On value frameworks and opportunity costs in health technology assessment

Short title: Economics, value and HTA

Author: Neill Booth

Affiliation: Faculty of Social Sciences, Tampere University, Finland

#### **ABSTRACT**

**Objectives:** Proceeding from a basic concept underpinning economic evaluation, opportunity cost, this study aims to explain how different approaches to economics diverge quite dramatically in their ideas of what constitutes appropriate valuation, both in principle and practice. Because the concept of opportunity cost does not inherently specify how valuation should be undertaken or specify how appropriate any economic value framework might be, the three main economics-based approaches to providing evidence about value for health technology assessment are described.

**Methods:** The paper describes how the three main economic value frameworks – namely, the extra-welfarist, welfarist, and classical – are most typically understood, applied, and promoted. It then provides clarification and assessment of related concepts and terminology.

**Results:** Although economic value frameworks differ, certain underlying characteristics of valuation were identified as fundamental to all approaches to economic evaluation in practice. The study also suggests that some of the rhetoric and terms employed in relation to the extra-welfarist approach are not wholly justified and, further, that only the welfarist approach ensures adherence to welfare-economic principles. Finally, deliberative analysis, especially when connected with a classical economic approach, can serve as a useful supplement to other analytical approaches.

**Conclusions:** All three approaches to economic evaluation have something to offer assessment processes, but they all display limitations too. Therefore, the author concludes that the language of economic evaluation should be used with sufficient humility to prevent overselling of economic value frameworks, especially with regard to the qualities of the evidence they provide for priority-setting processes.

Keywords: Costs and Cost Analyses; Priorities, Health; Technology Assessment, Health

# Acknowledgements

The author is indebted to Professor Steve Birch for his assistance with useful content for earlier drafts of the manuscript, along with valuable discussions. Professor Pekka Rissanen also deserves special thanks for helping provide the time and space necessary for undertaking the study. Of course, any mistakes that remain are entirely the responsibility of the author.

# **Sources of funding**

This work was supported by an unconditional grant from the Yrjö Jahnsson Foundation, with the funder having no other role in the study itself, in interpretation of the results, or in the writing of the manuscript.

## **CONFLICTS OF INTEREST**

The author has nothing to disclose.

#### Introduction

In a recent commentary piece in this journal (1), Professor Culyer usefully highlighted many of the issues in economics surrounding costs and context in health-economic evaluation for health-technology assessment (HTA). While making appropriate reference to both health economics and economics in general, Culyer neglected to mention that economics for HTA can encompass more than the extra-welfarist approach and that other economic value frameworks (EVFs) exist. Although his commentary helps to demystify the topic, still greater clarity and humility with regard to 'economic' perspectives on valuation could contribute to improved HTA processes. Indeed, assessing the quality and relevance of EVF outputs as information for priority-setting processes may become easier once the fundamental assumptions and value judgements related to EVFs are clarified.

This paper highlights two main alternatives to extra-welfarist economic value frameworks (EWEVFs) – the welfarist (WEVF) and the classical (CEVF) – and it describes how both can inform HTA decision-making processes. Each of the three economic approaches here depends on particular sets of premises (in essence, 'political' judgements) as to which sorts of value count and the extent to which those dimensions of value are covered. Hence, as Culyer and Jönsson note (2, p. 2), these can be seen as vital for correctly judging the applicability or relevance of any given EVF.

## Theoretical understanding of opportunity cost

This paper supplements earlier studies by clarifying several factors related to economic evaluation for HTA. Conceptual clarity is especially important both when defining opportunity costs and when actually carrying out any corresponding economic evaluation, on account of the implicit or explicit assumptions made, the limitations and uncertainties surrounding the measurement instruments, and the challenges involved in estimating any form of 'economic' efficiency. A clear, transparent approach is important also with regard to terminology: as Williams argued several decades ago, the role of economic evaluation in setting priorities for health technologies is easily oversold (3), and the relevance of this has been reaffirmed many times since (4, 5). Another important reason to strive for clarity lies in a shift witnessed in economic evaluation away from more welfarist views (6, p.64) and toward more narrowly focused extra-welfarist EVFs (7). Although the Culyer piece offers a textbook parable related to opportunity cost, it bears remembering that economists have

utilised the concept at least as far back as Adam Smith's day (8, Book I, Chapter VI, p. 1). The term 'opportunity-cost' itself was coined by Green, with the thrust of his definition already involving 'the opportunities foregone in accepting a certain line of action' (9). Differences between schools of economic thought notwithstanding, Green's definition seems to have been reinforced – by, among others, both Alchian (10) and Buchanan, with the latter stating that 'opportunity cost is the evaluation placed on the most highly valued of the rejected alternatives or opportunities' (11). Though there is fairly widespread agreement that economic evaluation is intended to **inform** HTA decision-making processes, how this principle gets applied in practical analysis of opportunity costs will reflect both the policy problems facing decision-makers and the research questions involved, along with the specific EVF chosen (1, 12).

