Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies

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**The author has issued a letter of dissent. It is available here: https://hemamethods.org/wp-content/uploads/2026/03/Letter-of-dissent-Steuten.pdf

HEMA's policies for managing potential conflicts of interest, and individual disclosures for all Working Group members, are available here: https://hemamethods.org/hema-working-group/

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Executive Summary

Background and context

The Institute for Clinical and Economic Review (ICER – USA), Canada's Drug Agency (CDA-AMC), and the National Institute for Health and Care Excellence (NICE - England) convened the Health Economics Methods Advisory (HEMA) group to provide independent and critical guidance on new methods and processes for economic evaluation. This first HEMA report focuses on potential extensions to the *benefits* considered in economic evaluation.

Economic evaluation used in the field of Health Technology Assessment (HTA) has largely relied on the "core" elements of net costs and health benefits reflected in changes in survival duration and/or health-related quality of life. There have been recent calls for "novel value elements" to be added to this standard approach. These include a variety of concepts such as broadening the perspective regarding which costs and whose benefits should be included, more fully reflecting individuals' preferences in relation to health benefits (e.g., attitudes to risk), incorporating additional costs, accounting for equity, including benefits which are unrelated to changes in health outcomes, and reflecting implications of funding decisions for innovation. These suggestions cover a range of different aspects of economic evaluation. *This report focuses on a subset: those "value elements" that relate to the measure of benefit used in such analyses*.

Why is economic evaluation undertaken?

Economic evaluation to support HTA decisions amounts to assessing the claims of different groups to draw on a health system's limited resources, which needs consideration of relevant benefits and costs. The specification of which benefits are relevant is normative rather than technical and, as for all policy areas, is open to debate. Once relevant benefits are defined, the magnitude of the additional benefits conferred by a given intervention is determined by evidence, which is also the case in estimating its additional cost.

Any decision about whether to fund the intervention, however, also needs to consider evidence on opportunity costs given limits on expenditure in all health systems. That is, the implications for others of any additional cost of the intervention in terms of forgone benefits when their services are displaced or unfunded. Decisions rest on the balance of evidence regarding a new technology's additional benefits and opportunity costs – is there a net gain in benefit across all individuals for whom the system is responsible? This evidential quantification of benefits, costs, and opportunity costs is essential to any economic evaluation. If relevant additional benefits are included in economic evaluation, the scope of opportunity costs considered must also expand to reflect the extent to which that additional benefit is forgone by those patients experiencing displaced or unfunded care due to the extra cost of the new intervention. Looking across HTA decisions for different types of interventions, such an extension in benefits may suggest some interventions are more valuable than with a narrower expression of benefits, and some may be less valuable.

Aims and objectives

The aim of the report is to provide a framework to help HTA organizations (specifically, those that have commissioned HEMA) to make decisions on possible changes to the specification of benefits they use in economic evaluation. It has three objectives:

- To propose a set of guiding principles to support HTA organizations in making decisions about potential changes in the benefit function used in economic evaluation.
- To appraise recent proposals to extend or adapt benefits used in economic evaluation for HTA.
- To apply the principles to these recent proposals with recommendations for HTA organizations.

Principles

The proposed set of principles applied are:

- ***Relevance***: benefits must be relevant for the decision-making HTA organization and for the decisions of interest. This should reflect the normative choices made by HTA organizations, which reflect their statutory, legal, or other authorities, as well as the expressed objectives and responsibilities of those responsible for decisions.
- ***Valuation***: different benefits must be aggregated with appropriate weighting (current approaches by HTA organizations use community preferences [valuations] rather than those of patients). Benefits need to be valued consistently across disease areas. Methods need to be practical, so that they can be applied straightforwardly and transparently in research and "real world" settings. Double-counting must be avoided.
- ***Opportunity cost***: there is a need to reflect any additional benefit in the assessment of opportunity costs. Any additional benefit should be reflected not just in the evaluation of new technologies, but also the outcomes that would have accrued to current or future patients had resources not been devoted to those new technologies.

Benefits considered

"Novel value elements" deemed in-scope for this discussion paper are benefits that constitute part of the objectives that decision makers may seek to achieve from health systems' limited resources. These include broad domains related to risk attitudes (e.g., the value of hope and insurance value); process benefits (such as the value of knowing about disease from diagnostics); equity (e.g., giving larger weight to potential health gains for those subject to unfair health inequalities); and expanding the perspective of economic evaluation (e.g., including productivity).

Risk Attitudes

The foundation for several proposed "novel value elements" is the claim that individuals' risk attitudes to their own health should be reflected in assessments of benefits. In particular, this relates to value elements termed "outcome certainty" and "disease risk reduction." This contrasts with the methods currently supported by HTA organizations, which effectively assume preferences over health are "risk neutral."

The Generalized Risk-Adjusted Cost-Effectiveness (GRACE) framework claims to bring individuals' risk attitudes into economic evaluation and leads to concepts like the value of hope and insurance. GRACE is not consistent about whose preferences should be used, varying between individuals assessing for themselves the benefits from available treatments, those considering the purchase of insurance, and the wider community.

Standard methods of economic evaluation place patients at the center of describing benefits by measuring the impact on patients' self-reported health. However, HTA agencies have adopted the normative position that the *valuation* of these health benefits should reflect the preferences of the broader community, consistent with the remits of their funders. The community does, of course, include past, current, and future patients. In this sense, the use of community preferences represents a collective perspective on how health gains should be valued across society. Patient input remains essential throughout economic evaluation. This role is distinct from the technical question of how benefits are ultimately valued and aggregated for decision making, but it reinforces that patients remain central to the purpose and practice of economic evaluation.

Methods used to derive the measure of lifetime health gain, such as the quality-adjusted life year or equal value of life years gained, make many simplifying assumptions, which means they cannot claim to represent preferences or utilities directly. These assumptions include independence of the assessment of health-related quality of life (HRQoL) from survival duration and vice versa, risk neutrality over survival, additivity over time, and constant proportional trade-off. There have been several attempts over the years to develop a simple preference-weighted measure of lifetime health gain that is closer to preferences or utilities. While some of these approaches offer theoretical advantages, these must be balanced against practical limitations. In practice, implementation of proposed alternatives has been very limited due to the need to repeat valuation studies for each new intervention under evaluation and the consequent burden on respondents.

If the remit of HTA agencies changes to account for individual risk preferences of the directly affected patients and patients impacted through the opportunity cost, some features like those addressed by the GRACE framework may need to be incorporated. Doing so would face practical barriers. However, there are also theoretical gaps in the currently proposed GRACE framework. Key studies undertaken as part of the development of GRACE need further extension and validation. Although such methods are not ready for "prime time" in HTA, further research on extending the measure of lifetime health gain to reflect preferences more fully – including but not necessarily limited to the incorporation of risk attitudes - may be

warranted. This should, however, consider emerging evidence on the extent to which such developments would materially affect the results of economic evaluations and HTA decisions.

