

This is a repository copy of *Country-level cost-effectiveness thresholds:initial estimates and the need for further research..*

White Rose Research Online URL for this paper:

<https://eprints.whiterose.ac.uk/id/eprint/135890/>

Version: Published Version

Monograph:

Woods, Beth orcid.org/0000-0002-7669-9415, Revill, Paul orcid.org/0000-0001-8632-0600, Sculpher, Mark orcid.org/0000-0003-3746-9913 et al. (1 more author) (2015) Country-level cost-effectiveness thresholds:initial estimates and the need for further research. Discussion Paper. CHE Research Paper . Centre for Health Economics, University of York , York, UK.

Reuse

Items deposited in White Rose Research Online are protected by copyright, with all rights reserved unless indicated otherwise. They may be downloaded and/or printed for private study, or other acts as permitted by national copyright laws. The publisher or other rights holders may allow further reproduction and re-use of the full text version. This is indicated by the licence information on the White Rose Research Online record for the item.

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.



THE UNIVERSITY *of* York



Country-Level Cost-Effectiveness Thresholds: Initial Estimates and the Need for Further Research

Beth Woods, Paul Revill, Mark Sculpher, Karl Claxton

CHE Research Paper 109

Country-level cost-effectiveness thresholds: initial estimates and the need for further research

Beth Woods^A
Paul Revill^A
Mark Sculpher
Karl Claxton

^AContributed equally

Centre for Health Economics, University of York, UK

March 2015

Background to series

CHE Discussion Papers (DPs) began publication in 1983 as a means of making current research material more widely available to health economists and other potential users. So as to speed up the dissemination process, papers were originally published by CHE and distributed by post to a worldwide readership.

The CHE Research Paper series takes over that function and provides access to current research output via web-based publication, although hard copy will continue to be available (but subject to charge).

Acknowledgements

This research report was produced as part of the Lablite project (<http://www.lablite.org/>), as well as the International Decision Support Initiative (www.idsihealth.org), a global initiative to support decision makers in priority-setting for universal health coverage. This work received funding support from Bill & Melinda Gates Foundation, the Department for International Development (UK), and the Rockefeller Foundation. The views expressed are those of the authors and not necessarily those of the funders.

Disclaimer

Papers published in the CHE Research Paper (RP) series are intended as a contribution to current research. Work and ideas reported in RPs may not always represent the final position and as such may sometimes need to be treated as work in progress. The material and views expressed in RPs are solely those of the authors and should not be interpreted as representing the collective views of CHE research staff or their research funders.

Further copies

Copies of this paper are freely available to download from the CHE website www.york.ac.uk/che/publications/. Access to downloaded material is provided on the understanding that it is intended for personal use. Copies of downloaded papers may be distributed to third-parties subject to the proviso that the CHE publication source is properly acknowledged and that such distribution is not subject to any payment.

Printed copies are available on request at a charge of £5.00 per copy. Please contact the CHE Publications Office, email che-pub@york.ac.uk, telephone 01904 321405 for further details.

Centre for Health Economics
Alcuin College
University of York
York, UK
www.york.ac.uk/che

© Beth Woods, Paul Revill, Mark Sculpher, Karl Claxton

Abstract

Healthcare systems in low- and middle-income countries (LMICs) face considerable population healthcare needs with markedly fewer resources than those in developed countries. The way in which available resources are allocated across competing priorities is crucial in affecting how much health is generated overall, who receives healthcare interventions and who goes without. Cost-effectiveness analysis (CEA) is one tool that can assist policy-makers in resource allocation. The central concern in CEA is whether the health gains offered by an intervention are large enough relative to its costs to warrant adoption. This requires some notion of the value that must be realized by an intervention, which is most frequently represented using a cost-effectiveness threshold (CET).

CETs should be based on estimates of the forgone benefit associated with alternative priorities which consequently cannot be implemented as a result of the commitment of resources to an alternative. For most health care systems these opportunity costs fall predominantly on health as a result of fixed budgets or constraints on health systems' abilities to increase expenditures. However, many CEAs to inform decisions in LMICs have used aspirational expressions of value, such as the World Health Organization's (WHO) recommended CETs (of 1-3 times GDP per capita in a country) which are not based upon opportunity costs. In contrast, we estimate CETs for a number of countries based upon recent empirical estimates of foregone benefit (from the English NHS) and international income elasticities of the value of health. The resulting CETs are much lower than those previously posited by WHO. There is no intention to provide definitive CETs; rather, the study is intended to provoke further research in this area of crucial policy importance and outlines how more robust estimates of CETs could be generated.

1. Introduction

Policy-makers in all healthcare systems face difficult choices about which interventions, programmes or activities (hereinafter referred to solely as ‘interventions’) should be funded from limited available resources. The tools of economic evaluation offer a variety of means to assist policymakers in the process of prioritization. A common approach is that of incremental cost-effectiveness analysis (CEA) which is based upon the comparative assessment of costs and health benefits. CEA seeks to identify which interventions offer health benefits large enough relative to costs to warrant adoption and those that do not.[1]

Results in CEA are often represented in the form of an incremental cost-effectiveness ratio (ICER); the ratio of incremental costs to incremental health benefits of one intervention compared to another mutually exclusive alternative ($\Delta \text{costs} / \Delta \text{health benefits}$).[1] Health benefits are often represented in the form of quality adjusted life years (QALYs); and so the ICER gives the ‘cost per QALY gain’ associated with an intervention. To determine whether an intervention’s ICER is likely to represent a ‘good buy’ requires comparison to some benchmark of value. The benchmark most frequently used is the cost-effectiveness threshold (CET). If an $\text{ICER} < \text{CET}$, an intervention’s health benefits are deemed large enough in comparison to costs (i.e. it is deemed ‘cost-effective’); but if $\text{ICER} > \text{CET}$ the benefits are insufficient in comparison to costs (i.e. it is not cost-effective).

