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Methodology

ICER Value Framework 2020 Update: Recommendations on the Aggregation of Benefits and Contextual Considerations

Aris Angelis, PhD,* Panos Kanavos, PhD, Lawrence D. Phillips, PhD

ABSTRACT

The Institute for Clinical and Economic Review (ICER) in the United States recently published a 2020 update to its value assessment framework. We are commenting on the method by which the benefits of health interventions are integrated, relating to contextual considerations and other factors relevant to an intervention's value. We start by discussing the theoretical foundations of decision analysis and its extension to multiple criteria decision analysis (MCDA). Then we provide a detailed, evidence-based response to some of the claims made by ICER with regard to the use of MCDA methods and stakeholder engagement. Finally, we provide a number of recommendations on the use of quantitative decision analysis and decision conferencing that could be of relevance to the ICER methodology. Overall, we agree that some of the proposed changes by ICER are moving in the right direction toward improving transparency in the value assessment process, but these changes are probably inadequate. We advocate that more serious attention should be paid to the use of quantitative decision analysis together with decision conferencing for the construction of value preferences via group processes for the integration of an intervention's various benefit components.

Keywords: decision conferencing, healthcare interventions, health technology assessement (HTA), Institute for Clinical and Economic Review (ICER), multiple criteria decision analysis (MCDA), quantitative decision analysis, value framework.

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Introduction

Since 2006, the Institute for Clinical and Economic Review (ICER) in the United States has been evaluating the clinical and economic value of innovative health interventions and has been making pricing recommendations with the goal of achieving "sustainable access to high value care for all patients."[1] The methodological framework it has developed focuses on the assessment of interventions' long-term value for money and short-term affordability.[1] In summary, the ICER value framework adopts a clear conceptual structure, as part of which an intervention's long-term value for money is measured through its incremental cost-effectiveness, with deliberative adjustments made possible for the existence of other benefits and contextual considerations via a majority voting process between members of its appraisal committee. More precisely, in terms of other benefits and contextual considerations, the appraisal committee members are asked to first vote individually on the existence or not of any other such benefits or disadvantages and contextual considerations, before being asked to reflect on the voting results as part of the final voting on the intervention's long-term value for money. Complementary to the intervention's long-term value for money, its short-term affordability is accounted for via the potential budget impact at health system level; if this is in excess of a national threshold (tied to the growth of the overall US economy), it acts as a signal for potential access challenges and possibly as a triggering mechanism for policy discussions and negotiation with the manufacturer.

Similar to the public engagement approach adopted by other healthcare evaluation agencies when seeking to revise their methods, ICER recently invited all interested parties to submit input for the 2020 update of its value assessment framework as part of an open consultation.[2] The fourth point of the consultation invitation focused on possible methods by which intervention benefits could be integrated, effectively relating to contextual considerations and other factors relevant when assessing an intervention's value, and possible ways of making them more explicit. Past experience and literature suggest that although similar types of evidence are being assessed during healthcare evaluations in different countries, the specific evaluation criteria used and the way they are incorporated vary, with their relative importance remaining largely unknown.[3] For example, a number of social value elements relating to the burden of disease, innovation level, socioeconomic impact, and

* Address correspondence to: Aris Angelis, PhD, LSE Health and Department of Health Policy, London School of Economics, Houghton Street, London, England WC2A 2AE, United Kingdom. Email: a.n.angelis@lse.ac.uk

other types of evidence are considered in the majority of cases; however, this usually takes place on an ad-hoc basis and lacks transparency regarding the role and impact of the various evidence components as part of a deliberative decision-making process.[3] Such differences in evaluation processes could partly explain the considerable variation observed in drug coverage decisions across countries,[4] with evidence suggesting the existence of poor to moderate agreement in health technology assessment (HTA) recommendations.[5] Any significant intercountry variability in the evaluation processes could have implications on efficiency and fairness that could risk the reasonableness and credibility of the decisions[6,7]; as such, any inconsistency deserves careful attention. In this article and in response to the ICER public consultation, we propose an improved way to incorporate benefits and other considerations in an effort to inform future updates of the value assessment framework.