Process benefits

Another suggested additional benefit relates to aspects of the process of health care which, despite not generating a change in health outcomes, might be something over which individuals have preferences. One example of this is what is referred to as the "value of knowing" in the broad area of diagnostics. Such interventions are routinely subject to economic evaluation in terms of the health benefit they generate by changing treatment decisions. The value of knowing suggests patients may derive benefit from the information diagnostics provide aside from its instrumental value in promoting changes to decisions that promote health for the patient. This opens up the stark choice for decision-makers about whether health benefits could legitimately be forgone to promote non-health changes in well-being (positive or negative) associated with the experience of having information, separate from any health benefits associated with acting on the information (which are already included).

Distinguishing health from "process" benefits of a health care intervention can be challenging conceptually and in terms of measurement. Before extending the measure of benefit used in economic evaluation to include these process effects, it would be important to understand whether they are (at least partially) included in existing measures of HRQoL used routinely in studies. If these are not covered, consideration should be given to more sensitive forms of measurement of HRQoL rather than adding new forms of valuation.

Equity

Although the focus of economic evaluation in HTA is to support decisions to enhance population health from available resources, incorporating equity considerations has been discussed for many years. The term "equity", often presented as a "novel value element", is used broadly and can encompass a range of concerns. A prominent example of equity in economic evaluation is to consider different types of unfair inequality in health outcomes and how these might be reflected in economic evaluation using distributional cost-effectiveness analysis (DCEA). However, reaching a broad consensus on exactly what constitutes fairness in resource allocation is challenging, mirroring the enduring practical barriers to quantifying health-related social welfare. Community preferences have been, and continue to be used in HTA, but decision makers need to determine which concept(s) of equity are most relevant to their remit to which these preferences relate – e.g., baseline health state, lifetime health, and/or social disadvantage.

If equity considerations are deemed important in the context of the evaluation of new technologies, they must also apply more generally across resource allocation decisions. This implies that equity must be reflected in valuing the health forgone in terms of opportunity costs. Where equity weighting is adopted, it should be used consistently, including in situations where interventions may increase as well as reduce inequalities. Furthermore, because of the

potential impact on equity through health forgone in opportunity costs, these methods should be used routinely whatever the impact on inequalities of the technology under evaluation. A reasonable exception might be where it can be shown empirically that any health opportunity costs are neutral with respect to the distribution of benefits (for example, through estimates of marginal productivity on the distributional effects of health system expenditure).

Perspective

Some proposed additional novel value elements may imply a broadening of the perspective of economic evaluation, beyond a focus on health-related benefits and costs falling on the health care system. The view that it is right for economic evaluation to consider benefits that fall outside of health and extend to other sectors of the economy is widely held and understandable.

Some broader effects that have been discussed in the literature, such as spillovers to carers and families in terms of health, are already recommended for inclusion as part of standard methods. In practice, adoption of these health impacts has been limited by evidential gaps. Progress has been made in recent years, particularly in relation to health impacts on family carers, but there remains significant scope for development here. When it comes to including a wider set of non-health impacts, such as productivity or impacts on other sectors like education, the challenge is to specify how health gain should be traded off against other socially valuable attributes of interventions, and in terms of opportunity costs. Although the widely used term "societal perspective" implies there is one way to aggregate across health and wider effects, this is not the case. Agreeing to a transparent and widely accepted set of weights to be used consistently in decision-making is likely to be a challenge. However, identifying and, where possible, quantifying these wider effects and their associated opportunity costs through approaches, such as an “impact inventory”, may improve transparency. Even where such effects are not formally incorporated into the benefit function, documenting them can help inform wider policy considerations when they are significant.

Based on this report, the following recommendations are made for HTA organizations:

1. When considering additional measures of benefit for economic evaluation, HTA organizations should assess these against the guiding principles of relevance, valuation, and opportunity cost outlined in this report.

2. No additional benefits should be routinely incorporated into economic evaluation until there is an evidential basis to reflect them in opportunity costs. This is essential to ensure comparability and consistency in decision-making, and to avoid inappropriate resource allocation.

3. The deliberative process within HTA may consider potential additional benefits qualitatively, but it should not be used in a way that bypasses the consideration of opportunity costs. HTA organizations should consider how the design of their processes,

including any pre-specification, supports transparent and consistent consideration of opportunity costs.

4. A clear normative and practical case for routinely incorporating risk preferences into a measure of lifetime health gain is necessary. This needs to consider both the theoretical merit of doing so and the importance of reflecting risk attitudes compared with other aspects of preferences that are simplified in standard methods.

5. The practical case for routinely incorporating risk preferences into a measure of lifetime health gain should consider: whose preferences should be elicited; over which aspects of health they should apply; the need to produce robust evidence for the relevant jurisdictions; and whether such developments would significantly affect HTA decisions.

6. HTA organizations that have adopted a normative position to use community preferences to define benefits for economic evaluation should be aware that simultaneously incorporating aspects of patients' preferences would be a departure from and inconsistent with this view.

7. Before considering whether specific benefits associated with the process of care (e.g., the value of knowing about disease prognosis) should be included in economic evaluation, further research is necessary to ensure these effects are not already being captured in HRQoL measures, or this could not be achieved with the use or development of more sensitive HRQoL measures.

8. HTA organizations should provide a clear normative basis and measurement approach when applying "modifiers" (e.g., for severity) as an expression of equity considerations.

9. Distributional cost-effectiveness analysis provides a framework for building distributional considerations into economic evaluation. If HTA organizations consider its use relevant to their responsibilities, this should relate to technologies which may increase as well as reduce inequalities, and opportunity costs should always reflect any impact of additional expenditure on inequalities.

10. The generation of improved empirical evidence of spillover health impacts on carers and other family members should be encouraged.

11. If broadening the perspective of economic evaluation to include benefits to the wider economy (e.g., productivity) or other sectors (e.g., education) is considered consistent with decision makers' remits, additional evidence requirements must be considered (e.g., opportunity costs by sector and trade-offs between different outcomes relevant to each sector).

12. HTA organizations should consider the routine use of "impact inventories" to understand and enhance transparency regarding any significant broader impacts of health technologies, but this should also quantify opportunity costs for relevant outcomes.

1. Introduction

1.1. Background

Health technology assessment (HTA) has been defined as a multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle.[6] It is used in many countries to assess and generate evidence to support decisions about what new medicines and other interventions should be funded from the resources available to the health system(s) in those jurisdictions, and at what prices. HTA processes are in place in various countries with health systems that draw on collective funding, through taxation, insurance, or combinations of both, to provide care and services to specified populations. Some of these use economic evaluation as part of HTA as a quantitative framework given the funding constraints that exist in all systems. In broad terms, economic evaluation in HTA seeks to establish whether the additional benefits generated by (typically new and mainly pharmaceutical) interventions can justify calls on limited available funding.