The choice of CET is, therefore, crucial in determining value from healthcare interventions when applying incremental CEA. A key concept in all economic analysis is that of ‘opportunity costs’.[2] All healthcare systems face resource constraints so if resources are committed to the funding of one intervention these are not available to fund and deliver others. Opportunity costs are the health benefits forgone due to the commitment of scarce resources to particular investments, or if additional resources are made available, the health that could have been gained by investing these resources elsewhere in the healthcare system. For CEA to be consistent with population health improvement there is a need for chosen CETs to reflect opportunity costs. However, the estimation of opportunity costs for different kinds of decisions remains a major challenge.

2. Understanding and estimating cost-effectiveness thresholds

Recent methods research has brought greater clarity as to normative basis for the use of CETs and how they can be appropriately estimated so as to improve population health.[3, 4] A clear distinction needs to be made between two related, but separate, concepts of opportunity costs: (i) opportunity costs in terms of health forgone – due to the commitment of limited collective healthcare resources to particular interventions; (ii) opportunity costs in terms of forgone consumption (the ‘consumption value of health’) when additional costs fall on consumption opportunities outside health care rather than on health care expenditure. The first, (i), can also be termed the ‘shadow price of the budget constraint’. It is an issue of ‘fact’, resulting from limits in the overall collective budget available for healthcare or constraints on health system’s abilities to increase expenditure. The second, (ii), is an issue of ‘value’ and depends upon how individuals value health as compared to other forms of consumption.

For economic evaluation of an intervention, it is important to consider what type of opportunity costs would result from investment in new activities. If opportunity costs result in the form of health forgone (e.g. through displacement of other health generating interventions funded from a collective healthcare budget), then the CET should reflect this – let’s denote this ‘ k ’ (the ratio of the cost reduction associated with displacing interventions to the QALYs lost). If opportunity costs are in terms of other forms of consumption (e.g. if the intervention relies on other sources of funding such as out-of-pocket contributions), the CET should reflect the consumption value of health - let’s denote this ‘ v ’.

Observing that an estimate of the consumption value of health is higher than the amount of healthcare resource required to improve health ($v > k$) suggests that the healthcare system is not meeting individual preferences, because individuals would be willing to give up more of the resources available to them to improve their own health than the healthcare system would require. Simply assuming that v is equal to k would be inappropriate since there are good reasons to expect $v > k$ not least the welfare losses associated with socially acceptable ways to finance healthcare systems (i.e. society would not increase health expenditure to the point where $v=k$).

For incremental CEA to suitably inform the allocation of healthcare expenditures, for which the primary purpose is generally regarded as being the generation of ‘health’ from limited collective healthcare resources, CETs reflecting the opportunity costs of healthcare spending (k) will always be required if there are any restrictions on the growth in health care expenditure. There are at least two ways in which k could be determined.

Firstly, a threshold can be chosen based upon what it is felt a health system *should* be willing to pay for health – for which distinction can be made between how much individuals would be willing to pay to improve health (v : the consumption value of health) and simply aspirational notions of how the world should be (or how much other individuals should be willing to spend to improve their health, without consideration of other calls on their resources).

Secondly, the relationship between changes in healthcare expenditure and health outcomes can be estimated (i.e. the marginal productivity of the healthcare system in generating health) as a direct measure of what is likely to be displaced when a cost-escalating intervention is adopted or what could be gained elsewhere if cost-savings are made or additional resources are made available.

The first of the approaches tends to dominate in practice in all healthcare systems. For instance, a value of US\$50,000 has been commonly applied in the United States.[5] Similarly, for low and middle income countries, the World Health Organization (WHO) has recommended thresholds of 1

to 3 times gross domestic product (GDP) per capita for use in low and middle income countries.[6] These values – from the US and from WHO – are not based upon assessment of health opportunity costs resulting from resource constraints. Instead they can be seen as statements of ‘value’; what it is felt health systems *should* be willing to pay for health gains (the US estimate motivated more by individuals’ expressions of willingness to pay for health gains; the WHO approach based on aspiration). However, their use is not necessarily consistent with population health improvement as they do not reflect the opportunity cost that is imposed on the health care system. They can therefore be seen as inappropriate measures of k that risk reducing, rather than increasing, population health.

The second approach is an empirical means to estimate k based upon assessment of health benefits forgone when funding is committed to particular interventions. Estimating k in this way provides a basis for making resource allocation decisions that increase population health. However, there is a paucity of estimates available in any jurisdiction using these approaches. One notable exception is Claxton et al.[4] who used local level programme expenditure data, in a range of disease areas, to estimate the relationship between changes in healthcare expenditure and health outcomes in the English National Health Service.

By exploiting the variation in expenditure and mortality outcomes, Claxton et al. estimate the relationship between changes in spending and mortality while accounting for endogeneity. With additional information about age and gender of the patient population these mortality effects were expressed as a cost per life year threshold (£25,241 per life year). These life year effects were adjusted for quality of life with additional information about quality of life norms by age and gender, as well as the quality of life impacts of different types of disease. 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 (i.e. that includes quality of life burden) a cost per QALY threshold was estimated of UK£12,936 (US\$20,212) per QALY.[4]

3. Estimating cost-effectiveness thresholds for other countries

There is a lack of empirically based estimates of k (based on opportunity costs in terms of health) for jurisdictions other than the UK despite growing recognition that such estimates are required to suitably inform resource allocation decisions.[7, 8] The Claxton et al. estimate of k is based upon estimates of the marginal productivity of healthcare spending in just one jurisdiction.[4] In principle, a similar approach could be adopted to estimate the relationship between healthcare spending and health outcomes internationally, using countries as units of analysis, to determine k in a wide range of settings.

