**Informing Decisions in Global Health: Cost Per DALY Thresholds and Health Opportunity Costs**

**Introduction**
Ensuring global access to proven interventions – including vaccines, drugs, and diagnostics, as well as prioritising the development of new health technologies – requires an assessment of whether the improvement in health outcomes they offer exceeds the improvement in health that would have been possible if the resources required had, instead, been made available for other health care activities. Therefore, some assessment of these health opportunity costs is required if the best use is to be made of the resources available for health care, existing technologies and the development of new ones.

**The relevance of health opportunity costs**
Evidence of the expected costs and health effects of making an intervention available to specific populations in particular settings and health care systems (HCS) are often summarized as cost per Disability Adjusted Life Year (DALY) ratios (Salomon et al, 2012). These provide a useful summary of how much additional resource is required to achieve a measured improvement in health (the additional cost required to avert one DALY), or how much health is delivered for an amount of additional resource (the DALYs averted per $1,000). Whether an effective intervention will improve health outcomes overall, because the cost per DALY it offers is judged to be cost-effective, requires a comparison with the likely health opportunity costs, i.e. the improvement in health that would have been possible if any additional resources required had, instead, been made available for other health care activities. An assessment of the likely health opportunity costs in different HCS means that evidence of the effectiveness and cost of an intervention can better inform decisions. Most importantly, it ensures that decisions improve rather than reduce health outcomes overall.

**Providing measures of value**
Evidence of the health opportunity costs faced by different HCS make it possible to report measures that reflect the value of providing access to an existing intervention, as well as investing in the discovery and development of new ones. Value can be expressed as the scale of the potential net health impact:
- Net DALYs averted, which is the difference between DALYs averted by an intervention and DALYs that could have been averted with any additional HCS resources required to implement it, or, if the intervention saves HCS costs, it is the DALYs averted by the intervention plus the DALYs that can also be averted with the cost savings offered.
- Global net DALYs averted are the net DALYs averted for all health care systems (countries) where the technology should be adopted and its implementation supported (where it offers positive net DALYs averted).

Value can also be expressed as the amount of additional health care resources which would be required to deliver similar net health impacts:
- $ value to a HCS is the amount of HCS resources that would be required to deliver the same amount of net DALYs averted.
- Global $ value is the $ values to all those HCS where the intervention should be adopted and implementation supported (where it offers positive net DALYs averted).

These measures of value, founded on an assessment of health opportunity cost, are not only useful to global bodies which make recommendations, purchase health technologies or prioritise the development of new ones (e.g., WHO, Global Fund, GAVI and BMGF), but also for decision makers in low- and middle-income countries (LMICs) and their negotiations with donor agencies and NGOs.

**Informing other decisions**
Evidence of the likely health opportunity costs faced in specific health care systems is also useful for a number of other reasons:

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• Exposes the implications of currently available resources for health care and the real value of increasing them. It contributes to greater accountability in low- and middle- as well as in high- income countries, for the health care and other expenditure decisions made at local, national and supra national levels.

• Demonstrates that the costs of an intervention are just as important as how effective it might be. Different HCS are likely to face different health opportunity costs so the maximum they can afford to pay for an intervention will also differ. This can inform evidence based tiered pricing mechanisms and value based purchasing negotiations.

• Identifies the value of more effective purchasing of other inputs (e.g. improvements to supply chains and encouragement of competitive generics market) and the most that might be offered as incentives to encourage implementation, e.g. through ‘payment by results’ mechanisms.

• Provides a benchmark to search for and explicitly identify other under exploited investments which could offer greater value, and existing commitments that could be disinvested to accommodate more valuable ones.

• Informs the content and scale of an Essential Health Package (EHP) with existing resources, the value of expanding the EHP and the incremental reallocation of resources, within the package.

• Prioritises implementation efforts and system strengthening. For example, measures of value (net DALYs averted and the $ value to the HCS) indicate the value of addressing existing constraints which might prevent the full implementation of valuable interventions. They can indicate the value of strengthening aspects of the HCS that are common constraints to the implementation of a number of interventions.

• The necessary trade-offs between health and other objectives can be identified and explicitly considered. For example, whether to provide access to an intervention that might not be judged cost-effective, so will reduce health outcomes overall, but would offer significant health or financial protection benefits to disadvantaged groups.

• Makes the strong ethical foundation of considering the costs and the cost-effectiveness of interventions less abstract and more easily communicated to the range of stakeholders. This can make the politically difficult decisions of which interventions can be provided, and which cannot, a more accountable, evidence based and, therefore, sustainable prospect.