The methods of economic evaluation have developed over time and have always been contentious, given that they expose a series of normative judgements about the objectives of collectively funded health care. In recent years, there have been calls for these approaches to incorporate additional or "novel value elements". These include a variety of concepts such as broadening the perspective regarding which costs and whose benefits should be included, reflecting more fully individuals' preferences (e.g., attitudes to risk), incorporating additional costs, accounting for equity, including benefits which are unrelated to changes in health outcomes, and reflecting implications of funding decisions for innovation. Many of these ideas have been summarized in the "ISPOR Value Flower" which followed the ISPOR (The Professional Society for Health Economics and Outcomes Research) task force on defining elements of value in health care.[7] "Generalized Cost-Effectiveness Analysis" (GCEA) is the term recently used to describe proposals to incorporate these ISPOR Value Flower elements into cost-effectiveness calculations.[8]

Some of these proposed methods are already in place in some jurisdictions. Others have been suggested previously, and some are new and are the subject of ongoing research. In this first Health Economics Methods Advisory (HEMA) report, we consider a specific area where extensions and adaptations in economic evaluation methods have been suggested – what is included in the measure of *benefit*. Other proposed elements of value may be considered in later reports. Alongside quantitative economic evaluation methods, HTA also typically includes deliberative processes to consider some evidence. Although deliberation is outside the scope of this report, Box 1 provides a brief description of its use alongside economic evaluation in HTA.

To distinguish the focus of the report from the broader interest in novel elements of value, it is important to define the term "benefit". Built into any economic evaluation is an assumption, understanding, or explicit instruction about decision-makers' objectives. That is, attributes of social value that decision makers consider they are tasked with promoting, given the limited

resources available and other constraints. These social objectives are normative in nature, so they cannot be defined using technical methods as right or wrong. They are also complex, and it is unlikely that a quantitative analysis will be able to capture them fully; there are also inevitable trade-offs between them. As such, “benefits" for the purpose of this report can be understood as measurable outcomes that reflect (unavoidably, partially, and imperfectly) these attributes of social value embedded in the authority (remits) of the organizations they represent, and for which those organizations are (at least in principle) held accountable. At the level of specific interventions, these attributes can be positive or negative (e.g., health benefits or harms).

The attributes of social value are distinct from the resources available to achieve them; for example, achieving cost savings by the introduction of a new technology is not considered a direct benefit, although they can generate benefits indirectly by freeing up resources for the management of other patients. There is significant variation between jurisdictions in the extent to which these attributes are explicitly defined in policy and reflected in HTA. Furthermore, there are inevitably multiple potential attributes, so it is helpful to think of a “benefit function” as an aggregation or “valuation” of measurable outcomes using weights reflecting the preferences of a relevant group (e.g., the community, patients, and decision makers).

Box 1. Deliberation in HTA

The focus of this report is quantitative economic evaluation to inform decisions. However, HTA organizations also use deliberation, typically by a multi-disciplinary panel that operates independently of the HTA agency or organization. One form of deliberation takes place in reviewing whether the modelling undertaken for economic evaluation is suitable to support decision-making – for example, does it represent the decision problem appropriately, are the model inputs the most suitable, etc.

Another way deliberation is used is to exchange views and perspectives on "contextual factors" or considerations that expand the evidence beyond quantification in analyses such as comparative-effectiveness and economic evaluation.[1,2] This report is focused on quantified benefits as well as their weighting and aggregation, leaving out contextual factors. However, in practice, as part of health care priority setting any benefits (or disbenefits in terms, for example, of side effects) that fit within the scope of the principles outlined in this report, but which cannot be quantified, can and often are moved to a deliberative step. Indeed, constructs such as equity in health decision-making and community-level benefits are often considered in HTA deliberation.[3] Like changes in weighting and aggregation of benefits, it is important for HTA organizations to acknowledge that movement to the deliberative step constitutes movement away from economic evaluation and into a broader decision process. For example, empirical evidence suggests group perceptions of the value of health technologies and coverage and reimbursement decisions are not always aligned with economic evaluation conclusions.[3,4]

While the specifics of this broader decision process are out of scope for this report, continued proposals to extend the benefit function may lead to HTA organizations asking how much "weight" should be placed on qualitative value elements against often quantitative evidence on the cost-effectiveness of new health care technologies.[5] In other words, any deliberative process may acknowledge opportunity cost as a factor, but a major challenge remains in appropriately accounting for the additional unquantified value elements in opportunity costs. Recent good practice recommendations on deliberative practices suggest prioritization as an important step for specifying the scope of deliberation to ensure transparency and consistency in decision-making.[1]

Given that economic evaluation supports decisions about how resources are allocated across different indications and clinical or service areas, a key principle is that the benefit function is "generic". This means the extra benefits associated with new interventions can be compared across disparate conditions, providing a common yardstick of performance. Importantly, any support for decisions where a new technology costs more overall than the intervention(s) it is replacing requires economic evaluation to reflect the benefits that could have been generated by using those additional resources elsewhere – in other words, the *opportunity costs*. A generic benefit function is also necessary so that it applies symmetrically to both the additional benefits of new investments and those forgone by other patients because of the cost of the new investments. Given the range of decisions HTA organizations need to take over disease areas and time, the definition of a benefit function that is consistent is important.

In the field of HTA, the benefit function has focused on health outcomes on the basis that, even if this does not cover the entirety of decision makers' remits, it is likely to be front and center. It has distinguished the potential impact of interventions on survival duration and health-related

quality of life (HRQoL). The scope of the former is uncontroversial, although the evidence is often a challenge to generate. The latter has generally reflected preferences of samples of individuals, but specific methods to elicit them have been a source of debate, and there is variation in how HRQoL is valued and its weights determined. The benefit function that has typically brought these two components of health benefit together is the quality-adjusted life year (QALY). Although this benefit function has been used in numerous evaluations over many years, it has been controversial, as would be any defined function. Alternatives to the QALY include the disability-adjusted life-year (DALY), the equal value life-year (evLY), and health years in total (HYT). There have been several attempts over the years to develop a simple preference-weighted measure of lifetime health gain that is closer to preferences or utilities. While some of these approaches may offer theoretical advantages, attempts to address the perceived weaknesses of the QALY have drawn further critiques.[9] A discussion of the relevant advantages and disadvantages of each measure is outside the scope of this report. Therefore, in the remainder of this report, we refer generally to any measure of preference-weighted health as "lifetime health gain."

1.2. Aims and Objectives

The aim of this report is to provide a framework to help decision-making (HTA) organizations decide on possible changes to the benefit function they use in economic evaluation. Although the framework is intended to be broadly applicable across HTA organizations, the focus is on the needs of three organizations: the National Institute for Health and Care Excellence (NICE) in England, Canada's Drug Agency (CDA-AMC), and the Institute for Clinical and Economic Review (ICER) in the USA. The health systems in which these organizations operate, their roles and responsibilities, and their current preferred methods of deriving benefit functions for economic evaluation differ in various ways (see Table 1), which may shape the extent to which modifications to the benefit function are feasible, appropriate, or desirable in each setting.

HEMA's role is to provide independent guidance on methods for these different organizations. Those HTA organizations have previously selected normative frameworks for their decision-making which reflect the remits and constraints of the health systems using their assessments. This includes decisions about the existing benefit functions they use in economic evaluation and aspects of how this is derived – for example, whose preferences are used as weights within the measure of lifetime health gain. These normative choices are open to debate, but they are not technically right or wrong, and the HTA organizations (and any organizations to which they report) are the appropriate sources of those judgments. As such, HEMA will take these normative positions as given and advise about the future methods developments needed to reflect the implications of these normative positions. However, it may also be the case that, despite these normative starting points, HEMA may identify and communicate weaknesses in current methods used or advocated by the HTA organizations, and it is not HEMA's responsibility to defend the methods decisions taken previously by these organizations.