To date, however, cross-country evidence on the productivity of healthcare spending has focused on answering the question “does healthcare spending improve health outcomes?” Recent research adjusting for potential reverse causality in this relationship (e.g. governments may spend more when health outcomes are worse) suggests that the answer to this question is yes.[9] However, the available literature does not focus on how the effect of healthcare spending on health outcomes varies according to the level of healthcare spending or country income. The analyses available do suggest that the marginal productivity of healthcare spending diminishes with healthcare spending or country income.[10-12] This indicates that the threshold should increase with country income or healthcare spending as the amount of health displaced by new resource commitments as country income / health care spending rises. However, there is little information about the rate at which this increase occurs¹. Understanding this would require careful exploration of the functional form of the relationship between healthcare spending and health outcomes.

However, there is a body of literature that estimates v (the consumption value of health) in different countries. Some of this literature is based upon stated preference elicitation of individuals’ willingness-to-pay (WTP) for morbidity adjusted life years (e.g. QALYs)[13, 14], but a larger body of work estimates the ‘value of a statistical life’ (VSL) from mortality reductions (e.g. through estimating compensating differentials for on the job risk exposure in labour markets).[15, 16] Moreover, the VSL literature also examines how the VSL varies across jurisdictions as a function of national per capita income (i.e. the elasticity of the VSL with respect to income, ϵ) (see below). This potentially provides information about the income elasticity of v if we can assume that the income elasticity of the VSL is equal to the income elasticity of the value of a life year, and this in turn is equal to the income elasticity of the value of a morbidity adjusted life year (e.g. QALY). For this to be the case across countries, a VSL must convert to the same number of QALYs across countries (the plausibility of this assumption is examined in the Discussion).

Understanding the income elasticity of v across countries of different income levels raises an interesting prospect. If a similar income elasticity of k exists as for v , income elasticities of the VSL can be applied to the Claxton et al. estimate of k for the English NHS to provide estimates of k in a wide range of jurisdictions. We follow this approach to provide estimates of k for application in different countries based upon their per capita income levels using the cost-effectiveness threshold for the NHS, per capita income in the UK and the elasticity of VSL with respect to income. (Figure 1). The approach is based upon two core assumptions: (1) that the discrepancy between v and k is constant across countries in percentage terms (i.e. that ‘underfunding’ of healthcare through collectively pooled resources relative to individual preferences over consumption and health is

¹ Typically constant elasticity production functions are modelled. These impose significant constraints on the way the threshold can vary with income or health care spending. Namely, values of the elasticity of health with respect to health care spending or income must be <1.0 for the threshold to be increasing in health care spending or income. However, values of the elasticity <1.0 also imply that the threshold increases at a diminishing rate with health care spending or income.

constant with respect to GDP p.c.); (2) that the UK is ‘typical’ of other countries with respect to the values of v and k . These assumptions are examined in the Discussion.

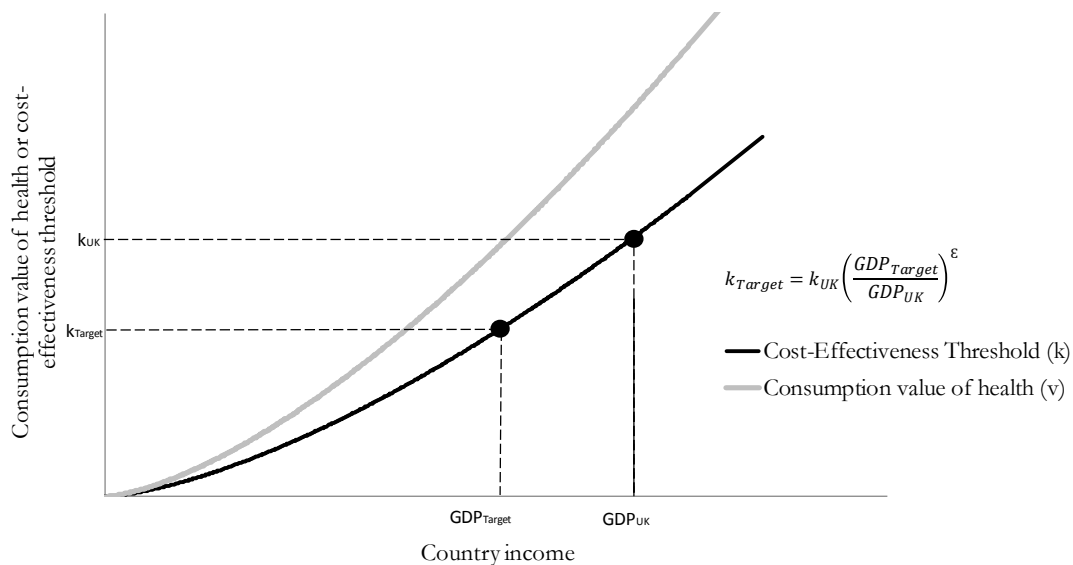


Figure 1: Method for inferring country-specific cost-effectiveness thresholds from UK threshold

4. What is known about the income elasticity of the value of health?

The relationship between the value of a statistical life (VSL) and per capita income at the level of jurisdictions (e.g. of countries) is investigated in a small but emerging literature.[16-18] The literature has evolved out of a longer standing body of work which has examined the relationship between income and health valuation at the level of individuals (i.e. 'within' countries).[15, 17]

Of central interest in both these bodies of work (within-group, at the individual level, and between-group, at the level of jurisdictions) is the income elasticity of the value of health and whether this is less than 1 (so health is a necessity good) or greater than 1 (so health is a luxury good); and whether the elasticity is likely to change for different levels of income.[17]

Initial research conducted primarily in higher income countries amongst individuals, and most often in the United States, suggested elasticities in the range 0.4-0.6.[15, 16] These estimates came mainly from cross-sectional studies looking at wage-risk premiums. However, the estimates have been described as 'nonsensical' when extrapolated to lower income countries since the corresponding VSL would be beyond the ranges deemed plausible in such settings.[16]

