Original Research

Reflecting the Health Opportunity Costs of Funding Decisions Within Value Frameworks: Initial Estimates and the Need for Further Research

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ABSTRACT

Purpose: Evaluating whether a new health technology provides good value for money requires an assessment of its opportunity cost. If the opportunity cost of the new health technology exceeds the benefits, however measured, a net loss is produced. Value frameworks using economic evaluation methods have been developed to guide the assessment of the value of new technologies within health care in response to rising spending. However, few explicitly consider health opportunity costs and fewer still base health opportunity costs on empirical estimates. This may partly be due to the dearth of estimates available, with only a handful of countries having estimates based on within-country data. To fill this gap, this study provides estimates of cost per disability-adjusted life year (DALY) averted for 33 high-income countries and the remaining Organization for Economic Cooperation and Development (OECD) and BRIICS countries (Brazil, Russia, India, Indonesia, China and South Africa).

Methods: Cost per DALY averted for each country was based on estimated elasticities of the health effects of changes in expenditure on health outcomes from applying an existing published econometric model that uses cross-country data to an expanded dataset and other existing elasticities drawn from selected UK within-country studies to country-level data on health expenditure, demographic characteristics, and burden of ill health. To provide a comprehensive picture of the state of research around empirical estimates of health opportunity costs for these countries, results from this study are reported against previously published estimates of cost per quality-adjusted life year (QALY) gained for the same countries.

Findings: All but one of the ranges estimated fall below 3× the gross domestic product (GDP) per capita, the upper end of the widely applied range of 1−3× GDP per capita. The range of estimates based on applying an existing published econometric model that uses cross-country data to an expanded dataset are higher than when cost per DALY averted is calculated from other existing elasticities of the health effects of changes in expenditure drawn from selected UK within-country studies. They also tend to be higher than published estimates of cost per QALY gained.

Implications: This study provides placeholder cost per DALY averted estimates that reflect health opportunity costs for 33 high-income countries and the remaining OECD and BRIICS countries. These estimates can be used to estimate the health opportunity costs of government health care expenditure until country-specific health opportunity cost are estimated using within-country data. (*Clin Ther*. 2020;42:44−59) © 2019 Elsevier Inc. All rights reserved.

Key words: value frameworks, opportunity costs, cost-effectiveness analysis, cost-effectiveness thresholds.

INTRODUCTION

Value frameworks have been developed to guide the assessment of the value of new technologies across

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disease areas within health care in response to rising spending on, for example, prescription drugs.[1] However, within these frameworks, too little effort has been placed on the consideration of health opportunity costs, potentially owing to a lack of available empirical estimates of health opportunity cost.[1–4] Improving population health is a key objective of health care expenditure.[5] Any new treatment under consideration for approval within the health care system (HCS) would undoubtedly be expected to generate an improvement in health among patients who directly benefit (ie, it is clinically effective); however, a necessary question is whether the money required to fund it would generate more health if spent on something else. This other potential way to spend the money is the "health opportunity cost" of funding the new treatment.

Consideration of health opportunity cost is essential to ensure that decisions improve health outcomes overall rather than reducing them. This is true regardless of whether the budget for health is fixed or flexible. It if is fixed, the question is: *What are the health effects of those things that would need to be given up if we commit these resources to this new technology?* If it is flexible, the question is: *What are the health effects of the other things that could be done with the money required to fund an intervention?* Few value frameworks explicitly account for health opportunity costs, although some governing bodies have tried to implicitly reflect health opportunity costs through the use of cost-effectiveness thresholds.

A cost-effectiveness threshold (often summarized as a cost per quality-adjusted life year [QALY] or disability-adjusted life year [DALY] threshold) that reflects health opportunity costs can be visually represented by using a bookshelf metaphor. In this metaphor, the width of each "book" (ie, health technology) represents its budget impact (a function of the cost per patient and number of patients in need), the height shows the health benefit (eg, QALYs gained or DALYs averted) per $1000 spent, and books are ranked from left to right, most to least cost-effective[6] (Figure 1). In the case of a fixed budget, a threshold that reflects health opportunity costs (ie, marginal cost per QALY or DALY) is the reciprocal of the effectiveness-cost of the least cost-effective intervention that is currently funded. In the case of a flexible budget, it is the reciprocal of the effectiveness-cost of the most cost-effective intervention that is not currently funded.

Although this bookshelf analogy provides a useful visual aid, in practice the effectiveness-cost of all available interventions is not known, cost-effectiveness is not the basis of all decisions made within health care, and, in the context of a fixed

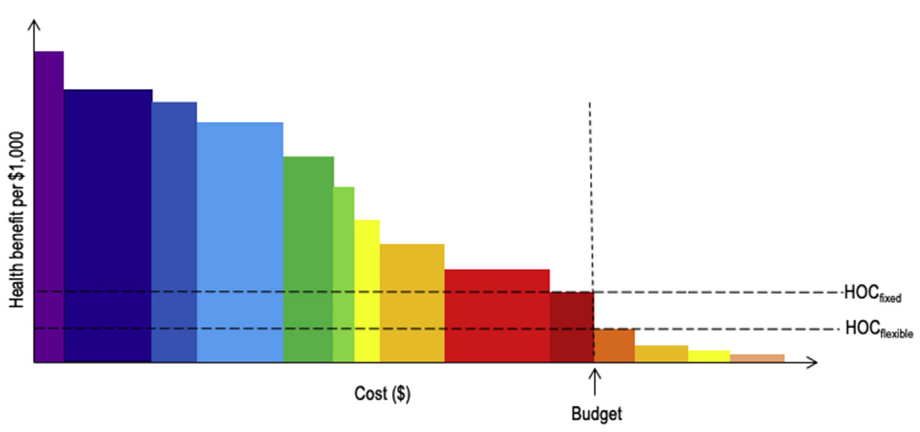

Figure 1. Cost-effectiveness threshold. In the case of a fixed budget, a threshold that reflects health opportunity costs (ie, marginal cost per QALY or DALY) is the reciprocal of the effectiveness-cost of the least cost-effective intervention that is currently funded (ie, HOC_{fixed}). In the case of a flexible budget, it is the reciprocal of the effectiveness-cost of the most cost-effective intervention that is not currently funded (ie, $HOC_{flexible}$.

budget, it is not typically possible to identify specific treatments that will be displaced (nor are disinvestment choices typically within the control of the decision-maker evaluating the new technology).[6–8] Instead, researchers have sought to empirically estimate the health effects of increasing/decreasing expenditure to determine the marginal cost per QALY or DALY.[9] To date, empirical estimates of health opportunity costs of government expenditure based on within-country data are available for only a few countries, including the United Kingdom, Spain, the Netherlands, and Australia.[10–14]

Placeholder estimates of health opportunity costs of government expenditure for a wider range of countries are available based on either extrapolating existing estimates or using published elasticities of the effect of expenditure on health. Cost per QALY estimates are available from Woods et al,[15] who extrapolate the UK estimate[10] to other countries using information about the income elasticity of demand. Ochalek et al[16] use published elasticities of the effects of government health care expenditure on health outcomes (expenditure elasticity of health) from Bokhari et al[17] to estimate cost per DALY averted for a range of low- and middle-income countries (LMICs).