Evidence to support the assessment of health opportunity costs

Health opportunity costs are the amount of health that a HCS currently delivers with more or less resources, so what is required are estimates of the health effects of changes in health expenditure (Martin et al 2008, 2012; Claxton et al 2015a). The effect of different levels of health care expenditure on mortality outcomes has been investigated in a number of published studies using country level data, many including LMICs (Gallet and Doucouliagos 2015). The challenge is to control for all the other reasons why mortality might differ between countries in order to isolate the causal effect of differences in health expenditure (Nakamura et al 2016). This is a particular challenge even if available measures are complete, accurate and unbiased because health outcomes are likely to be influenced by expenditure (increases in expenditure improves outcomes), but outcomes are also likely to influence expenditure (poor outcomes prompt greater efforts and increased expenditure). This problem of endogeneity risks underestimating the health effects of changes in expenditure.

Instrumental variables have been used in a number of studies to try and overcome this problem and estimate the proportionate effect on mortality of proportionate changes in health expenditure, or elasticities, for LMICs (e.g.- Bokhari et al 2007). These estimated elasticities can provide country specific cost per DALY averted values, taking account of measures of a country’s infrastructure, donor funding, population distribution, mortality rates, conditional life expectancies (all by age and gender), estimates of disability burden and total health care expenditure.

• Estimates of health opportunity costs (cost per DALY) are available for 123 counties (Ochalek et al 2015).

• Country specific estimates can be presented by GDP pc, health expenditure pc, under 5 mortality rate and by different grouping of countries (by region, GAVI eligible, LIC, MIC).

• These estimates can be updated for later waves of data on measures of infrastructure, donor funding, population, mortality rates, conditional life expectancies, disability burden and total health care expenditure for each county.

• Despite the challenges of estimation, the evidence suggests that elasticities appear to be relatively similar across countries with different levels of income. This means that it may be possible to project estimates over the longer run (subject to time variant interactions) based on projections of health expenditure, demographics and mortality rates.

• A meta regression of over 60 studies that have been published on the mortality and life expectancy effects of changes in health expenditure has been undertaken, which can be up-dated and refined as new evidence accumulates (Gallet and Doucouliagos 2015).

Other recommended thresholds

Cost-effectiveness ‘thresholds’ (e.g.- cost per DALY or cost per quality adjusted life year (QALY) thresholds) recommended or cited by decision making and advisory bodies (both national and supra national), reflect a lack of conceptual clarity about what they ought to represent and what type of evidence might inform their assessment (Revill 2014; Culyer 2015). As a consequence these values have simply become established norms or implied values, which describe the criteria used to judge cost-effectiveness. Other proposed thresholds reflect a view of what value ought to be placed on improvements in health. They imply what health care expenditure ought to be (the social demand for health) rather than an evidence based assessment of health opportunity costs given actual levels of expenditure, i.e. a ‘supply side’ estimate of the amount of health that a HCS currently delivers with more or less resources.

Established norms and implied values

Some implicit or explicit assessment of health opportunity cost is unavoidable because all decisions about health care imply one. A few HCS have revealed something about the criteria or threshold values likely to be used when making decisions (Vallejo-Torres et al, 2016). However, reimbursement agencies in only two HCS have been explicit about the threshold used to judge cost-effectiveness, although others seem likely to follow. For example, since 2004, the National Institute for Health and Care Excellence (NICE), which issues guidance to the UK NHS, has published an explicit range for the cost-effectiveness thresholds used in its deliberative decision-making process (£20,000 to £30,000 per QALY) (NICE, 2004). Although NICE makes clear that the threshold ought to represent the health consequences of additional NHS costs, this range was, in fact, founded on the values implied by the decisions it made.
between 1999 and 2003 (Rawlins and Culyer, 2004). The NICE thresholds are implied values from previous decisions and have been widely recognised for some time (including by NICE) as having little empirical foundation. This range has become an established norm, which is intended to represent how NICE makes its decisions, although recent evidence suggests that the thresholds implied by the decisions NICE actually makes are, in fact, much higher (Dakin et al., 2014). Neither the stated nor implied NICE thresholds are based on an evidenced based assessment of expected health opportunity costs (Claxton et al. 2015b). Other established norms are also evident in published economic evaluations. For example, in the US, thresholds of $50,000 to $100,000 per QALY have become increasingly cited but are also widely recognised as having little evidential foundation (Neumann et al. 2014).

The social value of health

Other suggested thresholds reflect a view of how much consumption should be given up to improve health. They imply what health care expenditure ought to be (the demand for health), rather than an assessment of the health effects of changes in actual health care expenditure, i.e. a ‘supply side’ assessment of health opportunity costs. Thresholds that reflect a view of the demand for health have been expressed in two subtly different ways: aspirational ones, which represent a particular view of what value ought to be placed upon health improvements and how much resources should be devoted to health care; and those based on evidence of how much consumption individuals are willing to give up to improve their health.