A range of different methods exist for the purpose of assessing the value of new health technologies as part of healthcare evaluation, an interdisciplinary scientific field also known as HTA. In current HTA practices, a number of value assessment approaches are used across different jurisdictions, which could be broadly divided into (1) comparative clinical benefit assessments, (2) economic evaluations, and (3) value-based assessments. We perceive the ICER methodology to pertain to the "value-based assessment" group of approaches, having as its mission a desire to serve the needs of decision makers interested in measuring the benefits of interventions that go beyond the clinical value added and cost-effectiveness, aiming to capture other aspects of value as part of a more comprehensive approach. This group of approaches is not yet characterized by a single or specific type of methodology, but most approaches have emerged because of the inadequacy of economic evaluations to capture the multidimensional nature of new medicines' value in a structured and consistent way. Given that economic evaluation is founded upon the utility-maximizing behavior of a single individual, a uniform cost-effectiveness criterion applied at a heterogeneous population level is unlikely to yield Pareto-optimal resource allocations.[8] The grounding of cost-effectiveness analysis in von Neumann-Morgenstern's utility theory depends on a set of restrictive utility assumptions, including that the quality-adjusted life-year (QALY), a measure of health benefit that accounts for both length of life and quality of life, adequately represents preferences; however, this is not always the case.[8,9] This idea has important implications for the incorporation of utilities at population level, such as equity, fairness, and a range of other aspects recently identified by a special International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Task Force Report.[10] Examples of such value-based approach efforts include the tiered incremental cost-effectiveness ratio threshold in England, which is based on additional value concerns relating to end-of-life criteria (that can effectively increase the valuation of a unit of health outcome for terminal illnesses) and ultra-rare conditions,[11–13] or the fluctuating threshold in Sweden, which is based on disease severity or need.[3,14,15]

In response to the desire to improve consistency in the consideration of additional benefits and the transparency of their influence on drug coverage decisions, multiple criteria decision analysis (MCDA) has emerged as a potential methodology for value-based assessment in HTA.[16–20] Besides the generation of guidelines for the conduct of MCDA in HTA,[21,22] a number of empirical studies have been conducted in collaboration with decision makers to test and advance these methods in practice.[23–27]

Decision Analysis and MCDA

We believe that the potential usefulness of decision analytic approaches for measuring the overall value of health interventions, including aggregating different benefit components, has not been fully appreciated by ICER. Despite evolving from expected utility theory, these approaches represent an alternative way of thinking to economic evaluation. Perhaps the most relevant theoretical framework to value measurement relates to decision theory, with decision analysis, its applied discipline, acting as the practical instrument of analysis.

Howard Raiffa first defined the spirit of decision analysis as "divide and conquer: decompose a complex problem into simpler problems, get one's thinking straight on these simpler problems, paste these analyses together with logical glue, and come out with a program of action for the complex problem" (page 271).[28] Different decision analysis approaches exist, which could be broadly divided into qualitative and quantitative types; all approaches contain the definition of objectives and criteria, the identification of alternatives and options, the collection of data and evidence, and the elicitation of consequences and preferences.[29] Quantitative approaches, however, move beyond this to quantify values (or utilities), trade-offs, and uncertainty, and aggregate all components together using an algorithm, which can be as simple as a weighted average. The extension of decision analysis applications to include decision problems with multiple objectives led to the foundations of MCDA,[30] effectively a fully quantitative decision analysis approach. The development of multiattribute utility theory from a utility framework is also well illustrated elsewhere.[31] The process of MCDA in the context of HTA could be summarized in the phases of problem structuring, model building, model assessment, model appraisal, and the development of action plans.[32] In turn, these phases include the steps of selecting and structuring criteria, measuring the performance of alternative options, scoring the options, weighting the criteria, calculating weighted aggregate scores, dealing with uncertainty, and examining the findings.[21]