The present study provides a range of plausible cost per DALY averted estimates that reflect health opportunity costs for high-income countries, 2 additional Organization for Economic Cooperation and Development countries, and the remaining BRIICS countries (Brazil, Russia, India, Indonesia, China, and South Africa) that can be used as placeholders for value frameworks. To do this, we apply the methods used by Ochalek et al[16] to data for these countries using the following: (1) the health effects of changes in expenditure on health outcomes (mortality, years of life lost [YLL], years of life disabled [YLD], and DALYs) from the econometric model developed in Bokhari et al[17]; and (2) other existing elasticities of the health effects of changes in expenditure drawn from selected UK within-country studies.[13,18] To provide a comprehensive picture of the state of research around cost-effectiveness thresholds for these countries, the cost per DALY averted estimates from the present study are reported against previously published estimates of cost per QALY gained for the same countries (ie, from Woods et al[15] and country-specific analyses using within-country data).[13,18]

MATERIALS AND METHODS

Estimates for the expenditure elasticity of health

Extending an existing econometric model

We applied the econometric specification of Bokhari et al,[17] and following Ochalek et al,[16] we expanded their dataset to include additional outcome measures that enabled us to assess the population-wide health effects of changes in expenditure.

Bokhari et al[17] estimated the effect of a change in health expenditure on under-5 and maternal mortality (where under-5 mortality is the cumulative probability of death by age 5) using cross-sectional data from the year 2000 for 127 countries. To do this, for each health outcome, H, the following econometric model is estimated:

$$\ln(H) = \beta_0 + \beta_1 \ln(E) + \beta_2 \ln(R) + \beta_3 \ln(S) + \beta_4 \ln(D) + \beta_5 \ln(I) + \beta_6 \ln(Gh) + \beta_7(\tilde{D} * \ln(Gh)) + \beta_8(R * \ln(Gh)) + \varepsilon \quad (1)$$

where E denotes the level of education, R, the paved roads per unit area; S, the level of sanitation and improved water service; D, the level of donor funding; I, income; Gh, government expenditures on health; $\tilde{D}$, deviation in donor funding from its historic average; and ε, an error term. As can be seen from equation (1), logarithmic transformation is undertaken for variables so that coefficients can be interpreted as elasticities. The model is estimated by using an instrumental variable approach in which $\ln(I)$, $\ln(Gh)$, and any interaction terms including these variables are considered endogenous. The authors use 4 instrumental variables to address this: military expenditure per capita of neighboring countries, the consumption-investment ratio, and 2 measures of institutional quality based on annual World Bank assessments. It is required that these instrumental variables are directly related to the level of government expenditure on health but are not directly related to health outcomes or any unobserved confounder between government expenditure on health and health outcomes. We added to their dataset additional outcome measures obtained from the Institute for Health Metrics and Evaluation Global Burden of Disease (GBD) project: adult female mortality, adult male mortality, YLD, YLL, and DALYs.[19] Owing to the use of interaction terms, estimated expenditure elasticities of health vary by country with respect to expenditure by the level of infrastructure (proxied by R) and shocks in donor funding (measured by $\tilde{D}$). The resulting elasticities on β_6 are used to calculate cost per DALY averted and are reported in Supplemental Appendix A (see the online version at doi:10.1016/j.clinthera.2019.12.002).

Existing elasticities drawn from selected within-country studies

Studies such as Bokhari et al using cross-country data face a number of significant econometric challenges.[17,20,21] Studies based on within-country data may be better able to overcome these challenges for 2 key reasons: (1) data are no longer constrained by international comparability, which means that more variables may be available; and (2) it may be easier to obtain plausible instrumental variables or natural experiments to inform an identification strategy. We used 2 recently published expenditure elasticities of all-cause mortality from the United Kingdom. These studies use similar data (variables collected at the level of regional health authorities) but have different approaches to identification of the causal effect of National Health Service expenditure on mortality.

Lomas et al[13] updates an earlier analysis by Claxton et al[10] in which disease-specific expenditure elasticities of mortality are estimated by using census data to obtain candidate instrumental variables, such as the proportion of households providing unpaid care (which is assumed to affect the level of disease-area spending but not affect mortality except indirectly through effects on expenditure). These elasticities were combined by using additional data and further estimates to provide an expenditure elasticity of all-cause mortality of −1.0278.[13]

In contrast, Andrews et al[18] directly estimate an expenditure elasticity of all-cause mortality by using instrumental variables comprising exogenous components of the resource allocation formula used to distribute funding across regional health authorities, assuming that adequate controls for health care need have been included. The resulting all-cause mortality elasticity is −0.705.

Calculating cost per DALY averted from elasticities of the health effects of expenditure

An estimate of the proportional effect of expenditure on health outcomes, such as an elasticity (eg, β_6 from equation (1)), is interesting in its own right, but an estimate of the absolute effect is required to inform the policy question of interest: what are the health opportunity costs of a change in expenditure? This is often summarized as a cost per DALY, which can be calculated for each country i as:

$$\textit{cost per DALY averted}_i = \frac{1\%{*}\textit{government expenditure on health}_i}{\textit{DALYs averted}_i} \quad (2)$$

The number of DALYs averted for each country i can be calculated from the estimated health outcome elasticities. Given the different possible health outcome measures, there are potentially 4 different

Table I. Disability-adjusted life year (DALY) methods and estimated expenditure elasticities of health according to source.

DALY method	DALY 1 (mortality)		DALY 2 (survival)	DALY 3 (morbidity)	DALY 4 (generic measure of health)
	Population-wide mortality (PM)	Under-5 mortality, adult female mortality, adult male mortality	Years of life lost (YLL)	Years of life disabled (YLD)	Disability adjusted life years (DALY)
This paper		✓	✓	✓	✓
Lomas et al (2019)	✓				
Andrews et al (2017)	✓				

ways to calculate DALYs, each with their own embedded assumptions. Table I summarizes which estimated expenditure elasticities of health are available from this study and two others (Lomas et al[13] and Andrews et al[18]) and which DALY method can be used to calculate cost per DALY averted from each outcome elasticity.