There is a large literature which has used stated preferences (hypothetical valuations) to estimate the consumption value or willingness to pay for a QALY. Most estimate how much consumption an individual is willing to give up to improve their own health. A few try to elicit how much individuals believe society should pay to improve health more generally. A wider literature, that extends beyond health, estimates the value of a statistical life based on how much consumption individuals are willing to give up to reduce their mortality risk. Some studies are based on stated preferences (hypothetical choices) but others identify situations where individuals actually make choices that imply a value, e.g. revealed preferences in the labour market. A cost per QALY or cost per DALY can be derived from these studies by making assumptions about age and gender distribution, conditional life expectancies and quality of life norms.

Recent reviews of this literature reveal very wide variation in values, even within countries (Vallejo-Torres et al, 2016; Ryen and Svensson, 2015; Robinson et al, 2016). However, some patterns do emerge. Reported values tend to be higher than available estimates of a ‘supply side’ assessment of health opportunity costs. This suggests a discrepancy between the demand and supply side of HCS. For example, if these estimates are regarded as an appropriate expression of social value, the difference would indicate that health care from collectively pooled resources is ‘underfunded’ compared to individual preferences about health and consumption. However, given the difficulties faced in the public financing of HCS in high income counties as well as LMICs this is what would be expected (Drummond et al. 2015; Woods et al. 2016). Since ‘demand side’ values, especially aspirational ones, are likely to be substantially higher than an assessment of the actual health opportunity costs (the supply side), their use is likely to reduce overall population health and underestimate the real value of devoting more resources to health care.

Thresholds currently used in LMICs

Some agencies have adopted or recommended explicit thresholds informed by these types of ‘demand side’ estimates. For example, in 2005 the World Health Organization recommended explicit cost per DALY thresholds to serve as a guide alongside WHO-CHOICE. They have been used as generic and internationally applicable criteria to classify interventions as highly cost-effective (less than one GDP pc), cost-effective (less than three GDP pc) or not cost-effective (three GDP pc or higher). They appear to have been based on estimates of the value of a statistical life reported in the Commission on Macroeconomics and Health 2001. Despite the widely recognised shortcomings of these GDP pc based thresholds (Newall et al. 2014; Marseille et al. 2015; Robinson et al. 2016; Bertram et al. 2016), they have nonetheless become established norms which are widely cited in published economic evaluations, have informed recommendations made by agencies and, in the absence of other country specific estimates, have been used as criteria to judge cost-effectiveness in LMICs. The current evidence suggests these established norms are substantially higher than available estimates of a ‘supply side’ estimate of health opportunity costs.

The only agency in a LMIC that has adopted an explicit evidence based country specific threshold is the Health Intervention and Technology Assessment Program (HITAP) in Thailand. HITAP adopted thresholds based upon estimates of individual stated preferences about health and consumption, which were intended to reflect the social value of health in Thailand; initially recommending a threshold of one GDP pc (120,000 THB per QALY) (Jirawattanapisal et al 2009). The organisation has continued to evolve and conduct research to inform this issue, raising the threshold to 160,000 THB per QALY in 2013 (Thavorncharoenasap et al 2013; Nimdet and Ngorsuracles 2015). These thresholds are country specific and empirically based estimates but represent a view of what the social value of health (relative to other consumption opportunities) ought to be, rather than a ‘supply side’ assessment of health opportunity costs based on evidence of the health effects of changes in actual health care expenditure.

Conclusions and recommendations

Some assessment of health opportunity costs is required if the best use is to be made of the resources available for health care, existing technologies and efforts to develop new ones.

• Cost per DALY threshold used to judge the cost-effectiveness of an intervention should reflect evidence of the likely health opportunity costs in the settings and health care system in which it will be used.

• Evidence of the health opportunity costs faced in different health care systems makes it possible to report measures that reflect the value of providing access to an existing intervention, as well as investing in the discovery and development of new ones (e.g. global and country specific net DALYs averted and the $ value to HCS).

• Health opportunity costs are the amount of health that a HCS currently delivers with more or less resources, so what is required are estimates of the health effects of changes in health expenditure.

1 The House of Commons investigation of NICE in 2008 identified that the thresholds used by NICE had little empirical foundation. This was reiterated during the 2008 review of its methods guidance, McCabe (2008). In response, NICE commissioned Appleby et al, 2009, and asked UK research funders to commission the research that was published in Claxton et al. 2015a.
• The effect of different levels of health care expenditure on health outcomes has been investigated in a number of published studies using country level data, many including LMICs.
• Despite the challenges of estimation, especially when based on country level data, some implicit or explicit assessment is unavoidable. Estimates are available for 123 countries. These estimates need to be updated and refined as more and better data become available.
• Cost-effectiveness ‘thresholds’ (cost per DALY or cost per QALY) that have been recommended or cited by decision making and advisory bodies are not founded on an assessment of the likely health opportunity costs. Their use is likely to reduce rather than improve health outcomes overall.

References: