Determining the efficiency path to universal health coverage: cost-effectiveness thresholds for 174 countries based on growth in life expectancy and health expenditures

Andres Pichon-Riviere, Michael Drummond, Alfredo Palacios, Sebastián Garcia-Marti, Federico Augustovski

Summary

Background Assessment of the efficiency of interventions is paramount to achieving equitable health-care systems. One key barrier to the widespread use of economic evaluations in resource allocation decisions is the absence of a widely accepted method to define cost-effectiveness thresholds to judge whether an intervention is cost-effective in a particular jurisdiction. We aimed to develop a method to estimate cost-effectiveness thresholds on the basis of health expenditures per capita and life expectancy at birth and empirically derive these thresholds for 174 countries.

Methods We developed a conceptual framework to assess how the adoption and coverage of new interventions with a given incremental cost-effectiveness ratio will affect the rate of increase of health expenditures per capita and life expectancy at the population level. The cost-effectiveness threshold can be derived so that the effect of new interventions on the evolution of life expectancy and health expenditure per capita is set within predefined goals. To provide guidance on cost-effectiveness thresholds and secular trends for 174 countries, we projected country-level health expenditure per capita and life expectancy increases by income level based on World Bank data for the period 2010–19.

Findings Cost-effectiveness thresholds per quality-adjusted life-year (QALY) ranged between US$87 (Democratic Republic of the Congo) and $95 958 (USA) and were less than 0·5 gross domestic product (GDP) per capita in 96% of low-income countries, 76% of lower-middle-income countries, 31% of upper-middle-income countries, and 26% of high-income countries. Cost-effectiveness thresholds per QALY were less than 1 GDP per capita in 168 (97%) of the 174 countries. Cost-effectiveness thresholds per life-year ranged between $78 and $80 529 and between 0·12 and 1·24 GDP per capita, and were less than 1 GDP per capita in 171 (98%) countries.

Interpretation This approach, based on widely available data, can provide a useful reference for countries using economic evaluations to inform resource-allocation decisions and can enrich international efforts to estimate cost-effectiveness thresholds. Our results show lower thresholds than those currently in use in many countries.

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Institute for Clinical Effectiveness and Health Policy (IECS), National Scientific and Technical Research Council, Buenos Aires, Argentina (Prof A Pichon-Riviere PhD, A Palacios MSc, S Garcia-Marti MD, F Augustovski PhD); **School of Public Health** (Prof A Pichon-Rivere, F Augustovski) **and Department of Economics** (A Palacios), **University of Buenos Aires, Buenos Aires, Argentina; Centre for Health Economics, University of York, York, UK** (M Drummond PhD)

Correspondence to: Prof Andres Pichon-Riviere, Institute for Clinical Effectiveness and Health Policy (IECS), National Scientific and Technical Research Council, Buenos Aires C1414CPV, Argentina **apichon@iecs.org.ar**

Introduction

In countries of all income levels, health-care systems face strong pressures to meet the increasing needs of populations with scarce resources. To approach universal health coverage along its three dimensions—who is covered, which services are provided, and at what financial burden for the population—decisions involve difficult trade-offs regarding costs and benefits (ie, efficiency), fairness, and other social values.[1]

Two of the four main goals for health systems are to improve health and to improve efficiency (broadly defined as how much health one country gets with the current level of spending).[2] To pursue an aim of evidence-based universal health coverage, assessment of efficiency is essential.[3] Additionally, most of the existing value frameworks agree that cost-effectiveness is a key value dimension to assess when deciding how to allocate health resources.[2,4–6] As such, economic evaluations have become key instruments to assess the efficiency of a wide range of health technologies or interventions.

The incremental cost-effectiveness ratio (ICER)—the primary metric of this type of study—expresses the efficiency of a given intervention in terms of additional costs per unit of additional benefit (frequently measured in quality-adjusted life years [QALY] or disability-adjusted life years [DALY]). A key factor in making the ICER actionable or useful for decision making is how to judge whether the health gains offered by a health technology are sufficiently large relative to the costs for the technology to be adopted. Whether the new benefits are greater than those to be displaced by the resources used to fund the new technology must also be evaluated.[7]

A crucial barrier to the widespread adoption of cost-effectiveness analysis for decision making is the absence of a widely accepted decision rule that can be used worldwide—ie, what is cost-effective in a particular

Research in context

Evidence before this study

We searched PubMed from database inception to June 30, 2022, without language restrictions, for previously published studies addressing the estimation of cost-effectiveness thresholds using the following search strategy: ("threshold*"[Title] OR "opportunity cost"[Title] OR "marginal cost"[Title]) AND ("cost-effectiveness"[Title/Abstract] OR "WTP"[Title/Abstract] OR "willingness to pay"[Title/Abstract] OR "opportunity cost"[Title/Abstract] OR "health technology assessment"[Title/Abstract]). We also reviewed references from retrieved articles to identify additional studies. The evidence showed that cost-effectiveness thresholds are paramount to making resource allocation decisions using economic evaluations. In the past decade, several studies have seriously challenged the previous WHO rule of thumb that considered a strategy to be cost-effective if a healthy year is gained at less than three times the gross domestic product (GDP) per capita. Most new threshold estimates in different countries show cost-effectiveness thresholds of less than 1 GDP per capita. However, no current method is considered the single best to empirically estimate thresholds. The approaches to estimating cost-effectiveness thresholds developed over the past ten years have constraints that limit their application in many contexts, as they depend on data availability and researchers to generate the estimates.

Added value of this study

We propose a simple and straightforward method to estimate cost-effectiveness thresholds based on per-capita health expenditures and life expectancy (or healthy life expectancy), enabling the definition of such thresholds based on target desired increases in health expenditures. Our approach can be complementary or represent an alternative to the available empirically derived estimates of the opportunity cost in each health system, which are more complex and require a quantity and quality of data that are usually unavailable in most countries (particularly in low-income and middle-income countries). We also provide guidance regarding reasonable values for cost-effectiveness thresholds according to the most recent data available for 174 countries (WHO and World Bank data from 2019). These values can be a useful reference for countries that do not have their own empirically derived estimates of the threshold (based, for example, on the opportunity cost) or to complement previous estimations. We present cost-effectiveness thresholds for 174 countries. These thresholds are less than 0·5 GDP per capita per quality-adjusted life-year in 51% of these countries and less than 1 GDP per capita in 97% of these countries.