Calculating cost per DALY averted from elasticities requires taking into account the age and sex structure of the population and the underlying burden of mortality and morbidity.[16] Therefore, data are required on the number of deaths in the population, disaggregated according to age and sex, as well as the size of the population, again disaggregated according to age and sex. The former is available from the Institute for Health Metrics and Evaluation GBD project and the latter can be calculated from GBD data on death rates.[19] Calculating the years of life lost requires data on conditional life expectancy, also available from GBD. We used YLD data from GBD and calculate DALYs as the sum of YLL and YLD for each country. We compared our results against gross domestic product (GDP) per capita (2015 US$) from the World Bank.[22] The 4 methods for calculating DALYs are described in detail elsewhere, and we summarize them here.[16]

DALY 1

DALY 1 uses mortality elasticities and a series of assumptions about survival and morbidity to obtain a cost per DALY averted. Population-wide all-cause mortality estimates are the most common health outcome available in the literature, and we began by calculating the deaths estimated to be averted from this outcome by applying the estimated elasticity to the number of absolute deaths in each 5-year age category for each country *i*. This is illustrated in Figure 2 for a hypothetical country using a hypothetical all-cause mortality elasticity of −1.0. The total height of each bar represents the absolute deaths occurring in the age category. The black part of the bar comprises those deaths that are expected to be averted by a 1% increase in health expenditure (ie, 1% of total deaths in each age category).

The number of deaths averted in each age category *a* is thus calculated as:

$$deaths\ averted_i^a = 1\% * \left|\varepsilon_i^{mortality^a}\right| * deaths_i^a \quad (3)$$

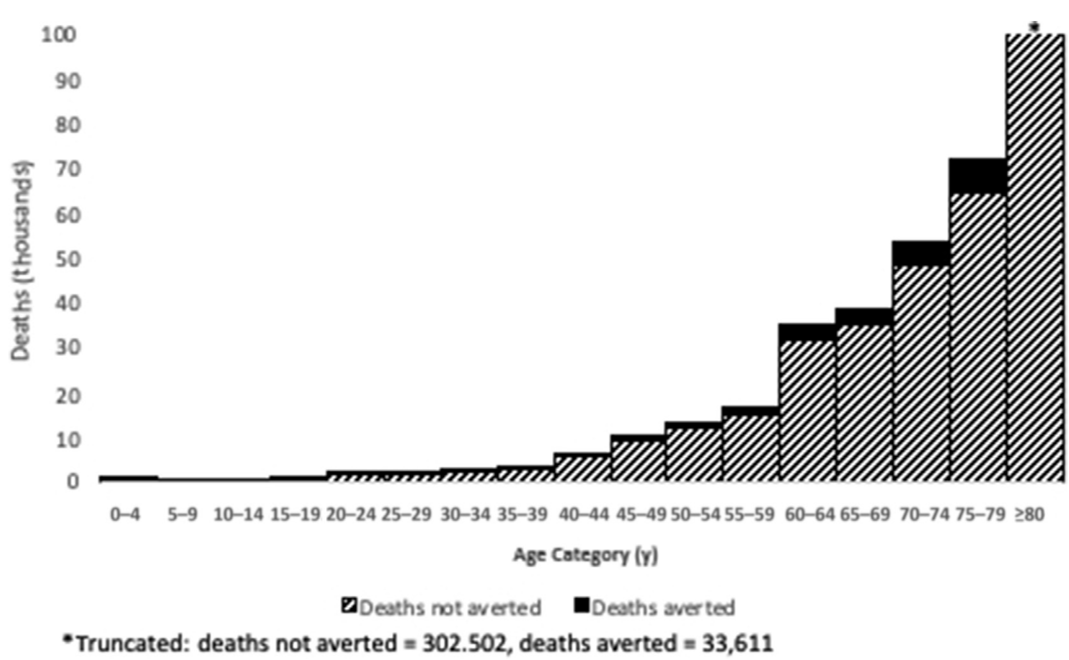

Figure 2. Absolute deaths averted and not averted for a hypothetical country.

Determining the age category within which each death is averted enables the calculation of survival effects (ie, YLL averted) by applying data on conditional life expectancy in each age category to the deaths in each age category:

$$YLL\ averted_i = \sum_{a=1}^{17} CLE_i^a * deaths\ averted_i^a \quad (4)$$

Where a population-wide all-cause mortality elasticity is not available, but age-group or sex-specific all-cause mortality elasticities are, and these can be used instead; an additional step is required, however, to obtain population YLLs. Our data enable the estimation of elasticities on under-5, adult female mortality, and adult male mortality. Figure 3A, B shows the averted and not averted adult female and male deaths, respectively, for a hypothetical 1% change in expenditure assuming an elasticity of −1.25 for adult female mortality and −0.75 for adult male mortality.

Total YLLs averted sex gender *g* (females or males) in the age category 15−60 years is then given by:

$$YLL\ averted_i^{15-60_g} = \sum_{a=1}^{9} CLE_i^{a_g} * deaths\ averted_i^{a_g} + \sum_{a=1}^{9} CLE_i^{a_g} * deaths\ averted_i^{a_g} \quad (5)$$

where there are 9 age groups (15−19 years, 20−24 years, and so forth, to 55−60 years) in the age category 15−60 years.

The YLLs averted among female subjects and among male subjects are added to the YLLs for the under-5 age category, which are also obtained by using equation (3) where there is only one age category (*a*, 0−4 years).

The result is YLLs averted among 0- to 4-year-olds and 15- to 60-year-olds. Thus, to calculate the YLLs averted among the whole population, we assume that the same proportion of YLLs that are averted among 0- to 5-year-olds and 15- to 60-year-olds are averted among 5- to 14-year-olds and those age ≥61 years. Determining the proportion of YLLs averted requires first calculating YLLs for the whole population using data on absolute deaths and conditional life expectancy for each of 17 age categories *a* as:

$$YLL_i = \sum_{g=1}^{2} \sum_{a=1}^{17} CLE_i^{a_g} * absolute\ deaths_i^{a_g} \quad (6)$$

Finally, we account for the direct and indirect effects of health expenditure on the burden of morbidity (measured by using YLD). Although an increase in expenditure would be expected to alleviate some of the YLD burden on one hand, on the other it would also be expected to increase it through extending survival (ie, alleviating some of the YLL burden). We account for the direct effect of expenditure on YLD burden by assuming that the same proportion of YLD burden is averted as YLL burden (ie, if our calculations show that YLL burden is alleviated by 15%, then we assume that 15% of the YLD burden is alleviated). We account for the indirect effect of expenditure by assuming that each YLL averted is subject to the existing per capita YLD burden. YLD burden data come from the GBD project. Therefore, the overall DALYs averted for the population are calculated as:

$$DALY\ averted_i = YLL\ averted_i + \left(YLD\ averted_i^{direct} - YLD\ gained_i^{indirect}\right) \quad (7)$$