The methods to estimate income elasticities of VSL have, therefore, been more carefully scrutinized in more recent years. In particular, cross sectional ('within group') estimates from earlier studies have been contrasted with longitudinal or cohort ('between group') studies (which typically estimate elasticities >1; even within countries) and reasons for inconsistencies explored.[16, 17, 19] For instance, Aldy and Smyth (2014) use a life-cycle model applied to US data of the consumption and labour supply choices faced by individuals with uncertain life expectancy and wage income to explain this discrepancy.[19] They argue that cross-sectional studies are more likely to capture changes in realised income, whereas longitudinal or across cohort studies capture the impact of permanent income which is more informative when translating VSL estimates across countries. Estimates of elasticity with respect to realised income are lower as realised income is more variable. Similarly, Getzen (2000) concludes that whereas 'within group' health may be deemed a necessity, analyses of expenditures 'between group' indicate it is almost certainly a luxury good at the national level.[17]

The recent consensus then is that the income elasticity of VSL to transfer estimates across countries should be >1.[16, 18] We choose to apply a range of elasticities (1.0, 1.5 and 2.0) to reflect uncertainty in the literature. Based upon Milligan et al (2014), a function is also applied of an elasticity of 2.5 for countries with gross domestic product (GDP) per capita < US\$10,725 (2005 price year) purchasing power parity (PPP) and of 0.7 for countries with per capita incomes greater than this level². [18]

² In line with the recommendations in Milligan et al. 2014 the elasticities from this study are applied to 2013 PPP-adjusted GDP, deflated to reflect 2005 international dollars. The resulting threshold values are then inflated to reflect 2013 international dollars.

5. Results: country level estimates of cost-effectiveness thresholds

The best estimate of the UK CET is £12,936 per QALY (US\$18,609 purchasing power parity (PPP) adjusted³). Gross domestic product (GDP) per capita estimates were obtained from the World Bank dataset for 2013.⁴ In line with the literature on the value of a statistical life we apply elasticities to countries' GDP per capita adjusted for purchasing power parity (see for example Milligan (2014)).^[18] CETs are reported in 2013 PPP adjusted US dollar values. Values without PPP adjustment are also provided for specific countries⁵.

Predicted CETs across country income levels are shown in Figure 2 for a range of income elasticities for the VSL. Higher income elasticities imply lower CETs in countries with lower GDP p.c. compared to the UK, and higher CETs in countries with higher GDP p.c. compared to the UK. The impact of alternative choices of elasticity is larger as the discrepancy between the GDP of the country of interest and UK GDP widens. Results for a selection of specific countries are shown in Table 1.

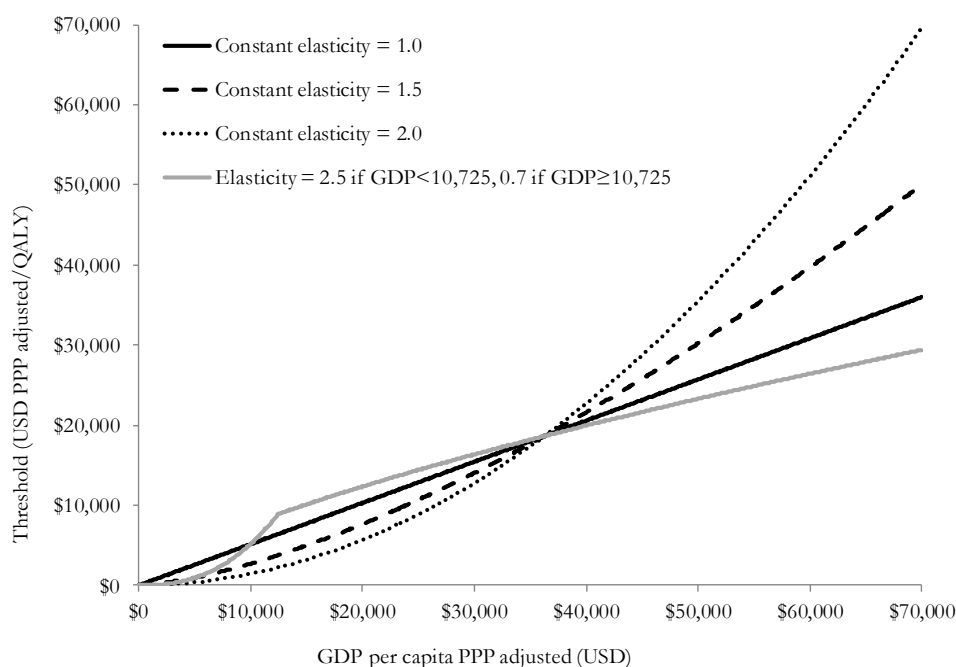


Figure 2: Predicted cost-effectiveness threshold (k) values by country income

³ This analysis uses the PPP conversion factor: <http://data.worldbank.org/indicator/PA.NUS.PPP>

⁴ This analysis uses PPP adjusted GDP per capita: <http://data.worldbank.org/indicator/NY.GDP.PCAP.PP.CD>

⁵ This analysis uses data on the ratio of the PPP conversion factor to the market exchange rate to remove the PPP adjustment but retain the presentation in dollars: <http://data.worldbank.org/indicator/PA.NUS.PPPC.RF>. Results are also presented in comparison to non-PPP adjusted GDP: <http://data.worldbank.org/indicator/NY.GDP.PCAP.CD>.