Evidence on whether or not the use of an algorithm is a necessary step for the aggregation of values, trade-offs, and uncertainty (eg, as part of MCDA), or whether it can be left to decision makers' own capabilities have existed in the cognitive psychology literature since the 1950s. In surveying the literature on the construction of complex values, Hastie and Dawes conclude that "the process of looking first *within* each attribute and then comparing across by some weighting system is superior to that of making global intuitive judgements *across* attributes."[33] The superiority is due in part to a limitation that Miller had noted earlier, namely that a human brain can at one time only retain 5 to 9 pieces of information.[34] In the behavioral economics literature over the last couple of decades, Thaler and Sunstein raised questions about the rationality of human judgments and decisions because of a number of biases and heuristics,[35] and, subsequently, Kahneman more thoroughly acknowledged that the human integrator has restricted capacity (or that the human brain lacks such an "integrator" altogether).[36] More recently, Montibeller and Winterfeldt described the focus on a small number of effects because of limited mental capacity as "myopic problem representation," explaining in detail the 12 cognitive biases and 14 motivational biases that can affect decision makers and experts when making judgments in decision and risk analyses.[37] Although the biases focus mainly on modeling uncertainty and values, they also include qualitative considerations associated with problem structuring. For all 26 biases, they include guidance about debiasing techniques that can eliminate or reduce them.

Response to the ICER Value Framework

Although we are not aware of the type of MCDA method(s) considered and tested by ICER, together with its independent committees, for weighting individual elements, we consider that dismissing these methods altogether on the ground that they are not "robust enough to add to reliability of value judgements" (pages 19-20)[2] to be exaggerated. A relevant question to ICER's rejection of MCDA methods would be, "Not robust compared with what?" As outlined below, there is an increasing accumulation of knowledge that the current process is flawed. At what point in time would the testing of other methods be acceptable?

There have been many successful applications of decision analysis methods across a number of areas, including in drug evaluation[26,38–43] and other nonhealth application contexts.[44–48] An insightful MCDA application is SMART Vaccines: Strategic Multi-Attribute Ranking Tool for Vaccines, developed by the Institute of Medicine in collaboration with the National Academy of Engineering.[49] From the initial conceptual demonstration of a prioritization framework to the final empirical application of a software tool for prioritizing new vaccines for development, this is a valuable open-access resource providing interested users with a hands-on experience with the concept and use of quantitative decision analysis modeling.

Another relevant MCDA application topic in the context of guiding the development of new health interventions would be along their clinical phases, using information from target product profiles (TPPs). A TPP, which provides a summary format for a new health intervention in development (eg, drug or vaccine), is described in terms of labeling concepts acting as the goal for the development program and is updated dynamically over time.[50] For example, the World Health Organization (WHO) TPPs provide sets of product attributes reflecting preferred and minimal product characteristics for specific disease areas, acting as benchmarks for product development by manufacturers.[51] Such information could be used for MCDA model building and assessment to construct value scales and score the performance of options against the attributes of interest, followed by their weighting. Therefore, in such contexts, well-designed MCDA models could act as mechanisms for guiding the development of future innovations in alignment with what decision makers value.

This is not to say that the application of MCDA in drug evaluation or HTA comes without challenges or limitations.[52–54] It might be more constructive, however, to view any robustness concerns of MCDA studies in alignment with their compliance to good methodological practice,[55] as something which has been shown to be poor in practice,[56] rather than prematurely dismissing this group of methods altogether, leaving no opportunity for their appropriate development and effective application.

Unavoidably, whether these methods are judged to be "too complicated for reliable use" (page 20)[2] or not, will depend on the knowledge, expertise, and experience of the people facilitating the overall process, especially during the stage of building a model of values by elicitating value preferences and their trade-offs. With regard to the claimed complexity and time required to build a fully quantitative MCDA model, the Benefit-Risk Project of the European Medicines Agency (EMA) created MCDA models in decision conferences for 5 new drugs, then under review by the Committee for Human Medicinal Products (CHMP), and easily created each benefit-risk balance model within just 6 hours.[57] In terms of their reliability, 3 separate studies modeling the harms of drugs with different groups of experts produced similar results with high correlations proving a high degree of reliability and accuracy.[58] Another early HTA study with 2 rounds of preference elicitation engaging participants from 3 different countries resulted in virtually identical results.[59] In any case, for some relatively easier decision problems the use of qualitative decision analysis (or other) methods may be adequate. Conditions for the choice of quantitative over qualitative approaches could be based on decision importance and analysis complexity, such as, for example, the severity of the disease indication, the unmet clinical need, the number of outcomes being assessed, the type of trade-offs to be valued, or the performance of the treatments.