Implications of all the available evidence

We provide an alternative approach to estimating cost-effectiveness thresholds using widely available, macro-level data. This approach is easy to apply to a wide range of countries and is easily updated when new data become available. The findings will inform policy makers on the thresholds to consider when deciding on the allocation of health resources. The most recent available evidence shows that cost-effectiveness thresholds could be substantially lower than those currently used by many countries (especially low-income and middle-income countries). The adoption of higher thresholds could lead to a high opportunity cost for health systems and drive increases in health expenditure per capita beyond current trends. The development of alternative approaches that use a range of methods and provide complementary evidence is an important contribution to inform the selection of cost-effectiveness thresholds and improve the evidence base for priority setting and patients' access to health care in the quest for universal health coverage.

country or jurisdiction, or what is the relevant cost-effectiveness threshold.[8,9]

The best known recommendations for cost-effectiveness thresholds are those published in a WHO document that derives thresholds on the basis of aspirational expressions of value in relation to gross domestic product (GDP) per capita per DALY averted, stating that an intervention is cost-effective if the cost per DALY averted is less than 3 GDP per capita and very cost-effective if it is less than 1 GDP per capita.[10] These recommendations used to be a widespread rule of thumb in the field; however, in the past decade several critiques and cautionary advice against the use of these WHO thresholds have arisen, both from within WHO and elsewhere,[11–14] generating a need to find new approximations for their estimation.

Two broad approaches have been proposed to estimate cost-effectiveness thresholds. The demand-side threshold relates to the willingness to pay for health improvements, and the supply-side threshold reflects the forgone benefits that could have been achieved if the same resources were used in their best alternative use.[8,15–17] Although the demand-side approach could be useful to inform the health budget, consensus states that the supply-side approach is the most relevant to inform decision making on resource allocation, because it reflects the opportunity cost associated with devoting a health system's resources to a particular use.[8,15] Several empirical estimates of the supply-side measure of opportunity cost of health have been published over the past decade,[17–22] showing substantially lower thresholds (ie, less than 1 GDP per capita per QALY) than the initial WHO thresholds. Although the existing approaches have greatly contributed to threshold estimation, they present several constraints that limit their application in many contexts. The most precise estimates exist for only a few countries, as they are dependent on data availability and researchers to generate the estimates. Both the empirical estimation of the marginal cost per unit of health, which has been the basis for estimating thresholds, and the

attempts to generate estimates for a wider range of countries, have their shortfalls.[23]

Therefore, a method to estimate cost-effectiveness thresholds that can be conducted easily, is based on public and widely available data, and can also reflect the differences among countries over time in their production of health in relation to health expenditure is needed. Policy makers will probably engage better with cost-effectiveness thresholds that are easier to understand and can align with their aspirations for universal health coverage in their country.

This Article presents a conceptual framework and a method to estimate cost-effectiveness thresholds and then empirically derives them for 174 countries, using public and widely available data on country-specific health expenditures and health outcomes.

Methods

Conceptual framework

Our approach is based on analysing how the adoption and coverage of new interventions, programmes, services, drugs, and other health technologies (hereafter collectively referred to as interventions) will affect, in a given country or health-care system, the rate of increase of both health expenditures per capita and life expectancy at birth at the population level. As we subsequently describe, after this relationship is quantified, the cost-effectiveness threshold can be calculated so that the influence of new interventions on the evolution of life expectancy and health spending is set within predefined goals.

At the population level, the evolution of health expenditure per capita and life expectancy (either measured in life-years or any variant of health-adjusted life expectancy, such as QALYs or DALYs) is a consequence of several factors, including many external to the health system, all of which act as vectors of different magnitude and direction. The final evolution of health spending and life expectancy will be the resultant vector of all the known and unknown factors that exerted any influence during a given period (figure).

The relationship between the ICER of new interventions and the rate of increase in health expenditure per capita and life expectancy at the country level or health-care-system level is the basis for our estimation of cost-effectiveness thresholds. The way in which a new intervention will affect health spending and life expectancy at the population level is derived mathematically in the appendix (p 2). The direction (ie, slope, m) of the influence vector of an intervention can be calculated from its ICER, the health expenditure per capita (HEpc), and the new life expectancy at the population level after the period during which the intervention was introduced (LE□):