On the conceptual level, identifying opportunity costs entails a two-part approach: firstly, the value of the 'new' technology at issue is estimated or defined; then, the estimate obtained is compared to the value placed on the class of all 'practicable' alternative technologies, however specified. The first of the two evaluative components assigns a value to the given health technology relative to at least one other way of serving the same group. This valuation addresses not only the estimated additional resource requirements of the new technology, but also takes into account its effectiveness; i.e., this first valuation reports or estimates a value for at least one of the outcomes produced by the health technology. The second component places a value on what would have to be forgone for in order to supply the resources needed for the chosen technology. The objective of any reputable economic evaluation is therefore to provide evidence on whether the technology's economic value (ascertained in the first component) outweighs the economic value of what is foregone (ascertained in the second component). The likely utility of economic evaluation for decision-making purposes is markedly lower when either of the two evaluative components lacks plausibility. Accordingly, this paper focuses on clarifying the nature of economic evaluations' information inputs to priority-setting processes. From this perspective, it outlines the orientation of three EVFs, which, to varying extents, can address policy problems and identify different forms of opportunity cost (1). The aim is a critical review of economists' attempts to adopt and operationalise these concepts, bundled as they are with particular aspirations, conditions, and premises.

## Concepts of opportunity cost in practice

There are three main 'economics'-based approaches to determining whether a given technology's economic value exceeds the value of any action forgone. Each type of EVF – the extra-welfarist, the welfarist, or the classical – imposes its own boundaries on how the valuation is undertaken. For each of the two components described above, the frameworks typically identify (or tacitly accepts) their own sources of 'value' and/or metrics thereof. These differences between EVFs stem predominantly from **what** is deemed to be of value, though EVFs also diverge in **how** the valuation is conducted.

For a backdrop to examination of differences between EVFs, it is useful to outline the scope of investigations that are possible as part of the economic evaluation of health-care technologies. There are at least five distinct levels at which concepts of opportunity cost can be considered: I) choices from among particular portfolios of public expenditure (13); II) choices from among the technology portfolios that constitute the basket of publicly provided services (7); III) choices between treatments within the limits set for total disease-specific expenditure (14); IV) choices between mutually exclusive treatments (15); and V) estimates of what may be forgone through using a specific input to the production process, or 'resource opportunity cost' (16). The focus here is on level II, because the portfolio-of-technology level represents the most prevalent scope adopted by economic evaluations aimed at informing processes of health-care resource allocation (17).

#### **Differences between EVFs**

The objective for extra-welfarist approaches is often characterised as being to 'maximise health' (18), where the matter of how 'health' is defined can be considered very important because of proxying; typically in EWEVFs, rather than 'health' *per se* being maximised, only an indicator of health is maximised. Under EWEVFs, 'health' usually refers to the amalgam of 1) an indicator reflecting some dimensions of perceived health status with 2) 'health-state valuations' connected with that indicator (19). Both many of the indicators, and many of the valuations thereof, are typically engineered by health economists themselves. Although extra-welfarist approaches do not dictate a given maximand, most EWEVF applications centre on maximising a **combination** of precisely this sort of 'social valuation' of states of health **with** estimates of length-of-life impacts, normally operationalised in the form of quality-adjusted life years (QALYs). Under EWEVFs, the first evaluative component's

output, typically a cost-per-QALY estimate, is compared with the second 'output', which represents 'opportunity cost' (an estimated mean cost per unit of health forgone through diverting resources from other activities). Thus, in principle, EWEVFs address whether total 'health' will increase if the new technology is introduced, but do so with an implicit assumption that both the new technology and the activities from which resources are diverted are, as economic theory suggests, perfectly divisible with constant returns to scale. However, as noted by Drummond (6) and illustrated by Birch and Donaldson (20), ascertaining the new technology's impact on efficiency (net impact on health) in a theoretically well-grounded manner requires avoiding such strict assumptions, which demands a mathematical-programming approach.

