difference in cost per death averted between the two countries.

Although cost per death averted is interesting, it is not reported here for two reasons. First, the number of deaths averted in each country is only useful for our purposes insofar as it can be used to calculate the survival effects of changes in expenditure, which constitute one part of DALYs. Second, the true cost per death averted is likely to be lower than what would be calculated from the above series of equations as it is reasonable to expect that changes in public expenditure on health affect mortality outside the 0-5 and 15-60 age groups. These issues are dealt with in the following section on the survival effects of changes in expenditure.

2.2 What are the survival effects of changes in expenditure?

To get closer to determining how changes in public expenditure on health affect a summary measure of mortality and morbidity (i.e., DALYs in this instance), we need to use information about the number of deaths that are averted as a result of changes in expenditure to calculate how many years of life that are not lost as a result. This gives us an estimate of YLLs averted, which when added to an estimate of years of life lost (YLDs) averted, a measure of morbidity, gives an estimate of the effect of changes in public expenditure on health on DALYs.

$$(16) \quad DALY_i = YLL_i + YLD_i$$

The effect of changes in public expenditure on YLLs can be obtained in two possible ways given the model and dataset used by Bokhari et al (2007). First, YLLs averted due to changes in expenditure can be *calculated* by combining information on the mortality effects of expenditure by age and gender from section 2.1 with information about conditional life expectancy (CLE) also by age and gender. However, as total YLLs for each country can themselves be calculated, we can also directly *estimate* the effect of changes in expenditure on YLLs. Each way of getting at the survival effects of changes in expenditure is explained in the two subsections that follow, and the associated assumptions are also explored.

2.2.1 Indirectly estimating effects on survival from mortality

The information from section 2.1 about the effect of a change in public expenditure on health on mortality (and therefore deaths averted) among 0-5 and 15-60 year olds can be used to calculate YLLs averted due to a change in public expenditure on health. We need to know two things in order to make this calculation:

- 1) YLLs associated with each averted death
- 2) YLLs averted among individuals ages 6-14 and 61+

The first—the number of YLLs associated with each death averted by a change in spending—depends upon the age at which each death is averted, as well as the gender of the individual and the country that they live in. We can apply country, gender and age-group-specific CLE to deaths averted among 0-5 and 15-60 year olds by five-year age-group calculated in the previous section. Summing the YLLs associated with each death averted among individuals aged 0-5 and 15-60 gives total YLLs averted among 0-5 and 15-60 year olds.

$$(17) \quad \text{mortality based YLL averted, ages 0 - 5 \& 15 - 60}_i = \sum_{j=1}^2 (CLE_{ij} * u5deathsaverted_{ij}) + \sum_{g=1}^2 \sum_{j=1}^9 (CLE_{ijg} * deathsaverted_{ijg})$$

In countries where 0-5 and 15-60 year olds account for a larger proportion of the total population, YLLs averted as a result of an increase in public expenditure on health will appear larger than in countries where these age groups make up a smaller proportion of the total population. This is particularly evident in countries where children under 5 comprise a relatively large share of the total

population for two reasons. First, CLE is higher among 0-5 year olds than any age between 15 and 60. Second, the elasticity on mortality in this group is generally greater in magnitude than the elasticities for adult female and adult male mortality.

Using CLE assumes that deaths averted are returned to the mortality risk of the general population matched for age and gender. This is likely to be optimistic with regard to survival effects as those individuals who have died are more likely to have comorbidities, and so averting their deaths may not necessarily restore them to the same morbidity level as the average living population. CLE is obtained from the Global Burden of Disease and is available only by five-year age category.

While equation 17 provides an estimate of the YLLs averted among 0-5 and 15-60 year olds based on mortality effects, we expect this to be an underestimate of total YLLs averted as it does not account for the potential effect of a change in expenditure on other age groups. One option would be to assume no effect on those other groups since this is not reported in the data, but this would be an extreme assumption. A more reasonable assumption is that the effect on YLLs among the total population is proportional to the estimated effect on YLLs among 0-5 and 15-60 year olds according to the baseline levels of YLLs in those age groups compared to the total population.

To apply this assumption we need to know the total YLLs that exist in a given country and those that exist among 0-5 and 15-60 year olds specifically. In our case YLLs represent the gap between age at death and the conditional life expectancy.¹² As such, total population YLLs are calculated for each country as the product of country-specific absolute numbers of deaths (from GBD data) and CLE by gender in each of 18 age categories comprised of ages 0-1, 80+ and sixteen five-year age categories covering ages 5-79 (also from GBD data). Summing across age categories and genders gives the total YLLs for each country.

$$(18) \quad YLL_i = \sum_{j=1}^{18} (CLE_{ij} * absolute\ deaths_{ij})$$

YLLs for 0-5 and 15-60 year olds are calculated as:

$$(19) \quad YLL, \text{ages } 0 - 5 \ \& \ 15 - 60_i = \sum_{j=1}^{11} (CLE_{ij} * absolute\ deaths_{ij})$$

Thus the ratio of YLLs among 0-5 and 15-60 year olds to YLLs for total population can be expressed as follows.¹³

$$(20) \quad \sigma_i = \frac{YLL, \text{ages } 0-5 \ \& \ 15-60_i}{YLL, \text{all ages}_i}$$

To apply the assumption that the effect on YLLs among the total population is proportional to the estimated effect on YLLs among 0-5 and 15-60 year olds, we simply scale up YLLs averted based on mortality effects using the ratio from (20):

$$(21) \quad \text{mortality and ratio based YLL averted, all ages}_i = (\text{mortality based YLL averted, ages } 0 - 5 \ \& \ 15 - 60_i) / \sigma_i$$

¹² Consistent with the YLLs calculated by World Health Organization age-weighting and time discounting are not used. YLLs calculated by WHO use a projected frontier life expectancy at birth for 2050 of 92 years instead of conditional life expectancy.

¹³ For middle-income countries mean=68%; min=37%; max=93%. For low-income countries mean=84%; min=49%; max=93%.

This assumes that the effect of health care on YLLs is distributed in proportion to the distribution of YLLs itself across age groups. Specifically, we assume that the proportion of YLLs averted of all YLLs in the 0-5 and 15-60 year olds is the same as in the total population. While this is generally a reasonable assumption, one could argue that an increase in public expenditure on health does not affect adolescents (i.e., 6-14 year olds) or older individuals (i.e., 60+ year olds) in the same way that it affects young children or the working age population. This may be the case, for example, if an increase in public expenditure on health is aimed toward interventions that affect under-5 mortality as it might be in a country working toward meeting the Millennium Development Goal to reduce child mortality that was set forth in 2000. However, the assumption may be considered more reasonable than assuming that health care expenditure does not affect mortality among adolescents and older individuals and is arguably the better option given data constraints.

2.2.2 *Directly estimating effects on survival*

The effect of changes in expenditure on survival can also be directly estimated by estimating the effect on population YLLs directly by employing YLL per capita as the outcome variable in the econometric model to generate YLL elasticities.

$$(22) \quad pc\ YLL_i = YLL_i/population_i$$

YLLs used are those calculated in equation 18. Directly estimating the effect on YLLs negates the need to use estimates of the mortality effect to calculate YLLs and also the need for the assumption that the effect on YLLs among the total population is proportional to the estimated effect on YLLs among 0-5 and 15-60 year olds. Using the same econometric model as described earlier for estimating the effect of expenditures on mortality, country-level YLL per capita elasticities of public expenditure on health were estimated. The range of estimated elasticities among LMICs was -0.26 – -0.30 with a mean value of -0.30.¹⁴

Cost per YLL averted is generally higher when it is based on mortality estimates, suggesting that the assumption of proportionality between YLLs averted among 0-5 and 15-60 year olds and those averted among the rest of the population underestimates total YLLs averted if direct estimation results in an estimate that is closer to the truth. Nonetheless, because the differences are small, where data on YLLs is unavailable basing cost per YLL averted on mortality effects would suffice, although this evidence suggests this may be optimistic.

2.3 **What are the morbidity effects of changes in expenditure?**

Changes in spending will likely affect morbidity (i.e., YLDs) as well as mortality. Having estimated the survival effects of changes in public expenditure on YLLs (using two methods: mortality based and direct estimation), we now consider the morbidity effects of changes in expenditure. Public expenditure on health can affect population level morbidity directly and indirectly.

The indirect effect of expenditure arises through changes in survival. We would not expect an individual whose death has been averted due to medical intervention to be in full health as deaths are generally the result of chronic or infectious diseases, which have an associated morbidity burden. Exceptions may include deaths caused by accidents (e.g., motor vehicle), but are a small percent of preventable deaths and amenable mortality.

¹⁴ In MICs the average elasticity on under-5 mortality is -0.33% (-0.27% to -0.36%), on adult female mortality is -0.18% (-0.11% to -0.20%) and on adult male mortality is also -0.18% (-0.13% to -0.20%). In LICs the average elasticity on under-5 mortality is -0.33% (-0.25% to -0.35%), on adult female mortality is -0.17% (-0.08% to -0.19%) and on adult male mortality is also -0.18% (-0.10% to -0.20%).

Increases in public expenditure on health also affect morbidity directly through the prevention and treatment of disease. For example, public health education campaigns and the distribution of condoms can help to prevent Hepatitis C. It can be treated and even cured with antiviral medication, but untreated can result in cirrhosis, liver cancer, liver failure and death. Increases in expenditure may result in decreased incidence of the disease and/or increased access to treatment, contributing to a reduction in population level burden of this disease, and through the same mechanisms other diseases.

There are three ways to get at the effect of changes in public expenditure on morbidity:

- 1) Using either survival effect a or b as a surrogate for morbidity effects and incorporating an indirect effect:
 - a. mortality-based survival effects
 - b. directly estimated survival effects
- 2) Directly estimating the effects of changes in public expenditure on health on YLDs averted

Each of these is outlined below with a description of what they capture (the direct or indirect effects) and the assumptions associated with each.

2.3.1 Indirectly estimating effects on morbidity from survival effects

When it is only possible to estimate the effect of changes in expenditure on mortality outcomes assumptions are required to move from the mortality to survival to the disability effects of expenditure. While one possibility is to assume that changes in expenditure only affect mortality and not morbidity, this is an extreme assumption. More likely, the effect on morbidity is proportional to the effect on survival. This relies on the assumption that the effect of changes in expenditure on YLL (as measured by mortality based estimates) is a surrogate for the effect on YLD and that the elasticity of the effect of a change in expenditure on YLD is similar to the elasticity of the effect of a change in expenditure on YLL. To implement this assumption we need to know the ratio of total YLDs in a given country to total YLLs in that country. For this we rely on WHO published estimates of YLD by country and YLL from (18). The ratio is expressed as:

$$(23) \quad \gamma_i = \frac{YLD_i}{YLL_i}$$

All ratios γ for LMICs are below 100% indicating that more than half of the overall survival and morbidity burden in these countries is comprised of mortality.¹⁵ This is neither obviously over- or under-optimistic with regard to health effects, but could be seen as optimistic if we think governments proportionally put greater priority on averting mortality than disability in LMICs. We can examine this through comparison with the other two ways of directly estimating these effects. YLDs averted for the population can thus be calculated from either indirectly obtained YLLs averted based on mortality estimates or directly estimated YLL averted (both represented by *YLL averted, all ages_i*):

$$(24) \quad \text{ratio based YLD averted}_i = \text{YLL averted, all ages}_i * \gamma_i$$

Where it is possible to estimate the effect of changes in public expenditure on health on survival directly, as can be done in this scenario, *YLL averted, all ages_i* in equation (24) can also be from directly estimated YLL averted. However, whether mortality effects or directly estimated YLLs

¹⁵ The mean ratio for middle-income countries is 1:0.61 with a range of 1:0.20 to 1:0.98. The mean ratio for low-income countries is 1:0.31 with a range of 1:0.14 to 1:0.75.

averted are used as a surrogate for morbidity effects, only the direct effect of changes in public expenditure on health on morbidity is captured. As such, we are implicitly assuming that each YLL averted is lived in full health, which we know is unlikely. WHO publishes country-level data on YLDs, providing an estimate of average population health per capita, which is calculated as:

$$(25) \quad \text{per capita YLD}_i = (\sum_{d=1}^n (P_{id} * DW_d)) / \text{population}$$

where P_{id} is the prevalence of disease d in country i , DW_d is the disability weight associated with disease d and there are n diseases.¹⁶ The disability weights reflect disease severity and are bounded between 0 (no morbidity) and 1 (death) (GHDx 2014).^{17,18}