DALY 2

DALY 2 uses YLL elasticities in combination with the same series of assumptions around the morbidity effects of expenditure as in DALY 1 to obtain a cost per DALY averted. First, population-wide YLL averted is calculated from the elasticity of the effect of expenditure on YLL as:

$$YLL\ averted = 1\% * \left|\varepsilon_i^{YLL}\right| * YLL_i^{all\ ages} \quad (8)$$

where population-wide YLL, $YLL_i^{all\ ages}$, is calculated by

$$YLL_i^{all\ ages} = \sum_{a=1}^{17} CLE_i^a * absolute\ deaths_i^a \quad (9)$$

The direct and indirect effects of expenditure on morbidity are then accounted for in the same way as for DALY 1, and DALYs averted are calculated by using equation (5).

DALY 3

DALY 3 uses YLL and YLD elasticities to obtain a cost per DALY averted. YLD averted are calculated as:

$$YLD\ averted = 1\% * \left|\varepsilon_i^{YLD}\right| * YLD_i^{all\ ages} \quad (10)$$

The calculated YLD averted (equation (10)) are added to the calculated YLL averted (equation (8)) to obtain DALYs averted.

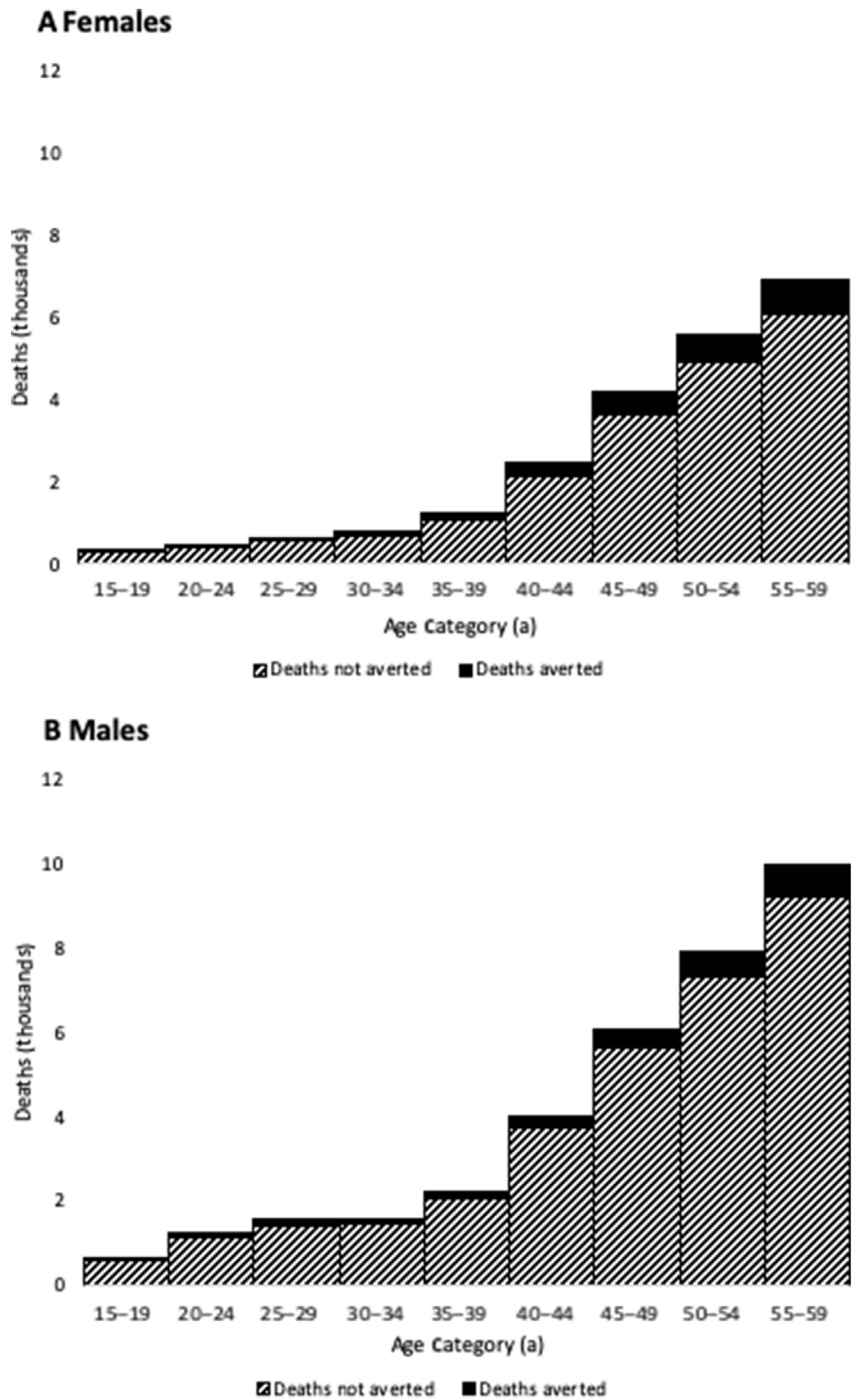

Figure 3. Absolute deaths averted and not averted for a hypothetical country. (A) Female subjects. (B) Male subjects.

DALY 4

DALY 4 uses DALY elasticities to obtain a cost per DALY averted, which is calculated by:

$$DALY\ averted = 1\% * \left|\varepsilon_i^{DALY}\right| * DALY_i^{all\ ages} \quad (11)$$

The results are given as cost per DALY averted in 2015 $US prices. To be able to compare the results of this analysis against the results of Woods et al,[15] which are reported in 2013 US$, we scale up their results using the growth in GDP between 2013 and 2015, which is:

$$GDP\ growth\ rate_i = \frac{GDP_i^{2015}}{GDP_i^{2013}} \quad (12)$$

This is then applied to the minimum and maximum estimates from Woods et al[15] to obtain minimum and maximum estimates in 2015 US$. The minimum estimate is calculated as:

$$minimum\ estimate_i^{2015} = minimum\ estimate_i^{2013} * 1 + GDP\ growth\ rate_i \quad (13)$$

The same calculation in equation (13) is done to scale the maximum estimate to 2015 US$.