The aim with welfarist approaches to economic evaluation is to maximise 'welfare', where analysis is undertaken to identify the improvements in the aggregate welfare of individuals (21). Valuation using WEVFs is based on the utility individuals gain from how the available resources are used, inclusive of any welfare impacts arising from the way commodities or outcomes are distributed within the population in connection with different uses of resources (22). 'Social welfare' or 'well-being' can be defined in terms of total net willingness to pay (WTP) (23), with contingent valuation methods constituting the main source of valuations in WEVFs (24). In more general terms, WEVF-based analysis compares the additional well-being produced by the new technology with that forgone through diversion of the required resources from elsewhere to support the new technology.

Finally, in classical approaches to economic evaluation, one of the central objectives is to supplement EWEVFs and WEVFs by accounting for preferences or values that are ascertainable only via deliberative methods. The label 'classical' refers to the long history of valuation in economics before such developments as the marginal revolution (25). With CEVFs, the goal is to identify and assess, rather than to define and maximise, 'health' or 'well-being'. That is, in place of a formalised maximand, the targets in a classical approach (26, p. 136) might involve satisficing (27) or sufficiency (28), in addition to interpreting, e.g., some EWEVF- or WEVF-derived indicator of 'economic' efficiency. Often, CEVFs operate with other, non-quantitative information too, and typically encompass deliberation (29). Perhaps their most important element is an attempt to avoid being constrained to focus on formal economic efficiency, i.e., on the type of neo-classical economic efficiency which is the result of quantitative or mathematical analysis.

# EVFs, opportunity cost, and the two components of valuation

As the name 'economic value framework' suggests, each EVF has its own approach to valuation embedded within it. Under EWEVFs, one frequent approach to judging what is forgone is to assume, both in principle and practice, that it is possible to quantify an opportunity cost and that this quantity is invariant to the size of the programme being evaluated, i.e., that there can be a fixed "cost per QALY" (30). However, this is inconsistent with the economic notion of resource scarcity and the general finding that the marginal utility of a good or service decreases as consumption increases. When EVFs employ comparison to some fixed monetary valuation of opportunity cost, they tend to ignore factors such as the potential budgetary impact of the intervention and the 'lumpiness' of health technologies (31, 32).

While all three EVFs entail estimating cost and effect differences for a new technology relative to a comparator, the discussion above should render it clear that there may be little deeper commonality in how EVFs assign value to alternative health technologies that might be displaced. The onus is generally on the user of the research to identify the possible implications of the chosen value system for the decision-making process it is purported to serve (33). The discussion below attempts to make the relevant implications clearer for each of the three main EVFs.

## Valuation and opportunity cost in EWEVFs

Under EWEVFs, the first evaluative component in defining opportunity cost is generally based on cost-effectiveness analysis, which yields an estimate of the mean cost-per-unit health benefit produced by the chosen intervention – i.e., an incremental cost-effectiveness ratio (ICER). In EWEVFs, this ratio, an estimate of the inverse of the mean rate of return on the additional investment required to fund the technology, is typically employed in an economic-efficiency metric entailing comparison with some predetermined benchmark ICER, i.e., some cost-effectiveness-ratio threshold (CERT) (34). The latter is usually exogenous to the study at hand. Only rarely under EWEVFs do the activities displaced by the additional investment of resources in the technology get identified, or be valued, on a case-by-case basis. While some CERTs involve estimates from econometric analysis of possible relationships between current resource use and health-related outputs (35, 36), they may also simply represent an arbitrary figure or diktat (37). Indeed, CERTs will generally fail to fully reflect the actual displacement

resulting from the technology's adoption (38). Many researchers continue to propose CERTs, of various types, despite evidence suggesting that thresholds are merely an economic abstraction and that a single appropriate CERT is likely to remain elusive in most contexts (39).

# WEVF-related valuation and opportunity cost

Under WEVFs, analysis focuses on individuals' preferences and technologies are evaluated for their impacts on 'well-being' (20). In some of these frameworks, the two evaluative components are brought together in a single model for analysis of portfolio choice through mathematical optimisation. By incorporating resource constraints into the model explicitly, thereby focusing attention on the well-being generated from the entire resource budget as opposed to a single programme's share of that budget, the approach addresses opportunity-cost considerations directly without requiring the separate valuation of the foregone alternatives that is typical under EWEVFs (40). Hence, the emphasis in WEVFs is on comparing across the well-being generated by various combinations (or portfolios) of 'health technologies' that the available resources can sustain, and on determining which combinations could improve 'welfare'. In addition, the approach can accommodate any other concrete constraints on preferences, in line with policy considerations related to equity, need, etc. (40). It is also important to note here that, in practice, WEVF utilises WTP estimates which typically rely on methods such as contingent valuation to compare WTP between the new technology in aggregate and whatever must be forgone (41).