Given the country level average morbidity burden is non-zero, it is unlikely that the indirect effect of spending on morbidity through YLLs averted is non-zero. To account for the fact that YLLs averted will not be lived in full health we can apply country specific per capita YLD burden to the country specific change in YLL (whether YLL averted is calculated indirectly from mortality estimates or estimated directly from YLL).

$$(26) \quad \text{indirect effect YLD}_i = \text{YLL averted, all ages}_i * (1 - \text{pc YLD}_i)$$

Adjusting YLDs averted to reflect the disability in which those life years are on average likely to be lived results in slightly higher costs per YLD averted as it reduces total YLD calculated to be averted by the change in public expenditure on health.

$$(27) \quad \text{YLD averted}_i = \text{ratio based YLD averted}_i - \text{indirect effect YLD}_i$$

2.3.2 Directly estimating effects on morbidity

YLD data (like YLL) are available for 2000, so the effect of changes in expenditure on YLDs can be estimated directly. Estimating this directly enables us to capture both channels through which changes in expenditure affect YLDs: through increases in YLDs from YLLs averted and decreases in YLDs from changes in expenditure, resulting in a net effect. Using the Bokhari et al. (2007) econometric model described earlier and estimating the country-level YLD per capita elasticities of public expenditure on health, the range of estimated elasticities among LMICs was -0.02% to -0.06% with a mean value of -0.03%.¹⁹ The per capita YLD burden following the change in expenditure is determined as:

$$(28) \quad \text{pc YLD}_{\text{post}_i} = \text{pc YLD}_{\text{pre}_i} - \text{pc YLD}_{\text{pre}_i} * (-1 * \text{YLD elasticity}_i)$$

YLDs averted by the change in expenditure are thus the difference between per capita YLD burden before and after the change in expenditure, multiplied by the population:

$$(29) \quad \text{YLD averted}_i = (\text{pc YLD}_{\text{pre}_i} - \text{pc YLD}_{\text{post}_i}) * \text{population}$$

¹⁶ YLDs are calculated from prevalence estimates that draw upon the Global Burden of Disease 2010 analysis, and are also adjusted for independent comorbidity. They are disaggregated by age and gender for countries for the year 2000. Age-weighting and time discounting are not used.

¹⁷ Disability weights come from the Global Burden of Disease study (2010) and are developed through surveys of the general public.

¹⁸ Although it is conceivable that countries with high disease prevalence and comorbidities could have per capita YLD values of greater than 1, this is not found to be the case. Among LICs (MICs) mean per capita YLD is 0.108 (0.106), with a range of 0.087 to 0.124 (0.082 to 0.138).

¹⁹ In low-income countries the mean elasticity on YLD is -0.00031 with a range of -0.0004 to -0.00027. In middle-income countries the mean elasticity on YLD is -0.00031 with a range of -0.00064 to -0.00024.

Having two estimates of YLDs averted (based on survival and directly estimated) enables us to examine the assumptions used to move from estimates of survival to morbidity, and this is done later on in 2.5.

2.4 Directly estimating the effect of changes in expenditure on disability and survival

Given that we have data on both YLLs and YLDs by country for the year 2000 we are able to construct DALYs, which are a summary measure of overall population mortality and morbidity. Each DALY represents one lost year of healthy life. Baseline per capita DALYs for each country i were constructed as follows:

$$(30) \quad pc \text{ DALY}_{pre_i} = pc \text{ YLL}_i + pc \text{ YLD}_i$$

where per capita YLL are calculated in equation 22 and per capita YLD are calculated in equation 25. The average elasticity for LICs is -0.21 (range -0.20 to -0.21) and for MICs is -0.21 (range -0.18 to -0.21). The country-specific elasticities are used to determine the change in DALYs per capita at the country level.

$$(31) \quad pc \text{ DALY}_{post_i} = pc \text{ DALY}_{pre_i} - pc \text{ DALY}_{pre_i} * (-1 * \text{DALY elasticity}_i)$$

This, in turn, is used to calculate overall DALYs averted in each country.

$$(32) \quad \text{DALY averted}_i = (pc \text{ DALY}_{pre_i} - pc \text{ DALY}_{post_i}) * \text{population}$$

This results in an average of 42,327 DALYs averted (range 503 to 864,175) in LICs and 25,159 (range 142 to 611,165) in MICs.

2.5 Estimates of cost per DALY averted thresholds

In sections 2.1 through 2.3 we presented a number of different ways of calculating YLLs and YLDs averted, ultimately leading to the direct estimation and calculation of DALYs averted in section 2.4. As DALYs are the sum of YLLs and YLDs there are four different ways of estimating DALYs averted that account for the effect of changes in expenditure on YLLs averted as well as both the direct and indirect effects on YLDs averted. These are presented in Table 2.

Table 2. Different methods for estimating and calculating DALYs averted from Bokhari et al (2007)

		1	2	3	4
YLL averted		Based on indirectly estimating effects on survival from mortality	Directly estimated	Directly estimated	
YLD averted	Direct effect	Uses indirectly estimated effects on survival from mortality as a surrogate for morbidity effects	Uses directly estimated survival effects as a surrogate for morbidity effects		Directly estimated
	Indirect effect	Uses average overall population health as a surrogate for increase in YLD burden associated with increase in YLLs averted	Uses average overall population health as a surrogate for increase in YLD burden associated with increase in YLLs averted	Directly estimated	

The estimates of DALY averted are then used to calculate cost per DALY averted as:

$$(33) \quad \text{cost per DALY averted}_i = (0.01 * \text{total public expenditure on health}_i) / \text{DALYs averted}_i$$

2.5.1 Low-income countries

Estimates of cost per DALY averted for the 53 LICs in Bokhari et al (2007)'s dataset all lie below the 1-3x GDP per capita rule of thumb commonly used in recommending the adoption of new interventions in LMICs.²⁰ (see Figure 1.) These results imply that even interventions adopted on the basis of being "highly cost-effective" at less than 1x GDP per capita displace more health than they generate if their cost per DALY averted is above the range of estimates provided here.

²⁰ Countries are classified according to the year 2000 World Bank income classifications.

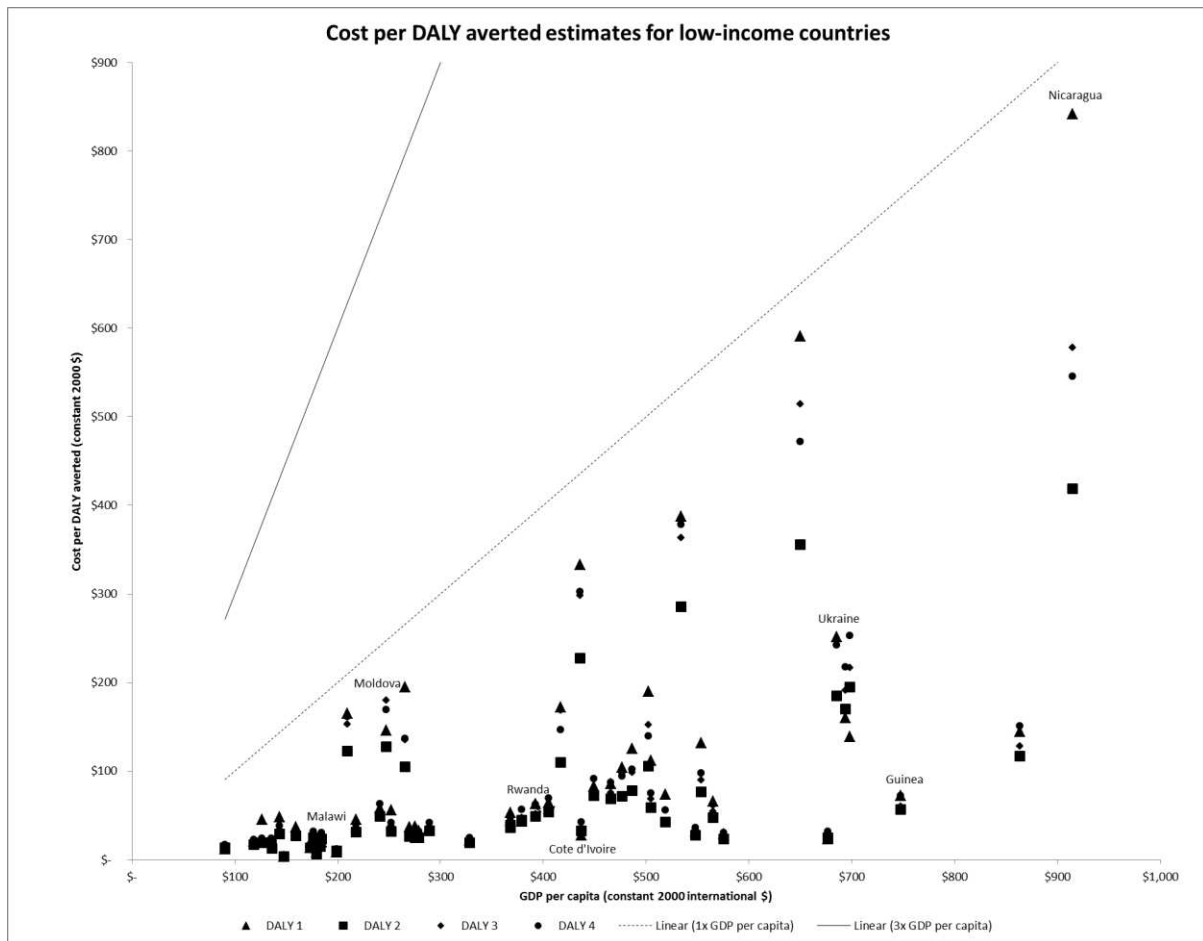


Figure 1. Cost per DALY averted estimates for low-income countries from Chapter 2²¹

The range of estimates for each country based on the input parameter estimates from Bokhari et al. (2007) enables us to compare 1) indirectly estimated effects on survival from mortality to directly estimated effects on survival and 2) indirectly estimated effects on morbidity from survival effects to directly estimated effects on morbidity. These comparisons allow us to make judgements about the assumptions used, which become important when using surrogacy assumptions in Chapter 3. Finally, we consider 3) whether there are any outliers, and what we can learn from them.

In order to make the first comparison, indirectly estimated effects on survival from mortality to directly estimated effects on survival, we can look at cost per DALY averted from DALYs 1 and 2. The difference between the two originates from how YLLs averted are estimated as both use YLLs averted as a surrogate for direct morbidity effects and average overall population health as a surrogate for indirect morbidity effects. In DALY 1 YLLs averted are based on mortality estimates and in DALY 2 they are directly estimated. DALY 2 gives the lowest cost per DALY averted estimate for 83% of countries, while DALY 1 gives the lowest for the other 17%. Indeed, more YLLs are estimated to be averted when YLLs are directly estimated (the same 83% of countries) as opposed to based on mortality effects. This suggests that basing YLLs averted on mortality effects results in an underestimate of YLLs averted and thus an overestimate of cost per DALY averted for most LICs.

To make the second comparison, indirectly estimated effects on morbidity from survival effects against directly estimated effects on morbidity, we can consider how DALY 3 and DALY 2 differ. YLLs

²¹ Converted from 2000 international \$, PPP using <http://data.worldbank.org/indicator/PA.NUS.PPPC.RF>, downloaded 13 November 2015.

averted from both are estimated directly, and the two differ only in how YLD averted are estimated. YLDs averted in DALY 3 are estimated directly, while in DALY 2 they are based on YLLs averted (i.e., directly estimated survival effects are used as a surrogate for morbidity effects). Cost per DALY averted from DALY 2 is always lower than DALY 3 for LICs. This results from the fact that on average, cost per YLD averted is highest when it is directly estimated. This suggests that the assumptions we employed around either the direct or indirect effect of changes in public expenditure on morbidity are imperfect. One reasonable explanation is that assuming that YLLs averted are lived out in average population morbidity is optimistic and they are likely lived in below average health. It is also possible that the direct effect of spending on morbidity is lower than the effect of it has on survival. If the latter is true, using the surrogacy assumption will result in an overestimate of YLDs averted.