RESULTS

Table II presents the estimates of cost per DALY averted for each country based on the elasticities estimated in this study (using DALYs 1, 2, 3, and 4), the elasticity –1.0278 from Lomas et al[13] (using DALY 1), the elasticity –0.705 from Andrews et al[18] (using DALY 1), and the range of cost per QALY estimates from Woods et al[15] in 2015 US$ along with the percentage of GDP per capita. The resulting estimates range from 5% to 376% of GDP per capita (India and Indonesia and the Netherlands, respectively).

The range of estimates for the United Kingdom from this study is $51,768 to $84,263 (approximately 1–2 × GDP per capita). Using the elasticity –1.0278 from Lomas et al[13] results in an estimate of $13,412 per DALY averted for the United Kingdom (31% of GDP per capita). The elasticity estimate from Andrews et al[18] is smaller in magnitude than that from Lomas et al.[13] It therefore results in a lower estimate of deaths averted by a 1% increase in expenditure and a higher estimate of cost per DALY averted of $19,553 (45% of GDP per capita). The finding that the estimates based on the Lomas et al and Andrews et al elasticities are lower than the range estimated in this study reflects the fact that the estimated elasticities of the effect of change in expenditure on under-5 and adult male and female mortality are lower in magnitude than the all-cause mortality elasticities from Lomas et al and Andrews et al. This also reflects that elasticities on the other health outcomes estimated (survival, morbidity, and DALYs) are also low enough to result in higher cost per DALY averted than are estimated using mortality outcomes by the other studies. The estimate from Claxton et al[10] (which forms the basis of the Woods et al[15] study) is $21,234 in 2015 US$ (48% of GDP per capita). This is lower than the range estimated in this study but higher than the estimates based on the elasticities of Lomas et al[13] and Andrews et al.[18]

The range estimated for Canada from this study ($53,048–$89,827) is also approximately 1–2 × GDP per capita. Again, this is higher than the range estimated by Woods et al[15] ($21,052–26,565 or 49%–61% of GDP per capita) or from using the elasticities from Lomas et al[13] and Andrews et al[18] ($15,848 and $23,104 or 37% and 53% of GDP per capita, respectively). The range from this study differs from that presented in a report for the Patented Medicine Prices Review Board in Canada.[23] Although the report uses the same methods as we apply here, it applies the estimated elasticities to data from Canadian life tables, and our study uses international data from the GBD project as was done in Ochalek et al.[16]

The same pattern emerging from the results for the United Kingdom and Canada is reflected in the range estimated for the United States. The range estimated in this study is $60,475 to $97,851, which is also approximately 1–2 × GDP per capita. Again, this is higher than the range estimated by Woods et al[15] ($25,690–$42,436 or 46%–76% of GDP per capita) or from using the elasticities from Lomas et al[13] and Andrews et al[18] ($17,465 and $25,462 or 31% and 45% of GDP per capita, respectively).

These results are plotted in Figure 4, which presents the estimates of cost per DALY averted by country against the GDP per capita alongside other published estimates for Australia, the Netherlands, and Spain.[11,12,14] The tightly dotted line represents 1 × GDP per capita and the loosely dotted line represents 3 × GDP per capita (representing the commonly applied 1 × and 3 × GDP per capita

Table II. Cost per disability-adjusted life year (DALY) averted or quality-adjusted life year (QALY) gained (2015 US$).

Country	GDP Per Capita (2015 US$)	Elasticities Estimated in Current Study (Range of Estimates From DALYs 1, 2, 3, and 4)		Lomas et al[13] (2019) Elasticities (DALY 1)		Andrews et al[18] (2017) Elasticities (DALY 1)		Woods et al[15] (2016) Results	
		Cost per DALY Range Averted (2015 US$)	% of GDP Per Capita	Cost per DALY Averted (2015 US$)	% of GDP Per Capita	Cost per DALY Averted (2015 US$)	% of GDP Per Capita	Cost per QALY Gained Range (2015 US$)	% of GDP Per Capita
Australia	56,311	61,294–110,152	109–196	18,298	32	26,677	47	27,356–34,836	49–62
Austria	43,775	72,500–120,212	166–275	17,332	40	25,268	58	20,548–26,638	47–61
Brazil	8539	6048–9318	71–109	1825	21	2660	31	1823–5747	21–67
Canada	43,249	53,048–89,827	123–208	15,848	37	23,104	53	21,052–26,565	49–61
Chile	13,416	8918–14,477	66–108	2669	20	3891	29	4175–8047	31–60
China	8028	3650–5669	45–71	1089	14	1587	20	1357–5366	17–67
Croatia	11,536	10,845–16,538	94–143	3193	28	4655	40	3351–6868	29–60
Estonia	17,119	12,139–18,941	71–111	3697	22	5390	31	5991–9693	35–57
Finland	42,311	45,417–73,276	107–173	13,581	32	19,799	47	20,547–22,085	49–52
France	36,206	59,273–94,104	164–260	15,535	43	22,648	63	18,032–18,496	50–51
Germany	41,313	54,021–85,569	131–207	15,322	37	22,337	54	19,584–24,775	47–60
Hungary	12,364	8697–12,929	70–105	2464	20	3593	29	3914–7129	32–58
India	1598	264–363	17–23	75	5	109	7	123–821	8–51
Indonesia	3346	535–778	16–23	157	5	229	7	455–1720	14–51
Italy	29,958	36,652–59,591	122–199	9479	32	13,819	46	14,065–15,088	47–50
Japan	34,524	49,334–75,174	143–218	11,833	34	17,251	50	17,666–17,742	51–51
South Korea	27,222	18,875–31,870	69–117	5469	20	7973	29	12,813–14,379	47–53
Lithuania	14,147	8670–12,520	61–89	2503	18	3649	26	5097–8091	36–57
Mexico	9005	5723–8730	64–97	1700	19	2478	28	2106–5896	23–65
The Netherlands	44,300	93,296–166,473	211–376	20,874	47	30,432	69	20,193–25,601	46–58
New Zealand	37,808	61,429–106,822	162–283	17,929	47	26,137	69	18,701–19,669	49–52
Portugal	19,222	18,872–30,929	98–161	5432	28	7920	41	6844–10,600	36–55
Russia	9093	4640–7424	51–82	1463	16	2133	23	3116–5296	34–58
Singapore	52,889	28,092–68,874	53–130	6476	12	9441	18	21,413–59,136	40–112
South Africa	5724	2480–3334	43–58	732	13	1067	19	1016–4077	18–71