$$m = \frac{ICER}{HEpc \times LE'} \quad (1)$$

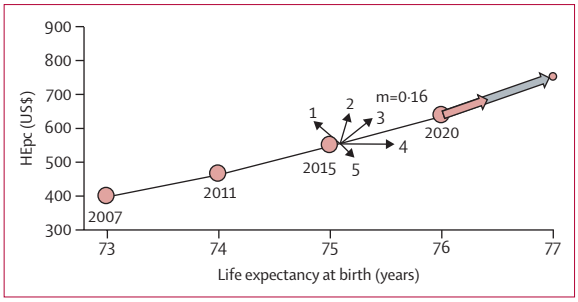

Figure: **Evolution of life expectancy and health expenditure per capita in a typical upper-middle-income country between 2007 and 2020**
The influence of distinct factors on the evolution of health spending and life expectancy is illustrated for 2015–2020. For example, an outbreak of a new disease can drive a decline in life expectancy and an increase in health-care costs, as shown by vector 1. Improvements in education, housing, nutrition, or other social determinants of health could drive increases in life expectancy without necessarily affecting health-care costs (vector 4). The adoption and coverage of new interventions will influence both life expectancy and costs. Health interventions affect both costs and benefits in the specific group of patients or subpopulation to which they are directed, affecting the evolution of health expenditures and life expectancy or HALE at the population level. A direct relationship exists between the ICER of the new interventions and the type of influence they will exert. For example, the adoption and coverage of a cost-saving intervention will produce health benefits and cost savings in the specific subgroup of patients to whom it is applied. These effects will also result in an increase in the life expectancy (or HALE) of the population and a reduction of health expenditure per capita at the country level or health-system level (vector 5), even though the effect of a single intervention at the population level will probably be minimal. On the other hand, an intervention that is more effective but more costly (ie, with an ICER in the upper-right quadrant of the cost-effectiveness plane) will improve life expectancy (or HALE) and increase health expenditures. An intervention with a more unfavourable ICER (vector 2) will be associated with a higher increase in health expenditures than a more cost-effective intervention (vector 3). This is reflected in the direction (slope) of the vectors (eg, vector 2 is steeper than vector 3). The ICER of the intervention determines the slope. Two interventions with the same ICER will be colinear vectors (ie, will have the same slope), although they could have different magnitude. An intervention aimed at a larger proportion of the population will be a vector of greater magnitude because it will be more influential. The slope (direction) of a vector (m) is calculated by finding the ratio of the vertical change to the horizontal change between two distinct points on the line. In this case, the vertical change will be the percentage increase in health expenditures per capita at the population level (%Δh) in a given period, and the horizontal change will be the corresponding change in life expectancy (ΔLE). For example, between 2015 and 2020, the resultant vector of all factors affecting health expenditures and life expectancy has a slope of m=0·16, as during this period all factors affecting health expenditures and life expectancy resulted in a change in life expectancy from 75 to 76 years (ΔLE=1 year), and a 16% change in health expenditure per capita, from US$549 to $639 (%Δh=0·16). The white and grey arrows show projections for the future. The white arrow is the expected resultant vector of all the known and unknown factors affecting health expenditure per capita and life expectancy during the time period. The grey arrow shows that the vector of influence of the new interventions will be colinear with the expected resultant vector if the ICER of new interventions is equal to m × HEpc × LE□ (equation 2). HALE=health-adjusted life expectancy. HEpc=annual total health expenditure per capita. ICER=incremental cost-effectiveness ratio.

See Online for appendix

This same equation, which enables quantification of the influence of a particular ICER on the rate of increase in health spending (expressed by m), can be applied to calculate the ICER consistent with a specific rate of increase in spending. From equation 1, if we solve for ICER, this value represents the cost-effectiveness threshold per life-year (CET_{LY}) that the interventions adopted in a given period should not exceed so that the

rate of increase in health expenditure per capita, driven by the newly adopted interventions, does not exceed the rate defined by m:

$$CET_{LY}(ICER)=m\times HEpc\times LE' \quad (2)$$

In other words, this equation enables calculation of what the ICER of the new interventions should be, on average, so that its influence vector is colinear with respect to a predefined target of progression of life expectancy and health expenditure per capita in a given period (defined by m). For example, for the case illustrated in the figure, if the country aims to maintain, from the year 2020, the same rate of increase in health expenditure and life expectancy as in the previous 5 years (m=0·16 during the period 2015–2020), then the ICER of the new interventions should not exceed, on average, the US$7·872 per life-year threshold (0·16 × $639 × 77, from equation 2).

As m=%Δh/ΔLE, where %Δh is the percentage increase in health expenditure per capita and ΔLE is the change in life expectancy in a given period, it is possible to estimate cost-effectiveness thresholds for any defined more stringent or less stringent targets of health expenditure and life expectancy increases, and equation 2 can also be re-expressed as:

$$CET_{LY}(ICER)=\frac{\%\Delta h\times HEpc\times(LE+\Delta LE)}{\Delta LE} \quad (3)$$

The adoption of this cost-effectiveness threshold per life-year ensures that the vector corresponding to the effect of new interventions will have the same direction as what is expected to be the evolution of population life expectancy and health expenditure per capita according to the goals set (%Δh and ΔLE). This does not imply that health expenditures and life expectancy will exactly evolve as defined by %Δh and ΔLE, as the adoption and coverage of new interventions will be just one of the many factors affecting the progress of life expectancy and health spending. However, although the magnitude of the vector corresponding to the new interventions might vary, the cost-effectiveness threshold indicates the value that should be observed to ensure that new interventions will exert a neutral influence (ie, will be colinear) on the direction of what is expected to be the evolution of health expenditure per capita and life expectancy.

The cost-effectiveness threshold for combined metrics of healthy life (ie, QALYs or DALYs) can be estimated following a similar approach, incorporating the ratio between the health-adjusted life expectancy and the life expectancy at birth at the population level (QYr=HALE/LE):

$$CET_{QALY}=\frac{\%\Delta h\times HEpc\times(LE+\Delta LE)}{\Delta LE\times QYr} \quad (4)$$

The approach described so far can provide guidance on the cost-effectiveness threshold for countries willing to accept increases in health expenditures to achieve better population health. Typically, but not exclusively, these are low-income or middle-income countries moving towards universal health coverage in which substantial health performance improvements are expected but where health spending is currently low. In a health system that is not willing or able to increase health expenditure, only cost-saving interventions can be adopted unless other interventions currently provided by the benefits package are displaced. If disinvesting in interventions currently being covered is an option, health systems could still finance new interventions with an ICER lower than a specified cost-effectiveness threshold, provided that this threshold ensures that there is room to displace interventions with a less favourable ICER that have been included in the benefits package in the past. We will refer to this cost-effectiveness threshold as the disinvestment CET (DisCET), which can be inferred from the previous period during which the last n years increase in life expectancy were achieved and during which it can be assumed that new interventions were included in the benefits package:

$$DisCET_{LY}=\frac{(HEpc-HEpc/(1+\%\Delta h)^{n/\Delta LE})\times LE}{n} \quad (5)$$

where ΔLE and %Δh are the mean annual increase in health expenditure and life expectancy in the previous period being used to estimate the threshold (appendix p 8). In this more restrictive context, new interventions should have a similar or better ICER than this DisCET to allow displacement of the less efficient interventions adopted in the past.

Derivation of country-level cost-effectiveness thresholds

The method described so far can be used by any country or health system to estimate cost-effectiveness thresholds when it is feasible to define a goal of increase in life expectancy and health expenditure per capita for a given period (or a reference period in the past for DisCET). Because most countries do not have explicit goals regarding the increase in life expectancy and health expenditure per capita, here we provide guidance cost-effectiveness thresholds for 174 countries. This guidance is based on the historical evolution of these two variables and assuming that the median increase in health expenditure per capita and life expectancy in countries with a similar income level is a reasonable goal.

