## Abstract

**Purpose:** Evaluating whether or not 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. Value frameworks employing 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, in part, 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 paper provides estimates of cost per DALY averted for 33 high-income countries and the remaining OECD and BRIICS countries.

**Methods:** We calculate cost per DALY averted for each country based on estimated elasticities of the health effects of changes in expenditure on health outcomes from applying: 1) an existing published econometric model that employs cross-country data to an expanded dataset; and 2) other existing elasticities drawn from selected UK within-country studies; to country-level data on health expenditure, demography and burden of ill health. In order to provide a comprehensive picture of the state of research around empirical estimates of health opportunity costs for these countries, the cost per DALY averted estimates from this paper are reported against previously published estimates of cost per QALY gained for the same countries.

**Findings:** All but one of the ranges estimated fall below 3x GDP per capita, the upper end of the widely applied range of 1-3x GDP per capita. The range of estimates based on applying 1) an existing published econometric model that employs cross-country data to an expanded dataset are higher than 2) 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 paper 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 more robust estimates of country-specific health opportunity cost are estimated using within country data.

## Introduction

Value frameworks have been developed to guide the assessment of the value of new technologies across 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 expendidure.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, i.e. it is clinically effective, but 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 that 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 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 summarised 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 using a bookshelf metaphor, where the width of each “book” (i.e., 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 (e.g., QALYs gained or DALYs averted) per $1,000 spent and books are ranked from left to right, most to least cost-effective.6 (See Figure 1.) In the case of a fixed budget, a threshold that reflects health opportunity costs (i.e., marginal cost per QALY or DALY) is the reciprocal of the effectiveness-cost of the least cost-effective intervention that is currently funded (i.e., HOCfixed). 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 (i.e., HOCflexible).

[INSERT FIGURE 1]

While 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 healthcare and, in the context of a fixed 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 handful of countries, including the UK, Spain, 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 al15, who extrapolate the UK estimate10 to other countries using information about the income elasticity of demand. Ochalek et al16 use published elasticities of the effects of government health care expenditure on health outcomes (expenditure elasticity of health) from Bokhari et al17 to estimate cost per DALY averted for a range of low- and middle-income countries (LMICs).

This paper provides a range of plausible cost per DALY averted estimates that reflect health opportunity costs for high-income countries, two additional OECD countries and the remaining BRIICs (Brazil, China, India, Indonesia and South Africa) that can be used as placeholders for value frameworks. To do this, we apply the methods employed by Ochalek et al16 to data for these countries using 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 al17, and 2) other existing elasticities of the health effects of changes in expenditure drawn from selected UK within-country studies.13,18 In order to provide a comprehensive picture of the state of research around cost-effectiveness thresholds for these countries, the cost per DALY averted estimates from this paper are reported against previously published estimates of cost per QALY gained for the same countries (i.e., from Woods et al, and country-specific analyses using within-country data).13,15,18

## Methods

### Estimates for the expenditure elasticity of health

#### Extending an existing econometric model

We apply the econometric specification of Bokhari et al17, and following Ochalek et al16 we expand their dataset to include additional outcome measures that enable us to assess the population-wide health effects of changes in expenditure.

Bokahari et al17 estimate the effect of a change in health expenditure on under-5 and maternal mortality using cross-sectional data from the year 2000 for 127 countries. To do this, for each health outcome, , the following econometric model is estimated:

(1)

 denotes the level of education, paved roads per unit area, level of sanitation and improved water service, level of donor funding, income, government expenditures on health, deviation in donor funding from its historic average and an error term. As can be seen from (1), logarithmic transformation is undertaken for variables so that coefficients can be interpreted as elasticities. The model is estimated using an instrumental variable (IV) approach where , and any interaction terms including these variables are considered endogenous. The authors use four IVs to address this: military expenditure per capita of neighbouring countries, consumption-investment ratio and two measures of institutional quality based on annual World Bank assessments. It is required that these IVs are directly related to the leave 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 add to their dataset additional outcome measures obtained from the Institute for Health Metrics and Evaluation (IHME) Global Burden of Disease (GBD) project: adult female mortality (AFM), adult male mortality (AMM), 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 ) and shocks in donor funding (measured by ). The resulting elasticities on are used to calculate cost per DALY averted and are reported in Appendix A.