Among the countries in the sample, the highest cost per DALY averted estimate is from either DALY 1 (51% of the sample) or DALY 4 (47%), with one exception, Moldova, where DALY 3 generates the highest cost per DALY averted. DALY 4 is generated by directly estimating the effect of changes in spending on per capita DALYs directly. Why directly estimating DALYs averted results in fewer averted in most LICs (87%) than directly estimated YLLs and YLDs averted and summing them isn't clear; however, the difference between cost per DALY averted from DALY 3 and 4 are very similar. Cost per DALY averted from DALY 4 is, on average among LICs in the sample, 12% higher than from DALY 3. As such, that cost per DALY averted is highest from DALY 3 for Moldova is random.

That DALY 1 results in the lowest cost per DALY averted for 17% of countries and the highest for 51% is, however, worth further exploration. The 17% of LICs for which cost per DALY averted from DALY 1 is the lowest estimate of cost per DALY averted are Cote d'Ivoire, the Democratic Republic of the Congo, Lesotho, Malawi, Niger, Nigeria, Rwanda, Sierra Leone and Zimbabwe, and these are the same 9 LICs for which mortality based estimates of cost per YLLs averted were lower than directly estimated YLLs averted. The number of mortality based YLLs averted between countries may differ for three main reasons.

One possibility is that YLLs among 0-5 and 15-60 year olds make up a small proportion of the total population, and so when the effect of spending on mortality is scaled up to the full population we estimate far more lives saved than in other countries. We find that this is not true for these countries. In fact, Niger and Sierra Leone have the highest ratio of individuals in the 0-5 and 15-60 age categories to total population. 0-5 and 15-60 year olds make up more than 92% of the total population in these countries. If anything these countries tend toward having 0-5 and 15-60 years constitute a disproportionately large proportion of the population.

A second possibility is that the elasticities on under-5, adult female and adult male mortality are higher in these countries than in other LICs. However, as the elasticities are perfectly in line with the other LICs, with no obvious outliers, this is not the explanation we are after.

A final possibility is that the mortality rates in these countries are much higher than in other countries, and indeed this plays the largest role in explaining why so many more YLLs are estimated to be averted in these countries when based on mortality effects. In particular, Zimbabwe, Sierra Leone, Malawi, Rwanda, Cote d'Ivoire, Nigeria and the Democratic Republic of the Congo all have adult male mortality rates of above 400 per 1,000, adult female mortality rates of above 350 per 1,000 and under-5 mortality rates of above 145 per 1,000. Lesotho suffers particularly high adult male and female mortality rates and Niger suffers from an especially high under-5 mortality rate of 227 per 1,000 (the second highest among LICs after Sierra Leone). As such, despite having very similar elasticities on these mortality rates to other LICs, when these elasticities are applied to the country specific mortality rate, far more lives are saved and thus YLLs averted than in other LICs with lower mortality rates.

Thus, for some countries basing YLLs averted on mortality effects underestimates total YLLs averted, while for others it may result in an overestimate. As such, it is not clear whether estimating YLLs directly is indeed a better measure, as it appears less sensitive to underlying mortality rates.

2.5.2 Middle-income countries

As shown in Figure 2, the range of cost per DALY averted estimates in middle-income countries crosses 1x GDP per capita for 21% of the 52 countries in this sample, but never reaches 3x GDP per capita. On average, the minimum cost per DALY averted estimate is 43% of 1x GDP per capita (range: 11% to 100%). For most middle-income countries, using a CET of 1x GDP per capita would lead to investment in interventions that displace more health than they generate.

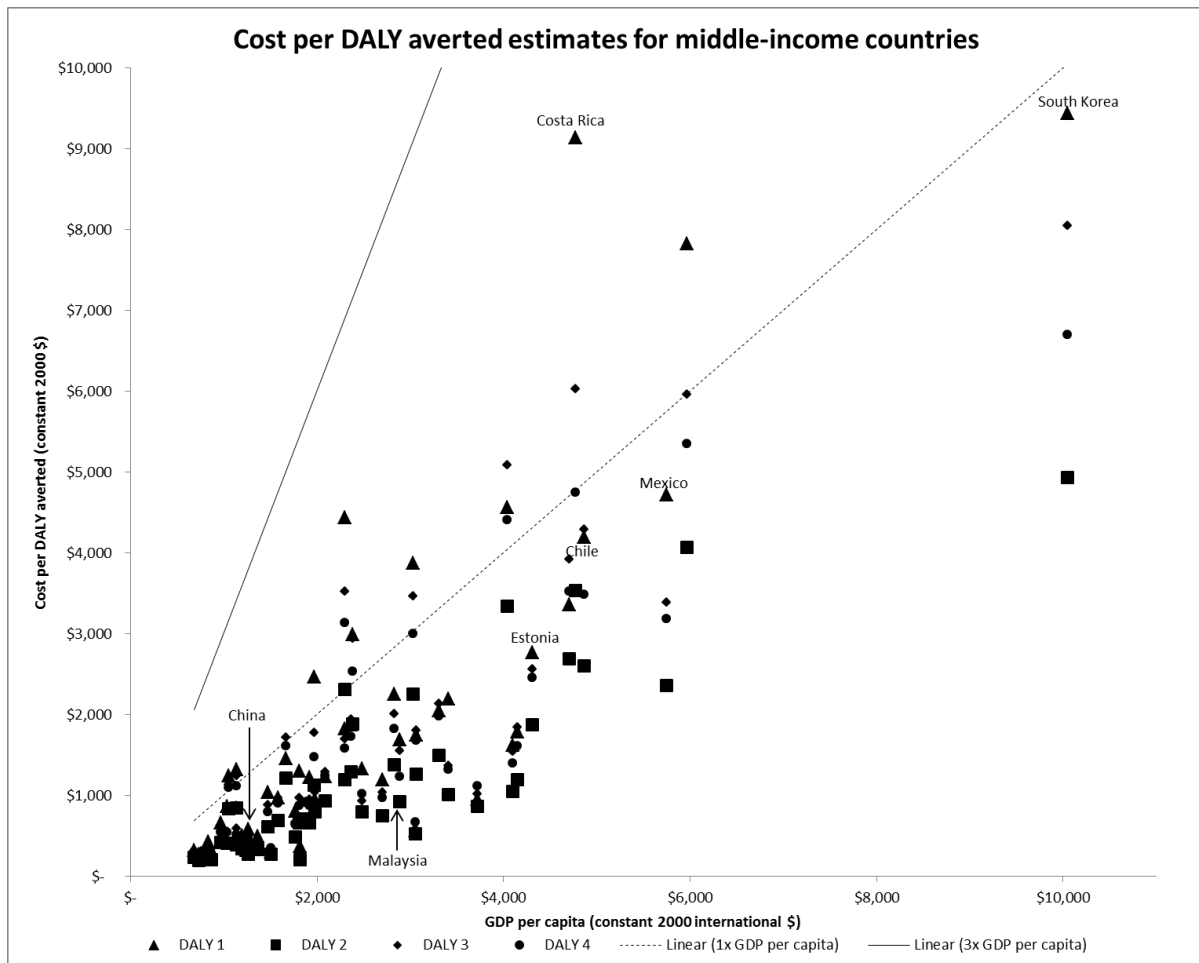


Figure 2. Cost per DALY averted estimates for middle-income countries from Chapter 2²²

The same general patterns are present in the cost per DALY averted estimates among middle-income countries that allowed us to compare 1) indirectly estimated effects on survival from mortality to directly estimated effects on survival and 2) indirectly estimated effects on morbidity from survival effects to directly estimated effects on morbidity, among low-income countries in the previous section. We also look at 3) whether there are any outliers, and what we can learn from them.

²² Argentina was in the original Bokhari et al (2007) dataset, but was dropped from the graph as no PPP conversion data was available. It is included in the Appendix. Converted from 2000 international \$, PPP using <http://data.worldbank.org/indicator/PA.NUS.PPPC.RF>, downloaded 13 November 2015. Equatorial Guinea was excluded as counter-intuitive sign of elasticity would make construction of a CET impossible.

In order to make the first comparison for middle-income countries, we can look at cost per DALY averted from DALYs 1 and 2. The lowest cost per DALY averted estimate was from DALY 2 for 98% of countries.²³ This is similar to LICs, where DALY 2 was the lowest for 83% of countries. As discussed in 2.5.1., DALY 1 and 2 differ from each other only in how YLLs averted are estimated, as they are estimated directly in DALY 2, but are based on mortality effects in DALY 1. Just as in low-income countries, directly estimating YLLs averted results in more YLLs averted for every middle-income country with one exception. Russia is the only middle-income country for which DALY 2 does not provide the lowest cost per DALY averted estimate, and this outlier is revisited later.

To make the second comparison for middle-income countries (comparing indirectly estimated effects on morbidity from survival effects against directly estimated effects on morbidity) we consider how DALY 3 and DALY 2 differ for this set of countries. The findings again mirror low-income countries: cost per DALY averted from DALY 2 is always lower than DALY 3. This strengthens the conclusion that the assumptions we employed around either the direct or indirect effect of changes in public expenditure on morbidity result in an overestimate of YLDs averted, thus leading to an underestimate of cost per DALY averted.

Just as in low-income countries, cost per DALY averted from DALY 3 and 4 are similar. Cost per DALY averted from DALY 3 is, on average among middle-income countries, 7% lower than from DALY 4.

Costa Rica stands out in Figure 2 as the middle-income country with the highest estimate of cost per DALY averted from DALY 1. Of all middle-income countries, Costa Rica's 1% increase in public expenditure on health per capita, whilst relatively high for its GDP per capita, generates the fewest DALYs averted per capita, owing to its baseline population distributions in terms of age and health. Since this is the denominator of the CET associated with DALY 1, it is understandably large in this sample of countries when viewed with countries' CETs ranked by GDP per capita.

Russia is a less obvious outlier as the only middle-income country for which DALY 2 is not the lowest cost per DALY averted estimate. As such, it presents an interesting case through which to better understand what drives each of the four estimates. It has a high adult male mortality rate at 443 per 1,000 as well as a high adult female mortality rate at 158 per 1,000, but a below median under-5 mortality rate among countries in the sample. However, the cost per DALY averted can't be driven by this aspect of YLLs averted alone as Botswana, Namibia, South Africa and Swaziland all have higher mortality rates among all three age groups than Russia does. It is instead the combination of two of the three factors driving YLLs averted in the LIC section above: mortality rates and the proportion of total population YLLs that YLLs among 0-5 and 15-60 year olds make up.

YLLs among 0-5 and 15-60 year olds make up a very high percentage of total YLLs in Botswana, Namibia, South Africa and Swaziland (87-93%), whereas in Russia YLLs among 0-5 and 15-60 year olds make up 57% of total YLLs. Thus when CLE is applied to the estimates of deaths averted, a large number of YLLs averted among adults in Russia results, and when YLLs are scaled up to be for the whole population this is carried through. Interestingly, basing YLLs averted on mortality effects results in a similar number of YLLs estimated to be averted compared to when YLLs averted are estimated directly (117,000 compared to 114,000 respectively).

Indeed, when using DALY 1 we find 161,000 DALYs averted compared to 157,000 in DALY 2 and 120,000 in DALY 3. That DALYs averted from DALY 1 and 2 are close is no surprise given how close

²³ There is no data on YLLs, YLDs or DALYs for Dominica, St. Kitts and Nevis, St. Lucia or St. Vincent and the Grenadines. As such, although these countries are included in Bokhari et al's (2007) dataset, we cannot get any further than cost per life saved among 0-5 and 15-60 year olds (as the ratio of YLLs among 0-5 and 15-60 year olds to YLLs in the total population is necessary), and so no results are reported for these countries.

the estimates of YLLs averted were, and that YLDs averted depend on YLLs averted for these two versions of DALYs. However, that estimated DALYs averted for DALY 3 is so much lower than DALY 1 or 2 makes clear how few YLDs are estimated to be averted when YLDs averted are directly estimated. Indeed, fewer than 6,000 are estimated to be averted in Russia when directly estimated.

The results of the four alternative approaches to calculating cost per DALY averted are presented in the Appendix for all countries where cost is measured in year 2000 international \$.

3. Estimates based on panel data

Moreno-Serra and Smith (2015) use a panel of 148 countries between 1995 and 2008 to investigate the effect of various types of health care expenditure on under-5 mortality, adult male mortality and adult female mortality.²⁴ Given the challenges associated with finding a suitable IV for health care expenditure, they instead implement the IV approach used by Brückner (2013) meaning that they use an IV to instrument the health outcomes rather than the health care expenditure and then explicitly account for the inherent reverse causality. In addition, a fixed effects specification is used to control for heterogeneity between countries. Unlike the Bokhari et al. (2007) model, where all variables are log-transformed prior to estimation, the Moreno-Serra and Smith (2015) model are estimated using raw values of variables and as such interpretation of regression coefficients is different. Instead of being interpreted as an elasticity, the reported results should be interpreted as estimates of deaths averted per 1,000 for an additional \$100 public expenditure on health per capita.