Similarly, in response to any concerns "that there are no validated or consensus methods to integrate these factors into overall judgements of value," quantitative decision analysis methods are probably the most validated methods known for carrying out such integration of partial components of value judgments and deriving an overall value function, as evident through the many theoretical and empirical applications in Keeney's landmark book, *Value Focused Thinking*.[60] In his book, Keeney explains how the overall value of an option is derived from the extent to which an objective or a number of objectives are judged to add value, and the elicitation of trade-offs that provide a common measure of added value. The implication for any drug evaluation process, including HTA, is that although clinical evidence on drug performance for efficacy, safety, and quality is based on objective evidence, subjective judgments are always needed for a number of context- and evidence-related concerns; for example, the appropriateness of the data for the intended disease indication, the clinical meaningfulness of the data, or the relative clinical relevance of different benefits and risks.[29] It is in regard to this subjective interpretation of objective data that the use of quantitative decision analysis methods can be of great significance, but also in regard to the overall valuation of evidence, spanning both performance and trade-offs; this is because they can accommodate these aspects in a structured and transparent way instead of leaving them to become randomly incorporated through ad hoc and vague efforts.

Furthermore, although the establishment of cost-effectiveness thresholds, and therefore any "value-based prices," are associated with a number of theoretical and practical challenges (if not limitations),[61,62] we are glad to see that one of the ultimate aims of ICER is to "engage all stakeholders in a shared process of learning" to "offer a transparent, reliable approach" (page 23) for the integration of benefits.[2] In this regard, the social psychology literature could be very insightful. In terms of learning processes, it should become clear that preferences do not just "sit in our heads" waiting to be extracted, but they need to become constructed in a process of value measurement as part of which "added value" is always a matter of judgment. Construction of preferences can be facilitated through group elicitation processes and it could be argued that "many heads are better than one," as it has been illustrated through an experiment on probability distributions obtained from individual versus group consensus.[63] Because of a number of problems relating to interaction processes and cognitive processing, interacting groups (process techniques) might fail to generate judgments as accurate as those of their most capable members, but a combination of group facilitation with judgment analysis and information technology can significantly improve the performance of a group's interaction.[64] Nevertheless, it should be noted that when making judgments in groups, decision makers and experts are affected by group-level biases.[65] As with the case of individual judgments, group judgments are subject to several biases, with their relative magnitudes depending on factors such

as group size, initial individual judgment, magnitude of bias among individuals, and the group-judgment process adopted.[66]

Recommendations on the Use of Quantitative Decision Analysis and Decision Conferencing

The ICER value framework adopts a clear conceptual structure and a well-defined set of benefits, with an incremental cost utility ratio (ie, incremental cost per QALY gained) acting as the key evaluation metric. Until recently, the appraisal committee members followed a deliberative voting process for the aggregation of any "other benefits or disadvantages" and "contextual considerations": there was an initial voting by each member on the existence of any such benefits and considerations, followed by a reflection of the voting results, before a final voting on the interventions' long-term value for money (Fig. 1A). The explicit consideration of well-specified "other benefits or disadvantages" (n = 7) and "contextual considerations" (n = 6) is unavoidably a noteworthy feature for improving the transparency of what influences an intervention's long-term value for money.

Following the submission and review of public input to the consultation, ICER published a summary of proposed changes to its 2020 value assessment framework update, rejecting the adoption of any formal multicriteria decision analytic approach.[67] Instead, it was proposed to retain a "modified approach to integrating other factors into deliberation and decision-making," (page 32),[67] using an expanded set of potential other benefits and contextual considerations for which independent evidence appraisal committee members could vote using a 3-level Likert-scale. After noting the proposed changes, ICER published the final 2020 updates, as part of which a revised list of other benefits and contextual considerations was considered (n = 9), using the new 3-level Likert-scale voting format ranging from "lower value" to "intermediate value" to "higher value" (see Fig. 1B).[68] The goal of this adaptation was to "provide the appraisal committees with a clearer understanding of the end of the spectrum within which they are expected to vote," having also the intention "to produce a more transparent record of how the appraisal committee feels that these considerations should be applied when integrated with the cost-effectiveness results in making decisions about pricing" (page 33).[68] Nevertheless, it is not entirely clear how the various value levels will inform decision making; for example, will the lower value levels be used to justify no value increment or to justify value decrement, in the form of unchanged or decreased health-benefit (ie, ex value-based) price benchmarks, respectively? Consider the case of the lower level of "uncertainty in model assumptions" (creating significant risk that the best-case cost-effectiveness estimates are too optimistic), which could be used as a decrement of value. The same might not hold true, however, for the lower value level of "mechanism of action" (being similar compared with other active treatments), which could be used to justify a lack of value increment rather than a decrement.