Table 1. Health Technology Assessment Descriptions

Health Technology Assessment Entity	Description
The National Institute for Health and Care Excellence (NICE)	NICE was formed in 1999 as a national advisory body accountable to the Secretary of State for Health with its functions set in legislation. NICE provides advice to the largely tax-funded National Health Service (NHS) in England on the clinical and cost effectiveness of health technologies. The NHS has a budget set by government. When NICE recommends a technology through its technology appraisal or highly specialized technologies program, the NHS must make sure funds are available within 3 months (unless otherwise specified) of the guidance publication. Under its statutory framework, NICE is required to have regard to the broad balance between the benefits and costs of the provision of health services or of social care in England, the degree of need of persons for health services or social care in England, and the desirability of promoting innovation in the provision of health services or of social care in England. This is reflected in NICE's statement of principles.
Canada's Drug Agency (CDA-AMC)	Canada's health-care system is publicly funded and provides universal coverage for hospital and physician services. Coverage for prescription drugs is made up of public and private insurance. CDA-AMC is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the appropriate use of drugs and medical devices in the health care system. CDA-AMC's Drug Reimbursement Reviews provide non-binding recommendations to federal, provincial, and territorial public drug plans. Different plans have different mandates and priorities and make their decisions independent of one another.
Institute for Clinical and Economic Review (ICER)	In the United States, the Institute for Clinical and Economic Review (ICER) is an independent, non-profit research institute that conducts evidence-based reviews of health care interventions, including prescription drugs, other treatments, and diagnostic tests. In collaboration with patients, clinical experts, and other key stakeholders, ICER analyzes the available evidence on the benefits and risks of these interventions to measure their value and suggest fair prices. ICER also regularly reports on the barriers to care for patients and recommends solutions to ensure fair access to prescription drugs.

The specific objectives of this HEMA report are:

I. To define a set of guiding principles to support HTA organizations' decisions about potential changes in the benefit function used in economic evaluation.

II. To appraise recent proposals to extend or to adapt the benefit function used in HTA. Attention is given to frameworks, such as the ISPOR Value Flower and GCEA, which have shaped much of the recent debate. Others are also considered. No attempt is made to be exhaustive regarding these proposals.

III. To apply the proposed principles to these additional benefits and generate recommendations for HTA organizations.

We first set out the purpose of economic evaluation in the context of health care decision making (Section 2). We then propose a set of key principles to be used to determine which benefits are relevant (Section 3). Section 4 provides an overview of proposed additional value elements and classifies these according to the issues they refer to, and identifies which are of potential relevance to the assessment of benefits. Those elements considered in scope for the assessment of benefits are assessed according to the key principles. Section 5 provides a discussion, and Section 6 offers key recommendations for HTA organizations when considering additions to the benefit function.

2. Why Is Economic Evaluation Undertaken?

Economic evaluation seeks to inform collective-level decisions regarding the adoption of and/or the reimbursement/funding for specific interventions using a defined benefit function and funding envelope. Inevitably, the specification of a benefit function is contested – both its constituent parts and the weights necessary for valuation. This reflects a broader understanding of the challenges of defining what economists call "social welfare" for policy making. For many years, economists have debated the role economic analysis should play in policy decisions (more generally called "social choice"), and the field of health has been central to these deliberations.[9] Some have argued that it is possible to define social welfare by observing competitive markets and, where these do not exist, by measuring individuals' preferences – so-called "welfarists".[10] Others have argued that, although individual preferences are important, there are other considerations, such as people's actual conditions and values, termed "extra-welfarists" or "non-welfarists".[11,12] The latter approach has dominated the development of economic evaluation in health, which has adopted a more modest approach to inform decisions. This has involved using the (inevitably incomplete) information about the normative values, objectives, and constraints delegated to decision makers by relevant "higher authorities" such as regional or central government.[13] Using available evidence, economic evaluation exposes relevant trade-offs and reflects the implications of decisions back to those making them which, in principle, can hold these governance arrangements to account.

On the cost side of resource allocation decisions, economic evaluation needs to recognize the constraints facing health care systems, most obviously limits on the additional expenditure they can devote to new interventions. In some health care systems (e.g., the NHS in the UK), there are explicit budget constraints set by governments for specific time periods. Deficits may sometimes be run or changes made to planned budgets, but this does not detract from the fact that expenditure is obviously constrained. In other systems, decision makers do not face explicit budgets, but there are still limits to the extent to which expenditure can be increased, at least in the short term. In the context of collectively funded health care (whether those funds come from taxation or insurance, or some combination of these), all systems must contend with limits in their ability to increase expenditure to fund more expensive medical interventions as they become available.

The consequence of constraints on health system expenditure is that new medicines and other technologies are competing for limited resources, although the details of what resources are available will vary by system. In effect, multiple claims are being made, through HTA submissions, on behalf of different groups of patients and other recipients, on health systems' constrained ability to fund. Whenever additional funding is granted to a new technology which benefits one group of patients, there are inevitable negative consequences for the benefits of others as their claim on resources has been weakened. These negative consequences constitute *opportunity costs* and can come in different forms, partly depending on the system. In

a tax-funded and budgeted system like the NHS in the UK, additional spending on a new technology will inevitably mean less funding being available to meet the claims of other patients, either in terms of other potentially fundable new technologies or the rules or timing of access to existing care and interventions. In insurance-based systems, opportunity costs can be incurred through different routes, such as increased premiums, out-of-pocket costs, such as co-payments, or offsetting reductions in coverage. The Canadian system is a decentralized, federated model where these constraints are primarily realized within the budgets of individual provincial and territorial health systems, so opportunity costs are incurred at the province/territory level.

Although overall expenditure may increase over time in the health systems of high-income countries, there is no automatic linkage between a decision to fund a new technology and an increased funding envelope. Hence, opportunity costs mean decrements in health to real patients, although these individuals may not be easily identifiable, in contrast to those identifiable individuals who stand to benefit from new interventions for specific diseases. Across jurisdictions, evidence on the quantification of opportunity costs associated with increased expenditure is only now (and only partially) being reflected in economic evaluation in health.[14] To ensure that the interests of all patients are reflected in HTA decisions, opportunity costs must be routinely considered in the methods used. Indeed, any analysis to inform HTA decisions without evidential consideration of opportunity costs cannot be defined as economic evaluation.

This reality has clear implications for how benefits are considered in economic evaluation. The purpose of economic evaluation is to ensure that any new intervention generates more benefit than the forgone benefit imposed on others as opportunity costs. If the measure of benefit is extended or adapted for a new intervention, this can advantage some patients in the claim made on their behalf. However, for the economic evaluation framework to be coherent as well as fair, that same extended definition of benefit must be applied to other patients who potentially bear the opportunity cost. Hence, economic evaluations would need to reflect the extended benefits symmetrically: both in terms of the gains from a new intervention and the benefits forgone by others due to depleted resources. In other words, if benefits are valued differently across populations of patients, some patients will be advantaged while others will be disadvantaged, but this would not be fully reflected in the economic analysis. If relevant additional benefits are included in economic evaluation, the scope of opportunity costs considered must also expand to reflect the extent to which additional benefit is forgone by those patients experiencing displaced or unfunded care due to the extra cost of the new intervention. Looking across HTA decisions for different types of interventions, such an extension in benefits may suggest some interventions are more valuable than with a narrower expression of benefits, and some may be less valuable.