#### 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 two key reasons: 1) data is no longer constrained by international comparability, which means that more variables may be available, 2) it may be easier to obtain plausible IVs or natural experiments to inform an identification strategy. We use two recent published expenditure elasticities of all-cause mortality from the UK. 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 NHS expenditure on mortality.

Lomas et al13 updates an earlier analysis by Claxton et al10 where disease-specific expenditure elasticities of mortality are estimated using census data to obtain candidate IVs, 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 are combined using additional data and further estimates in order to provide an expenditure elasticity of all-cause mortality of -1.0278.13

In contrast, Andrews et al18 directly estimate an expenditure elasticity of all-cause mortality using IVs comprising of exogenous components of the resource allocation formula used to distribute funding across regional health authorities assuming adequate controls for healthcare need have been included. The resulting all-cause mortality elasticity is -0.705.18

### 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 (e.g., 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 summarised as a cost per DALY, which can be calculated for each country *i* as:

(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 four different ways to calculate DALYs, each with their own embedded assumptions. Table 1 summarises which estimated expenditure elasticities of health are available from this paper and two others: Lomas et al13 and Andrews et al18, and which DALY method can be used to calculate cost per DALY averted from each outcome elasticity.

[INSERT TABLE 1]

Calculating cost per DALY averted from elasticities requires taking into account the age and gender structure of the population and the underlying burden of mortality and morbidity.16 Therefore, data is required on the number of deaths in the population, disaggregated by age and gender, as well as the size of the population, again disaggregated by age and gender. The former is available from the IHME 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 (CLE), also available from GBD. We use years of life disabled (YLD) data from GBD, and calculate DALYs as the sum of YLL and YLD for each country. We compare our results against GDP per capita (2015 US$) from the World Bank.22 The four methods for calculating DALYs are described in detail elsewhere, and we summarise 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 begin by calculating the deaths estimated to be averted from this outcome by applying the estimated elasticity to the number of absolute deaths in each five-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 are those deaths that are expected to be averted by a 1% increase in health expenditure (i.e., 1% of total deaths in each age category).

[INSERT FIGURE 2]

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

(3)

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

(4)

Where a population-wide all-cause mortality elasticity is not available, but age-group or gender-specific all-cause mortality elasticities are these can be used instead, but an additional step is required to obtain population YLLs. Our data enable the estimation of elasticities on under-5, adult female mortality and adult male mortality. Figures 3a and 3b show 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 AFM and -0.75 for AMM.

[INSERT FIGURES 3a AND 3b]

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

(5)

where there are nine age groups (15-19, 20-24, … , 55-60) in the 15-60 category.

The YLLs averted among females and among males are added to the YLLs for the under-5 age category, which are also obtained using equation 3 where there is only one age category *a,* 0-4.

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

(6)

Finally, we account for the direct and indirect effects of health expenditure on the burden of morbidity (measured by years of life disabled, YLD). While an increase 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 (i.e., 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 (i.e., 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 Global Burden of Disease. Therefore, the overall DALYs averted for the population are calculated as

(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:

(8)

where population-wide YLL, , is calculated by

(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 using equation 5.

**DALY 3**

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

 (10)

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

**DALY 4**

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

(11)

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

(12)

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

(13)

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

## Results

Table 2 presents the estimates of cost per DALY averted for each country based on the elasticities estimated in this paper (using DALYs 1, 2, 3 and 4), the elasticity -1.0278 from Lomas et al13 (using DALY 1), the the elasticity -0.705 from Andrews et al18 (using DALY 1) and the range of cost per QALY estimates from Woods et al15 in 2015 US$ along with the percent of GDP per capita. The resulting estimates range from 5% to 376% of GDP per capita (India and Indonesia and the Netherlands respectively).

[INSERT TABLE 2]

The range of estimates for the UK from this paper are $51,768-$84,263 (approximately 1-2x GDP per capita). Using the elasticity -1.0278 from Lomas et al13 results in an estimate of $13,412 per DALY averted for the UK (31% of GDP per capita). The elasticity estimate from Andrews et al18 is smaller in magnitude than that from Lomas et al13 and 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). That the estimates based on the Lomas et al13 and Andrews et al18 elasticities are lower than the range estimated in this paper 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 al13 and Andrews et al18. 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 (which forms the basis of the Woods et al study) is $21,234 2015 US$ (48% of GDP per capita)15,23 . This is lower than the range estimated in this paper, but higher than the estimates based on the Lomas et al13 and Andrews et al18 elasticities.