We agree that the Likert-scale format change is a step in the right direction toward improving the transparency that different factors exert on decision makers' judgments; but it is still inadequate, because transparency requires access to both the underlying performance data and the model structure, in which case it relates both to valuation of performance and valuation of trade-offs. The very last stage of "human integration" required for aggregating together all these additional components into the intervention's core cost-utility ratio to derive its long-term value for money lacks transparency and, more importantly, is prone to failure and susceptible to bias, mainly because of the limited human mental capacity to support such complex tasks, as evident in the behavioral and decision science literature.[33,34,36,37,69] Incorporating additional factors without a clear conceptual framework for the expression of preferences and judgments can degrade the validity of rankings, as has already been demonstrated elsewhere.[70]

Among the most important features of quantitative decision analysis approaches and MCDA is the encompassing integration of all relevant benefits for a decision problem, and their value trade-offs, into an overall value function. Recently, the ISPOR Special Task Force on US Value Assessment Frameworks reviewed the use of MCDA for the aggregation of benefits into a single value metric and recommended further research on its use through testing in real-life decision settings because it might provide the best opportunity for improvement.[71] In the public policy domain, HM Treasury in the UK recently updated the content of The Green Book regarding guidelines on the appraisal and evaluation of central government projects and programmes to recommend the use of MCDA for estimating the value of social benefits (and costs), including for the consideration of trade-offs.[72]

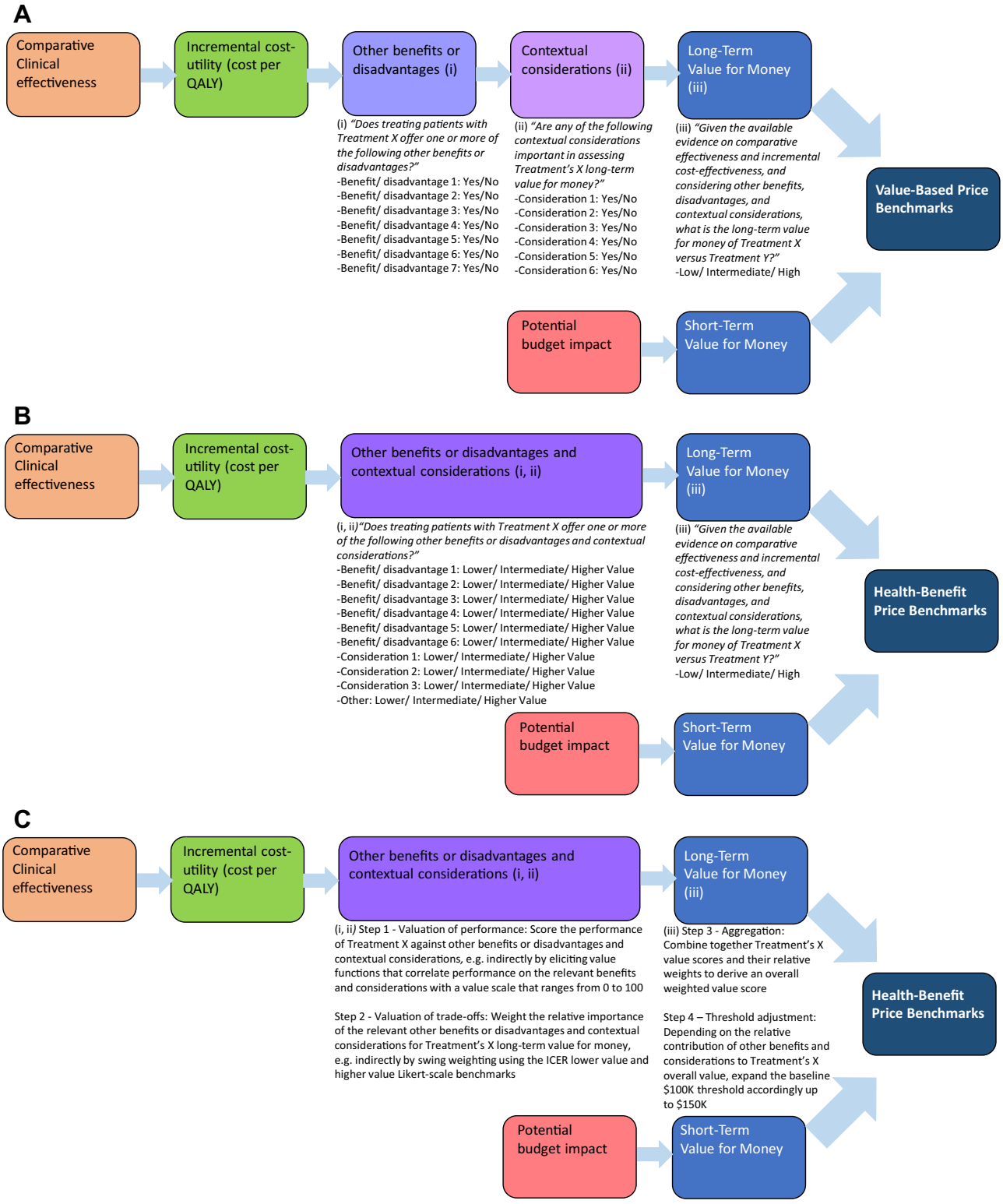
Value preferences could be constructed via decision conferencing, defined as "a gathering of key players who wish to resolve important issues facing their organization, assisted by an impartial facilitator, using a model of relevant data and judgements created on-the-spot to assist the group in thinking more clearly about the issues" (page 54).[61] Typical stages of decision conference workshops include exploring the issues, structuring and building the model, exploring the model, and agreeing on the way forward, all of which can be in alignment with requisite modeling: a decision model whose form and content are sufficient to solve a particular problem.[73]