# Valuation and opportunity cost in classical economic approaches

CEVFs can be viewed as a reaction to various limitations of EWEVFs and WEVFs in practice, especially as the latter are designed to 'maximise' via an objective function of one type or another. CEVFs represent an alternative approach, one that need not focus on a single maximand (as EWEVFs typically do) or on a single source of preferences (as is typical under WEVFs, the source being individuals) yet CEVFs can still be in line with conventional interpretations of opportunity cost (5).

## How CEVF approaches can help in HTA

In light of the above, CEVFs are proposed as an alternative that affords wider scope than either 'health maximisation' under EWEVFs or 'maximisation of economic welfare' under WEVFs, as they allow for qualitative use of preferences from groups of individuals, or directly from other stakeholders. Rather than rejecting use of the other EVFs, the CEVF approach supplements them with further information or deliberative analysis, such as incorporating community values (42) canvassed through various evidence-gathering processes (43-45).

A CEVF approach can help inform HTA in three main ways. Firstly, CEVFs can add information to the evidence provided by EWEVF and WEVF approaches on the relative efficiency with which 'health' and 'welfare' are produced, respectively. While WEVFs may include strong evidence about budget- or resource impacts, additional, related information (with either a short or a long time horizon) can still be produced or utilised within a CEVF (46). Secondly, CEVFs can identify any qualifications or caveats to the EWEVF or WEVF findings, aiming to ensure that the information they provide is interpreted correctly, through an appropriate appraisal of their quality. While such appraisal is already addressed by many existing HTA processes, it could have greater value due to being integral to a CEVF approach, in line with an iterative, classical vision of valuation (26). The third main advantage would be that CEVFs can provide fuller awareness of the nature of the research question and its connection with the policy problem, as well as of the types and levels of uncertainty and relevance carried by information from other EVFs (47, 48). One major contribution that CEVFs can make to HTA processes is to force more clarity into the terminology surrounding EVFs. This point will be returned to below.

CEVFs allow inclusion of dimensions of value that might not be measurable in the commensurate units 'required' by EWEVFs or WEVFs (49). Because they can account for informal analysis during an iterative process of deliberation, CEVFs could prove highly relevant for decision-makers (50). This might involve, for instance, **A**) confirming, doubting, or disproving the suitability of standard health-economic outcome metrics for the technology in question, partly through questioning the assumptions underlying information outputs from other EVFs, and **B**) establishing additional objectives or outcome measurements relevant for the technology in question (51, p. 149). For item **A**, deliberative analysis may assist in identifying any need to supplement other EVFs, because it is probable that no single

overriding 'efficiency' principle meets all the desiderata for allocation, and there may be good reasons to consider multiple prioritisation principles (29). For instance, some opportunity costs may not be quantifiable (52) and might lend themselves only to deliberation, as in the case of rights-based deontological or paternalistic considerations (53). In addition, with regard to item **B**, for some technologies there may be little pertinent quantitative information available from formal analysis, and stakeholders may hold diverse, conflicting views (54). The appraisal process may embody a range of considerations that might not all be well-defined prior to, or even during, economic evaluation. There are numerous situations in which deliberative analysis via CEVFs may provide a useful extension that improves on purely formal analysis, and a variety of evidentiary inputs may be used, as necessary, on a case-by-case basis (1, 55).

In general, although analytic endeavours within EWEVFs or WEVFs can reveal some of the implications of particular choices (33), CEVFs may add a platform that stimulates discussion of more communitarian values (e.g., (56, 57)). With CEVFs, the aim is what some have called 'higher-level efficiency', rather than efficiency in the more neo-classical sense found in the more formal approaches of EWHEE and WHEE (58, p. 125).