The range estimated for Canada from this paper ($53,048-$89,827) is also approximately 1-2x GDP per capita. Again, this is higher than the range estimated by Woods et al15 ($26,565-43,249 or 49-61% of GDP per capita) or from using the elasticities from Lomas et al13 and Andrews et al18 ($15,848 and $23,104 or 37% and 53% of GDP per capita respectively). The range from this paper differs from that presented in a report for the Patented Medicine Prices Review Board in Canada24. Although the report uses the same methods as we apply in this paper, it applies the estimated elasticities to data from Canadian life tables while this paper uses international data from the Global Burden of Disease as was done in Ochalek et al16.

The same pattern emerging from the results for the UK and Canada is reflected in the range estimated for the USA. The range estimated in this paper is $60,475- $97,851, which is also approximately 1-2x GDP per capita. Again, this is higher than the range estimated by Woods et al15 ($25,690-$42,436 or 46-76% of GDP per capita) or from using the elasticities from Lomas et al13 and Andrews et al18 ($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 Spain11,12,14. The tightly dotted line represents 1x GDP per capita and the loosely dotted line represents 3x GDP per capita (representing the commonly applied 1x and 3x GDP per capita norms).25 The same estimates are presented against under-5 mortality in Appendix B. It can be seen that, in general, cost per DALY averted is increasing with GDP per capita, but the relationship is not fixed, nor is it monotonic. The variability of estimates between countries results from variability in country-specific characteristics, such as its demography and epidemiology and how much it spends on healthcare. As a result, there is no fixed proportion of GDP per capita that can reliably be used to estimate health opportunity costs.

[INSERT FIGURE 4]

These patterns are evident across countries where the estimates based on the population-wide all-cause mortality elasticities from Lomas et al13 result in the lowest estimate for each country. The ranges from Woods et al15 are all below 1x GDP per capita with the exception of Singapore (40%-112% of GDP per capita). The ranges estimated in this paper are all below 3x GDP per capita (apart from the Netherlands, which is 211% - 376%). Ochalek et al16, on which the methods used here are based, report results for LMICs only and most of the estimated ranges are below 1x GDP per capita. This is mainly due to two 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 al16 also depend on a country’s underlying mortality rates, demography and epidemiology.

The ranges this paper and the results from Woods et al15 tend to widen as GDP increases in Figure 4. The ranges from Woods et al15 widen as GDP per capita diverges from the UK value estimated by Claxton et al23 since these results extrapolate from that value. The width of the range of estimates for each country from this paper 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 (i.e., as government expenditure on health tends to increase with GDP), but differing levels of uncertainty exist in the denominator for each country.

## Discussion

Evaluating whether or not 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. While 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 (NICE) specifies an explicit range for the cost-effectiveness thresholds used in its deliberative decision-making process (£20,000 to £30,000 per QALY)26 based on implied values from previous decisions27, which have been widely recognised for some time (including by NICE) as having little empirical foundation.28–30 Other established norms include the thresholds of $50,000 to $150,000 per QALY in the US31, which have become increasingly cited but are also widely recognised as having little evidential foundation32, and the range of 1x to 3x GDP per capita, which have been widely used for decision making in LMICs after being recommended by the World Health Organization (WHO).33 The shortcomings of applying these thresholds in decision making in LMICs have been thoroughly established34–36, and the WHO has since distanced itself from them.37 Employing 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.16 11

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 is 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 paper provide a range of placeholder estimates for the health opportunity costs of government health care expenditure, which can be used to assess the cost-effectiveness of new technologies that impose costs on government funded components of a HCS.

The validity of the approach employed in this paper rests on 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 IVs with either approach. In practice, IVs 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 upon 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 al17 model may present similar issues if the interaction terms employed 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. Where the outcome measure is DALYs (or even QALYs) no assumptions are needed, except that the measure is accurately and consistently recorded (as with all measures). However, where the outcome measure is not a generic measure of health, it is necessary to employ assumptions to account for any components of health not part of the outcome measure, and where the outcome measure applies only to part of the population, some assumptions are needed to account for the total population health effects. Where mortality outcome measures are used we assume that the same proportion of deaths are averted across the population (i.e., 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 U5M being of greater magnitude than those on AFM or AMM. As such, using population segment-specific mortality elasticities (as done in this paper) may be more accurate than population-wide mortality elasticities as done in, e.g., Lomas et al13, Andrews et al18, and Edney et al38. 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 (i.e., 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 produces the most accurate cost per DALY averted is a matter of question resting on judgements about the validity of the construction of DALYs and the assumptions employed.