Among the requirements for constructive decision conferencing processes are ensuring that a diversity of perspectives is represented and that a feeling of "cohesiveness" exists between participants as part of which different opinions are being heard in a trusted manner; group numbers of between 7 and 15 participants have shown to be ideal because they are small enough to allow participants to reach an agreement but sufficiently large to represent all perspectives and interests.[74] Together with appropriate facilitation from a decision analysis expert, this can engage participants in constructive discourse and peer review, thus enabling the group outputs to be better than those of the best individual in the group.[64] Hundreds of successful decision analysis applications exist worldwide for which preferences have been constructed using decision conferencing.[75,76]

A recent MCDA pilot study in collaboration with European HTA bodies revealed how the application of quantitative decision analysis in combination with decision conferencing could take place by adopting a clean slate approach without the use of economic evaluations.[27] A number of evaluation criteria were incorporated in each jurisdiction's value model and decision-maker value preferences were elicited during the decision conferences, including performance scores and criteria weights. Following the estimation of the drugs' overall benefits, a subsequent consideration of drug costs enabled the demonstration of value for money in the form of estimated "cost per unit of value" ratios. Although findings revealed some differences in value preferences across countries, drug rankings remained consistent. Importantly, the study demonstrated how MCDA could act as a decision support tool for HTA, because of the transparency in the construction of value preferences in a collaborative manner.

In the context of HTA decision making, assuming that an agreement has been reached regarding the level of the cost-effectiveness threshold(s), adjusting the threshold or the interventions' incremental cost utility ratio to accommodate other benefits and contextual considerations should be possible. For example, as part of an incremental MCDA approach to economic

Figure 1. Previous (A), newly updated (B), and recommended (C) ICER Value Assessment Framework stages focusing on the aggregation of (1) other benefits or disadvantages and (2) contextual considerations, for (3) estimating long-term value for money.



ICER indicates Institute for Clinical and Economic Review.

evaluation, a "baseline" threshold could be expanded proportionally with any additional value not captured by the QALY component.[77] Alternatively, as part of a clean slate approach independent from economic evaluations, assuming the existence of a defined budget (eg, within a particular indication or therapeutic area), a value function could be used with the purchasing

costs of the interventions to calculate multidimensional value for money ratios; this could be followed by a multicriteria portfolio decision analysis aiming to maximize benefits given the budget constraint, while allowing for opportunity costs to be naturally incorporated.[78] In any case, further research would be required to develop and test such new methodological applications.