Table 1: Example results for a range of countries and the World Bank income classification cut-offs

Country/classification	PPP-adjusted (2013 USD)		Actual values (2013 USD)		Threshold as % GDP
	GDP p.c.	Threshold range ⁺	GDP p.c.	Threshold range ⁺	
Malawi	780	9 - 401	226	3 - 116	1% - 51%
Indonesia	9,559	1,298 - 4,914	3,475	472 - 1,786	14% - 51%
Chile	21,911	6,819 - 13,141	15,732	4,896 - 9,436	31% - 60%
Kazakhstan	23,206	7,648 - 13,675	13,610	4,485 - 8,018	33% - 59%
United kingdom	36,197	18,609 - 18,609	41,787	20,223 - 20,223	48% - 48% [#]
Canada	43,247	21,051 - 26,564	51,958	25,292 - 31,915	49% - 61%
United states	53,143	24,283 - 40,112	53,042	24,283 - 40,112	46% - 75%
Norway	65,461	28,057 - 60,862	100,819	43,211 - 93,736	43% - 93%
Low/middle income*	1,045	16 - 537	Not available		1% - 51%
Middle/high income*	12,746	2,307 - 9,028			18% - 71%

* We have assumed Gross National Income per capita to be the same as PPP adjusted GDP. These values relate to the income cut-offs for low to middle income and middle to high income countries as defined by the World Bank. ⁺ Reflects range of values obtained when using elasticity estimates of 1.0, 1.5, 2.0 and 2.5 for GDP less than \$10,725 and 0.7 for GDP greater than \$10,725. [#] For the UK the World Bank ratio of PPP conversion factor to market exchange rate did not correspond to the ratio of reported actual GDP to reported PPP-adjusted GDP. The threshold as a % GDP value for the UK therefore depends on whether PPP-adjusted or actual data are used (51% and 48% respectively).

The estimated CETs are substantially lower than those currently used by decision-making agencies and international organizations. Compared to a threshold of US\$50,000 per QALY that has been conventionally applied in the US, our approach estimates a CET in the range US\$24,283-US\$40,112 per QALY. Even more starkly, in comparison to thresholds of 1-3 times GDP per capita recommended by the WHO, the upper bounds of our estimates indicate values of 51% GDP p.c. for countries classified as low income and 71% GDP p.c. for those classified as middle income.

US dollar CET values with and without PPP adjustment are provided in the appendix for all countries for which data was available from the World Bank database for 2013. Values without adjustment for PPP can be converted to local currency using standard exchange rates.

6. Discussion

Policymakers in all countries face difficult decisions about how to allocate scarce healthcare resources to maximize health gains for their populations. Cost-effectiveness analysis offers a means by which to compare the costs and health gains from alternative interventions as a basis to inform investment. For the results of CEA to align with population health improvement requires that health gains from recommended interventions exceed the opportunity costs of health forgone when resources are committed to those interventions. The health opportunity costs should be reflected in the cost effectiveness threshold (k). Health opportunity costs can be contrasted to the consumption value of health (v) based upon individuals' expressions of the value of health gains.

In this paper we provide estimates of cost-effectiveness thresholds (the ' k 's) in a number of countries based upon assessment of the likely marginal productivity of their healthcare systems. This has required (i) an estimate of the marginal productivity in the English NHS from Claxton et al.; (ii) estimates of the GDP p.c. of the UK and other countries of interest; and (iii) estimates of the elasticity of the value of health (' v ') with respect to countries' per capita income (proxied by income elasticities of the value of a statistical life (VSL)). We estimate thresholds far lower than those conventionally applied; which implies that CEAs are likely to be recommending interventions which lead to reductions in population health.

The results presented rely upon some core assumptions if they are to be reasonable extrapolations to reflect the marginal productivity of other (non-UK) healthcare systems: (1) that the discrepancy between the consumption value of health (v) and cost-effectiveness threshold for health (k) is constant in percentage terms across countries; (2) that the UK is 'typical' of other countries with respect to the values of v and k ; and (3) that the income elasticity of VSL equals the income elasticity of the consumption value of a QALY.

Two reasons why the proportional discrepancy between k and v may differ across country income levels include: (i) non-constant ratios between individual and societal valuations of health (e.g. due to differences in understanding of health production functions and the trade-off associated with an implied v); (ii) constraints on the size of the health care budget differing for reasons other than societal valuations of healthcare spending (e.g. differences in tax generating abilities due to technical/administrative reasons). The ratio of v/k represents the value of collective compared to private resource or the shadow price of public expenditure.

The assumption that the UK is 'typical' of countries with respect to health production possibilities in part relies upon the UK healthcare system (the NHS) being of 'typical' efficiency in converting health sector resources to health gains for a country of its income level. There is some limited evidence the UK NHS may incur less waste than other health sectors (as indicated for example by relatively high use of generic drugs [20]) or be more efficient due to bodies such as the National Institute for Health and Care Excellence. If the UK is more productive, this means our analysis over-estimates the marginal productivity of other healthcare systems and under-estimates k . However, if the UK is less wasteful than other countries, the UK estimate of k can be considered relevant to a higher income level than UK GDP (as waste is simply lost income), this suggests our analysis may over-estimate k . Depending on the magnitude of these effects our analysis may over or under-estimate the marginal productivity of other healthcare systems and under- or over-estimate k . However, if this were the case, it also implies that perhaps other countries could seek efficiency gains by reassessing what interventions they currently provide and at what cost, rather than evaluating new interventions more leniently.

For the elasticity of the VSL to equal the elasticity of the consumption value of health (v), a statistical life should provide the same units of morbidity-adjusted health (e.g. QALYs) across countries. This could be questioned if lives-saved were expected to generate very different remaining morbidity-adjusted life expectancies. Although life expectancy at birth varies considerably across countries, remaining life expectancy differs much less due to differences in age demographics (e.g. Hammitt and Robinson, 2011, find remaining life expectancies between 34 and 45 years in countries with widely varying per capita incomes as a result of much older populations in countries with higher life expectancies at birth[16]). Again, although quality of life is likely to be increasing in income, older populations would also be expected to have higher levels of morbidity so differences in QALYs gained may also be small.

Therefore, although our results are embedded with many assumptions, it is not immediately clear whether these are likely to lead to our estimates of k being positively or negatively biased.