The approach adopted in this paper is quite different to that adopted by Woods et al15 where the Claxton et al10 estimate of health opportunity costs of NHS expenditure is extrapolated to other countries using the income elasticity of the value of a statistical life (VSL). The assumptions underlying this approach therefore centre on the econometric and modelling assumptions within the Claxton et al10 estimate and also on the appropriateness of applying the income elasticity of VSL to extrapolate this estimate. While 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 UK.

Another difference between the estimates reported by Woods et al15 and those reported here is that the former are given in cost per QALY gained while 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. While both are generic measures of health encompassing changes in both length and quality of life, QALYs represent health that stands to be gained while 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.39

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. Where 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.40–42 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 healthcare through increased insurance premiums. Healthcare is then rationed through price rather than waiting times, which results in health opportunity costs falling on individuals who are ‘priced out’, i.e. cannot afford the healthcare they need.43,44

While 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 seeks to capture the effect of a new technology across a range of objectives, which is summarised by way of an ‘impact inventory’. 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”.45 Regardless of the number of objectives are 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.46

## Conclusion

This paper makes an important contribution towards considering opportunity costs within economic evaluation of new health technologies. We provide placeholder estimates for 33 high-income countries and the remaining OECD and BRIICS countries, which can be used to estimate the health opportunity costs of government health care expenditure until more robust estimates of country-specific health opportunity cost are estimated using within country data. While 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.

## References

1. Neumann PJ, Willke RJ, Garrison LP. A Health Economics Approach to US Value Assessment Frameworks-Introduction: An ISPOR Special Task Force Report [1]. *Value Health*. 2018;21(2):119-123. doi:10.1016/j.jval.2017.12.012

2. Garrison LP, Pauly M V, Willke RJ, Neumann PJ. An Overview of Value, Perspective, and Decision Context-A Health Economics Approach: An ISPOR Special Task Force Report [2]. *Value Health*. 2018;21(2):124-130. doi:10.1016/j.jval.2017.12.006

3. Danzon PM, Drummond MF, Towse A, Pauly M V. Objectives, Budgets, Thresholds, and Opportunity Costs-A Health Economics Approach: An ISPOR Special Task Force Report [4]. *Value Health*. 2018;21(2):140-145. doi:10.1016/j.jval.2017.12.008

4. Sculpher M, Claxton K, Pearson SD. Developing a Value Framework: The Need to Reflect the Opportunity Costs of Funding Decisions. *Value Heal*. 2017;20(2):234-239. doi:10.1016/j.jval.2016.11.021

5. Murray CJ, Frenk J. A framework for assessing the performance of health systems. *Bull World Health Organ*. 2000;78(6):717-731.

6. Culyer AJ. Cost-effectiveness thresholds in health care: a bookshelf guide to their meaning and use. *Heal Econ Policy Law*. 2016;11(04):415-432. doi:10.1017/S1744133116000049

7. Culyer AJ. Cost, context, and decisions in health economics and health technology assessment. *Int J Technol Assess Health Care*. 2018;34(5):434-441. doi:10.1017/S0266462318000612

8. van Baal P, Perry-Duxbury M, Bakx P, Versteegh M, van Doorslaer E, Brouwer W. A cost-effectiveness threshold based on the marginal returns of cardiovascular hospital spending. *Health Econ*. 2019;28(1):87-100. doi:10.1002/hec.3831

9. Thokala P, Ochalek J, Leech AA, Tong T. Cost-Effectiveness Thresholds: the Past, the Present and the Future. *Pharmacoeconomics*. February 2018. doi:10.1007/s40273-017-0606-1

10. Claxton K, Martin S, Soares M, et al. Methods for the estimation of the National Institute for Health and Care Excellence cost-effectiveness threshold. *Health Technol Assess (Rockv)*. 2015;19(14):1-504. doi:10.3310/hta19140

11. Edney LC, Haji Ali Afzali H, Cheng TC, Karnon J. Estimating the Reference Incremental Cost-Effectiveness Ratio for the Australian Health System. *Pharmacoeconomics*. December 2017. doi:10.1007/s40273-017-0585-2

12. Vallejo-Torres L, García-Lorenzo B, Serrano-Aguilar P. *Estimating a Cost-Effectiveness Threshold for the Spanish NHS*. Madrid; 2016. http://documentos.fedea.net/pubs/eee/eee2016-22.pdf. Accessed July 31, 2017.