Spain	25,832	30,803–51,813	119–201	8275	32	12,064	47	11,485–13,434	44–52
Sweden	50,580	82,716–136,789	164–270	23,828	47	34,738	69	23,692–30,155	47–60
Switzerland	80,945	92,240–159,319	114–197	27,620	34	40,266	50	34,988–58,549	43–72
Trinidad and Tobago	17,322	8045–11,883	46–69	2253	13	3285	19	7487–9389	43–54
Turkey	9126	7446–13,032	82–143	2204	24	3213	35	2454–5707	27–63
United Kingdom	43,876	51,768–84,263	118–192	13,412	31	19,553	45	21,234–21,234	48–48
United States	56,116	60,475–97,851	108–174	17,465	31	25,462	45	25,690–42,436	46–76
Uruguay	15,574	13,800–22,591	89–145	4118	26	6003	39	4332–9665	28–62

GDP = gross domestic product.

norms).[24] The same estimates are presented against under-5 mortality in Supplemental Appendix B (see the online version at doi:10.1016/j.clinthera.2019.12.002). It can be seen that, in general, cost per DALY averted is increasing with GDP per capita, but the relationship is neither fixed nor monotonic. The variability of estimates between countries results from variability in country-specific characteristics, such as its demographic characteristics and epidemiology and how much it spends on health care. As a result, there is no fixed proportion of GDP per capita that can reliably be used to estimate health opportunity costs.

These patterns are evident across countries where the estimates based on the population-wide all-cause mortality elasticities from Lomas et al[13] result in the lowest estimate for each country. The ranges from Woods et al[15] are all below 1 × GDP per capita with the exception of Singapore (40%–112% of GDP per capita). The ranges estimated in this study are all below 3 × GDP per capita (apart from the Netherlands, which is 211%–376%). Ochalek et al,[16] on which the methods used here are based, report results for LMICs only, and most of the estimated ranges are below 1 × GDP per capita. This outcome is mainly due to 2 factors: countries with higher GDP per capita tend to spend more on health, and government health expenditure forms the numerator of cost per DALY averted; and countries with higher GDP per capita tend to have better baseline health outcomes, meaning that the same proportional effect will result in a smaller denominator. The estimated ranges are, however, not a simple function of GDP per capita, as variation is evident in Figure 4, and estimated ranges based on Ochalek et al also depend on a country's underlying mortality rates, demographic characteristics, and epidemiology.

The ranges in this study and the results from Woods et al[15] tend to widen as GDP increases in Figure 4. The ranges from Woods et al[15] widen as GDP per capita diverges from the UK value estimated by Claxton et al[10] because these results extrapolate from that value. The width of the range of estimates for each country from this study generally expands as GDP increases, but the pattern is less straightforward. Some portion of this is explained by the uncertainty in the denominator being scaled up by a larger numerator (ie, as

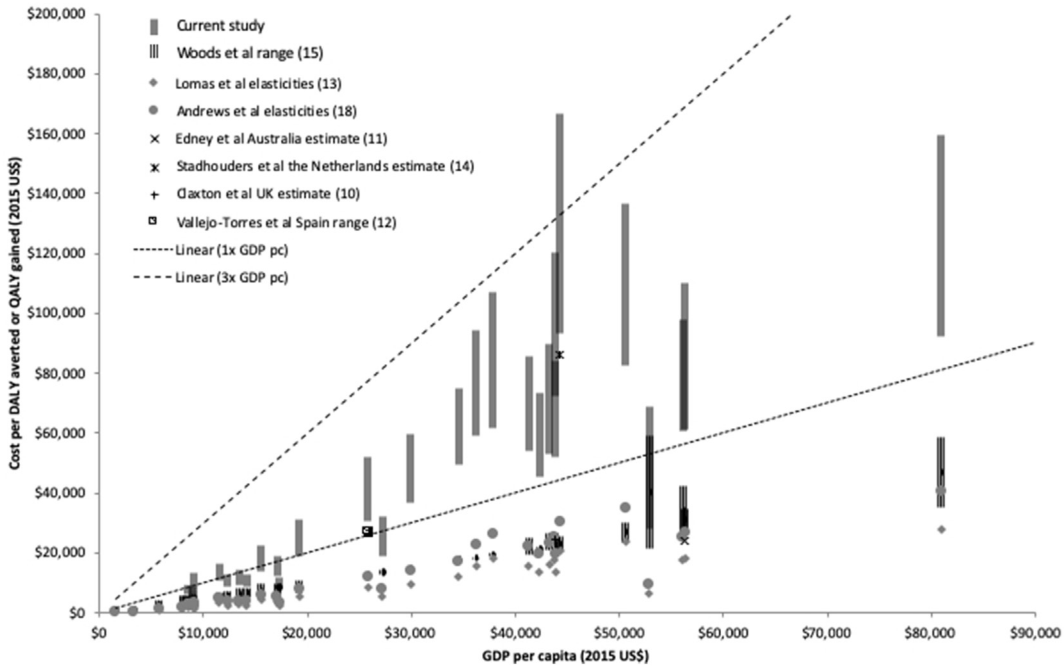

Figure 4. Range of cost per disability-adjusted life year (DALY) averted or quality-adjusted life year (QALY) gained estimates by method for each country and gross domestic product (GDP) per capita.

government expenditure on health tends to increase with GDP), but differing levels of uncertainty exist in the denominator for each country.

DISCUSSION

Evaluating whether a new health technology provides good value for money requires an assessment of its opportunity cost. If the opportunity cost of the new health technology exceeds the benefits, however measured, then a net loss is produced. Although much attention has been given to the estimation of costs and benefits in cost-effectiveness analysis, too little has been devoted to the estimation of opportunity costs.

The National Institute for Health and Care Excellence in the United Kingdom specifies an explicit range for the cost-effectiveness thresholds used in its deliberative decision-making process (£20,000 to £30,000 per QALY)[25] based on implied values from previous decisions,[26] which have been widely recognized for some time (including by the National Institute for Health and Care Excellence) as having little empirical foundation.[27–29] Other established norms include the thresholds of $50,000 to $150,000 per QALY in the United States,[30] which have become increasingly cited but are also widely recognized as having little evidential foundation.[31] Also used is the range of 1 × to 3 × GDP per capita, which has been widely used for decision-making in LMICs after being recommended by the World Health Organization.[32] The shortcomings of applying these thresholds in decision-making in LMICs have been thoroughly established,[33–35] and the World Health Organization has since distanced itself from them.[36] Using a threshold for decision-making that is not based on an empirical estimate of health opportunity cost risks decisions reducing rather than improving health outcomes overall.[15,16]

Estimating the effect of a change in health expenditure on health outcomes as a basis for health opportunity costs is a data-intensive exercise, for which adequate within-country data are often unavailable or inaccessible. Estimates based on cross-country data or from other within-country studies may be the best available until bespoke estimates from within-country data are produced. The results presented in this study provide a range of placeholder estimates for the health opportunity costs of government health care expenditure that can be used to assess the cost-effectiveness of new technologies that impose costs on government-funded components of an HCS.