These results should, however, only be regarded as a first attempt to inform this area of crucial policy importance. The estimates can be used to inform policy decisions, particularly in the absence of other estimates based upon an assessment of health opportunity costs; but they should be applied cautiously. They can in some ways be regarded as a provocation to inspire more research. What research could then be undertaken to better inform thresholds for use within countries?

Aside from the relatively elaborate analysis of Claxton et al. being repeated in every country, which would likely not be possible due to data constraints in many jurisdictions, econometric analyses of policy reforms and other natural experiments could inform the marginal productivity of health sectors. Another approach could be to explore the cost-effectiveness of interventions currently provided within a country and those falling outside of the budget envelope. In this way, policymakers can undergo a process of 'threshold seeking'[21] and become more informed about k as the number of CEAs in their jurisdiction increases. One example of a study using an approach similar to this is from Malawi - the country with the lowest per capita income from those presented in this paper – and suggests a threshold of no more (and perhaps less) than US\$150 in that country.[22] Encouragingly, this is slightly above the range (US\$3-US\$116) that we estimate.

As has already been highlighted, an analysis of cross-country data with countries as units of analysis could be used to inform international estimates of marginal productivity of healthcare. Moreno-Serra and Smith (2014), adopting an approach similar to this but focused on mortality, estimate a marginal cost of only \$145 per life year saved from public healthcare expenditure in a typical low and middle income country.[10] Another alternative could be a hybrid-type approach whereby a small number of within-country empirical estimates of thresholds are produced which are then extrapolated across income levels to provide estimates for a greater number of countries.

All such analyses are likely to have important roles in the quest for greater allocative efficiency, leading to overall population health gains, in health sectors across the world.

7. Conclusion

The cost-effectiveness thresholds presented in this paper are much lower than those previously applied in many countries (e.g. using WHO recommended cost-effectiveness thresholds of 1-3 times GDP per capita). The results have potentially profound consequences for resource allocation. It is hoped they will provoke further research on this topic.

References

1. Drummond, M., et al., *Methods for the Economic Evaluation of Health Care Programmes*. 3rd Edn. 2005: Oxford Medical Publications.
2. Palmer, S. and J. Raftery, Economic Notes: opportunity cost. *BMJ*, 1999. **318**(7197): p. 1551-2.
3. Claxton, K., Walker, S., Palmer, S., Sculpher, M., *Appropriate Perspectives for Health Care Decisions*. 2010.
4. Claxton, K., Martin, S., Soares, M., Rice, N., Spackman, E., Hinde, S., Devlin, N., Smith, P.C., Sculpher, M., *Methods for the estimation of the NICE cost-effectiveness threshold*. 2013, Centre for Health Economics, University of York.
5. Neumann, P.J., J.T. Cohen, and M.C. Weinstein, Updating cost-effectiveness--the curious resilience of the \$50,000-per-QALY threshold. *N Engl J Med*, 2014. **371**(9): p. 796-7.
6. WHO. *World Health Organization, Cost-Effectiveness Thresholds*. http://www.who.int/choice/costs/CER_thresholds/en/index.html. 2012 April 30, 2012].
7. Revill, P., Walker, S., Madan, J., Ciaranello, A., Mwase, T., Gibb, D.M., Claxton, K., Sculpher, M., Using cost-effectiveness thresholds to determine value for money in low- and middle-income country healthcare systems: are current international norms fit for purpose?, in *University of York, Centre for Health Economics Research Paper 98*. 2014.
8. Newall, A.T., M. Jit, and R. Hutubessy, Are current cost-effectiveness thresholds for low- and middle-income countries useful? Examples from the world of vaccines. *Pharmacoeconomics*, 2014. **32**(6): p. 525-31.
9. Moreno-Serra, R. and P.C. Smith, Does progress towards universal health coverage improve population health? *Lancet*, 2012. **380**(9845): p. 917-23.
10. Moreno-Serra, R., Smith, P.C., Broader health coverage is good for the nation's health: evidence from country level panel data. *Journal of the Royal Statistical Society*, 2014.
11. Bokhari, F.A., Y. Gai, and P. Gottret, Government health expenditures and health outcomes. *Health Econ*, 2007. **16**(3): p. 257-73.
12. Farahani, M., S.V. Subramanian, and D. Canning, Effects of state-level public spending on health on the mortality probability in India. *Health Econ*, 2010. **19**(11): p. 1361-76.
13. Shiroya, T., et al., International survey on willingness-to-pay (WTP) for one additional QALY gained: what is the threshold of cost effectiveness? *Health Econ*, 2010. **19**(4): p. 422-37.
14. Ryen, L. and M. Svensson, The Willingness to Pay for a Quality Adjusted Life Year: A Review of the Empirical Literature. *Health Econ*, 2014.
15. Viscusi, W.K. and J.E. Aldy, The value of a statistical life: A critical review of market estimates throughout the world. *Journal of Risk and Uncertainty*, 2003. **27**(1): p. 5-76.

16. Hammitt, J.K., Robinson, L.A., The income elasticity of the value per statistical life: transferring estimates between high and low income populations. *Journal of Benefit-Cost Analysis*, 2011. **2**(1): p. 2152-2812.
17. Getzen, T.E., Health care is an individual necessity and a national luxury: applying multilevel decision models to the analysis of health care expenditures. *J Health Econ*, 2000. **19**(2): p. 259-70.
18. Milligan, C., Kopp, A., Dahdah, S., Montufar, J., Value of a statistical life in road safety: a benefit-transfer function with risk-analysis guidance based on developing country data. *Accident Analysis and Prevention*, 2014. **71**: p. 236-247.
19. Aldy, J.E., Smyth, S.J., Heterogeneity in the value of life, in *Resources for the Future Discussion Paper No. 14-13*. 2014.
20. OECD, Health at a Glance 2013: *OECD Indicators*. 2013.
21. Culyer, A., et al., Searching for a threshold, not setting one: the role of the National Institute for Health and Clinical Excellence. *J Health Serv Res Policy*, 2007. **12**(1): p. 56-8.
22. Bowie, C. and T. Mwase, Assessing the use of an essential health package in a sector wide approach in Malawi. *Health Res Policy Syst*, 2011. **9**: p. 4.