#### **Discussion**

Each mode of economic thinking outlined in this paper can offer useful information for priority-setting processes, even though each EVF involves its own particular aims, assumptions, and value judgements. Whichever EVF is applied, evaluating opportunity cost requires **some** valuation of what is given up (59); hence, the aim here is not to denigrate or promote any particular mode of economic evaluation but to promote solid awareness of the information that each can provide. In all cases, it should be acknowledged that economic approaches to assessing opportunity costs are information-intensive in their input requirements and that their use often suffers from a lack of appropriate information (60), especially as pathways to health are often quite complex (61). One should also bear in mind that any method which gives consistent or accountable answers in a systematic manner is unlikely to yield truly comprehensive evaluation (62). There are many circumstances wherein measurements fail to cover relevant aspects of the changes in 'states of health' (32, 63) or do not capture changes in capabilities or in patient-reported experiences, not to mention the fact that 'social valuations' of such changes in health status do not fully capture society's values

(5). On account of the measurement issues surrounding WTP, there may be many situations in which no valid and reliable methods of operationalising WEVFs exist (41, 64).

#### Problems with the EVF lexicon

While choice processes for allocating health-care resources should lead to transparent mechanisms for valuation of the various options and their opportunity costs (65, p. 138), terminology can make economic evaluation more opaque. This is evident from the declining use of terminology relating to intangibles and incommensurability, which could be seen as arrogant in a sub-discipline that often preaches humility. On account of space restrictions, the discussion here focuses on the terms 'cost', 'threshold', 'decision rule' and 'value for money'.

'Cost' has multiple meanings in both lay and specialist use, as Culyer noted when deeming it naïve to employ the term 'cost' for undesirable attributes (1). An alternative interpretation to that offered by Culyer is to take the undesirable attributes of an intervention as also representing a cost. Of course, at the level of valuing what may be forgone through using a specific input to the production process, or 'resource opportunity cost', i.e., at the level of building the pool from Alchian's and Culyer's examples, then 'undesirable attributes' should not be referred to as costs. On the other hand, the use of the term 'cost' for an undesirable attribute, a harm, or a negative benefit, could legitimately be used to refer to its part in an estimate of higher-level opportunity cost, i.e., when assessing the value of the pool per se. Indeed, at the portfolio-of-technology level, such undesirable attributes can be seen as an essential component of any EVF. Undesirable attributes are important when forming a valuation; Alchian expresses it thus: 'The decision maker must choose among events that are amalgams of goods and bads' (10). Therefore, in addition to the **things** forgone, such as the financial costs and the resources tied up, other aspects of the value forgone, for example, the 'costs' in terms of harms to health will also have a legitimate place in economic evaluations' definitions of (opportunity) costs (66). In practice, economic evaluations do typically include undesirable attributes in their analysis; for instance, EWEVFs do tend to utilise something akin to Alchian's amalgam approach when they promote a metric expressing the estimated cost divided by the estimated incremental overall population-'health impact'. For the purposes of HTA, it seems reasonable to suggest that any sound economic evaluation involves taking both pros and cons into account: focusing on both the undesirable and the

desirable attributes of technology, in line with the foundations of technology assessment (67). While, obviously, pain and suffering need not involve resources *per se*, the principle of opportunity cost encompasses the benefit forgone, so any robust measurement of higher-level opportunity cost should also take the 'cost', in terms of related pain and suffering, into account.

Some extra-welfarist economists and even some HTA practitioners take the perspective that 'thresholds' can and should be quantified. However, economising in line with these assumptions may be less intuitive for others involved in prioritisation processes and seem rather perfunctory with respect to 'societal values' (68, 69). As is noted above, defining opportunity cost as a single threshold estimate can be seen as a typical economic abstraction. While economic evaluation must always operate at some level of abstraction in practice, the fairy tale of a single threshold (CERT), or threshold range, can be regarded as unhelpful. As no such one-size-fits-all threshold exists in reality, even within a well-bounded single jurisdiction, employing the term 'thresholds' seems to oversell EWEVFs. The problematic terminology is compounded by the use of connected phrasings such as 'decision rules' and 'value for money'. For instance, the real-world applicability of so-called decision rules of EWEVFs is crucially reliant on the framework's inherent value judgements and assumptions. Indeed, these 'rules' are typically valid only within the confines of the EWEVF in question, and there is a danger that the term 'decision rules' could be construed to carry a similar meaning beyond this arcane hypothetical setting. Furthermore, claims of ICERs revealing 'value for money' seem quite arrogant, in that EWEVFs often offer only a highly abstracted indicator of value. Although the concise term 'value for money' may be much easier to sell to HTA decision-makers than, e.g., 'estimated mean valuation of estimated change in mean health status divided by the estimated change in mean health-care costs', the former loses too much in precision; it seems much less honest. Since loose language could result in dire consequences of economic evaluation being oversold to the HTA community, it should be avoided at all costs.