To calculate these thresholds, we first estimated the expected annual increases in health expenditure per capita and life expectancy according to the income-level stratum of each country (low income, lower-middle income, upper-middle income, and high income). We estimated these two parameters from World Bank data from 2010 to 2019 (the most recent 10-year data available) as the observed median increase in life expectancy and total health

	Life expectancy, years*	Health-adjusted life expectancy, years*	GDP per capita, US$*	HEpc, US$*	%Δh, median (IQR)	ΔLE, median (IQR)
High-income countries	..	..	..	..	1·7% (0·8 to 3·3)	0·18 (0·14 to 0·24)
Australia	82·9	70·9	$54 875	$5427	..	..
Canada	82·0	71·3	$46 329	$5048	..	..
Germany	81·3	70·9	$46 795	$5440	..	..
Israel	82·8	72·4	$43 951	$3456	..	..
Japan	84·4	74·1	$40 458	$4360	..	..
South Korea	83·2	73·1	$31 902	$2625	..	..
UK	81·2	70·1	$43 070	$4313	..	..
USA	78·8	66·1	$65 095	$10 921	..	..
Upper-middle-income countries	..	..	..	..	2·4% (1·2 to 4·8)	0·21 (0·15 to 0·31)
Argentina	76·7	67·1	$10 076	$946	..	..
Brazil	75·9	65·4	$8876	$853	..	..
China	76·9	68·5	$10 144	$535	..	..
Iran	76·7	66·3	$3514	$470	..	..
Russia	73·1	64·2	$11 536	$653	..	..
South Africa	64·1	56·2	$6625	$547	..	..
Thailand	77·2	68·3	$7814	$296	..	..
Türkiye	77·7	68·4	$9122	$396	..	..
Lower-middle-income countries	..	..	..	..	2·6% (−0·5 to 4·4)	0·28 (0·21 to 0·40)
Bolivia	71·5	63·3	$3552	$246	..	..
Honduras	75·3	63·0	$2574	$188	..	..
India	69·7	60·3	$2072	$64	..	..
Kenya	66·7	57·7	$1909	$83	..	..
Nigeria	54·7	54·4	$2230	$71	..	..
Pakistan	67·3	56·9	$1482	$39	..	..
Philippines	71·2	62·0	$3485	$142	..	..
Ukraine	71·8	64·3	$3661	$248	..	..
Low-income countries	..	..	..	..	2·8% (0·1 to 4·8)	0·44 (0·38 to 0·61)
Afghanistan	64·8	54·0	$494	$66	..	..
DR Congo	60·7	54·1	$597	$21	..	..
Ethiopia	66·6	59·9	$856	$27	..	..
Haiti	64·0	55·8	$1313	$57	..	..
Mali	59·3	54·6	$879	$34	..	..
Rwanda	69·0	60·2	$820	$51	..	..
Uganda	63·4	58·2	$799	$32	..	..

GDP=gross domestic product. HEpc=annual total health expenditure per capita. %Δh=expected annual increase in HEpc. ΔLE=expected annual increase in life expectancy (years). *Data from the World Bank database and the WHO database, accessed November, 2022. The most recent data in these databases are for 2019.

Table 1: **Expected annual increases in health expenditures per capita and life expectancy according to income level; and main country-level parameters used to estimate the cost-effectiveness thresholds**

For the **World Bank database** see https://databank.worldbank.org/

For the **WHO database** see https://www.who.int/data/gho/data/themes/topics/indicator-groups/indicator-group-details/GHO/healthy-life-expectancy-(hale)

expenditure per capita in each income level stratum (this is the observed evolution of these two variables; this method does not seek to establish a causal relationship). Increases in health expenditure per capita were analysed in constant local currency units to avoid the influence of inflation and exchange rates and then the cost-effectiveness thresholds were calculated from equations 3 and 4. This approach enabled us to provide guidance cost-effectiveness thresholds for countries that, in the medium-term, consider it a reasonable target to behave like a typical country in each income stratum (ie, to see a rate of increase in health expenditure per capita and life expectancy in the median of values for countries with a similar income). DisCETs (equation 5) were estimated using the period in which the previous two additional life-years' increase in life expectancy were achieved (n=2,

	High-income countries (n=54)	Upper-middle-income countries (n=48)	Lower-middle-income countries (n=49)	Low-income countries (n=23)	Total (n=174)
Cost-effectiveness thresholds per QALY					
In US$ (2019)					
Range	$5480–$95 958	$1108–$10 638	$190–$3249	$87–$320	$87–$95 958
Median (IQR)	$18 218 ($10 229–$43 175)	$4355 ($2886–$5301)	$745 ($451–$1389)	$163 ($131–$229)	$3192 ($533–$9512)
As a proportion of GDP per capita					
Range	0·18–1·47	0·22–1·34	0·14–0·96	0·14–0·65	0·14–1·47
Median (IQR)	0·68 (0·50–0·88)	0·58 (0·44–0·76)	0·35 (0·23–0·48)	0·24 (0·18–0·32)	0·49 (0·32–0·70)
Less than 0·5 GDP per capita	26%	31%	76%	96%	51%
Less than 1·0 GDP per capita	94%	94%	100%	100%	97%
Less than 1·5 GDP per capita	100%	100%	100%	100%	100%
Less than 2·0 GDP per capita	100%	100%	100%	100%	100%
In annual health expenditures per capita					
Range	7·61–9·12	7·22–10·64	5·23–8·77	3·53–5·08	3·53–10·64
Median (IQR)	8·78 (8·31–8·90)	9·61 (9·27–9·92)	7·56 (6·97–7·82)	4·38 (4·18–4·60)	8·41 (7·39–9·06)
Cost-effectiveness thresholds per life-year					
In US$ (2019)					
Range	$4553–$80 529	$970–$9158	$171–$2679	$78–$274	$78–$80 529
Median (IQR)	$16 031 ($8887–$37 251)	$3772 ($2541–$4684)	$642 ($399–$1175)	$150 ($118–$203)	$2775 ($476–$8307)
As a proportion of GDP per capita					
Range	0·15–1·24	0·20–1·16	0·12–0·74	0·13–0·54	0·12–1·24
Median (IQR)	0·59 (0·44–0·76)	0·51 (0·39–0·67)	0·31 (0·20–0·43)	0·22 (0·16–0·30)	0·43 (0·28–0·61)
Less than 0·5 GDP per capita	39%	48%	88%	96%	63%
Less than 1·0 GDP per capita	98%	96%	100%	100%	98%
Less than 1·5 GDP per capita	100%	100%	100%	100%	100%
Less than 2·0 GDP per capita	100%	100%	100%	100%	100%
In annual health expenditures per capita					
Range	6·88–7·89	6·62–9·04	5·17–7·31	3·33–4·43	3·33–9·04
Median (IQR)	7·59 (7·27–7·74)	8·39 (8·14–8·64)	6·62 (6·14–6·83)	3·87 (3·79–4·03)	7·29 (6·46–7·84)

QALY=quality adjusted life-year. GDP=gross domestic product.

Table 2: **Cost-effectiveness thresholds per life-year and per QALY according to country income level**

roughly equivalent to a period of 8–10 years), with the same %Δh and ΔLE estimates used for the cost-effectiveness thresholds. Countries that changed income-level stratum during the period analysed provided information to the category in which they were classified during most of the years between 2010 and 2019. To incorporate the uncertainty in cost-effectiveness thresholds, ranges were estimated in the sensitivity analysis on the basis of the 95% CI of the ratio between the median increase in health expenditure per capita and the median increase in life expectancy in each income stratum (appendix p 11).

All thresholds estimated for each country are reported in US dollars (2019). Cost-effectiveness thresholds are also reported in units of GDP per capita and in per capita health expenditure units for ease of comparability and generalisability. Information on how to update the threshold values is shown in the appendix (p 12) and on the web platform, which allows thresholds to be updated or adapted to different contexts.

For the **web platform** see https://www.iecs.org.ar/en/thresholds/

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The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

In total, sufficient information was present in the World Bank database to conduct the analysis for 174 countries. During the 2010–19 period, the median annual increase in per capita health-care spending was 2·8% (IQR 0·1 to 4·8) for low-income countries, 2·6% (–0·5 to 4·4) for lower-middle-income countries, 2·4% (1·2 to 4·8) for upper-middle-income countries, and 1·7% (0·8 to 3·3) for high-income countries, and the corresponding median increases in life expectancy were 0·44 years (IQR 0·38 to 0·61), 0·28 years (0·21 to 0·40), 0·21 years (0·15 to 0·31), and 0·18 years (0·14 to 0·24). This information and the main parameters used to estimate the cost-effectiveness thresholds (life expectancy, health-adjusted life expectancy, GDP per capita, and health

expenditure per capita) are summarised for selected countries in table 1; information for all countries is available in the appendix (p 17).

Table 2 summarises the cost-effectiveness thresholds by income level, and table 3 shows the cost-effectiveness thresholds per QALY in a sample of countries (for all countries, see appendix p 25). The median cost-effectiveness threshold per QALY was $18 218 for high-income countries, $4355 for upper-middle-income countries, $745 for lower-middle-income countries, and $163 for low-income countries (table 2). The cost-effectiveness thresholds per QALY were less than 0·5 GDP per capita in 88 (51%) of the 174 countries analysed. However, this proportion varied in the different income categories: 22 (96%) of the 23 cost-effectiveness thresholds in low-income countries were less than 0·5 GDP per capita compared with only 14 (26%) among 54 high-income countries. Cost-effectiveness thresholds were less than 1 GDP per capita in all low-income countries and in 51 (94%) of 54 high-income countries (table 2). In total, 168 (97%) of the 174 cost-effectiveness thresholds were less than 1 GDP per capita (appendix p 15).

The country-level cost-effectiveness thresholds per QALY estimated through our approach ranged from $87 (Democratic Republic of the Congo) to $95 958 (USA). In terms of proportion of GDP, cost-effectiveness thresholds ranged from 0·14 GDP (Djibouti) to 1·47 GDP (USA) and from 3·53 (Chad) to 10·64 (Lebanon) when measured in units of annual health expenditures per capita. In terms of life-years, cost-effectiveness thresholds ranged from $78 to $80 529 and from 0·12 to 1·24 GDP per capita. Table 2 presents the summary per income level. Results for all countries are available in the appendix (p 21). DisCET values were 7–12% lower. The DisCETs for life-years and QALYs for all countries are shown in the appendix (pp 29, 33).

These results are useful for countries that consider the median increase in health expenditures and life expectancy of countries at the same income level to be an appropriate target. However, some countries might prefer to calculate their threshold on the basis of their own estimates of how they expect health spending and life expectancy to behave. In this case, it is necessary to define the expected %Δh and ΔLE for a given period to estimate the cost-effectiveness threshold. For example, in the USA, the Institute for Clinical and Economic Review calculated a budget impact threshold for new drugs on the basis of an estimated annual %Δh of 3·75% (GDP average growth of 2·75% plus an additional 1%).[24] Regarding ΔLE, a yearly increase in life expectancy of 0·2 years can be considered a reasonable target for a country such as the USA (50% of high-income countries showed annual increases of life expectancy between 0·14 and 0·24 in the past 10 years). If we assume that these estimates of %Δh and ΔLE are reasonable goals for the USA, they can be used in equation 4 to estimate the cost-effectiveness threshold that will be consistent with these goals, resulting in a threshold of $192 855 per QALY (%Δh=0·0375, ΔLE=0·2, LE=78·8, HEpc=$10 921, QYr=0·8388). This threshold differs from that presented for the USA in table 3 ($95 958 per QALY) because the estimates are based on different assumptions. In table 3, cost-effectiveness thresholds were estimated assuming that, for all countries, behaving like the median of countries in their income stratum is a reasonable target. For example, the median increase in health expenditure per capita in high-income countries was 1·7% (table 1), and this value was used to estimate the cost-effectiveness thresholds for the USA in table 3 instead of the 3·8% annual increase used here.

A country might prefer different targets for health expenditures and life expectancy increases than what

	US$	Proportion of GDP	Units of HEpc
High-income countries			
Australia	$49 211 ($41 884–$61 634)	0·90 (0·76–1·12)	9·07 (7·72–11·36)
Canada	$44 638 ($37 992–$55 907)	0·96 (0·82–1·21)	8·84 (7·53–11·07)
Germany	$47 461 ($40 395–$59 443)	1·01 (0·86–1·27)	8·72 (7·43–10·93)
Israel	$30 641 ($26 079–$38 376)	0·70 (0·59–0·87)	8·86 (7·55–11·10)
Japan	$39 190 ($33 355–$49 084)	0·97 (0·82–1·21)	8·99 (7·65–11·26)
South Korea	$23 285 ($19 818–$29 163)	0·73 (0·62–0·91)	8·87 (7·55–11·11)
UK	$37 952 ($32 302–$47 532)	0·88 (0·75–1·10)	8·80 (7·49–11·02)
USA	$95 958 ($81 672–$120 181)	1·47 (1·25–1·85)	8·79 (7·48–11·00)
Upper-middle-income countries			
Argentina	$9329 ($6805–$16 419)	0·93 (0·68–1·63)	9·86 (7·19–17·36)
Brazil	$8462 ($6173–$14 894)	0·95 (0·70–1·68)	9·92 (7·23–17·45)
China	$5203 ($3795–$9157)	0·51 (0·37–0·90)	9·72 (7·09–17·11)
Iran	$4701 ($3429–$8275)	1·34 (0·98–2·35)	9·99 (7·29–17·59)
Russia	$6123 ($4466–$10 776)	0·53 (0·39–0·93)	9·37 (6·84–16·49)
South Africa	$4512 ($3292–$7941)	0·68 (0·50–1·20)	8·25 (6·02–14·53)
Thailand	$2909 ($2122–$5119)	0·37 (0·27–0·66)	9·82 (7·16–17·28)
Türkiye	$3940 ($2874–$6934)	0·43 (0·32–0·76)	9·94 (7·25–17·49)
Lower-middle-income countries			
Bolivia	$1889 ($965–$2396)	0·53 (0·27–0·67)	7·68 (3·92–9·74)
Honduras	$1603 ($819–$2033)	0·62 (0·32–0·79)	8·55 (4·36–10·84)
India	$487 ($249–$618)	0·24 (0·12–0·30)	7·64 (3·90–9·69)
Kenya	$612 ($312–$776)	0·32 (0·16–0·41)	7·33 (3·74–9·30)
Nigeria	$374 ($191–$474)	0·17 (0·09–0·21)	5·23 (2·67–6·63)
Pakistan	$299 ($153–$379)	0·20 (0·10–0·26)	7·56 (3·86–9·59)
Philippines	$1105 ($564–$1401)	0·32 (0·16–0·40)	7·78 (3·97–9·86)
Ukraine	$1892 ($966–$2400)	0·52 (0·26–0·66)	7·62 (3·89–9·67)
Low-income countries			
Afghanistan	$320 ($101–$503)	0·65 (0·20–1·02)	4·86 (1·53–7·64)
DR Congo	$87 ($28–$137)	0·15 (0·05–0·23)	4·25 (1·34–6·68)
Ethiopia	$124 ($39–$194)	0·14 (0·05–0·23)	4·62 (1·45–7·26)
Haiti	$261 ($82–$410)	0·20 (0·06–0·31)	4·58 (1·44–7·20)
Mali	$138 ($43–$216)	0·16 (0·05–0·25)	4·02 (1·26–6·31)
Rwanda	$254 ($80–$398)	0·31 (0·10–0·49)	4·93 (1·55–7·75)
Uganda	$139 ($44–$219)	0·17 (0·05–0·27)	4·30 (1·35–6·76)

Data are threshold (range). QALY=quality-adjusted life-year. GDP=gross domestic product per capita. HEpc=health expenditure per capita.

Table 3: **Cost-effectiveness threshold per QALY in US$ (2019) for selected countries**

might be considered typical for countries in the same income stratum for several reasons. For example, total health expenditures in India represent only 3·09% of its GDP, a low value even compared with other countries in the same income stratum, in which health spending is closer to 5% of GDP. Therefore, India could have reasons to be more ambitious when defining a target of health expenditure increases, which would affect the threshold estimate. For example, if India sets a goal for the next 5 years to reach a health expenditure that represents 5% of its GDP, and projecting an annual GDP growth of 6%, the yearly increase in health expenditure per capita necessary to achieve this goal in 5 years is calculated as:

$$\left(1+\frac{0{\cdot}05\times(1+0{\cdot}06)^{5}-0{\cdot}031}{0{\cdot}031}\right)^{1/5}-1=0{\cdot}1663 \text{ (or } 16{\cdot}63\%)$$

In turn, the life expectancy in India is currently lower than in other lower-middle-income countries, so it is reasonable to expect a higher rate of increase. In the past 10 years, the annual increase in life expectancy in India was 0·34 years, a value greater than the median increase in lower-middle-income countries. Therefore, India could calculate its threshold under this new assumption (%Δh of 16·63% and ΔLE of 0·34) instead of the median increases in lower-middle-income countries presented in table 1 (%Δh of 2·6% and ΔLE of 0·28). Applying equation 4, the resulting cost-effectiveness threshold for India would be $2534 per QALY (%Δh=0·1663, ΔLE=0·34, LE=69·7, HEpc=$64, QYr=0·8651). This threshold is around 1 GDP per capita, very different from that estimated for India in table 3, which was closer to 0·25 GDP. This difference is mainly explained by the fact that the cost-effectiveness threshold of a country would be higher if the country would be willing to increase health expenditure per capita by 16·6% annually instead of expecting only a 2·6% increase. Alternative scenarios for the estimation of cost-effectiveness thresholds in different countries can be explored on the web platform. An additional example of the application of this method at the health-system level is shown in the appendix (p 13).

Discussion

We propose a simple and straightforward method to estimate cost-effectiveness thresholds based on per-capita health expenditures and life expectancy or healthy life expectancy. We apply this method to empirically derive cost-effectiveness thresholds in 174 countries. Our approach proposes a conceptual framework for analysing how new interventions adopted by health systems will affect the rate of increase in life expectancy and health expenditure per capita at the population level and, by extension, the way in which the choice of a cost-effectiveness threshold will influence this rate of increase.