Appendix: All country values

The table below presents the PPP-adjusted and non-adjusted range of threshold values for each country for which PPP-adjusted GDP was reported in the World Bank database. In some cases data was not available to remove the PPP-adjustment and only PPP-adjusted threshold values are reported.

Country	Cost-effectiveness threshold range	
	(USD, PPP adjusted)	(actual USD)
Afghanistan	56 - 1,023	19 - 349
Albania	1,563 - 5,816	702 - 2,612
Algeria	2,514 - 9,300	1,012 - 3,743
Angola	807 - 3,875	603 - 2,897
Antigua and Barbuda	6,250 - 12,750	3,965 - 8,090
Armenia	858 - 3,997	387 - 1,801
Australia	21,153 - 26,938	32,771 - 41,732
Austria	21,355 - 27,684	23,727 - 30,759
Azerbaijan	4,172 - 11,085	1,901 - 5,051
Bahrain	21,245 - 27,277	11,962 - 15,358
Bangladesh	93 - 1,315	30 - 427
Belarus	4,407 - 11,297	1,895 - 4,857
Belgium	20,060 - 23,111	22,570 - 26,003
Belize	1,012 - 4,340	584 - 2,503
Benin	46 - 921	20 - 414
Bhutan	835 - 3,943	267 - 1,258
Bolivia	534 - 3,151	250 - 1,474
Bosnia and Herzegovina	1,318 - 4,952	644 - 2,421
Botswana	3,490 - 10,419	1,621 - 4,839
Brazil	3,210 - 10,122	2,393 - 7,544
Brunei Darussalam	29,901 - 73,137	16,065 - 39,294
Bulgaria	3,609 - 10,541	1,720 - 5,025
Burkina Faso	38 - 840	17 - 379
Burundi	8 - 396	3 - 137
Cabo Verde	584 - 3,297	343 - 1,935
Cambodia	131 - 1,564	44 - 518
Cameroon	104 - 1,394	49 - 654
Canada	21,051 - 26,564	25,292 - 31,915
Central African Republic	5 - 310	3 - 171
Chad	61 - 1,070	31 - 540
Chile	6,819 - 13,141	4,896 - 9,436
China	2,013 - 7,957	1,151 - 4,550
Colombia	2,174 - 8,754	1,370 - 5,518
Comoros	35 - 801	19 - 452
Congo, Dem. Rep.	8 - 384	5 - 230
Congo, Rep.	489 - 3,016	264 - 1,628
Costa Rica	2,733 - 9,574	2,006 - 7,027

Country	Cost-effectiveness threshold range	
	(USD, PPP adjusted)	(actual USD)
Cote d'Ivoire	129 - 1,548	61 - 737
Croatia	6,206 - 12,720	3,953 - 8,101
Cyprus	12,318 - 16,130	11,020 - 14,430
Czech Republic	10,620 - 15,322	7,325 - 10,569
Denmark	20,888 - 25,974	28,767 - 35,771
Djibouti	128 - 1,541	71 - 857
Dominica	1,429 - 5,205	991 - 3,611
Dominican Republic	1,943 - 7,618	937 - 3,675
Ecuador	1,557 - 5,788	858 - 3,191
Egypt, Arab Rep.	1,745 - 6,669	522 - 1,993
El Salvador	856 - 3,991	422 - 1,967
Equatorial Guinea	16,150 - 17,717	9,843 - 10,798
Eritrea	20 - 615	9 - 280
Estonia	8,912 - 14,418	6,574 - 10,636
Ethiopia	26 - 696	10 - 255
Fiji	897 - 4,086	507 - 2,307
Finland	19,334 - 20,781	23,867 - 25,653
France	18,861 - 19,347	21,168 - 21,713
Gabon	5,268 - 12,018	3,164 - 7,218
Gambia, The	39 - 857	12 - 252
Georgia	729 - 3,683	366 - 1,850
Germany	21,080 - 26,668	21,933 - 27,747
Ghana	224 - 2,043	104 - 951
Greece	9,345 - 14,658	7,982 - 12,520
Grenada	1,878 - 7,302	1,272 - 4,948
Guatemala	756 - 3,750	360 - 1,788
Guinea	22 - 645	9 - 269
Guinea-Bissau	22 - 639	9 - 256
Guyana	610 - 3,368	348 - 1,924
Haiti	41 - 875	20 - 421
Honduras	299 - 2,360	149 - 1,177
Hong Kong SAR, China	24,302 - 40,202	17,409 - 28,801
Hungary	7,434 - 13,540	4,268 - 7,773
Iceland	19,942 - 22,720	22,567 - 25,712
India	416 - 2,781	115 - 770
Indonesia	1,298 - 4,914	472 - 1,786
Iran, Islamic Rep.	3,450 - 10,378	1,054 - 3,171
Iraq	3,276 - 10,194	1,504 - 4,679
Ireland	21,071 - 26,634	23,063 - 29,153
Israel	15,243 - 17,366	16,821 - 19,163
Italy	16,712 - 17,928	16,867 - 18,094
Jamaica	1,122 - 4,570	668 - 2,719
Japan	18,651 - 18,731	19,769 - 19,854