#### **Conclusions**

Rather than economists holding a uniform, all-encompassing view, there are three main approaches to economic thinking for HTA, accompanied by a multitude of ways to implement each of these. Instead of a single notion of economics embodied by one EVF, the study found EWEVFs, WEVFs, and CEVFs, each with corresponding problems and potential. Therefore, all approaches to economic evaluation should be checked for quality and relevance before being used to inform prioritisation processes. Applying more precise vocabulary, coupled with greater understanding of the limits to analysis of any kind, should help decision-makers engage in appropriate deliberation and interpretation in their HTA endeavours. The ways in which notions of opportunity cost are translated into practice and interpreted are likely to have great importance, not only for priority-setting but also for the long-term health and sustainability of health-care systems.

## FINANCIAL SUPPORT

This work was supported by the Yrjö Jahnsson Foundation (grant number 6572).

#### References

- 1. Culyer AJ. Cost, context, and decisions in health economics and health technology assessment. *International Journal of Technology Assessment in Health Care*. 2018;34(5):434-41.
- 2. Culyer AJ, Jönsson B, editors. *Public and Private Health Services: Complementarities and Conflicts*. Oxford: Basil Blackwell; 1986.
- 3. Williams A. The cost-benefit approach. *British Medical Bulletin*. 1974;30(3):252-6.
- 4. Birch S, Gafni A. Cost effectiveness/utility analyses. Do current decision rules lead us to where we want to be? *Journal of Health Economics*. 1992;11(3):279-96.
- 5. Coast J. Is economic evaluation in touch with society's health values? *BMJ*. 2004 November 20, 2004;329(7476):1233-6.
- 6. Drummond M. *Principles of Economic Appraisal in Health Care*. Oxford: Oxford University Press; 1980.
- 7. Drummond M, Sculpher M, Claxton K, et al. *Methods for the Economic Evaluation of Health Care Programmes*. Fourth ed. Oxford: Oxford University Press; 2015.
- 8. Smith A. *An inquiry into the nature and causes of the wealth of nations*. London: Strahan and Cadell; 1776: Book I, Chapter VI, p. 1.
- 9. Green DI. Pain-Cost and Opportunity-Cost. *The Quarterly Journal of Economics*. 1894;8(2):218-29.
- 10. Coase RH, editor. *Economic forces at work (A collection of papers by Armen Albert Alchian)*. Indianapolis: Liberty Press; 1977.
- 11. Buchanan JM. Opportunity Cost. The New Palgrave Dictionary of Economics. Second ed. London: Palgrave Macmillan UK; 2008. p. 1-5.
- 12. McIntosh E, Donaldson C, Ryan M. Recent advances in the methods of cost-benefit analysis in healthcare. Matching the art to the science. *Pharmacoeconomics*. 1999;15(4):357-67.
- 13. Sloan FA, Hsieh CR. *Health Economics (second edition)*. Cambridge, Massachusetts: MIT Press; 2017.
- 14. Tianviwat S, Chongsuvivatwong V, Birch S. Optimizing the mix of basic dental services for Southern Thai schoolchildren based on resource consumption, service needs and parental preference. *Community dentistry and oral epidemiology*. 2009;37(4):372-80.
- 15. Edlin R, McCabe C, Hulme C, et al. *Cost effectiveness modelling for health technology assessment: a practical course.* London: Adis; 2015.
- 16. Brent RJ. *Cost-benefit analysis and health care evaluations (second edition)*. Cheltenham: Edward Elgar; 2014.
- 17. Neumann PJ, Ganiats TG, Russell LB, et al., editors. *Cost-effectiveness in health and medicine (second edition)*. Oxford: Oxford University Press; 2016.
- 18. Culyer AJ. Why do/should we do economic evaluation? *Value & Outcomes Spotlight*. 2015;1(2):8-10.
- 19. Karimi M, Brazier J. Health, Health-Related Quality of Life, and Quality of Life: What is the Difference? *PharmacoEconomics*. 2016 2016/07/01;34(7):645-9.
- 20. Birch S, Donaldson C. Applications of cost-benefit analysis to health care: Departures from welfare economic theory. *Journal of Health Economics*. 1987 1987/9;6(3):211-25.
- 21. Sendi P, Gafni A, Birch S. Opportunity costs and uncertainty in the economic evaluation of health care interventions. *Health economics*. 2002;11(1):23-31.
- 22. Birch S, Gafni A. The Inconvenient Economic Truth: Benefits Forgone as an Input to Economic Evaluation and Implications for Decision-making. In: Rosen B, Israeli A, Shortell S, editors. *Improving Health and Healthcare Who is Responsible? Who is Accountable?* Jerusalem, Israel: The Israel National Institute for Health Policy Research; 2011. p. 601-22.