13. Lomas J, Martin S, Claxton K. Estimating the Marginal Productivity of the English National Health Service From 2003 to 2012. *Value Heal*. 2019;0(0). doi:10.1016/j.jval.2019.04.1926

14. Stadhouders N, Koolman X, Dijk C, Jeurissen P, Adang E. The marginal benefits of healthcare spending in the Netherlands: Estimating cost‐effectiveness thresholds using a translog production function. *Health Econ*. August 2019. doi:10.1002/hec.3946

15. Woods B, Revill P, Sculpher M, Claxton K. Country-Level Cost-Effectiveness Thresholds: Initial Estimates and the Need for Further Research. *Value Heal*. 2016;19(8):929-935. doi:10.1016/j.jval.2016.02.017

16. Ochalek J, Lomas J, Claxton K. Estimating health opportunity costs in low-income and middle-income countries: a novel approach and evidence from cross-country data. *BMJ Glob Heal*. 2018;3(6):e000964. doi:10.1136/bmjgh-2018-000964

17. Bokhari FAS, Gai Y, Gottret P. Government health expenditures and health outcomes. *Health Econ*. 2007;16(3):257-273. doi:10.1002/hec.1157

18. Andrews M, Elamin O, Hall AR, Kyriakoulis K, Sutton M. Inference in the presence of redundant moment conditions and the impact of government health expenditure on health outcomes in England. *Econom Rev*. 2017;36(1-3):23-41. doi:10.1080/07474938.2016.1114205

19. Institute for Health Metrics and Evaluation. Global Burden of Disease Study 2015 (GBD 2015) Data Resources | GHDx. http://ghdx.healthdata.org/gbd-2015. Published 2018. Accessed March 21, 2018.

20. Gravelle HSE, Backhouse ME. International cross-section analysis of the determination of mortality. *Soc Sci Med*. 1987;25(5):427-441. doi:10.1016/0277-9536(87)90167-5

21. Nakamura R, Lomas J, Claxton K, Bokhari F, Serra RM, Suhrcke M. *Assessing the Impact of Health Care Expenditures on Mortality Using Cross-Country Data*. York; 2016. https://www.york.ac.uk/media/che/documents/papers/researchpapers/CHERP128\_health\_care\_expenditures\_mortality\_cross-country\_data.pdf. Accessed May 3, 2017.

22. World Bank. GDP per capita (current US$) | Data. https://data.worldbank.org/indicator/NY.GDP.PCAP.CD. Accessed October 31, 2017.

23. Claxton K, Martin S, Soares M, et al. Methods for the estimation of the National Institute for Health and Care Excellence cost-effectiveness threshold. *Health Technol Assess*. 2015;19(14):1-503, v-vi. doi:10.3310/hta19140

24. Ochalek J, Lomas J, Claxton K. *Assessing Health Opportunity Costs for the Canadian Health Care Systems*.; 2018.

25. Cameron D, Ubels J, Norström F. Global Health Action On what basis are medical cost-effectiveness thresholds set? Clashing opinions and an absence of data: a systematic review medical cost-effectiveness thresholds set? Clashing opinions and an absence of data: a systematic review On what basis are medical cost-effectiveness thresholds set? Clashing opinions and an absence of data: a systematic review. *Glob Health Action*. 1447;11(1). doi:10.1080/16549716.2018.1447828

26. NICE. Guide to the Technology Appraisal Process (reference N0514). 2004.

27. Rawlins MD, Culyer AJ. National Institute for Clinical Excellence and its value judgments. *BMJ*. 2004;329(7459):224-227. doi:10.1136/bmj.329.7459.224

28. Committee H of CH. NICE: First report of the Health Committee 2007-2008. Presented at the: 2008.

29. Committee H of CH. NICE response to the first report of session 2007-2008. HC550. Presented at the: 2008.

30. Committee H of CH. The government’s response to the Health Select Committee’s first report of session 2007-08 on the National Institute for Health and Clinical Excellence. Cm7331. Presented at the: 2008.