In a similar fashion, for the context of ICER's assessments, the selection and aggregation of any relevant "other benefits or disadvantages" and "contextual considerations," including the assignment of relative weights of importance, could be implemented at the level of the independent evidence appraisal committees (see Fig. 1C). Given ICER's use of value-based price benchmarks representing acceptable long-term value for money, a possible way to fuse together the MCDA results with the use of a baseline incremental cost-utility ratio could be by expanding the latter proportionally to reflect how much of the model's total value is accounted for by the non-QALY component.[77]

ICER's Past Assessment of Tisagenlecleucel for Pediatric B-cell Acute Lymphoblastic Leukemia

As an illustrative example, the case of tisagenlecleucel's ICER assessment for the treatment of pediatric B-cell acute lymphoblastic leukemia (ALL) could be considered.[79] With regard to "other benefits or disadvantages," the question was first asked: "Does treating patients with tisagenlecleucel offer one or more of the following other benefits?" and then 6 different benefit aspects were specified (Table 1). The 13-member evidence committee unanimously (13 out of 13) voted that the "intervention offers a novel mechanism of action or approach that will allow successful treatment of many patients who have failed other available treatments." The majority of the evidence committee (9 out of 13) also voted that the "intervention will have a significant impact on improving return to work and/or overall productivity." Finally, only a minority of the committee voted in favor that the "intervention will significantly reduce caregiver or broader family burden" (4 out of 13), and no member of the committee voted in favor of the existence of any other benefits.

With regard to "contextual considerations," the evidence committee was then asked: "Are any of the following contextual considerations important in assessing tisagenlecleucel's long-term value for money?", followed by the specification of 6 different contextual aspects (Table 2). The majority of the committee (12 out of 13) voted that the "intervention is intended for the care of individuals with a condition of particularly high severity," that there is "significant uncertainty about the long-term risk of serious side effects" (9 out of 13), and that there is "significant uncertainty about the magnitude or durability of the long-term benefits" (9 out of 13). A minority of the committee voted that the "intervention is the first to offer any improvement for patients with this condition" (5 out of 13), that "there are additional contextual considerations that should have an important role in judgments of the value of this intervention" (4 out of 13), and that "the intervention is intended for the care of individuals with a condition that represents a particularly high lifetime burden of illness" (1 out of 13).

After these 2 voting procedures, the last voting question corresponded to tisagenlecleucel's overall long-term value for money based on the totality of the evidence: "Given the available evidence on comparative effectiveness and incremental cost-effectiveness, and considering other benefits, disadvantages, and contextual considerations, what is the long-term value for money of treatment with tisagenlecleucel versus treatment with clofarabine (Table 3)?" In response to that question, 7 members voted "intermediate," 3 members voted "high," and 1 member voted "low," with 2 members abstaining; panel members that voted "intermediate" or "low" noted that "the high degree of uncertainty regarding long-term benefits and harms" led them to vote for a lower category of value than they would have done otherwise, with the two abstaining members also disclosing the same uncertainty issues responsible for precluding their ability to assess long-term value for money.

Based on the above, it becomes evident that the overall 3-step voting process relating to other benefits, contextual considerations, and overall long-term value for money is associated with various challenges. Initially, the binary voting on the existence of other benefits and contextual considerations in the first 2 stages excludes performance valuation, towards understanding the magnitudes of committee members' value preferences. This could be partially addressed through the use of the recently introduced Likert-scale but still, the relationship between product performance (in terms of benefits) or condition characteristics (in terms of contextual considerations) and value preferences would be characterized by limited granularity. Beyond that, valuation of trade-offs associated with the relative importance of the various aspects (pertaining to other benefits and contextual considerations against each other, and versus the core cost per QALY metric) would still remain completely unaccounted for. Ultimately, the robustness-determining step of the overall process would be the overly complex integration of all the evidence pieces together in the last stage that also remains completely unfacilitated and which is limited by restricted human mental capacity to carry out such tasks.

Assuming that a threshold range of $100 000 to $150 000 per QALY reflects the maximum acceptable long-term value for money based on which health-benefit (ie, ex value-based) price benchmarks are estimated, $100 000 per QALY could hypothetically be chosen as the baseline threshold for interventions whose value is not associated with any other benefits or contextual

Table 1. List of relevant "other benefits or disadvantages" and respective voting results for tisagenlecleucel in the ICER assessment.