3. Principles Guiding Benefits

Although HTA organizations have defined the benefit functions they currently wish to see used in economic evaluation, these can change over time if changes can be justified. A series of principles are proposed to guide whether a suggested change in the benefit function warrants inclusion in HTA-based economic evaluation as described in Table 2. The proposed principles flow logically from the fundamental objective of economic evaluation used to support HTA; namely, to ensure the resources available to a health care system are used for the greatest benefit for current, future, and potential patients.

Table 2. Summary of Principles Guiding Specific Benefit Inclusion in Economic Evaluations

Principle	Brief Description	Rationale
Benefits must be relevant for the decision-making organization and for the decisions of interest.	This should reflect the normative choices made by HTA organizations which reflect their statutory, legal, or other authorities, as well as the expressed objectives and responsibilities of those responsible for decisions. In general, under current approaches, health, as opposed to patients' preferences (utility) or happiness, is the key benefit of interest for HTA organizations. Preferences play a role in quantifying health, reflecting key trade-offs in some aspects of HRQoL and length of life.	All three HTA organizations for which this report is developed state a focus on health as opposed to patients' utility. NICE's stated perspective on outcomes is "health effects, whether for patients or, when relevant, carers."[15] Canada's Drug Agency (CDA-AMC) describes its primary goal as generating "better health, better patient experience, and better value for Canadians."[16] The Institute for Clinical and Economic Review (ICER) states that the end goal of its work on comparative clinical effectiveness and cost-effectiveness is to ensure "sustainable access to high-value health care for all Americans."[17]

Principle	Brief Description	Rationale
Benefits must be aggregated (or valued) appropriately.	Current approaches by HTA organizations use community preferences (i.e., of the general population including prior, current, and potential future patients) rather than patients identified with a specific current condition. Benefits need to be valued consistently across disease areas. Methods need to be practical, so that they can be applied straightforwardly and transparently in research and "real-world" settings.	HTA informs population-level decisions around coverage and reimbursement of new medicines and health technologies.[18] Individual health care decisions are made downstream between physicians, patients and families. This reflects the current position of the three HTA organizations for whom this report is developed.[15,18,19] Consistent valuation across diseases is necessary to compare benefits and opportunity costs, and these need to be implemented in a practical way that supports transparency.
There is a need to reflect any additional benefit in the assessment of opportunity costs.	Any additional benefit should be reflected not just in the evaluation of new technologies but also in the benefits that would have accrued to current or future patients had additional resources not been allocated to those new technologies.	In resource constrained health systems, policy making involves trade-offs where allocation of a limited resource involves benefits for some patients and lost benefits for other patients in the system. NICE's principles indicate that "Resources need to be allocated appropriately and fairly. They must provide the best outcomes for the finite resources available while balancing the needs of the overall population and of specific groups".[20] The current NICE Methods Manual states "Given the fixed budget of the NHS, the appropriate maximum acceptable ICER to be considered is that of the opportunity cost of programs displaced by new, more costly technologies."[15] ICER is explicit that it seeks to consider opportunity costs.[18] CDA-AMC states that it adopts a "supply-side" estimate of the cost-effectiveness threshold, which assumes that reimbursing a new technology will displace some other technology or health care service.[19]

3.1. Relevance

As outlined in Section 1, HTA organizations generate guidance for different parts of health care systems. While these organizations can, to some degree, determine the methods used to produce this guidance, they must be relevant to the needs of the health care systems they impact. The objectives and constraints of those systems may have been defined in relevant documentation or agreed with limited transparency when the HTA organizations were founded, so there is inevitably variation in the extent to which these are explicit and in their level of detail. However, HTA organizations need to reflect these as clearly as possible in their approaches to economic evaluation. In most jurisdictions, this has led to a focus on health as the key benefit of interest, typically measured using some measure of lifetime health gain as the measure of benefit. Health is the focus of evaluation not only because it contributes to the utility of individuals, but as a socially valuable objective in its own right. Clearly, the experience of patients living with a given condition is critical to ensuring that the description and measurement of the effects of treatment is accurately and appropriately captured. However, the valuation of health, such as the relative importance of length of life versus HRQoL or trade-offs across different dimensions of health, is typically based on the preferences of the wider community (see Section 3.2).

This differs fundamentally from approaches rooted in mainstream micro-economic theory, where the utility of individuals consuming interventions is the focus under the assumption of perfect market conditions. However, in the context of health care decision making, several concerns have been raised about relying solely on patient utilities. These include the possibility of inappropriately reflecting adaptation to ill health; reluctance to treat people differently according to their ability to pay; and, more broadly, the standard model of consumer behavior (and associated concepts of individual consumer sovereignty as well as willingness and ability to pay) are not appropriate for health and health care.[10,12]

This distinction between utility of individuals versus health as (one of) the benefits of relevance in healthcare is a key normative debate between what has been termed “welfarism” and “extra or non-welfarism” based approaches referred to in Section 2.[13] While the details of this debate need not be revisited here, it underscores the importance of considering whether the proposed benefit is relevant to the decision-making context, how it may relate to these normative concepts of health versus utility, and whether it is consistent with other benefits advocated for inclusion in economic evaluation.[6,10,17,21-26]

For the three HTA organizations for which this report is primarily developed, the focus on health can be justified because it aligns with their institutional mandates or statements of remit (Table 2).

3.2. Valuation

Valuing benefits involves aggregating different types of benefit and making trade-offs explicit within the benefit function. This involves subjective judgment, and preferences inevitably shape valuation. As discussed in Section 3.1, there is a clear distinction between valuation approaches that align more closely with the mainstream microeconomic "welfarist" paradigm versus those that purposely depart from it. The welfarist approach holds that rational individuals act to maximize their own utility (well-being) within their available resources, and that policies should be assessed based on the preferences of those who consume services and bear the associated opportunity cost. Extending this to health care, this paradigm holds that it is the patients or those directly affected by health technologies whose preferences count for the valuation of benefits. However, economic evaluation generally used in HTA, and specifically by the HTA organizations that are the focus of this report, deliberately departs from this approach. This is because a normative position has been accepted both by using "health" as the primary category of benefit (see Section 3.1) but also in that health benefits are valued to reflect the preferences of the broader community. This approach is consistent with the view of the 2nd Panel on Cost-Effectiveness in Health and Medicine.[27] The preferences elicited from the community are used to inform how individuals trade-off length of life for HRQoL, and how different dimensions of HRQoL, such as physical functioning, pain, and mental health, are weighted relative to one another.