31. Anderson JL, Heidenreich P, Barnett P, et al. ACC/AHA Statement on Cost/Value Methodology in Clinical Practice Guidelines and Performance Measures: A Report of the American College of Cardiology/American Heart Association Task Force on Performance Measures and Task Force on Practice Guidelines. 2014;63(21). doi:10.1016/j.jacc.2014.03.016

32. Neumann PJ, Cohen JT, Weinstein MC. Updating Cost-Effectiveness — The Curious Resilience of the $50,000-per-QALY Threshold. *N Engl J Med*. 2014;371(9):796-797. doi:10.1056/NEJMp1405158

33. Commission on Macroeconomics and Health. *Macroeconomics and Health: Investing in Health for Economic Development*. Geneva; 2001. http://www1.worldbank.org/publicsector/pe/PEAMMarch2005/CMHReport.pdf. Accessed July 31, 2017.

34. Newall AT, Jit M, Hutubessy R. Are current cost-effectiveness thresholds for low- and middle-income countries useful? Examples from the world of vaccines. *Pharmacoeconomics*. 2014;32(6):525-531. doi:10.1007/s40273-014-0162-x

35. Marseille E, Larson B, Kazi DS, Kahn JG, Rosen S. Thresholds for the cost-effectiveness of interventions: alternative approaches. *Bull World Health Organ*. 2015;93(2):118-124. doi:10.2471/BLT.14.138206

36. Robinson LA, Hammitt JK, Chang AY, Resch S. Understanding and improving the one and three times GDP per capita cost-effectiveness thresholds. *Health Policy Plan*. 2017;32(1):141-145. doi:10.1093/heapol/czw096

37. Bertram MY, Lauer JA, De Joncheere K, et al. Cost-effectiveness thresholds: pros and cons. *Bull World Health Organ*. 2016;94(12):925-930. doi:10.2471/BLT.15.164418

38. Karnon J, Afzali H, Edney L. Estimating a Reference ICER for Australia. In: *Boston 2017 Congress - International Health Economics Association*. Boston; 2017.

39. Augustovski F, Colantonio LD, Galante J, et al. Measuring the benefits of healthcare: DALYs and QALYs – Does the choice of measure matter? A case study of two preventive interventions. *Int J Heal Policy Manag*. 2018;7(2):120-136. doi:10.15171/ijhpm.2017.47

40. Appleby J, Devlin N, Parkin D, Buxton M, Chalkidou K. Searching for cost effectiveness thresholds in the NHS. *Health Policy (New York)*. 2009;91(3):239-245. doi:10.1016/j.healthpol.2008.12.010

41. Daniels T, Williams I, Robinson S, Spence K. Tackling disinvestment in health care services. *J Health Organ Manag*. 2013;27(6):762-780. doi:10.1108/JHOM-11-2012-0225

42. Chen TC, Wanniarachige D, Murphy S, Lockhart K, O’Mahony J. Surveying the Cost-Effectiveness of the 20 Procedures with the Largest Public Health Services Waiting Lists in Ireland: Implications for Ireland’s Cost-Effectiveness Threshold. *Value Heal*. 2018;21(8):897-904. doi:10.1016/J.JVAL.2018.02.013

43. Vanness DJ. Measuring Opportunity Costs of Health Technology Adoption as Morbidity and Mortality of the Uninsured. In: *International Health Economics Association*. ; 2017.

44. Reinhardt UE, Krugman PR, Frist WH. *Priced out : The Economic and Ethical Costs of American Health Care*.; 2019.

45. Lakdawalla DN, Doshi JA, Garrison LP, Phelps CE, Basu A, Danzon PM. Defining Elements of Value in Health Care-A Health Economics Approach: An ISPOR Special Task Force Report [3]. *Value Health*. 2018;21(2):131-139. doi:10.1016/j.jval.2017.12.007

46. Walker S, Griffin S, Asaria M, Tsuchiya A, Sculpher M. Striving for a Societal Perspective: A Framework for Economic Evaluations When Costs and Effects Fall on Multiple Sectors and Decision Makers. *Appl Health Econ Health Policy*. May 2019. doi:10.1007/s40258-019-00481-8

**Table 1. DALY methods and estimated expenditure elasticities of health by source**

**Table 2. Estimates of cost per DALY or QALY averted of marginal government healthcare expenditure for each country**

**Figure 1. Cost-effectiveness threshold**

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

**Figures 3a and 3b. Absolute deaths averted and not averted for a hypothetical country (females and males)**

**Figure 4. Range of cost per DALY averted or QALY gained estimates by method for each country and GDP per capita**