This intervention offers reduced complexity that will significantly improve patient outcomes.	0/13
This intervention will reduce important health disparities across racial, ethnic, gender, socioeconomic, or regional categories.	0/13
This intervention will significantly reduce caregiver or broader family burden.	4/13
This intervention offers a novel mechanism of action or approach that will allow for successful treatment of many patients who have failed other available treatments.	13/13
This intervention will have a significant impact on improving return to work and/or overall productivity.	9/13
There are other important benefits or disadvantages that should have an important role in judgments of the value of this intervention.	0/13

ICER indicates Institute for Clinical and Economic Review.

Table 2. List of relevant "contextual considerations" and respective voting results for tisagenlecleucel in the ICER assessment.

This intervention is intended for the care of individuals with a condition of particularly high severity in terms of impact on length of life and/or quality of life.	12/13
This intervention is intended for the care of individuals with a condition that represents a particularly high lifetime burden of illness.	1/13
This intervention is the first to offer any improvement for patients with this condition.	5/13
Compared with the clofarabine or comparable chemo- or immunotherapy, there is significant uncertainty about the long-term risk of serious side effects of this intervention.	9/13
Compared with the clofarabine or comparable chemo- or immunotherapy, there is significant uncertainty about the magnitude or durability of the long-term benefits of this intervention.	9/13
There are additional contextual considerations that should have an important role in judgments of the value of this intervention.	4/13

considerations. This baseline threshold could then be expanded up to $150 000 per QALY if the intervention fully satisfies all the additional benefit and contextual consideration–related value aspects, or a certain number of them deemed to be sufficient for reaching the maximum threshold (see Fig. 1C). For this to take place, the relative importance of each additional value aspect that is relevant for the particular decision context would need to be elicited as part of each technology's evidence appraisal, such as, for example, using swing weighting via decision conferencing.

Ultimately, the decision of whether an intervention's long-term value for money is acceptable and at what price would be fully transparent. This would be reflected based on the intervention's performance on an explicit set of evaluation criteria but also the relevance and relative importance of this performance for the particular decision context, as judged by the members of the evidence appraisal committee. Nevertheless, the details of such a socio-technical process would require much attention and it should be clear that MCDA, as an approach, does not provide an "off-the-shelf" template. Instead, it must be tailor-made for each field of inquiry, as it has been evident from past experience with EMA and EU HTA bodies, both of which took several years to establish MCDA feasibility tests and methodological developments.

Conclusion

Overall, we propose that the combination of quantitative decision analysis together with decision conferencing to be considered by ICER for the purpose of integrating together the various benefit components of interventions through the engagement of different stakeholders following group processes for the construction of value preferences. Ideally, any potential dismissal of MCDA methods by decision-makers and HTA institutions, including healthcare evaluation agencies like ICER, should be preceded by adequate research in their development and application; for example, this could take the form of case study work involving specific MCDA techniques and the conduct of participatory processes to arrive at the value of interventions for different contexts. We believe that through further collaborative work and improvement by MCDA practitioners and HTA researchers, quantitative decision analysis methods could act as valuable decision-making tools for ICER and other organizations keen in using value-based assessment approaches for HTA. Furthermore, given their explicit and transparent nature, such methods could serve as a template for future innovation, by guiding the development of new health interventions to what the relevant actors and society value most. We would therefore recommend their meticulous hands-on testing via continuous practical applications, in collaboration with the relevant HTA institutions, decision makers, and stakeholders. ICER's mantra is known to be "Fair Pricing, Fair Access, Future Innovation"; however, fair pricing relies on accurate, consistent, and transparent assessment, for which the appropriate construction of value preferences and aggregation of benefits is crucial.

Table 3. Voting results for tisagenlecleucel's overall long-term value for money in the ICER assessment.

Low: 1/13	Intermediate: 7/13	High: 3/13	Abstain: 2/13

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Author's Affiliations: Department of Health Policy, London School of Economics, London, England, UK (Angelis, Kanavos); Department of Management, London School of Economics, London, England, UK (Phillips).

Author Contributions: *Concept and design*: Angelis, Kanavos, Phillips
Acquisition of data: Angelis
Analysis and interpretation of data: Angelis, Kanavos, Phillips
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