The proposed approach can be complementary or an alternative to the available empirically derived estimates of the opportunity cost in each health system, which are complex and require a quantity and quality of data that are usually not available in many countries—particularly in low-income and middle-income countries. Our approach uses a simpler and single input: health systems define the path of health spending and life expectancy increases in which they expect to remain in a given period. The cost-effectiveness threshold to adopt is just a consequence of this decision. The advantage of this approach is that it is focused on a more mundane parameter—easier to understand by policy makers and directly relevant to budget holders. Furthermore, this approach allows decision makers to decide how aspirational they want to be while being able to see the consequences in terms of necessary increase in health expenditure. Another important aspect is the direct relationship between our estimate of the threshold and the budget. The close link between threshold and budget is well known. As expressed by Culyer:[15] "One way of looking at the threshold is nonetheless as a demand concept—an implication of a collective willingness to pay for health as expressed by the size of the health budget." If a country decides to increase the health budget, and consequently the annual rate of increase in health spending, this increase will be directly reflected in the estimation of the threshold according to our method.

Other notable characteristics of our approach are as follows. First, the estimation of cost-effectiveness thresholds is based on per-capita expenditure on health, not GDP, so is sensitive to differences in the efficiency of health spending among countries with a similar GDP; second, the approach is easy to extend to subnational levels or subsectors within a single country, enabling the estimation of different thresholds, which could be very relevant in most low-income and middle-income countries with fragmented and decentralised health-care systems; third, it forms a basis for planning and monitoring (eg, considering what increase in health expenditure to make and what health gain would be expected on the basis of a country's past performance); fourth, it has few assumptions, is simple, and is based on widely available, macro-level data, and therefore, unlike other approaches, can be easily applied to a wide range of countries; and finally, it can be easily updated.

The present approach enriches the current evidence base of the international threshold estimation efforts and can be considered as a kind of supply-side cost-effectiveness threshold, which is more relevant for decision making. The approach is based on current health system efficiency and efficiency trends, and has the opportunity cost as a core principle: if a health system decides to cover interventions with an ICER beyond the defined cost-effectiveness threshold, forgone health benefits will imply that the system reaches its cost increase target without reaching the health benefits goals. However, the present approach also implies a willingness-to-pay concept as in the demand-side thresholds. The evolution, over the years, of the rate of increase in health spending

and life expectancy in a given country reflects, at a very high policy level, a collective willingness of society to pay for the increase in life expectancy of the population.

In addition to presenting an innovative method to estimate cost-effectiveness thresholds, our study also provides guidance regarding what could be reasonable values for these thresholds according to the most recent data available for 174 countries. These values can be a useful reference for countries that do not have their own estimates of the threshold—eg, based on the opportunity cost—and in which there are no obvious reasons to justify a radically different behaviour regarding health expenditures and life expectancy to that of other countries in the same income stratum. The results obtained show cost-effectiveness thresholds per QALY of less than 0·5 GDP in half of the countries, and less than 1 GDP in 97% of the 174 countries analysed, consistent with the most recent empirical estimates of cost-effectiveness thresholds. Our results show lower thresholds, relative to GDP, in low-income countries. In only 26% of high-income countries did we observe cost-effectiveness thresholds per QALY of less than 0·5 GDP, compared with 31% of upper-middle-income countries, 76% of lower-middle-income countries, and 96% of low-income countries. Lower-income countries typically have a smaller share of their GDPs devoted to health care than countries of a higher income level. Therefore, when judging the cost-effectiveness of interventions, there is no reason to expect that lower-income countries would apply higher or similar thresholds (in terms of GDP per capita per QALY) than those used in high-income countries. Our results also show considerably lower thresholds than those postulated previously by WHO.[10]

Despite using a different approach and a very simple method, our study shows results consistent with other studies from the past decade, with differences of less than 30% in most cases. Some examples are our estimate of $24 733 per QALY in Spain compared with $26 600 estimated by Vallejo-Torres and colleagues,[22] 0·51 GDP per QALY in China versus 0·63 GDP per DALY estimated by Ochalek and colleagues,[20] $50 978 versus $44 200 per QALY in Sweden,[21] $3532 versus $5200 per QALY in Peru and $8462 versus $7700 per QALY in Brazil,[17] and $4512 per QALY versus $3015 per DALY in South Africa according to Edoka and Stacey.[25] Our results are also broadly in line with experts' recommendations,[9,26] and with the thresholds currently in use by many countries.

An important limitation of our method is that we use a macro-level approach based on the current efficiency (or inefficiency) of the health system. If a more inefficient country estimates cost-effectiveness thresholds on the basis of its current performance, it will estimate higher thresholds, further promoting the escalation of inefficiency. For this same reason, the country-level guidance thresholds that we produced on the basis of the income level of each country could be overestimated in the case of countries with more efficient spending (within their income strata) and underestimated in the most inefficient countries, as we are assuming that countries will see increases in both life expectancy and health expenditure per capita that are in the median of their income level stratum.

Another limitation is that our approach estimates the degree of increase in health expenditures driven by the coverage of new interventions on the basis of only a few parameters. The actual increase could be higher or lower according to the influence of other factors that also affect life expectancy, health expenditures, or both (eg, a health system can disinvest by eliminating obsolete technologies or achieve other efficiencies and therefore can prevent, or reduce, the increase in spending driven by new interventions). This limitation is also present in other approaches to estimate cost-effectiveness thresholds,[23] but because we are using country-group-specific estimates of health expenditure growth and health gain, we partly account for the effects of these other influences. The estimates produced by our approach assume that all interventions will have an ICER at the threshold level. However, health systems can finance a combination of interventions with ICERs above and below the threshold and maintain the increase in spending within the limits established (appendix p 7).

This model will eventually be extended and refined after further thoughts, discussion, and the consideration of issues such as how different population age structures or different per-capita health expenditure by age could affect threshold estimation and how new interventions interact with other factors that also influence life expectancy and health expenditure per capita.

Additionally, a limitation of the DisCET is that, by using values derived from analysing countries' expenditures, it implies an assumption either that the whole growth observed (both in health expenditure and life expectancy) derives from past decisions regarding the adoption of new interventions, which may not be the case, or that these decisions fostered a pace of increase at a similar rate to the one driven by other factors, which is almost impossible to verify.