The current normative position of HTA organizations reflects the collective nature of health system funding, whether tax- or insurance-funded. The community includes past, current, and potential future patients across all health conditions. This has been referred to as the "Insurance Principle".[28,29] At the same time, limiting the source of values to patient preferences presents practical and conceptual challenges. Individuals living with conditions may adapt to changes in health over time.[30] In addition, it may be difficult to identify patients who have experienced all relevant health states and adverse events or to ensure that valuations are not influenced by personal interests.[31] For these reasons, community preferences are often used to support consistent and comparable valuation across different conditions and interventions. Importantly, this does not diminish the central role of patients. Patient experience is critical to identifying, describing, and measuring the health impacts of interventions that are subsequently valued within economic evaluation. Patient engagement to inform economic evaluation should be seen as complementary to the use of community preferences in valuation.

Whether preferences should be drawn from patients or the community is a normative value judgment that is the legitimate domain of decision makers and the organizations they represent. Hence, the principle that any additional benefit is valued appropriately is, in part, based on the normative starting point about the use of community preferences used in most economic evaluations in general and the HTA organizations commissioning this work. Furthermore, the approach to valuation needs to be applied consistently across evaluations, whatever disease or service areas are affected. This is because the numerous new and existing interventions available to health systems are all making claims on the same resource base. As such, it is important for the valuation in the measure of benefit to contribute to a common yardstick of value.

Appropriate valuation also needs to attend to practical considerations. One aspect is that the methods that are required across numerous evaluations should be straightforward to use. It is not sufficient that they meet some theoretical criteria if their implementation in routine research studies and the real world is excessively costly, complex, or lacking transparency. Trade-offs may exist when considering adopting a new method that has theoretical strengths but is burdensome and costly to implement. In such situations, there should be careful consideration of how the adoption of such methods is expected to impact HTA decisions. It should also be recognized that the existing elements of the benefit function are themselves based on evolving and imperfect empirical representations. A second aspect of these practical considerations is the need to avoid the error of counting the same benefit multiple times. This requires an assessment of each category of benefit to ensure it does not overlap in full or in part with other types of benefits. Where such overlap potentially exists, accurate measurement methods that facilitate the identification of and control for double-counting are required.

3.3. Opportunity Costs

Economic evaluation in HTA is fundamentally concerned with measuring and valuing the benefits of alternative health care technologies and comparing these to their opportunity costs. The latter needs assessment of both the net costs of the new interventions compared to what they seek to replace, and the benefits forgone elsewhere in the health system because of any additional net cost. As presented in Section 2, this means that *any aspect of benefit* must be considered symmetrically both for health technologies that are the direct subject of the economic evaluation and for any existing or potential health care that is displaced because of additional spending. This is not a normative position but, rather, an evidential requirement for any economic evaluation in the context of constrained expenditure. Despite the centrality of such evidence to all collectively funded systems, the role of evidence of opportunity cost is limited in economic evaluation under current HTA arrangements, even in relation to publicly funded and explicitly budget-constrained health care systems. For example, in Canada, despite accepting the principle of opportunity cost (see Table 2), HTA practice relies on conventional benchmarks (e.g., CAD $50,000-$100,000 per QALY gained). Policy-makers should exercise caution around claims that any additional type of benefit applies only to special case new technologies, such that the impact on opportunity cost is trivial or non-existent and may safely be ignored. Estimates of opportunity cost in the form of the marginal change in health outcomes given a marginal change in expenditure have been generated in several countries, including the UK and USA,[32] generally based on regression models using aggregate national or international data. As for much evidence used in HTA, including the health effects of new interventions compared with existing forms of management, current estimates of opportunity cost are subject to uncertainty and would be improved by additional data collection and further development in methods. In standard economic evaluation, the way opportunity cost is introduced conceptually is usually through a cost-effectiveness “threshold” against which an intervention’s incremental cost-effectiveness ratio is compared to inform a funding, reimbursement, or pricing decision. However, these thresholds are often not made public or reflect a range of considerations that

may or may not include opportunity costs. This has led to the suggestion that thresholds should be seen as “approval norms” and distinct from opportunity cost estimates; however, the latter should still be reflected in HTA decisions and available to support transparency.[33]

Given that evidence on opportunity costs (whether through cost-effectiveness thresholds or other means) is currently limited in HTA, it could be argued that ensuring any additional aspect of the benefit function is mirrored by an equivalent measure of estimated opportunity cost is unnecessary. The risk of failing to reflect evidence on opportunity costs is that less benefit is generated from available resources that could otherwise be achieved. There is also an equity concern as some patients may end up with greater reductions in benefit compared to those who gain. This remains a current challenge for HTA, which should be addressed. The risks to public health of misallocating resources will be exacerbated if additional items of benefit are added to economic evaluation without symmetrical consideration of opportunity costs. This risk can be illustrated by research that explored the implications of NICE adding productivity to its measure of benefit. Productivity can be added, presumably expressed in monetary terms, to the estimated additional benefits of a new intervention because of improved health in the indicated population. However, any additional cost to the health service due to the new intervention will have negative effects on other patients’ health, which will also be reflected in productivity, and therefore needs to be included. Otherwise, the analysis is only partial and provides potentially misleading information to decision makers. For example, if a new cancer drug generates lifetime health gain against standard therapy, this may have a positive impact on productivity, but its additional cost will reduce funding for other services, which impose reduced health on other types of patients, again with productivity consequences. The extent of the error in failing to reflect opportunity costs associated with all (new and existing) measures of benefit depends on the magnitude of the productivity effects. However, the earlier analysis showed that, when NICE makes decisions to recommend a new technology that imposes additional costs on the NHS and hence involves other patients foregoing health, each lost QALY in opportunity cost is also associated with an average net productivity effect of £11,600.[34]

The US system, in particular, deviates from that in the UK and Canada, with no central insurance or funding system facilitating access to health care for all citizens. Identifying where opportunity costs fall in the US, or any system with mixed funding, is challenging for multiple reasons. For example, state-based Medicaid plans are statutorily required to balance budgets each year while covering the most vulnerable populations (e.g., approximately 25 percent of total Medicaid enrollment is through disability and aging eligibility pathways[35]). Yet the Medicaid system is not closed for the duration of an individual’s life, as members may rely on coverage at one point in time (e.g., over 50% of children rely on Medicaid coverage at one point in their lives[36]) and later move to a private insurance plan through an employer. In this example, the lack of ability to follow and “track” health outcomes (e.g., as a function of restricted coverage) along with the mix of tax-payer funding and private funding makes it difficult to identify causal links between marginal changes in health outcomes from marginal changes in expenditure. Research is necessary to understand further how opportunity costs manifest themselves in US systems and the implications for measurement. Despite this uncertainty in estimating opportunity costs, ignoring them in economic evaluations, with or without additional benefit

measures, risks misallocating resources. Existing estimates, although uncertain, are the best available and need to be reflected in analyses to inform HTA decisions.

One approach in the literature to estimating opportunity costs in the USA is to rely on private insurance mechanisms for funding health. For example, private insurance plans in the US can increase premiums or make other changes that impose higher costs on beneficiaries to cover new interventions. This mechanism may lead to the loss of plan members who cannot afford premium increases. Among those who drop coverage, a proportion experience higher mortality and morbidity from lost access, which has been estimated through a simulation approach to amount to 10 QALYs lost in population health for every $1 million increase in insurance expenditures (i.e., in the form of pass-through premium increases).[37] There are alternative approaches to estimating opportunity costs, including a macro-level approach that derived thresholds for multiple countries using the effect of new interventions on life expectancy and per capita health expenditures. Findings suggest a similar health opportunity cost threshold in the US as was found through the mechanism described previously using insurance and coverage.[32]

Despite the difficulty in establishing causal links to estimate these opportunity costs, the US remains a place where millions of people have no access to care, in many cases leading to financial ruin for people facing injuries, accidents, or cancer diagnoses that reduce their survival and increase their morbidity. As of 2024, 27 million Americans were uninsured, with a disproportionate share falling on racial and ethnic minorities. Some have argued that cost-effectiveness thresholds should reflect the “willingness to pay” of those covered by a health system for additional health (i.e., their willingness to forgo their own consumption in exchange for improved health).[38] Sometimes called a “demand-side” threshold, this unrealistically assumes that the funding available to systems through insurance premiums, taxation, or otherwise, adjusts to reflect those willingness to pay preferences. Such an approach can potentially guide the level of *future* health expenditure, but does not directly address the affordability of new technologies given *current* funding levels.[39]

4. Additional Value Elements

This section examines proposed additional value elements from the health economics and related literature with a goal of determining their fit within a health benefit function using the principles outlined in Section 3. The literature on additional value elements continues to expand. Therefore, we do not aim to be exhaustive in covering this, but rather to illustrate some examples, mostly from the original ISPOR Task Force,[7] against the principles outlined in Section 3.

The “petals” of the value flower include scientific spillovers, equity, real option value, value of hope, severity of disease, fear of contagion and disease, insurance value, value of knowing, productivity, and family spillovers, in addition to core elements including lifetime health gain and net costs. Recent versions of the value flower have grouped more value elements into four categories: uncertainty, dynamics, beneficiary, and additional elements.[8] Other concepts of benefit are referred to which have been mentioned in the literature. The proposed principles need not be applied solely to existing proposals for additional value elements but also to any emerging in the future.

4.1. Do Proposed Value Elements Relate to Benefits?

Each proposed novel value element is, firstly, assessed for whether it constitutes a benefit for inclusion in economic evaluation. Table 3 briefly summarizes those elements that were considered a potential component of the “benefit function” and that meet the scope of the report. We group these elements into four categories: Risk Attitudes, Non-Health Benefits from the Process of Care, Equity, and Perspective. Each category, and different aspects within it, is further described in Sections 4.2 - 4.5, where we apply the principles that were proposed in Section 3.

Table 3. Value Elements in Scope

Domain	Alternative Names and/or Elements Within Domains	Description of the Value in Relation to a Health Intervention	Justification
1. Risk Attitudes			
Outcome Certainty	(i) Value of reducing risk in health outcomes; (ii) Value of hope	(i) The value of reducing risk in health outcomes. (ii) The value of the potential for favorable outcomes from a health technology.	(i) Patients value more certainty in health outcomes (ii) Incorporating risk attitudes (e.g., risk-seeking or risk-averse) may reveal a subset of patients willing to trade-off certain health outcomes for a small probability of achieving an above average health outcome.[8]
Risk Protection (Insurance Value)	Peace of mind value; Insurance value; Physical risk protection and financial risk protection; Disease risk reduction	Availability of the technology reduces risk of disease and its unfavorable physical and financial consequences	A medical technology can reduce physical risk for healthy consumers who might get sick in the future. New technologies make illness less unpleasant and thus effectively raise utility. Medical technology expands insurance possibilities by converting some aspects of previously uninsurable physical risk into a potentially insurable financial risk. Financial insurance value is the incremental gain to risk-averse consumers from gaining access to financial health care insurance.[40]
Patient-Centered Health Improvements	GRA-QALY (Generalized Risk-Adjusted QALY)	HRQoL and length of life gains are benefits but the way in which they are calculated differs from standard approaches.	Incorporating risk attitudes of patients into benefits replaces the existing HRQoL weights used in HTA with expected utility as a function of the probability distribution of possible health outcomes along with a HRQoL utility function.

Domain	Alternative Names and/or Elements Within Domains	Description of the Value in Relation to a Health Intervention	Justification
2. Non-Health Benefits from the Process of Care			
Process Utility Value of Knowing	(i) Value of diagnostics; (ii) value related to care and delivery of services	(i) Value of informed treatment decisions, reducing uncertainty surrounding a patient's health status. (ii) Aspects of interventions not directly impacting health (e.g., information, relationships with providers)	(i) Specific value from diagnostics may reveal future risk of disease and offer patients informed decisions in advance of care. (ii) Other aspects of the process of care can impact patients' satisfaction with services but not their health outcomes. Depending on the condition, this may impact HRQoL in positive as well as negative ways.[8]
3. Equity			
Equity	DCEA (Distributional Cost-Effectiveness Analysis)	Societal preferences for reductions in health inequalities deemed unfair.	Explicit incorporation of weighting of health benefits across heterogeneous patient populations to potential health gains for disadvantaged populations.
4. Perspective			
Family and Caregiver Spillovers		Patients' family members and friends are also affected by the financial and non-financial burdens of providing care.	Incorporation of the effect of a treatment on caregiver HRQoL and the financial impacts at the family and/or caregiver level.

Domain	Alternative Names and/or Elements Within Domains	Description of the Value in Relation to a Health Intervention	Justification
Community Spillovers		Individuals not infected by an infectious disease can be impacted via behavioral change in response to fear of infection e.g. closing of schools in COVID.	Incorporated into economic evaluation through behavioral impacts, medical costs, and non-medical costs.
Productivity	Work loss, presenteeism, absenteeism, labor market participation	Reduced productivity while at work or reduced ability to go to work.	Disease-specific productivity impacts presenteeism, absenteeism, unemployment, productivity loss due to premature death, and gains in productivity gains from life extension. Differences in productivity are potential positive impacts of health interventions and therefore benefits, even though expressed in monetary units. That is, they are distinct from the cost of resources used to improve health and are only realized because of improvements in health outcomes.

Table 4. Additional Value Elements Out of Scope

Domain	Alternative Names and/or Elements Within Domains	Description of the Value in Relation to a Health Intervention	Justification	Rationale for Exclusion
Dynamic Pricing	Dynamic net health system costs	Price changes both pre- and post-loss of exclusivity for a technology or class of technologies.	In certain monopolist environments, manufacturers may increase prices during a period of exclusivity after initial market approval; oligopolist scenarios reduce the price during patent exclusivity; genericization may be implemented by government entities or because of post-exclusivity competition.[8]	Relates to how possible price changes over time might be handled in economic evaluation which varies by health system. The proposed inclusion of dynamic pricing is independent of (and involves no change in) the existing benefit function.
Dynamic Disease Prevalence	Stacked cohorts	Technology will impact the prevalence of a condition beyond its direct impact on the current cohort.	If there are substantial differences in cost-effectiveness between cohorts or if the technology has shared effects.[41]	This is a modelling issue, which changes how net costs or epidemiology evolve over time and involves no change to what is considered in the benefit function.
Option Value	Real option value	The value of a technology to extend life for an average patient to take advantage of future approved technologies. Safrin et al. (2024) further distinguish ex ante from ex post.	The concept that health benefits and costs in the future may be impacted by innovation in present day.[8]	This relates to whether the additional benefits associated with keeping patients' options open should count and, if so, how. It does not redefine which types of benefits should be considered.