- 23. Nyborg K. Project evaluation with democratic decision-making: What does cost–benefit analysis really measure? *Ecological Economics*. 2014 2014/10/01/;106:124-31.
- 24. Shackley P, Donaldson C. Willingness to pay for publicly-financed health care: how should we use the numbers? *Applied Economics*. 2000 2000/12/01;32(15):2015-21.
- 25. Quade ES. A history of cost-effectiveness. Santa Monica, CA.: RAND Corporation, 1971.
- 26. Franklin B. Memoirs of Benjamin Franklin. New York: Harper & Brothers; 1842.
- 27. Simon HA. Administrative behavior: a study of decision-making processes in administrative organization. New York: Macmillan; 1957.
- 28. Ilias G, Joanna C, Ed D, et al. Maximizing Health or Sufficient Capability in Economic Evaluation? A Methodological Experiment of Treatment for Drug Addiction. *Medical Decision Making*. 2016;37(5):498-511.
- 29. Daniels N, van der Wilt GJ. Health technology assessment, deliberative process, and ethically contested issues. *International Journal of Technology Assessment in Health Care*. 2016;32(1-2):10-5.
- 30. Claxton K. The irrelevance of inference: A decision-making approach to the stochastic evaluation of health care technologies. *Journal of Health Economics*. 1999;18(3):341-64.
- 31. Paulden M. Opportunity cost and social values in health care resource allocation. Alberta: University of Alberta; 2016.
- 32. Hurley J. Chapter 16: Welfarism, extra-welfarism and evaluative economic analysis in the health sector. In: Barer ML, Getzen TE, Stoddart GL, editors. *Health, health care and health economics: perspectives on distribution*: Chichester: Wiley; 1998. pp. 373-95.
- 33. Mooney G. Values in health care. In: Lee K, editor. Economics and health planning. London: Croom Helm; 1979. p. 23–44
- 34. Culyer AJ. Cost-effectiveness thresholds in health care: a bookshelf guide to their meaning and use. *Health Economics, Policy and Law.* 2016;11(4):415-32.
- 35. Thokala P, Ochalek J, Leech AA, Tong T. Cost-Effectiveness Thresholds: the Past, the Present and the Future. *Pharmacoeconomics*. 2018;36(5):509-22.
- 36. Claxton K, Martin S, Soares M, et al. Methods for the Estimation of the NICE Cost Effectiveness Threshold. *Health Technology Assessment*. 2015;19(14), pp. xxix–xxxiv.
- 37. Birch S, Gafni A. The biggest bang for the buck or bigger bucks for the bang: the fallacy of the cost-effectiveness threshold. *Journal of Health Services Research and Policy*. 2006;11:46-51.
- 38. Caro JJ. Pursuing Efficiency: A Dead End for HTA? Value in Health. 2009;12:S49.
- 39. Cleemput I, Neyt M, Thiry N, et al. Using threshold values for cost per quality-adjusted life-year gained in healthcare decisions. *International Journal of Technology Assessment in Health Care*. 2011;27(1):71-6.
- 40. Birch S, Gafni A. Population Needs, Opportunity Costs and Economic Methods for Financial Sustainability in Health Care Systems. In: Ethgen O, Staginnus U, editors. *The Future of Health Economics*. London: Routledge; 2016, pp. 169–180.
- 41. Gafni A. Economic Evaluation of Health-care Programmes: Is CEA Better than CBA? *Environmental and Resource Economics*. 2006;34(3):407-18.
- 42. Mooney G. *The Health of Nations: Towards a New Political Economy*. London: Zed Books; 2012.
- 43. Vickers G. Systems Analysis: A Tool Subject or Judgment Demystified? *Policy Sciences*. 1981;14(1):23.
- 44. Baltussen R, Jansen MPM, Bijlmakers L, et al. Value Assessment Frameworks for HTA Agencies: The Organization of Evidence-Informed Deliberative Processes. *Value in Health*. 2017;20(2):256-60.
- 45. 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 in Health*. 2018;21(2):161-5.