The validity of the approach used in this study rests on the following: (1) the underlying assumptions within the econometrics used to estimate the expenditure elasticity of health; and (2) the assumptions required to calculate cost per DALY averted from the estimated elasticities. Econometric analysis based on cross-country data has for a long time proven challenging, but recent advances in data collection have enabled more promising within-country data approaches. However, as has been noted in the econometrics literature, it is not possible to directly test the exogeneity of instrumental variables with either approach. In practice, instrumental variables are likely contaminated to some extent, which introduces additional inevitable structural uncertainty around resulting estimates. In addition, for a given country, the validity of the overall approach depends on whether the estimated elasticity can appropriately be applied. For example, where differences between HCS exist, the expenditure elasticity of health from UK data may not be transferable to other countries. The expenditure elasticity of health estimates from the Bokhari et al[17] model may present similar issues if the interaction terms used are not sufficient to capture the differences between jurisdictions.

Calculating cost per DALY averted from estimated expenditure elasticities of health may require assumptions depending on what the health outcome measure used is. No assumptions are needed when the outcome measure is DALYs (or even QALYs), except that the measure is accurately and consistently recorded (as with all measures). However, when the outcome measure is not a generic measure of health, it is necessary to use assumptions to account for any components of health not part of the outcome measure, and when the outcome measure applies only to part of the population, some assumptions are needed to account for the total population health effects. When mortality outcome measures are used, we assume that the same proportion of deaths are averted across the population (ie, the elasticity applies equally to each age group). However, it is plausible that a change in expenditure may have differential effects across different segments of the population, and this is borne out in the elasticities on under-5 mortality being of greater magnitude than those on adult female mortality or adult male mortality. As such, using population segment-specific mortality elasticities (as done in this study) may be more accurate than population-wide mortality elasticities as done in, for example, the studies of Lomas et al,[13] Andrews et al,[18] and Edney et al.[11] However, the former requires assumptions to account for the mortality effects of expenditure on segments of the population not covered by the outcome elasticity. Neither mortality nor YLL outcome measures account for changes to the burden of morbidity (ie, YLD) that may result from changes in health expenditure. We therefore assume that YLD is reduced in proportion to the reduction in YLL. Which methods produce the most accurate cost per DALY averted is a matter of question, resting on judgments about the validity of the construction of DALYs and the assumptions used.

The approach adopted in this study is different from that adopted by Woods et al,[15] where the Claxton et al[10] estimate of health opportunity costs of National Health Service expenditure is extrapolated to other countries using the income elasticity of the value of a statistical life (VSL). The assumptions underlying this approach therefore center on the econometric and modeling assumptions within the Claxton et al estimate and also on the appropriateness of applying the income elasticity of VSL to extrapolate this estimate. Although there is no direct connection between individuals' VSL and the marginal productivity of government expenditure on health, they may be linked indirectly if HCS respond to individuals' preferences in a similar way to the United Kingdom.

Another difference between the estimates reported by Woods et al[15] and those reported here is that the former are given in cost per QALY gained whereas the latter are cost per DALY averted. Whether a new health technology whose benefits are assessed in QALYs can be compared against a cost per DALY averted threshold (and vice versa) is an important question. Although both are generic measures of health encompassing changes in both length and quality of life, QALYs represent health that stands to be gained, whereas DALYs are a measure of disease burden that stands to be averted. Therefore, comparing them requires the assumption that the quality of life associated with a health condition is equivalent to the level of disability it confers.[37]

Health opportunity costs are relevant regardless of how the HCS is financed; they exist in systems that are primarily government funded as well as those that are primarily privately funded. When a new treatment displaces a treatment currently available in a government-funded HCS, health opportunity costs may manifest in a number of ways, such as the extension of waiting times for existing procedures.[38–40] The ratio of changes in incremental costs on government-funded HCS to health effects of displacement of this kind are hereafter referred to as the health opportunity costs of government health care expenditure. In contrast, HCS with voluntary health insurance may obtain additional resources for health care through increased insurance premiums. Health care is then rationed through price rather than waiting times, which results in health opportunity costs falling on individuals who are "priced out" (ie, cannot afford the health care they need).[41,42]

Although an important objective of health care expenditure is the improvement of population health, other objectives could be considered as part of the economic evaluation of a new health technology. The societal perspective proposed by the 2nd US panel on cost-effectiveness analysis seeks to capture the effect of a new technology across a range of objectives, which is summarized by way of an "impact inventory."[43] For example, one such widely discussed objective is the contribution to economic output more generally, referred to as net production. Other possible objectives include educational outcomes or other aspects of value such as those included in the "value flower."[44] Regardless of the number of objectives considered, the opportunity costs of increased expenditure should be accounted for in decision-making. The extended impact inventory provides a framework for the inclusion of opportunity costs as part of the estimation of net effects on a number of objectives.[45]

CONCLUSIONS

This study makes an important contribution toward considering opportunity costs within economic evaluation of new health technologies. We provide placeholder estimates for 33 high-income countries and the remaining Organization for Economic Cooperation and Development and BRIICS countries. These values can be used to estimate the health opportunity costs of government health care expenditure until more robust findings of country-specific health opportunity costs are estimated using within-country data. Although the question of what constitutes value is essentially normative, the estimation of the opportunity costs of what is valued (however defined) is an empirical question. For value frameworks to inform decisions in a way that results in improvements in the objectives of the HCS, answers are required to these questions.

DISCLOSURES

The authors have indicated that they have no conflicts of interest regarding the content of this article. This study was unfunded. Neither author has received any previous support from industry or organizations that may have influenced this work.

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Both authors contributed to the design of this study and the undertaking and interpretation of the analysis. Jessica Ochalek wrote the original draft and both authors reviewed and approved the final version.