Country	Cost-effectiveness threshold range	
	(USD, PPP adjusted)	(actual USD)
Jordan	1,971 - 7,757	872 - 3,432
Kazakhstan	7,648 - 13,675	4,485 - 8,018
Kenya	73 - 1,164	32 - 519
Kiribati	49 - 954	43 - 848
Korea, Rep.	15,598 - 17,505	12,227 - 13,722
Kosovo	1,085 - 4,493	473 - 1,961
Kyrgyz Republic	147 - 1,651	58 - 649
Lao PDR	329 - 2,474	113 - 852
Latvia	7,532 - 13,602	5,133 - 9,270
Lebanon	4,187 - 11,098	2,420 - 6,416
Lesotho	95 - 1,329	41 - 581
Liberia	11 - 451	6 - 234
Libya	6,503 - 12,927	3,697 - 7,349
Lithuania	9,175 - 14,565	5,598 - 8,886
Luxembourg	35,195 - 117,072	43,092 - 143,342
Macao SAR, China	48,116 - 288,671	30,832 - 184,977
Macedonia, FYR	1,978 - 7,791	824 - 3,246
Madagascar	28 - 717	9 - 235
Malawi	9 - 401	3 - 116
Malaysia	7,709 - 13,712	3,481 - 6,192
Maldives	1,929 - 7,550	1,103 - 4,318
Mali	38 - 844	17 - 368
Malta	12,965 - 16,419	10,138 - 12,838
Marshall Islands	196 - 1,908	182 - 1,774
Mauritania	131 - 1,564	46 - 550
Mauritius	4,202 - 11,112	2,248 - 5,945
Mexico	3,850 - 10,780	2,410 - 6,749
Micronesia, Fed. Sts.	180 - 1,829	162 - 1,646
Moldova	310 - 2,400	148 - 1,151
Mongolia	1,264 - 4,849	543 - 2,085
Montenegro	2,912 - 9,786	1,464 - 4,921
Morocco	736 - 3,702	316 - 1,590
Mozambique	16 - 537	8 - 294
Namibia	1,332 - 4,979	791 - 2,958
Nepal	72 - 1,154	22 - 357
Netherlands	21,104 - 26,757	23,153 - 29,354
New Zealand	17,226 - 18,117	20,555 - 21,619
Nicaragua	297 - 2,350	118 - 937
Niger	12 - 469	5 - 213
Nigeria	446 - 2,880	239 - 1,545
Norway	28,057 - 60,862	43,211 - 93,736
Oman	21,322 - 27,562	
Pakistan	314 - 2,416	87 - 669

Country	Cost-effectiveness threshold range	
	(USD, PPP adjusted)	(actual USD)
Palau	3,235 - 10,149	2,531 - 7,940
Panama	5,352 - 12,083	3,042 - 6,869
Papua New Guinea	92 - 1,305	75 - 1,073
Paraguay	919 - 4,135	484 - 2,179
Peru	1,969 - 7,747	1,114 - 4,383
Philippines	606 - 3,358	256 - 1,421
Poland	7,694 - 13,703	4,440 - 7,908
Portugal	9,527 - 14,756	7,738 - 11,985
Puerto Rico	17,145 - 18,088	14,075 - 14,849
Qatar	45,558 - 246,565	31,105 - 168,345
Romania	4,932 - 11,746	2,467 - 5,875
Russian Federation	8,263 - 14,046	5,007 - 8,511
Rwanda	30 - 746	13 - 323
Samoa	363 - 2,598	265 - 1,897
Sao Tome and Principe	125 - 1,527	68 - 827
Saudi Arabia	24,484 - 41,080	11,799 - 19,797
Senegal	73 - 1,166	34 - 544
Serbia	2,175 - 8,760	1,061 - 4,275
Seychelles	8,310 - 14,074	5,470 - 9,265
Sierra Leone	53 - 990	23 - 435
Singapore	31,889 - 88,068	22,342 - 61,701
Slovak Republic	9,686 - 14,841	6,561 - 10,053
Slovenia	11,374 - 15,690	9,135 - 12,603
Solomon Islands	61 - 1,063	57 - 1,004
South Africa	2,221 - 8,909	1,175 - 4,714
South Sudan	77 - 1,198	40 - 617
Spain	14,638 - 17,124	13,277 - 15,531
Sri Lanka	1,346 - 5,005	453 - 1,686
St. Kitts and Nevis	6,222 - 12,731	4,110 - 8,409
St. Lucia	1,584 - 5,914	1,107 - 4,133
St. Vincent and the Grenadines	1,615 - 6,058	998 - 3,746
Sudan	162 - 1,734	84 - 901
Suriname	3,740 - 10,672	2,286 - 6,525
Swaziland	634 - 3,436	288 - 1,559
Sweden	21,148 - 26,917	28,306 - 36,028
Switzerland	24,450 - 40,914	36,661 - 61,348
Tajikistan	90 - 1,291	37 - 533
Tanzania	45 - 912	18 - 357
Thailand	2,941 - 9,820	1,181 - 3,943
Timor-Leste	71 - 1,153	
Togo	27 - 715	13 - 327
Tonga	399 - 2,726	333 - 2,275
Trinidad and Tobago	13,159 - 16,503	7,941 - 9,959

Country	Cost-effectiveness threshold range	
	(USD, PPP adjusted)	(actual USD)
Tunisia	1,747 - 6,680	678 - 2,592
Turkey	5,114 - 11,895	2,950 - 6,861
Turkmenistan	2,784 - 9,635	1,588 - 5,495
Tuvalu	188 - 1,870	200 - 1,991
Uganda	28 - 725	11 - 293
Ukraine	1,097 - 4,518	487 - 2,005
United Kingdom	18,609 - 18,609	20,223 - 20,223
United States	24,283 - 40,112	24,283 - 40,112
Uruguay	5,450 - 12,160	4,548 - 10,147
Uzbekistan	379 - 2,656	138 - 965
Vanuatu	127 - 1,538	139 - 1,685
Venezuela, RB	4,701 - 11,553	3,724 - 9,151
Vietnam	398 - 2,721	144 - 982
Yemen, Rep.	223 - 2,035	83 - 757
Zambia	144 - 1,635	68 - 768
Zimbabwe	41 - 874	21 - 455