- 46. Mauskopf JA. Prevalence-based economic evaluation. Value in Health. 1998 Nov;1(4):251-9.
- 47. Deaton A, Cartwright N. Understanding and misunderstanding randomized controlled trials. *Social Science & Medicine*, 2018;210:2-21.
- 48. Manski CF. The lure of incredible certitude. *Economics and Philosophy*. 2019 (Forthcoming).
- 49. Oortwijn W, Sampietro-Colom L, Habens F. Developments in value frameworks to inform the allocation of healthcare resources. *International Journal of Technology Assessment in Health Care*. 2017;33(2):1-7.
- 50. Schultze CL. Why Benefit-Cost Analysis? In: Hinrichs HH, Taylor GM, editors. *Program budgeting and benefit-cost analysis: cases, text and readings*. Pacific Palisades: Goodyear Publishing Company, Inc., 1969. pp. 1-8.
- 51. Enthoven AC. Operations research at the national policy level. In: Tucker SA, editor. *A modern design for defense decision: a McNamara-Hitch-Enthoven anthology*. Washington: Industrial College of the Armed Forces; 1966. pp. 149–160.
- 52. Marsh KD, Sculpher M, Caro JJ, Tervonen T. The Use of MCDA in HTA: Great Potential, but More Effort Needed. *Value in Health*. 2018;21(4):394-7.
- 53. Culyer AJ, Bombard Y. An Equity Framework for Health Technology Assessments. *Medical Decision Making*. 2012;32(3):428-41.
- 54. Williams B. Conflicts of values. In: Williams B, editor. *Moral Luck: Philosophical Papers 1973–1980*. Cambridge: Cambridge University Press; 1981. p. 71-82.
- 55. European network for Health Technology Assessment (EUnetHTA) project. HTA Core Model: version 3.0. <a href="http://www.corehta.info/model/HTACoreModel3.0.pdf">http://www.corehta.info/model/HTACoreModel3.0.pdf</a>. 2016 (Accessed 31st December 2018).
- 56. Sandel MJ. Market Reasoning as Moral Reasoning: Why Economists Should Re-engage with Political Philosophy. *Journal of Economic Perspectives*. 2013;27(4):121-40.
- 57. Mooney G. "Communitarian claims" as an ethical basis for allocating health care resources. *Social Science & Medicine*. 1998;47(9):1171-80.
- 58. Hitch CJ, McKean RN. *The economics of defense in the nuclear age*. Cambridge, Mass.: Harvard University Press; 1960.
- 59. Wildavsky A. *Speaking truth to power: the art and craft of policy analysis.* New Brunswick (N.J.): Transaction; 1993.
- 60. Mooney G. Priority setting in mental health services. *Applied Health Economics and Health Policy*, 2002;1(2):65-74.
- 61. Birch S. As a matter of fact: evidence-based decision-making unplugged. *Health Economics*. 1997;6(6):547-59.
- 62. Stone DA. Policy paradox: the art of political decision making. New York: W.W. Norton; 2002.
- 63. Brazier JE, Rowen D, Lloyd A, Karimi M. Future Directions in Valuing Benefits for Estimating QALYs: Is Time Up for the EQ-5D? *Value in Health*. 2019;22(1):62-8.
- 64. Culyer AJ, Chalkidou K. Economic Evaluation for Health Investments En Route to Universal Health Coverage: Cost-Benefit Analysis or Cost-Effectiveness Analysis? *Value in Health*. 2019;22(1):99-103.
- 65. Mooney G, Russell E, Weir R. Choices for health care. London: MacMillan; 1980.
- 66. O'Donnell R. Complexities in the examination of opportunity cost. *Journal of Economic Education*. 2016;47(1):26-31.
- 67. Daddario EQ. House of Representatives Bill 6698. Washington: U.S. Govt. Print. Off., March 7, 1967.
- 68. Macfie AL. What Kind of Experience is Economizing? *Ethics*. 1949;60(1):19-34.
- 69. Marseille E, Larson B, Kazi DS, et al. Thresholds for the cost-effectiveness of interventions: alternative approaches. *Bulletin of the World Health Organization*. 2015;93(2):118-24.