In their main model, the effect of public expenditure on health per capita on deaths per 1,000 is assumed to be constant across all countries. As such there are no interaction terms employed in their main model. In order to detect some non-linearities of the effect of public expenditure on health on mortality outcomes with respect to GDP per capita, Moreno-Serra and Smith (2015) implement a model where the public expenditure on health variable is interacted with LMIC status. The relevant effects of public expenditure on health on mortality outcomes for LMICs in each model are reported below.

Table 3. Estimates of deaths averted per 1,000 population for an additional \$100 public expenditure on health per capita (adapted from: Moreno-Serra and Smith (2015))

	Under-5 mortality	Adult female mortality	Adult male mortality
Effect for all countries in main model	-13.193	-2.583	-2.210
Effect for LMICs in interacted model	-90.772	-18.414	-12.004

No further outcomes are estimated using the Moreno-Serra and Smith (2015) model since it uses panel data and cannot be used to directly estimate effects on YLL per capita, YLD per capita or DALY per capita that are not available on a year-by-year basis. Therefore the corresponding CETs are derived using modelling assumptions to extrapolate beyond mortality effects of changes in expenditure. These are described in the sections below, and comparison is drawn between these results and those obtained in Chapter 2 throughout.

3.1 What are the mortality effects of changes in expenditure?

This estimated effect of a \$100 increase in government expenditure per capita on mortality²⁵ among children under-5, adult males and adult females from Moreno-Serra and Smith (2015) can be translated into a proportional change in the average mortality rate (across the years 1995-2008) in each of the three groups g by dividing the absolute value of the coefficient for each group by the average mortality rate for that group within Moreno-Serra and Smith (2015)'s sample of countries

²⁴ LMICs that are included in Moreno-Serra and Smith's original 2015 analysis, but not reported in the figures in the sections that follow are those that are not included in the Bokhari et al (2007) analysis and for which, therefore, there is not information from which to draw ratios necessary to estimate all of the possible DALY figures.

²⁵ Consistent with Moreno-Serra and Smith (2015), mortality rates are the average across the years included in the sample for each country.

from 1995 to 2008.²⁶ Dividing the resulting value by 100 gives the effect per dollar increase per capita (instead of per hundred dollars).

$$(34) \quad p_g = \frac{|coefficient_g|}{average MR_g} / 100$$

The average mortality rate for adults represents the cumulative probability of death by age 60 conditional on being alive at age 15 and these data, like that from Bokhari et al (2007), come from the World Bank. The mortality rates for children under-5 are obtained from Institute for Health Metrics and Evaluation (IHME) and represent the cumulative mortality rate for the first five years of life.

Table 4. Proportional effects of a \$1 increase in government expenditure on health

	children under age 5	adult females aged 15-60	adult males aged 15-60
% change in mortality rate p_g	1.43%	0.07%	0.06%

The calculated proportional effect for each group p_g can be applied to the average mortality rates of individual countries to obtain country specific effects. For each country and group, therefore, the proportional change in mortality resulting from a \$1 increase per capita in government spending reduces the mortality rate among children under 5, adult females and adult males by 1.43%, 0.07% and 0.06% respectively. To determine the number of lives saved among adult males and adult females resulting from the hypothetical change in spending we first determine the pre-change annual mortality rate $AMR_{pre_{ig}}$ from the mortality rate provided by the World Bank for either group g of males or females in country i using equation (1) from section 2.²⁷ (We again assume at first an annual constant probability over 45 years, and divide by 1,000 as the mortality rates are expressed as per 1,000.) As we know the risk of death is not constant between ages 15 and 60, we obtain five-year age specific mortality rates by weighting the constant annual mortality rates calculated by (33) by known mortality rates, which were calculated in (2).²⁸ The absolute baseline number of deaths among adult males or adults females can then be calculated by equation (3). The mortality rate after the hypothetical change in spend for country i and age group g is determined by:

$$(35) \quad MR_{post_{ig}} = (1 - p_g) * MR_{pre_{ig}}$$

This corresponds to equation (4) in Chapter 2, but here we are using the proportional effect calculated in (34) instead of a country specific elasticity as was done in Chapter 2. This is converted into an annual rate using equation 5. The constant rates are then weighted using the weights from (2) again, and the absolute number of deaths following the change in spend is calculated by equation (6). The number of deaths calculated among adults is then calculated by equation (7).

For under-5 mortality, although the data source used by Moreno-Serra and Smith (2015) is different to that used by Bokhari et al (2007), we can still apply the same set of calculations to get at deaths averted in children under-5 from a hypothetical change in government expenditure on health. We

²⁶ It must be transformed into a proportional effect instead of used directly because the outcome variables estimated by Moreno-Serra and Smith are not logged.

²⁷ We use the mortality rate used by Moreno-Serra and Smith (2015), which is the average mortality rate in a given age group in a given country across the years 1995-2008.

²⁸ We are using the year 2000 rates as these most closely correspond to the average between 1995 and 2008 that is available in public data.

use equations (8) through (14), but replace equation (11) with corresponding version of equation (35).

Any difference in calculated cost per deaths averted among adults between section 2.1 and this section will arise due to the different datasets, estimation methods as described earlier in the paper and the difference in baseline mortality rates (i.e., in 2000 versus on average between 1995 and 2008). Although the same outcome measure is used by both Bokhari et al (2007) and Moreno-Serra and Smith (2015) for adults, Bokhari et al (2007) use a cross-section from 2000 while Moreno-Serra and Smith (2015) use panel data from 1995-2008. Among children under-5 differences in the hypothetical cost per deaths averted will arise for the same reasons as for adults, but additional differences may also be due to the different datasets used for this variable.²⁹

3.2 What are the survival effects of changes in expenditure?

As the model employed by Moreno-Serra and Smith (2015) requires panel data, we cannot estimate the effect of changes in government expenditure on survival directly. The data used to construct YLLs (conditional life expectancy and mortality rates) from GBD are only available at 10 year intervals. While it is conceivable that a panel could be constructed using this data and annual data on the cumulative probability of death for individuals aged 0-5 and 15-60 available from the World Bank, doing so would require a number of assumptions with regard to, for example, if and how conditional life expectancies change between decades, that would render the data subject to additional assumptions and uncertainty. Additionally, lack of natural variation in conditional life expectancies between years would limit the variation in YLL to the variation in mortality in the 0-5 and 15-60 age categories only. Instead, we rely on what we learn from the effect of changes in expenditure on mortality. There are two ways that we can calculate the survival effects of changes in expenditure using what we know about the mortality effects.

- 1) Based on the estimated mortality effects of expenditure
- 2) Based on what we know from estimating YLLs averted from section 2.2

Each will be described below.

3.2.1 Indirectly estimating effects on survival from mortality

The same as in section 2.2, YLLs averted by the change in expenditure depends upon the age at which each life saved is saved, the gender of the individual and the country that they live in. Country, gender and age-specific CLE for year 2000 is applied to each life saved (i.e., death averted) among individuals aged 0-5 and 15-60 to determine YLL averted in this population using equation 17 from section 2.2. The same assumption applies: that individuals return to the country-specific mortality risk of the general population (matched for age and gender), and is likely to be optimistic with regard to life year effects. In addition, this estimate of YLL averted doesn't account for the effect that expenditure has on individuals within the population who do not fall into the 0-5 and 15-60 year age categories. As discussed earlier in this paper, assuming that expenditure affects only 0-5 and 15-60 year olds would be an extreme assumption, and instead we make a less strong assumption—that the effect on YLLs among 6-14 and 61+ year olds is proportional to the estimated effect on YLLs among 0-5 and 15-60 year olds. Further details on how this assumption is implemented are available in section 2.2. This is calculated using equation (21), which relies on the ratio of YLLs among 0-5 and 15-60 year olds to YLLs among the total population from equation (20).

²⁹ Under-5 mortality rates from the World Bank are estimates developed by the UN Inter-agency Group for Child Mortality Estimation (UNICEF, WHO, World Bank, UN DESA Population Division. More information on the estimation method is available at <http://www.ploscollections.org/article/browseIssue.action?issue=info:doi/10.1371/issue.pcol.v07.i19>. More information on the method used by IHME is available at [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(10\)60703-9/abstract](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(10)60703-9/abstract).

3.2.2 Adjusting for directly estimated effects on survival

Although we cannot estimate the effect of expenditure on YLLs directly using Moreno-Serra and Smith (2015), we can still use what we know about the effect of expenditure on YLLs from what was estimated in section 2.2 using Bokhari et al (2007)'s model. More specifically, we can assume that the ratio between directly estimated YLLs averted and calculated YLLs averted from mortality estimates using Bokhari et al (2007)'s model and data would be similar. That ratio is calculated as:

$$(36) \quad \theta_i = \frac{\text{directly estimated YLLs averted}_i}{\text{mortality based YLLs averted, all ages}_i}$$

The numerator is calculated in second part of section 2.2.2 (directly estimating the effect of changes in expenditure on survival) and the denominator is calculated by equation (21). Multiplying θ_i by scaled up YLLs averted based on estimated mortality effects from section 3.2 gives an estimate of the YLLs we would expect to be estimated to be averted if we were able to estimate YLLs averted directly, assuming the relationship between direct estimation of YLLs averted and calculated scaled up YLLs averted is the same as it was when Bokhari et al (2007)'s model and data were used.

$$(37) \quad YLL \text{ averted, all ages} = \theta_i * YLL \text{ averted, all ages}_i$$

Consistent with Chapter 2, average cost per YLL averted was generally lower when it was “directly estimated” (i.e., the ratio θ_i was applied) than when it was based on scaled up mortality effects.

In MICs the cost per YLL averted is higher on average (whether mortality or direct estimation based) when using the model and data (with the addition of adult female and male mortality) of Bokhari et al (2007) than Moreno-Serra and Smith (2015). However, in LICs the opposite is true, with cost per YLL being higher on average when based on Moreno-Serra and Smith (2015). (See Table 5³⁰.)

Table 5. Cost per YLL averted

		(1)	(2)	(3)	(4)
MICs	AVERAGE	\$ 7,474	\$ 4,516	\$ 2,628	\$ 1,653
	MAX	\$ 32,126	\$ 13,480	\$ 6,761	\$ 3,662
	MIN	\$ 1,025	\$ 829	\$ 684	\$ 401
LICs	AVERAGE	\$ 585	\$ 405	\$ 816	\$ 582
	MAX	\$ 3,396	\$ 2,489	\$ 3,057	\$ 2,680
	MIN	\$ 20	\$ 22	\$ 146	\$ 149

(1) Estimated in Section 2.2.1
 (2) Estimated in Section 2.2.2
 (3) Estimated in Section 3.2.1
 (4) Estimated in Section 3.2.2

Cost per YLL averted for each country is based on the following three core issues, each of which differ depending upon whether the Bokhari et al (2007) or the Moreno-Serra and Smith (2015) model and dataset are used:

³⁰ Only the mortality based estimates of cost per YLL averted can be calculated for Bahrain, Czech Republic, Djibouti, Fiji, Iran, Iraq, Latvia, Maldives, Malta, Oman, Poland, Saudi Arabia, Suriname, Syria, Bhutan, Central African Republic, Laos, Liberia, Solomon Islands and Timor-Leste as there are no ratios from section 2 for these. They are therefore not included in the estimations of the averages.

1. Econometric estimates (i.e., elasticities versus proportional effects)
2. Baseline mortality rates (i.e., year 2000 versus average over 1995-2008)
3. Costs (i.e., 1% of public expenditure on health versus \$1 per person)

While econometric estimates differ between chapters 2 and 3, within each chapter they differ very little if at all between MICs and LICs. Using Moreno-Serra and Smith (2015), the same proportional effects for under-5s, adult females and adult males are applied in LICs as in MICs. Using Bokhari et al (2007), the elasticities differ little between MICs and LICs, with the average elasticity for under-5 and adult male being the same between the two and the average elasticity for adult female mortality being 0.01% lower in magnitude in LICs than MICs.³¹ As such, the difference must be driven by either baseline mortality rates or costs.

The comparable proportional effects for Moreno-Serra and Smith (2015) do not differ by country and were given in Table 4. The proportional effect on under-5 mortality is larger (1.43%) than the corresponding average elasticity from Bokhari et al (2007), while the effects on adult female and adult male were smaller (0.07% and 0.06% respectively). Given that CLE is higher for children under-5 than for adults, we would expect more YLLs to be gained when using Moreno-Serra and Smith (2015)'s model if all else was the same.

Baseline mortality rates differ between MICs and LICs. Moreno-Serra and Smith (2015) use an average of the years 1995-2008 for which observations exist as the mortality rate, and in their dataset the average under-5 mortality rate is 3.3 times higher in LICs than in MICs and the average adult female (male) mortality rate is 1.9 (1.4) times higher in LICs than MICs. Similarly in Bokhari's dataset and additional World Bank data on adult female and adult male mortality rates in 2000, the under-5 mortality rate is 3.5 times higher in LICs than MICs, while the adult female (male) mortality rate is 1.4 (2.0) times higher.

Whilst Moreno-Serra and Smith (2015) considers a \$1 increase in public expenditure on health per capita Bokhari et al (2007) considers a 1% increase. Therefore, although elasticities vary little for Bokhari et al (2007) and do not change in Moreno-Serra and Smith (2015) and the patterns of baseline mortality rates do not grossly differ between the two time periods, cost per DALY averted may vary with income group owing to the assumptions around the change in public expenditure on health. On average, a \$1 increase in public expenditure on health per capita is 2.56 times greater for an LIC than a MIC. The corresponding figure for a 1% increase in public expenditure on health per capita shows a completely different relationship with the absolute number of \$s being 4.53 times greater for a MIC, on average, than a LIC. Therefore we would expect the cost per YLLs averted from Moreno-Serra and Smith (2015) to be relatively high for LICs and relatively low for MICs in comparison with Bokhari et al (2007).

3.3 What are the morbidity effects of changes in expenditure?

In section 2.3 three ways of getting at the morbidity effects of changes in expenditure were presented. Only the first of these two was based only on mortality effects. The second was based on the effect of expenditure on YLL and the third involved directly estimating YLD averted. As the model employed by Moreno-Serra and Smith (2015) requires panel data, we cannot estimate YLDs directly. Nonetheless, we can make use of what was learned in section 2.3 about the effect of expenditure on YLDs relative to the effect of expenditure on mortality based estimates of survival. Thus we retain different options for calculating the effect of changes in expenditure on YLDs. These are based on:

³¹ See footnote 7 for more details.

- 1) survival effects as a surrogate for morbidity effects
 - a. mortality based survival effects
 - b. survival effects based on the relationship between directly estimated survival effects from section 2.2 and mortality-based survival effects
- 2) the relationship between directly estimated effects on YLDs averted from section 2.2 and mortality-based survival effects

As in section 2.3, each of these is outlined below with a description of what they capture (the direct or indirect effects) and the assumptions associated with each. The results are then compared to those from section 2.3.

3.3.1 Indirectly estimating effects on morbidity from survival effects

As we did previously in section 2.3, we can assume that the effect of changes in expenditure on YLLs (as measured by mortality based estimates or using the ratio from equation 36) is a good surrogate for the effect on YLD. In other words, the proportional effect of the effect of a change in expenditure on YLD is the same as the proportional effect of the effect of a change in expenditure on YLL. To implement this assumption, we need the ratio of total YLDs in a given country to total YLLs in that country, which are calculated by equation (23). We apply this ratio γ_i to the estimates of change in YLL due to changes in spending to obtain changes in YLD resulting from the hypothetical change in spend using equation (24). If we believe that LMIC governments will give greater priority to averting mortality than morbidity, our assumption is optimistic and will provide an overestimate of YLDs averted. Nonetheless, it is unlikely that changes in spending will have no effect at all on morbidity, and so the assumption we have made represents one option on a spectrum of possibilities.

Using survival effects as a surrogate for morbidity captures the direct effect that changes in government spending on health will have on morbidity, but does not capture the indirect effect that spending will have through YLLs averted. As in section 2.3, we can account for this effect by assuming that YLLs averted will be lived in average health. This may be optimistic (as deaths averted may be among individuals with below average health), but represents a reasonable assumption. Thus this indirect effect can be calculated by equation (26) and YLDs averted are calculated by (27).

3.3.2 Adjusting for directly estimated morbidity

Although we cannot estimate the effect of changes in spending on YLDs directly in this section, we were able to in the previous section (2.3) since that model required only cross-sectional data. We therefore do know something about the relationship between the effect of changes in spending on mortality and morbidity that can be applied here. Specifically, we know the ratio between the directly estimated effect of spending on mortality and the directly estimated effect of spending on morbidity from section 2, which is expressed as:

$$(38) \quad \varphi_i = \frac{YLD_i}{YLL_{averted,all\ ages_i}}$$

The numerator is the number of YLDs averted in a given country based on the direct estimation of the effect of changes in spending on YLDs from the first part of section 2.3 and the denominator is the number of YLLs averted in that country based on the estimation of the effect of changes in spending on mortality (which have been scaled up to reflect the effect at the population level) from equation (21). We can take this ratio and apply it to the estimate of the effect of changes in spending on mortality from the Moreno-Serra and Smith (2015) model to get an estimate of what we might have estimated in terms of YLDs averted if there was panel data for YLDs and we could directly estimate it with this model.

$$(39) \quad YLD \text{ averted, all ages} = \varphi_i * YLL \text{ averted, all ages}$$

Because this method uses a ratio that includes directly estimated YLDs from section 2, and directly estimated YLDs capture both the direct and indirect effects of changes in spending on morbidity, there is no need to make an adjustment to the YLLs calculated in section 3.2 when summing them to obtain DALYs.

3.4 Adjusting for directly estimated effect on survival and morbidity

We would ideally like to be able to estimate the effect of changes in government spending on health (as represented by DALYs, a summary measure of morbidity and mortality) directly, but due to the lack of panel data for DALYs we cannot. We can, however, use what we know about the relationship between the estimate of the effect on survival and the direct estimation of DALYs from section 2.4 by utilizing the following ratio:

$$(44) \quad \omega_i = \frac{DALY \text{ averted}_i}{YLL \text{ averted, all ages}_i}$$

This assumes that the relationship between the effect of changes in spending on DALYs and survival (as calculated by the scaled up YLL averted effects based on mortality effects) would be the same if we could directly estimate DALYs averted with the Moreno-Serra and Smith (2015) dataset and model. Because the ratio includes directly estimated DALYs averted, and that accounts for both the direct and indirect effect of changes in spending on morbidity, there is no need to adjust these estimates.

3.5 Estimates of cost per DALY averted thresholds

Using additional information gained in section 2 with GBD data from 2000, we are able to calculate four possible estimates of cost per DALY averted, each specific to a country's health expenditure, age and gender distributions, baseline mortality rates, conditional LEs, and 2000 YLL and YLD burden. (See Table 6.)

Table 6. Different methods for estimating and calculating DALYs averted from Moreno-Serra and Smith (2015)

		1	2	3	4
YLL averted		Based on indirectly estimating effects on survival from mortality	"Directly estimated" (i.e., ratio of directly estimated to based on mortality effects from Bokhari)	"Directly estimated" (i.e., ratio of directly estimated to based on mortality effects from Bokhari)	
YLD averted	Direct effect	Uses mortality-based survival effects as a surrogate for morbidity effects	Uses "directly estimated" survival effects as a surrogate for morbidity effects	"Directly estimated" (i.e., ratio of directly estimated to based on mortality effects from Bokhari)	"Directly estimated" (i.e., ratio of directly estimated to based on mortality effects from Bokhari)
	Indirect effect	Uses average overall population health as a surrogate for increase in YLD burden associated with increase in YLLs averted	Uses average overall population health as a surrogate for increase in YLD burden associated with increase in YLLs averted		

DALY 1 can be estimated from both Bokhari et al (2007)'s data and model as well as Moreno-Serra and Smith (2015)'s data and model. Owing to lack of panel data over the years 1995 to 2008 on YLLs, YLDs and DALYs, DALYs 2-4 cannot be directly generated from the results of the Moreno-Serra and Smith (2015) model for Chapter 3. The relationship between each of DALY 2, 3 and 4 in section 3 and DALY 2, 3 and 4 in section 2 can be boiled down to the relationship between mortality based YLLs averted in each section. And given that the same assumptions apply in each section with regard to obtaining YLDs averted, we can simplify the DALY calculation for DALYs 2, 3 and 4 to:

$$(45) \quad Ch. 3 DALY x = Ch. 2 DALY x * \frac{Ch.3 DALY 1}{Ch. 2.DALY 1}$$

As in section 2.5, each estimate of DALYs averted is used to calculate a cost per DALY averted by equation (33). The ranking of DALYs 1, 2 3 and 4 is unchanged between Chapters 2 and 3, and the observations reported in section 2.5 remain true here. Namely, that when YLLs cannot be estimated directly, mortality based estimates of YLLs averted are a good alternative. On the other hand, directly estimating YLDs averted results in far fewer averted than assuming that the effect of

changes in spending is the same on morbidity as it is on YLLs averted (whether mortality based or directly estimated), and as such where this assumption is applied the CET is likely to be an underestimate. These are forgone conclusions given the ratios we've used to obtain DALYs 2-4 in section 3.

However, more interestingly we can compare cost per DALY averted for DALY 1 between the Chapters 2 and 3. Given that YLDs are not directly estimated in DALY 1, whether cost per DALY averted is higher or lower when based on Moreno-Serra and Smith (2015) hinges upon whether cost per YLL averted from Chapter 3 is higher or lower than in Chapter 2. This is discussed in detail in 3.2, where we show that the primary driver in differences between the two models is costs (i.e., 1% of public expenditure on health versus \$1 per person).

3.5.1 Low-income countries

Figure 3 shows cost per DALY averted for LICs using Moreno-Serra and Smith's (2015) model and data. Cost per DALY averted is given in 2005 international \$³²; however, GDP per capita from Chapter 2 is used and is therefore given in 2000 international \$.³³

The full range of cost per DALY averted estimates lies below 1x GDP per capita for 3 of the 45 countries on the graph. For more than half, the highest cost per DALY averted estimate is lower than 50% of 1x GDP per capita. This further underscores the message from 3.5 that interventions adopted using a 1x GDP per capita threshold will displace more health than they generate.

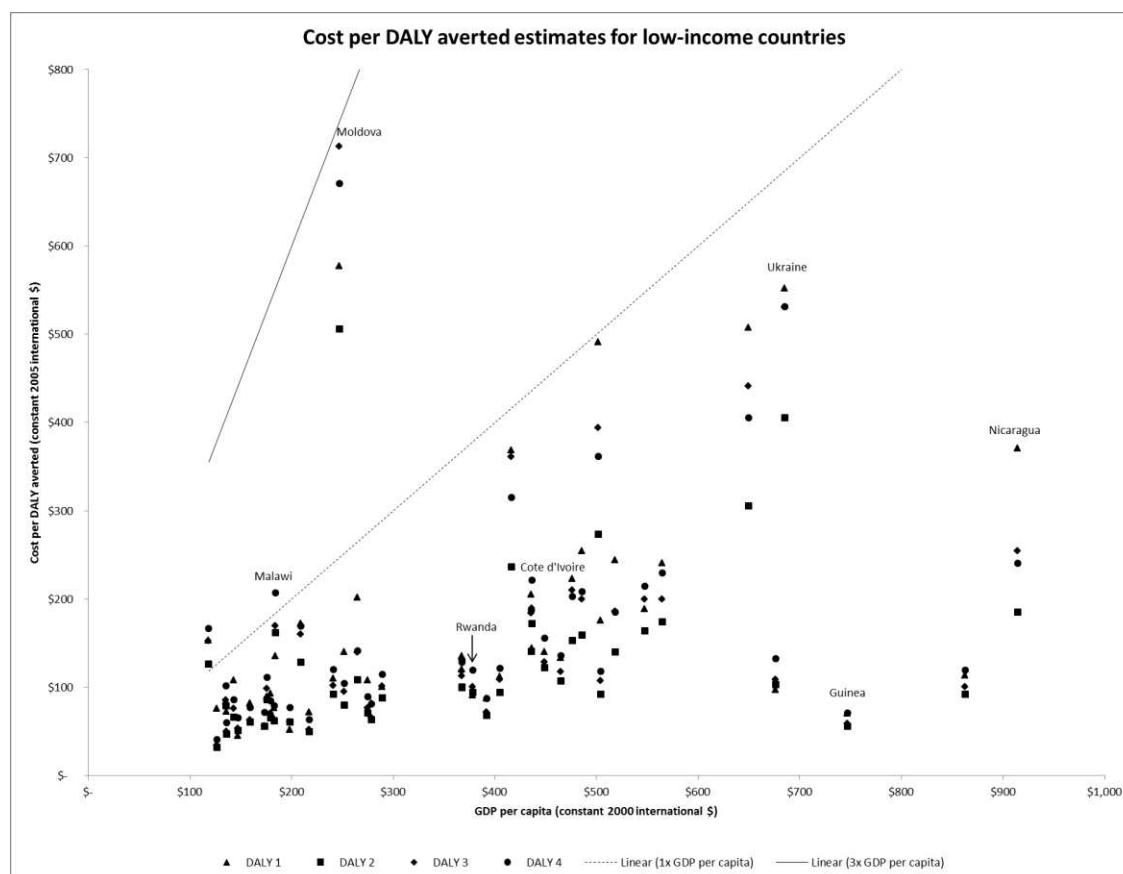


Figure 3. Cost per DALY averted estimates for low-income countries from Chapter 3

³² Converted from PPP using <http://data.worldbank.org/indicator/PA.NUS.PPPC.RF>, downloaded 13 November 2015.

³³ Only LICs for which all 4 CETs could be estimated are included. Countries which were not included in Bokhari et al's (2007) dataset are therefore excluded.

Given that the relative ranking of the cost per DALY averted estimates remains the same for each country in this chapter as in Chapter 2, all of the conclusions reached there remain true here. However, comparing cost per DALY averted between Chapters 2 and 3, we find that, on average, for countries in both samples, cost per DALY averted for DALY 1 is 223% higher in Chapter 3 than in Chapter 2.

3.5.2 Middle-income countries

Unlike in Chapter 2 where most cost per DALY averted estimates for middle-income countries fell below 1x GDP per capita, in Chapter 3 all fall below that arbitrary line, strengthening the point that the adoption of interventions or programmes using GDP based CETs will lead to a net health loss.

In fact, the estimates of cost per DALY averted for middle-income countries are on average 57% as high as those estimated in Chapter 3.³⁴ The range of estimates from Chapter 3 is also generally lower than from Chapter 2 for each country. This results from the fact that all the variation within cost per DALY estimates from each section arises from the difference in the DALY estimates (and not the costs) and the cost per DALY averted thresholds are inversely proportional to the DALY estimates. Hence it is not a surprise that the absolute range is larger when the change in spending is higher.

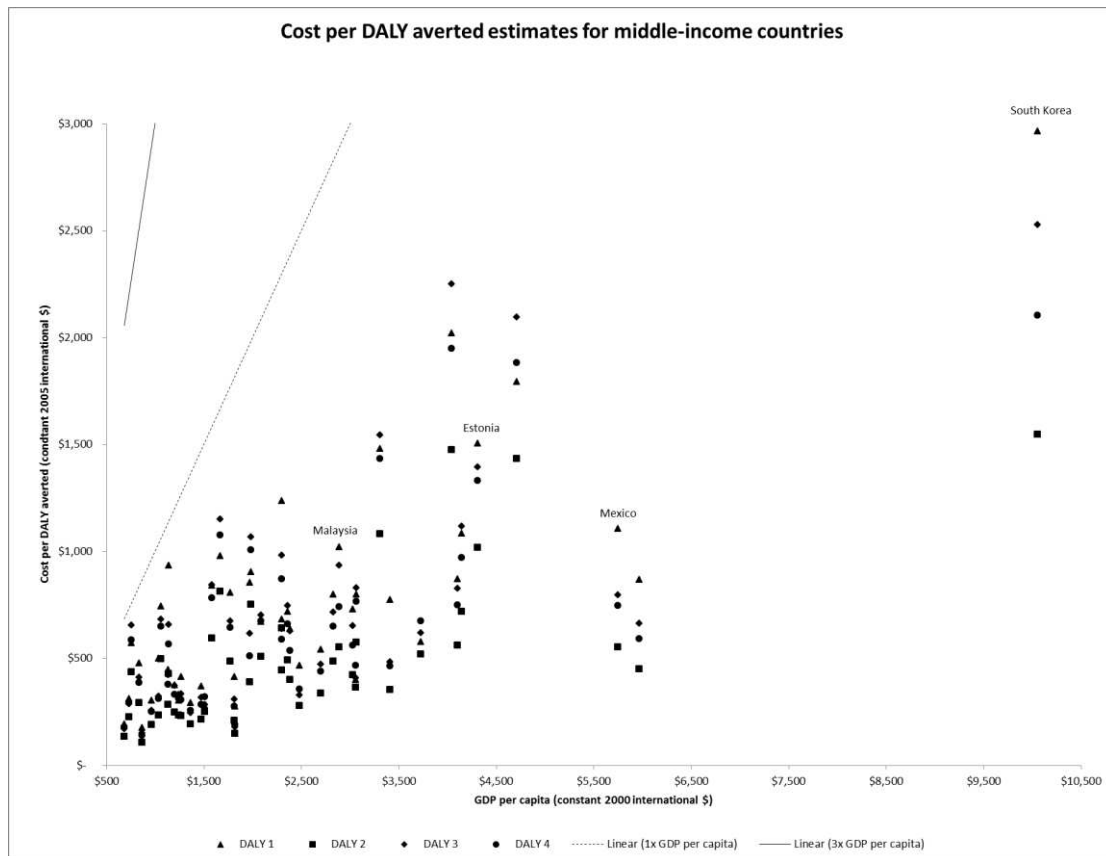


Figure 4. Cost per DALY averted estimates for middle-income countries from Chapter 3³⁵

³⁴ China and Costa Rica are omitted although they were included in Moreno-Serra and Smith’s (2015) dataset as there was no data on adult female and adult male mortality for these countries.

³⁵ Only MICs for which all 4 CETs could be estimated are included. Countries which were not included in Bokhari et al’s (2007) dataset are therefore excluded. Jamaica was converted from PPP using the 2006 conversion factor as no conversion factor was available for 2005.

4. Implications for policy and research

The framework of analysis set out in this paper can be applied to the results of any econometric study which is thought to identify plausible effects on mortality of changes or differences in health expenditure. The examples used illustrate two different, but sophisticated, approaches to identification in situations where country level cross section or panel data are available. The analysis has demonstrated how survival effects can be derived when mortality effects are estimated as either elasticities or as absolute effects, whilst reflecting the epidemiology and demographics of specific countries. The assumptions required to move from estimates of the effect of changes in expenditure on mortality to survival, morbidity, and ultimately to DALYs are made explicit. By extending the cross sectional analysis to include other outcome data (see Chapter 2), it is also possible to estimate the effects on survival, morbidity and DALYs directly. This provides the opportunity to evaluate the assumptions required when estimating CETs from mortality effects alone. The results indicate that, when summary measures of survival and health are estimated directly, the distribution of CETs is similar to those based only on estimated mortality effects. This suggests that the assumptions required to move from estimates of mortality effects to DALYs are not unreasonable.

An important criticism of the Bokhari et al. (2007) and Moreno-Serra and Smith (2015) papers is that the identification strategy relies on an empirically observable relationship between contemporaneous public expenditure on health and mortality. This has two drawbacks: i) the effect of spending on mortality is likely to be lagged, where spending in a year affects mortality not only in the present year, but in future years too; and ii) the relationship between different types of healthcare expenditures is not explicitly modeled, so, for example, an increase in public expenditure on health may be offset by a decrease in private expenditure on health. Both limitations point to an underestimation of the effect of public expenditure on health, since neither lagged effects are captured, nor are substitution effects fully accounted for. The implication of this is that the CETs are likely overestimated, since the relevant health effects are likely to have been underestimated.

Using the data and models of Bokhari et al. (2007) and Moreno-Serra and Smith (2015), we are able to calculate a range of CETs for each LMIC. All fall below 3x GDP per capita, a commonly accepted level above which a treatment or intervention is judged to be cost-ineffective, and nearly all are also below 1x GDP per capita, the commonly accepted level below which something is deemed highly cost-effective. This suggests that current interventions acceptable at a 1x GDP per capita threshold (or even below it) may be displacing more health than they generate. This is in line with the conclusion of Woods et al (2015), who also calculate CETs well below 1-3x GDP per capita. We are able to compare the full range of estimates from Woods et al (2015) and from this study for countries included in both and for which all eight CETs could be calculated. Our minimum and maximum estimates are generally lower than those found by Woods et al (2015), and when we use a crude method to inflate our estimates to 2013 international \$ they are always lower.³⁶

Very few LMICs have estimated their own CETs, and while these estimates provide a range that can serve as a guide, within country estimates are ideal. However, the only country to have conducted such a study to date is the UK where expenditure and mortality data are available at a local area and disease-specific level. Such data is unlikely to be available for LMICs and further research is required which can make best use of what is currently available or could be easily collected or extracted from existing sources. Within country estimates are preferable because they are best placed to directly estimate the opportunity cost of expenditure in a given country. The approach taken in this paper is to use an identification strategy based on an international health production function, which is then used to inform an approximation of a country-specific health production function. This second best

³⁶ Cost per DALY averted/(2000 GDP per capita/2013 GDP per capita)

approach is applied to country-specific baseline data to give country-specific CETs. As such, these estimates can be considered as an improvement upon the type of norms that have been widely cited and could be used as interim guidance while research on within country estimates is undertaken.

The major contribution of this paper, however, is not the specific range of estimates for particular countries but the demonstration that it is now possible to make what was previously an abstract and confused concept real. Clarity about both the concept and the type of empirical analysis that can support its assessment can help inform decision making within low- and middle-income countries and influence how other supra national bodies make recommendations and investment and purchasing decisions. As well as identifying the real value of devoting more resources to health care, these continuing research efforts can contribute to greater accountability in low- and middle-, as well as in high-income countries, for the health care and other expenditure decisions made at a local, national and supra national levels.

References

- Bokhari, F.A.S., Gai, Y., Gottret, P. Government health expenditures and health outcomes. *Health Economics*, 16(3), pp257-273. <http://onlinelibrary.wiley.com/doi/10.1002/hec.1157/abstract> [Accessed December 3, 2015].
- Brückner, M., 2013. On the simultaneity problem in the aid and growth debate. *Journal of Applied Econometrics*, 28(1), pp.126–150. Available at: <http://doi.wiley.com/10.1002/jae.1259> [Accessed December 3, 2015].
- Cawley, J., 2015. A selective review of the first 20 years of instrumental variables models in health-services research and medicine. *Journal of Medical Economics*, 18(9), pp.721–34. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25899087> [Accessed December 1, 2015].
- Claxton, K., Sculpher, M., et al., 2015. Causes for concern: is NICE failing to uphold its responsibilities to all NHS patients? *Health Economics*, 24(1), pp.1–7. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25488707> [Accessed November 27, 2015].
- Claxton, K., Martin, S., et al., 2015. Methods for the estimation of the National Institute for Health and Care Excellence cost-effectiveness threshold. *Health Technology Assessment (Winchester, England)*, 19(14), pp.1–503, v–vi. Available at: <http://www.journalslibrary.nihr.ac.uk/hta/volume-19/issue-14#abstract> [Accessed November 17, 2015].
- Cochrane, A.L., St Leger, A.S. & Moore, F., 1978. Health service “input” and mortality “output” in developed countries. *Journal of Epidemiology & Community Health*, 32(3), pp.200–205. Available at: <http://jech.bmj.com/content/32/3/200> [Accessed November 30, 2015].
- Dakin, H. et al., 2014. The influence of cost-effectiveness and other factors on NICE decisions. *Health Economics*. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25251336> [Accessed December 2, 2015].
- Devlin, N. & Parkin, D., 2004. Does NICE have a cost-effectiveness threshold and what other factors influence its decisions? A binary choice analysis. *Health Economics*, 13(5), pp.437–52. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/15127424> [Accessed December 2, 2015].
- Drummond, M. et al., 2015. The cost effectiveness threshold. In *Methods for the Economic Evaluation of Health Care Programs*. Oxford: Oxford University Press, pp. 83–98.
- Epstein, D.M. et al., Efficiency, equity, and budgetary policies: informing decisions using mathematical programming. *Medical Decision Making :An International Journal of the Society for Medical Decision Making*, 27(2), pp.128–37. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17409363> [Accessed November 30, 2015].
- Filmer, D. & Pritchett, L., 1999. The impact of public spending on health: does money matter? *Social Science & Medicine* (1982), 49(10), pp.1309–23. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/10509822> [Accessed November 30, 2015].
- Getzen, T.E., 2000. Health care is an individual necessity and a national luxury: applying multilevel decision models to the analysis of health care expenditures. *Journal of Health Economics*, 19(2), pp.259–270. Available at: <http://ideas.repec.org/a/eee/jhecon/v19y2000i2p259-270.html> [Accessed December 3, 2015].

GHDx, 2014. Global Burden of Disease Study 2010 (GBD 2010) Disability Weights. Available at: <http://ghdx.healthdata.org/record/global-burden-disease-study-2010-gbd-2010-disability-weights> [Accessed December 3, 2015].

Gravelle, H.S.E. & Backhouse, M.E., 1987. International cross-section analysis of the determination of mortality. *Social Science & Medicine*, 25(5), pp.427–441. Available at: <http://www.sciencedirect.com/science/article/pii/0277953687901675> [Accessed November 30, 2015].

Grosse, S.D., 2008. Assessing cost-effectiveness in healthcare: history of the \$50,000 per QALY threshold. *Expert Review of Pharmacoeconomics & Outcomes Research*, 8(2), pp.165–78. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20528406> [Accessed November 17, 2015].

Hammitt, J.K. & Robinson, L.A., 2011. The Income Elasticity of the Value per Statistical Life: Transferring Estimates between High and Low Income Populations. *Journal of Benefit-Cost Analysis*, 2(1). Available at: <http://www.degruyter.com/view/j/jbca.2011.2.1/jbca.2011.2.1.1009/jbca.2011.2.1.1009.xml> [Accessed December 3, 2015].

Jamison, D.T. et al., 2013. Global health 2035: a world converging within a generation. *Lancet*, 382(9908), pp.1898–955. Available at: <http://www.thelancet.com/article/S0140673613621054/fulltext> [Accessed July 10, 2014].

Jirawattanapaisal, T. et al., 2009. Evidence-based decision-making in Asia-Pacific with rapidly changing health-care systems: Thailand, South Korea, and Taiwan. *Value in Health : The Journal of the International Society for Pharmacoeconomics and Outcomes Research*, 12 Suppl 3, pp.S4–11. Available at: <http://www.sciencedirect.com/science/article/pii/S1098301510603336> [Accessed November 21, 2015].

Marseille, E. et al., 2015. WHO | Thresholds for the cost–effectiveness of interventions: alternative approaches. *Bulletin of the World Health Organization*, 93(2), pp.118–124. Available at: <http://www.who.int/bulletin/volumes/93/2/14-138206-ab/en/> [Accessed November 27, 2015].

Martin, S., Rice, N. & Smith, P.C., 2008. Does health care spending improve health outcomes? Evidence from English programme budgeting data. *Journal of Health Economics*, 27(4), pp.826–842. Available at: <http://ideas.repec.org/a/eee/jhecon/v27y2008i4p826-842.html> [Accessed November 30, 2015].

Milligan, C. et al., 2014. Value of a statistical life in road safety: A benefit-transfer function with risk-analysis guidance based on developing country data. *Accident Analysis & Prevention*, 71, pp.236–247. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24952315> [Accessed October 1, 2015].

Moreno-Serra, R. & Smith, P.C., 2015. Broader health coverage is good for the nation’s health: evidence from country level panel data. *Journal of the Royal Statistical Society. Series A, (Statistics in Society)*, 178(1), pp.101–124. Available at: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4280714&tool=pmcentrez&rendertype=abstract> [Accessed November 27, 2015].

National Institute for Clinical Excellence, 2004. *Guide to the Methods of Technology Appraisal*, London. Available at:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/191504/NICE_guide_to_the_methods_of_technology_appraisal.pdf [Accessed December 2, 2015].

Neumann, P.J., Cohen, J.T. & Weinstein, M.C., 2014. Updating cost-effectiveness—the curious resilience of the \$50,000-per-QALY threshold. *The New England Journal of Medicine*, 371(9), pp.796–7. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25162885> [Accessed November 22, 2015].

Newall, A.T., Jit, M. & Hutubessy, R., 2014. Are current cost-effectiveness thresholds for low- and middle-income countries useful? Examples from the world of vaccines. *PharmacoEconomics*, 32(6), pp.525–31. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/24791735> [Accessed November 24, 2015].

Nimdet, K. & Ngorsuraches, S., 2015. Willingness to pay per quality-adjusted life year for life-saving treatments in Thailand. *BMJ Open*, 5(10), p.e008123. Available at: <http://bmjopen.bmj.com/content/5/10/e008123.full> [Accessed November 9, 2015].

Nixon, J. & Ulmann, P., 2006. The relationship between health care expenditure and health outcomes. Evidence and caveats for a causal link. *The European Journal of Health Economics : HEPAC : Health Economics in Prevention and Care*, 7(1), pp.7–18. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16429295> [Accessed November 24, 2015].

Or, Z., 2001. Exploring the Effects of Health Care on Mortality Across OECD Countries. Available at: http://www.oecd-ilibrary.org/social-issues-migration-health/exploring-the-effects-of-health-care-on-mortality-across-oecd-countries_716472585704 [Accessed November 30, 2015].

Rawlins, M.D. & Culyer, A.J., 2004. National Institute for Clinical Excellence and its value judgments. *BMJ (Clinical Research ed.)*, 329(7459), pp.224–7. Available at: <http://www.bmj.com/content/329/7459/224> [Accessed November 29, 2015].

Revill, P. et al., 2014. *Using cost-effectiveness thresholds to determine value for money in low- and middle-income country healthcare systems: are current international norms fit for purpose?*, York. Available at: https://www.york.ac.uk/media/che/documents/papers/researchpapers/CHERP98_costeffectiveness_thresholds_value_low_middle_income_countries.pdf [Accessed November 27, 2015].

Ryen, L. & Svensson, M., 2014. The willingness to pay for a quality adjusted life year: a review of the empirical literature. *HealthEconomics*. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/25070495> [Accessed October 15, 2015].

Salomon, J.A. et al., 2012. Common values in assessing health outcomes from disease and injury: disability weights measurement study for the Global Burden of Disease Study 2010. *Lancet (London, England)*, 380(9859), pp.2129–43. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/23245605> [Accessed November 19, 2015].

Stinnett, A.A. & Paltiel, A.D., 1996. Mathematical programming for the efficient allocation of health care resources. *Journal of Health Economics*, 15(5), pp.641–653. Available at: <http://www.sciencedirect.com/science/article/pii/S0167629696004936> [Accessed October 4, 2015].

Thavorncharoensap, M. et al., 2013. Estimating the willingness to pay for a quality-adjusted life year in Thailand: does the context of health gain matter? *ClinicoEconomics and Outcomes Research : CEOR*, 5, pp.29–36. Available at: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3548562&tool=pmcentrez&rendertype=abstract> [Accessed December 1, 2015].

The Subcommittee for Development of the National List of Essential Medicines, 2007. The threshold at which an intervention becomes cost-effective.

Viscusi, W.K. & Aldy, J.E., 2003. The Value of a Statistical Life: A Critical Review of Market Estimates throughout the World. Available at: <http://www.nber.org/papers/w9487> [Accessed December 2, 2015].

Wagstaff, A. & Claeson, M., 2004. *Rising to the Challenges*, Washington D.C. Available at: <http://web.worldbank.org/archive/website01063/WEB/IMAGES/296730PA.PDF> [Accessed November 30, 2015].

Weinstein, M. & Zeckhauser, R., 1973. Critical ratios and efficient allocation. *Journal of Public Economics*, 2(2), pp.147–157. Available at: <http://ideas.repec.org/a/eee/pubeco/v2y1973i2p147-157.html> [Accessed November 30, 2015].

WHO, 2015. Cost effectiveness and strategic planning (WHO-CHOICE). Available at: http://www.who.int/choice/costs/CER_levels/en/ [Accessed December 4, 2015].

WHO, 2001. *Macroeconomics and Health: Investing in Health for Economic Development*, Geneva. Available at: <http://www1.worldbank.org/publicsector/pe/PEAMMarch2005/CMHReport.pdf> [Accessed December 4, 2015].

Woods, B. et al. Country-level cost-effectiveness thresholds: initial estimates and the need for further research. CHERP109. Centre for Health Economics, University of York. https://www.york.ac.uk/media/che/documents/papers/researchpapers/CHERP109_cost-effectiveness_threshold_LMICs.pdf

Appendix 1: Elasticities

Table 7. Elasticities on YLLs, YLDs and DALYs averted for low- and middle income countries

	YLL	YLD	DALY		YLL	YLD	DALY		YLL	YLD	DALY
Albania	-0.29	-0.03	-0.21	Morocco	-0.30	-0.03	-0.21	Haiti	-0.29	-0.04	-0.21
Algeria	-0.30	-0.03	-0.21	Namibia	-0.30	-0.04	-0.21	India	-0.29	-0.03	-0.20
Argentina	-0.30	-0.03	-0.21	Panama	-0.30	-0.03	-0.21	Indonesia	-0.30	-0.03	-0.21
Belarus	-0.30	-0.03	-0.21	Paraguay	-0.29	-0.04	-0.21	Kenya	-0.30	-0.03	-0.21
Belize	-0.30	-0.03	-0.21	Peru	-0.30	-0.03	-0.21	Kyrgyz R	-0.29	-0.04	-0.21
Bolivia	-0.30	-0.03	-0.21	Philippines	-0.30	-0.03	-0.21	Madagascar	-0.30	-0.03	-0.21
Botswana	-0.30	-0.03	-0.21	Romania	-0.29	-0.03	-0.21	Malawi	-0.30	-0.03	-0.21
Brazil	-0.30	-0.03	-0.21	Russia	-0.30	-0.03	-0.21	Mali	-0.30	-0.03	-0.21
Bulgaria	-0.30	-0.03	-0.21	South Africa	-0.30	-0.03	-0.21	Mauritania	-0.30	-0.03	-0.21
Cape Verde	-0.29	-0.03	-0.21	Sri Lanka	-0.26	-0.02	-0.18	Moldova	-0.29	-0.03	-0.21
Chile	-0.30	-0.03	-0.21	Swaziland	-0.30	-0.03	-0.21	Mongolia	-0.30	-0.03	-0.21
China	-0.30	-0.03	-0.21	Thailand	-0.30	-0.03	-0.21	Mozambique	-0.30	-0.03	-0.21
Colombia	-0.30	-0.03	-0.21	Trinidad & Tobago	-0.28	-0.03	-0.20	Nepal	-0.30	-0.03	-0.21
Costa Rica	-0.30	-0.03	-0.21	Tunisia	-0.30	-0.03	-0.21	Nicaragua	-0.29	-0.04	-0.21
Croatia	-0.29	-0.03	-0.21	Turkey	-0.30	-0.03	-0.21	Niger	-0.30	-0.03	-0.21
Dominican Republic	-0.29	-0.04	-0.21	Uruguay	-0.30	-0.03	-0.21	Nigeria	-0.30	-0.03	-0.21
Ecuador	-0.30	-0.03	-0.21	Venezuela	-0.30	-0.03	-0.21	Pakistan	-0.30	-0.03	-0.21
Egypt	-0.30	-0.03	-0.21	Armenia	-0.29	-0.03	-0.20	Rwanda	-0.30	-0.03	-0.21
El Salvador	-0.30	-0.03	-0.21	Azerbaijan	-0.30	-0.03	-0.21	Senegal	-0.30	-0.03	-0.21
Equatorial Guinea	-0.26	-0.06	-0.20	Bangladesh	-0.30	-0.03	-0.21	Sierra Leone	-0.30	-0.03	-0.21
Estonia	-0.30	-0.03	-0.21	Benin	-0.30	-0.03	-0.21	Sudan	-0.30	-0.03	-0.21
Gabon	-0.30	-0.03	-0.21	Burkina Faso	-0.30	-0.03	-0.21	Tajikistan	-0.30	-0.03	-0.21
Guatemala	-0.30	-0.03	-0.21	Burundi	-0.30	-0.03	-0.21	Tanzania	-0.30	-0.03	-0.21
Guyana	-0.30	-0.03	-0.21	Cambodia	-0.30	-0.04	-0.21	Togo	-0.30	-0.03	-0.21
Honduras	-0.30	-0.03	-0.21	Cameroon	-0.30	-0.03	-0.21	Turkmenistan	-0.30	-0.03	-0.21
Hungary	-0.28	-0.03	-0.20	Chad	-0.30	-0.03	-0.21	Uganda	-0.30	-0.03	-0.21
Jamaica	-0.27	-0.02	-0.19	Comoros	-0.30	-0.03	-0.21	Ukraine	-0.30	-0.03	-0.21
Jordan	-0.30	-0.03	-0.21	Congo, DR	-0.30	-0.03	-0.21	Uzbekistan	-0.30	-0.03	-0.21
Kazakhstan	-0.30	-0.03	-0.21	Congo, R.	-0.30	-0.03	-0.21	Vietnam	-0.30	-0.03	-0.21
S. Korea	-0.29	-0.03	-0.20	Cote d'Ivoire	-0.30	-0.03	-0.21	Yemen	-0.30	-0.03	-0.21
Lebanon	-0.29	-0.03	-0.20	Eritrea	-0.30	-0.03	-0.21	Zambia	-0.29	-0.04	-0.21
Lesotho	-0.30	-0.03	-0.21	Ethiopia	-0.30	-0.03	-0.21	Zimbabwe	-0.30	-0.03	-0.21
Lithuania	-0.28	-0.02	-0.19	Gambia	-0.30	-0.03	-0.21				
Macedonia	-0.29	-0.03	-0.21	Georgia	-0.30	-0.03	-0.21				
Malaysia	-0.30	-0.03	-0.21	Ghana	-0.30	-0.03	-0.21				
Mauritius	-0.28	-0.03	-0.20	Guinea	-0.30	-0.03	-0.21				
Mexico	-0.30	-0.03	-0.21	Guinea-Bissau	-0.30	-0.03	-0.21				

Appendix 2: CETs

Table 8. Cost per DALY averted estimates for low-income countries

	Section 2				Section 3			
	DALY 1	DALY 2	DALY 3	DALY 4	DALY 1	DALY 2	DALY 3	DALY 4
Armenia	\$591	\$356	\$514	\$472	\$507	\$305	\$441	\$405
Azerbaijan	\$104	\$71	\$98	\$94	\$223	\$153	\$210	\$203
Bangladesh	\$125	\$78	\$98	\$102	\$255	\$159	\$200	\$208
Benin	\$38	\$25	\$27	\$31	\$108	\$70	\$77	\$89
Bhutan					\$233			
Burkina Faso	\$32	\$25	\$26	\$32	\$82	\$63	\$66	\$81
Burundi	\$19	\$12	\$13	\$16	\$73	\$47	\$50	\$60
Cambodia	\$112	\$58	\$69	\$75	\$176	\$91	\$108	\$118
Cameroon	\$29	\$24	\$26	\$30				
Central African Republic					\$171			
Chad	\$18	\$15	\$15	\$19	\$77	\$62	\$64	\$79
Comoros	\$66	\$47	\$54	\$62	\$241	\$174	\$200	\$229
Congo, Dem. Rep.	\$23	\$25	\$26	\$32	\$97	\$103	\$109	\$132
Congo, Rep.	\$37	\$26	\$29	\$34				
Cote d'Ivoire	\$28	\$33	\$36	\$42	\$144	\$172	\$190	\$221
Eritrea	\$45	\$19	\$20	\$24	\$76	\$32	\$34	\$40
Ethiopia	\$8	\$6	\$6	\$8	\$93	\$65	\$70	\$85
Gambia, The	\$145	\$116	\$128	\$151	\$114	\$92	\$101	\$119
Georgia	\$190	\$106	\$152	\$140	\$491	\$273	\$394	\$361
Ghana	\$37	\$32	\$37	\$42	\$100	\$88	\$102	\$114
Guinea	\$72	\$57	\$60	\$72	\$71	\$56	\$59	\$71
Guinea-Bissau	\$45	\$31	\$33	\$40	\$72	\$50	\$52	\$63
Haiti	\$132	\$77	\$90	\$98				
India	\$32	\$27	\$34	\$36	\$189	\$163	\$200	\$214
Indonesia	\$74	\$42	\$56	\$56	\$244	\$139	\$186	\$185
Kenya	\$58	\$48	\$54	\$63	\$110	\$92	\$102	\$120
Kyrgyz Republic	\$195	\$105	\$135	\$136	\$202	\$108	\$140	\$141
Lesotho	\$139	\$194	\$217	\$253				
Liberia					\$77			
Madagascar	\$26	\$24	\$28	\$32	\$90	\$85	\$99	\$111
Malawi	\$20	\$24	\$25	\$30	\$136	\$161	\$170	\$207
Mali	\$13	\$13	\$13	\$17	\$56	\$55	\$56	\$71
Mauritania	\$64	\$54	\$63	\$69	\$112	\$94	\$109	\$121
Moldova	\$146	\$128	\$180	\$169	\$577	\$506	\$713	\$670
Mongolia	\$165	\$122	\$153	\$162	\$173	\$128	\$160	\$169
Mozambique	\$83	\$72	\$76	\$92	\$140	\$122	\$129	\$155
Nepal	\$56	\$32	\$38	\$41	\$141	\$80	\$95	\$104
Nicaragua	\$842	\$419	\$578	\$545	\$371	\$185	\$255	\$240

Niger	\$8	\$10	\$10	\$12	\$52	\$60	\$61	\$77
Nigeria	\$3	\$3	\$4	\$4	\$45	\$51	\$53	\$65
Pakistan	\$44	\$36	\$43	\$48	\$121	\$100	\$119	\$131
Rwanda	\$43	\$44	\$48	\$57	\$91	\$94	\$100	\$119
Senegal	\$86	\$68	\$76	\$87	\$134	\$107	\$118	\$136
Sierra Leone	\$12	\$13	\$14	\$17				
Solomon Islands					\$724			
Sudan	\$22	\$19	\$21	\$25				
Tajikistan	\$20	\$17	\$20	\$22	\$153	\$126	\$153	\$166
Tanzania	\$20	\$19	\$20	\$24	\$85	\$78	\$85	\$101
Togo	\$53	\$39	\$44	\$50	\$135	\$100	\$113	\$128
Turkmenistan	\$387	\$285	\$364	\$378				
Uganda	\$63	\$49	\$52	\$63	\$88	\$68	\$72	\$87
Ukraine	\$252	\$185	\$242	\$242	\$552	\$405	\$531	\$531
Uzbekistan	\$333	\$228	\$298	\$302	\$206	\$141	\$184	\$187
Vietnam	\$172	\$110	\$168	\$147	\$369	\$236	\$362	\$315
Yemen, Rep.	\$48	\$29	\$34	\$38	\$108	\$66	\$76	\$86
Zambia	\$36	\$27	\$28	\$34	\$82	\$60	\$63	\$77
Zimbabwe	\$160	\$170	\$191	\$218				

Table 9. Cost per DALY averted estimates for middle-income countries

	Section 2				Section 3			
	DALY 1	DALY 2	DALY 3	DALY 4	DALY 1	DALY 2	DALY 3	DALY 4
Albania	\$840	\$386	\$592	\$510	\$931	\$428	\$656	\$565
Algeria	\$507	\$337	\$503	\$450	\$374	\$248	\$371	\$332
Argentina					\$1707*	\$1037*	\$1541*	\$1379*
Bahrain					\$1289			
Belarus	\$1244	\$835	\$1140	\$1092	\$741	\$497	\$679	\$651
Belize	\$2190	\$1005	\$1367	\$1321	\$772	\$354	\$482	\$465
Bolivia	\$323	\$231	\$287	\$303	\$189	\$136	\$168	\$178
Botswana	\$567	\$521	\$580	\$667	\$397	\$365	\$406	\$467
Brazil	\$1747	\$1259	\$1809	\$1675	\$798	\$575	\$826	\$765
Bulgaria	\$967	\$686	\$973	\$904	\$837	\$594	\$842	\$782
Cape Verde	\$1220	\$662	\$955	\$872				
Chile	\$4194	\$2598	\$4294	\$3488				
China	\$584	\$369	\$523	\$496				
Colombia	\$1827	\$1190	\$1702	\$1581	\$681	\$444	\$635	\$589
Costa Rica	\$9137	\$3532	\$6034	\$4747				
Croatia	\$4569	\$3336	\$5090	\$4410	\$2019	\$1474	\$2249	\$1949
Czech Republic					\$1740			
Djibouti					\$252			
Dominican Republic	\$1194	\$743	\$1041	\$974	\$539	\$335	\$470	\$440
Ecuador	\$431	\$265	\$372	\$351	\$474	\$291	\$409	\$386
Egypt, Arab Rep.	\$324	\$199	\$280	\$264	\$173	\$106	\$149	\$141
El Salvador	\$1234	\$936	\$1286	\$1242	\$670	\$508	\$699	\$674
Estonia	\$2770	\$1874	\$2566	\$2452	\$1503	\$1017	\$1393	\$1330
Fiji					\$838			
Gabon	\$369	\$201	\$237	\$257	\$272	\$148	\$175	\$190
Guatemala	\$495	\$330	\$413	\$437	\$290	\$194	\$242	\$256
Guyana	\$657	\$417	\$552	\$548	\$301	\$191	\$252	\$251
Honduras	\$868	\$410	\$556	\$542	\$498	\$235	\$319	\$311
Hungary	\$3357	\$2685	\$3921	\$3527	\$1792	\$1433	\$2092	\$1882
Iraq					\$168			
Jamaica	\$950	\$794	\$1121	\$1062	\$902**	\$753**	\$1064**	\$1008**
Jordan	\$1316	\$840	\$1239	\$1121	\$445	\$284	\$419	\$379
Kazakhstan	\$269	\$196	\$247	\$257	\$310	\$226	\$284	\$296
Korea, Rep.	\$9444	\$4934	\$8049	\$6705	\$2962	\$1548	\$2525	\$2103
Latvia					\$936			
Lebanon	\$4441	\$2308	\$3523	\$3132	\$1235	\$642	\$979	\$871
Lithuania	\$2046	\$1496	\$2134	\$1983	\$1478	\$1081	\$1541	\$1433
Macedonia, FYR	\$2468	\$1128	\$1781	\$1478	\$852	\$389	\$614	\$510
Malaysia	\$1691	\$918	\$1551	\$1233	\$1017	\$552	\$933	\$742
Maldives					\$780			
Malta					\$2444			

Mauritius	\$1791	\$1192	\$1847	\$1609	\$1082	\$720	\$1115	\$972
Mexico	\$4716	\$2364	\$3389	\$3183	\$1105	\$554	\$794	\$746
Morocco	\$478	\$268	\$385	\$355	\$412	\$231	\$332	\$306
Namibia	\$1330	\$799	\$932	\$1022	\$464	\$279	\$325	\$357
Oman					\$856			
Panama	\$3874	\$2251	\$3463	\$3000	\$726	\$422	\$649	\$562
Paraguay	\$1037	\$608	\$884	\$798	\$368	\$216	\$314	\$283
Peru	\$1300	\$659	\$967	\$875	\$411	\$208	\$306	\$277
Philippines	\$410	\$321	\$447	\$426	\$301	\$235	\$328	\$313
Poland					\$1781			
Romania	\$1459	\$1215	\$1716	\$1609	\$976	\$813	\$1148	\$1077
Russian Federation	\$688	\$705	\$926	\$914				
Saudi Arabia					\$619			
South Africa	\$955	\$860	\$1022	\$1119	\$576	\$519	\$617	\$675
Sri Lanka	\$267	\$204	\$305	\$274	\$571	\$437	\$653	\$587
Suriname					\$415			
Swaziland	\$303	\$276	\$311	\$352	\$275	\$250	\$282	\$319
Thailand	\$805	\$486	\$672	\$644	\$805	\$486	\$672	\$644
Trinidad and Tobago	\$1623	\$1048	\$1543	\$1401	\$868	\$561	\$826	\$750
Tunisia	\$2989	\$1884	\$2939	\$2530	\$635	\$400	\$624	\$538
Turkey	\$2249	\$1374	\$2009	\$1830	\$798	\$487	\$713	\$649
Uruguay	\$7827	\$4070	\$5961	\$5348	\$866	\$450	\$660	\$592
Venezuela	\$1875	\$1290	\$1945	\$1729	\$717	\$493	\$744	\$661
* Estimates presented in PPP (conversion factor not available)								
** PPP conversion factor from 2006 used (conversion factor for 2005 not available)								