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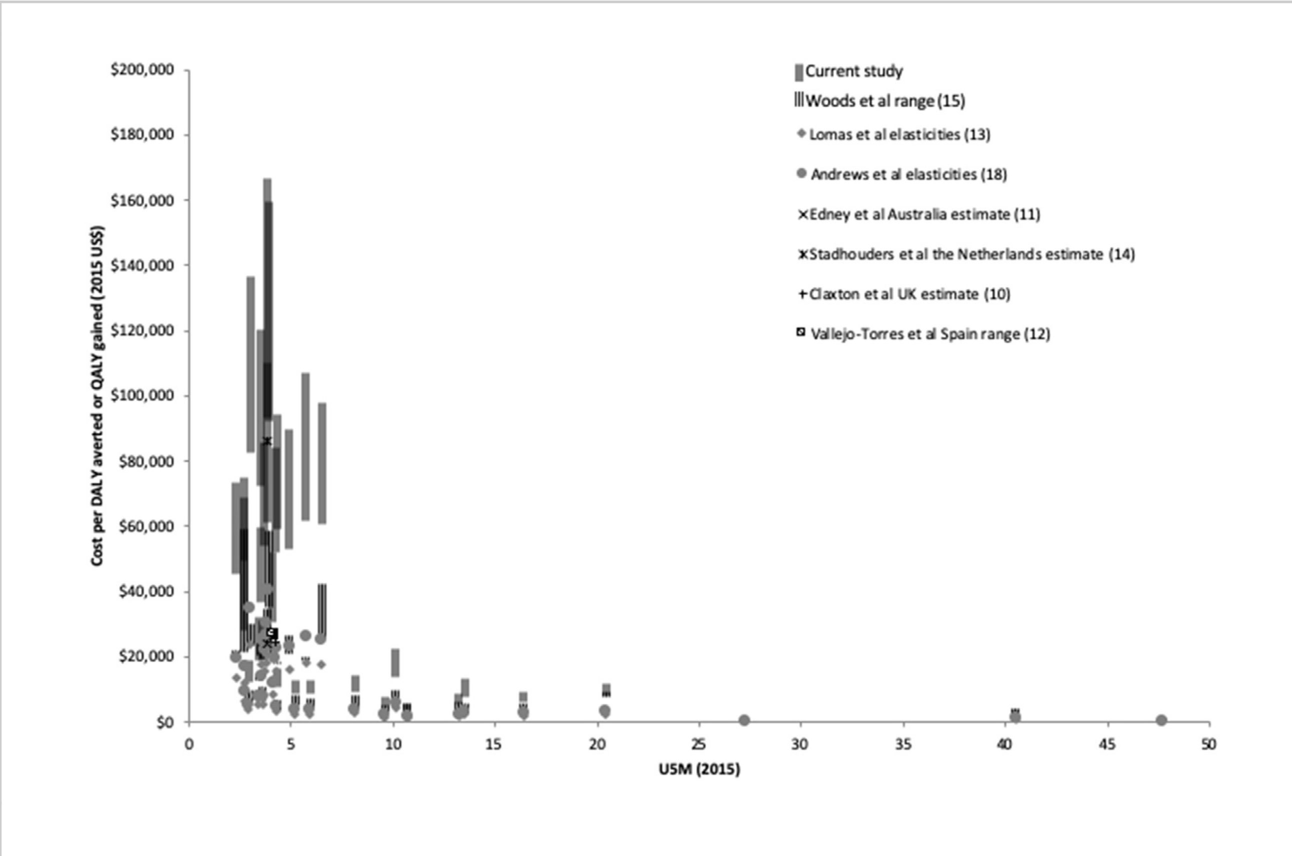
APPENDIX A

Estimated expenditure elasticities of health for six health outcomes

Country	Under-5 mortality (U5M)	Adult female mortality (AFM)	Adult male mortality (AMM)	Years of life lost (YLL)	Years of life disabled (YLD)	Disability adjusted life years (DALY)
Australia	−0.341	−0.192	−0.193	−0.303	−0.029	−0.214
Austria	−0.378	−0.202	−0.214	−0.241	−0.018	−0.165
Brazil	−0.341	−0.192	−0.193	−0.303	−0.029	−0.213
Canada	−0.341	−0.192	−0.193	−0.303	−0.029	−0.214
Chile	−0.333	−0.182	−0.184	−0.302	−0.030	−0.213
China	−0.343	−0.193	−0.194	−0.300	−0.029	−0.211
Croatia	−0.347	−0.193	−0.196	−0.292	−0.027	−0.205
Estonia	−0.344	−0.192	−0.194	−0.297	−0.028	−0.209
Finland	−0.344	−0.193	−0.194	−0.299	−0.029	−0.210
France	−0.366	−0.199	−0.207	−0.261	−0.022	−0.181
Germany	−0.351	−0.195	−0.198	−0.286	−0.026	−0.200
Hungary	−0.353	−0.194	−0.199	−0.280	−0.025	−0.196
India	−0.348	−0.194	−0.197	−0.290	−0.027	−0.203
Indonesia	−0.337	−0.187	−0.189	−0.300	−0.030	−0.212
Italy	−0.366	−0.199	−0.207	−0.261	−0.022	−0.181
Japan	−0.378	−0.202	−0.214	−0.240	−0.018	−0.165
South Korea	−0.351	−0.195	−0.198	−0.286	−0.026	−0.201
Lithuania	−0.357	−0.196	−0.202	−0.276	−0.024	−0.192
Mexico	−0.342	−0.192	−0.193	−0.302	−0.029	−0.213
Netherlands	−0.388	−0.204	−0.219	−0.224	−0.015	−0.152
New Zealand	−0.344	−0.193	−0.195	−0.298	−0.028	−0.209
Portugal	−0.351	−0.195	−0.198	−0.287	−0.026	−0.201
Russia	−0.341	−0.192	−0.193	−0.303	−0.029	−0.213
Singapore	−0.417	−0.212	−0.236	−0.174	−0.005	−0.113
South Africa	−0.341	−0.191	−0.192	−0.301	−0.029	−0.212
Spain	−0.361	−0.198	−0.204	−0.269	−0.023	−0.187
Sweden	−0.347	−0.194	−0.196	−0.293	−0.027	−0.206
Switzerland	−0.341	−0.192	−0.193	−0.303	−0.029	−0.213
Trinidad and Tobago	−0.353	−0.195	−0.200	−0.282	−0.025	−0.197
Turkey	−0.343	−0.192	−0.193	−0.299	−0.029	−0.210
United Kingdom	−0.364	−0.198	−0.206	−0.263	−0.022	−0.183
United States	−0.347	−0.194	−0.196	−0.293	−0.027	−0.206
Uruguay	−0.311	−0.156	−0.164	−0.298	−0.033	−0.212

APPENDIX B


Current study
Woods et al range (15)
Lomas et al elasticities (13)
Andrews et al elasticities (18)
Edney et al Australia estimate (11)
Stadhouders et al the Netherlands estimate (14)
Claxton et al UK estimate (10)
Vallejo-Torres et al Spain range (12)
Cost per DALY averted or QALY gained (2015 US$)
$200,000
$180,000
$160,000
$140,000
$120,000
$100,000
$80,000
$60,000
$40,000
$20,000
$0
0
5
10
15
20
25
30
35
40
45
50
U5M (2015)