Decision rules for the allocation of health resources that do not prioritise on the basis of appropriate guidance, either through the absence of a cost-effectiveness threshold or by using a misguided threshold, will lead to suboptimal solutions. Inappropriate prioritisation could result in reimbursing interventions that are not cost-effective or in limiting access to effective and efficient interventions, exacerbating health inequalities and ultimately worsening the performance of the health system. However, no current method is considered the single best to empirically estimate thresholds.[8,27] The development of alternative approaches that use a range of methods and provide complementary evidence is an important contribution to inform the selection of cost-effectiveness thresholds, to improve the evidence base for priority setting, and to improve patients' access to health care in the quest for universal health coverage.

Contributors
AP-R, AP, SG-M, and FA were responsible for the analysis. AP-R conceptualised the work and, along with MD and FA, designed the methodology. MD supervised the work. AP-R and AP were responsible for data curation and software management. All authors participated in writing, reviewing, and editing the manuscript, and have read and agreed to the published version. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests
We declare no competing interests.

Data sharing
The full dataset and the STATA do-file detailing the variable construction and statistical analyses are available in the appendix.

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References

1 WHO. The world health report 2010: health systems financing: the path to universal coverage. 2010. https://apps.who.int/iris/handle/10665/44371 (accessed April 1, 2022).
2 WHO. Everybody's business—strengthening health systems to improve health outcomes: WHO's framework for action. 2007. https://apps.who.int/iris/handle/10665/43918 (accessed April 1, 2022).
3 WHO. Making fair choices on the path to universal health coverage: final report of the WHO consultative group on equity and universal health coverage. 2014. https://apps.who.int/iris/handle/10665/112671 (accessed April 1, 2022).
4 Garrison LP Jr, Neumann PJ, Willke RJ, et al. A health economics approach to US value assessment frameworks—summary and recommendations of the ISPOR Special Task Force report [7]. *Value Health* 2018; **21:** 161–65.
5 Anderson JL, Heidenreich PA, Barnett PG, 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. *Circulation* 2014; **129:** 2329–45.
6 Pichon-Riviere A, Garcia-Marti S, Oortwijn W, Augustovski F, Sampietro-Colom L. Defining the value of health technologies in Latin America: developments in value frameworks to inform the allocation of healthcare resources. *Int J Technol Assess Health Care* 2019; **35:** 64–68.
7 Drummond MF, Sculpher MJ, Claxton K, Torrance GW, Stoddart GL. Methods for the economic evaluation of health care programmes, 4th edn. Oxford: Oxford University Press, 2015.
8 Chi YL, Blecher M, Chalkidou K, et al. What next after GDP-based cost-effectiveness thresholds? *Gates Open Res* 2020; **4:** 176.
9 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:** 118–24.
10 WHO Commission on Macroeconomics and Health. Macroeconomics and health: investing in health for economic development/report of the Commission on Macroeconomics and Health. 2001. https://apps.who.int/iris/handle/10665/42435 (accessed April 1, 2022).
11 WHO. Using health technology assessment for universal health coverage and reimbursement systems. Nov 2, 2015. https://www.who.int/publications/m/item/using-health-technology-assessment-for-universal-health-coverage-and-reimbursement-systems (accessed April 1, 2022).
12 Faria R, Duarte A, McKenna C, et al. Guidelines for the economic evaluation of healthcare technologies in Colombia: technical support documents. Instituto de Evaluación Tecnológica en Salud. August, 2014. https://www.iets.org.co/Archivos/66/Documentos_tecnicos_en_ingles.pdf (accessed April 1, 2022).
13 Revill P, Sculpher M. Cost effectiveness of interventions to tackle non-communicable diseases. *BMJ* 2012; **344:** d7883.
14 Shillcutt SD, Walker DG, Goodman CA, Mills AJ. Cost effectiveness in low- and middle-income countries: a review of the debates surrounding decision rules. *PharmacoEconomics* 2009; **27:** 903–17.
15 Culyer AJ. Cost-effectiveness thresholds in health care: a bookshelf guide to their meaning and use. *Health Econ Policy Law* 2016; **11:** 415–32.
16 Woods B, Revill P, Sculpher M, Claxton K. Country-level cost-effectiveness thresholds: initial estimates and the need for further research. *Value Health* 2016; **19:** 929–35.
17 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 Health* 2018; **3:** e000964.
18 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:** 1–503, v–vi.
19 Edney LC, Haji Ali Afzali H, Cheng TC, Karnon J. Estimating the reference incremental cost-effectiveness ratio for the Australian health system. *PharmacoEconomics* 2018; **36:** 239–52.
20 Ochalek J, Wang H, Gu Y, Lomas J, Cutler H, Jin C. Informing a cost-effectiveness threshold for health technology assessment in China: a marginal productivity approach. *PharmacoEconomics* 2020; **38:** 1319–31.
21 Siverskog J, Henriksson M. Estimating the marginal cost of a life year in Sweden's public healthcare sector. *Eur J Health Econ* 2019; **20:** 751–62.
22 Vallejo-Torres L, García-Lorenzo B, Serrano-Aguilar P. Estimating a cost-effectiveness threshold for the Spanish NHS. *Health Econ* 2018; **27:** 746–61.
23 Edney LC, Lomas J, Karnon J, et al. Empirical estimates of the marginal cost of health produced by a healthcare system: methodological considerations from country-level estimates. *PharmacoEconomics* 2022; **40:** 31–43.
24 Pearson SD. The ICER value framework: integrating cost effectiveness and affordability in the assessment of health care value. *Value Health* 2018; **21:** 258–65.
25 Edoka IP, Stacey NK. Estimating a cost-effectiveness threshold for health care decision-making in South Africa. *Health Policy Plan* 2020; **35:** 546–55.
26 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:** 796–97.
27 Karlsberg Schaffer S, Cubi-Molla P, Devlin N, Towse A. Shaping the research agenda to estimate relevant cost-effectiveness thresholds for health technology assessment decision making: report for ABPI. April, 2016. https://www.ohe.org/publications/shaping-research-agenda-estimate-cost-effectiveness-thresholds-decision-making (accessed April 1, 2022).