Domain	Alternative Names and/or Elements Within Domains	Description of the Value in Relation to a Health Intervention	Justification	Rationale for Exclusion
Scientific Spillover	Novel mechanism of action	A new mechanism of action can be of value because it can have positive spillover effects in other clinical areas.	A drug with a new mechanism of action might not in itself be very valuable, but the knowledge that the mechanism works might lead to other more valuable drugs in the future, even to treat very different diseases. The first drug with a novel mechanism of action unlocks the value of the later innovations.[7,8]	This relates to whether the benefits of future R&D in terms of new products because of expenditure on current products should be counted and if so how. It does not relate to which benefits of current and future products should be considered. The case for reflecting such spillovers applies whether the benefit function is defined, for example, in terms of health, or health plus productivity and would not change that choice of benefit.
Societal Discount Rate		Standard analyses use a discount rate for costs and benefits. GCEA proposes to use empirically derived societal discount rates based on positive or normative approaches.	The positive approach treats health as an asset whose opportunity cost should be compensated by future returns to health, represented by a risk-free interest rate. While the normative approach utilizes the Ramsey equation to derive a Pareto efficient optimal rate.	No consideration of an alternative or additional items in the benefit function.

Domain	Alternative Names and/or Elements Within Domains	Description of the Value in Relation to a Health Intervention	Justification	Rationale for Exclusion
Adherence		Better adherence generates greater (health) benefits and should be reflected.	Incorporating possible differences in use of a medicine between clinical trials and real-world clinical practice.	The proposal is to consider adherence as a mechanism that generates health benefits; there is no suggestion that improved adherence should be considered as a benefit independently of its impact on health outcomes. To include adherence separately in addition to health effects derived from adherence would double count.
Direct Non-Medical Costs		Incurring direct non-medical costs to accommodate disability and diminished HRQoL.	Additional costs to include may involve travel costs or other costs associated with receiving care but not directly tied to paying for a particular health service or intervention.	This relates to costs rather than benefits.

Several value elements that have been proposed are not relevant to the benefit function. These elements are listed in Table 4 together with justification for their exclusion. The overarching principle here is that value elements that do not propose changes to what is included in the benefit function (as described in Section 1) are not within scope for this report. Benefits are the measurable outcomes of interventions and policies which reflect the attributes of social value relevant to the objectives and responsibilities of the HTA organizations covered by this report and the health systems they represent. Those out of scope "novel value elements" relate to costs, or different approaches to economic evaluation. Whether these alternative approaches should be used and, if so, how they are implemented are separate questions from what constitutes an appropriate benefit function.

4.2. Risk Attitudes

The foundation for several proposed new value elements is the claim that individuals' risk attitudes with respect to their own health should be reflected in assessments of benefits. This applies to those elements categorized under "outcome certainty" ("value of reducing risk in health outcomes" and "value of hope"), and "disease risk protection" (or "insurance value") in Table 3. Generalized Risk Adjusted Cost Effectiveness (GRACE) provides a potential approach for incorporating these risk attitudes into the measure of benefit.[42,43] Advocates of the approach argue that this would have implications for the benefits that would be attributed in different scenarios and for different types of health technologies. The GRACE framework comprises two elements: Generalized Risk Adjusted (GRA) QALYs on the benefits side, and Risk and Severity Adjusted Willingness to Pay (RASA-WTP). The GRA-QALY departs from standard methods for the assessment of benefits, incorporating attitudes to risk and anticipating that this will reveal the relevant level of risk aversion. This is advocated to reflect considerations labeled "Outcome Certainty", "Disease Risk Reduction", and "Patient Centered Health Improvements", and contrasts with the standard approach to economic evaluation, where the measure of lifetime health gain does not generally reflect risk attitudes when measuring preferences. RASA-WTP creates a variable WTP threshold with adjustments based on these same risk preferences, according to the severity of the condition and any pre-existing disability.

Diminishing marginal utility is a fundamental economic concept that holds that the utility a consumer obtains from consumption of each unit of a good or service eventually declines as consumption increases. Where there is diminishing marginal utility of health, this implies risk-aversion. If this is reflected in health (as suggested in the GRA-QALY framework), this means that, where the health effect of an intervention is uncertain, the expected (mean) level of lifetime health gain used in standard economic evaluation will overestimate the *certainty equivalent* level of health gain. The certainty equivalent is the level of health gain for certain that is considered equally good as the uncertain distribution of health. When an individual has preferences that exhibit risk aversion, their certainty equivalent is lower than the expected (mean) level, in effect penalizing health interventions with greater uncertainty. Where the distributions of health benefits are symmetrical around the same mean for both a clinically effective new health technology and its comparator, and less variable for the comparator than the new technology,

the expected benefit of the new technology will be lower if incorporating risk aversion (as per GRA-QALYs) than under standard approaches. Assuming risk aversion, GRA-QALYs penalize greater uncertainty in patient outcomes. (See Box 2, Figure 1).

Whether the pattern of health effects shown in Box 2 Figure 1 (i.e., the same mean, symmetric distribution, new technology is more variable) will occur in practice is highly technology- and disease-specific. However, in general, longer periods of clinical experience and opportunity to develop relevant evidence might be expected to reduce the degree of variation in health effects (though it is worth noting here that such effects are rarely fully captured in economic evaluation). Also note that the issue here is not the degree of uncertainty in the sense used in relation to parameters in economic evaluation, such as the degree of uncertainty in the mean treatment effect, which is resolvable by increasing research sample size.[44] Although related, this is, rather, the degree of variability of treatment benefit faced by individual patients and may be expected to reduce with clinical and research experience. In some settings, new classes of targeted treatments and personalized medicine may demonstrate less variability in patient outcomes and, therefore, generate even higher GRA-QALY benefits when compared to existing treatments with greater variability in health outcomes.

A further implication that is claimed from incorporating risk attitudes into the benefit function using GRACE is a concept termed the “value of hope”, which is described in existing literature in two different ways. The first is based on the claim that patients with severe conditions hold risk-seeking preferences.[7] This means that, for a new technology with the same mean health but with greater variance than its comparator, the certainty equivalent of a risk-seeking patient is higher than with standard methods: such patients “hope” that they will be in the right-hand tail of the distribution following treatment. A second explanation found in more recent accounts suggests that people are not only risk-averse but may also be “prudent” - where a treatment has a right-skewed distribution of health benefits, a prudent individual will prefer this to a comparator treatment that has the same mean and variance but has less of a right hand skew, including a symmetric or left hand skew.[42,43] (See Box 2, Figure 2.) “Prudence” in individual preferences follows if there is diminishing marginal utility but this never becomes negative (there is no level of health beyond which the addition of extra health units leads to a reduction in patient utility). We refer to descriptions of the “value of hope” below.

Box 2: Probability Density Functions of Three Treatments with the Same Expected Health

Figure 1: Two Treatments with Symmetric Distributions with Different variation

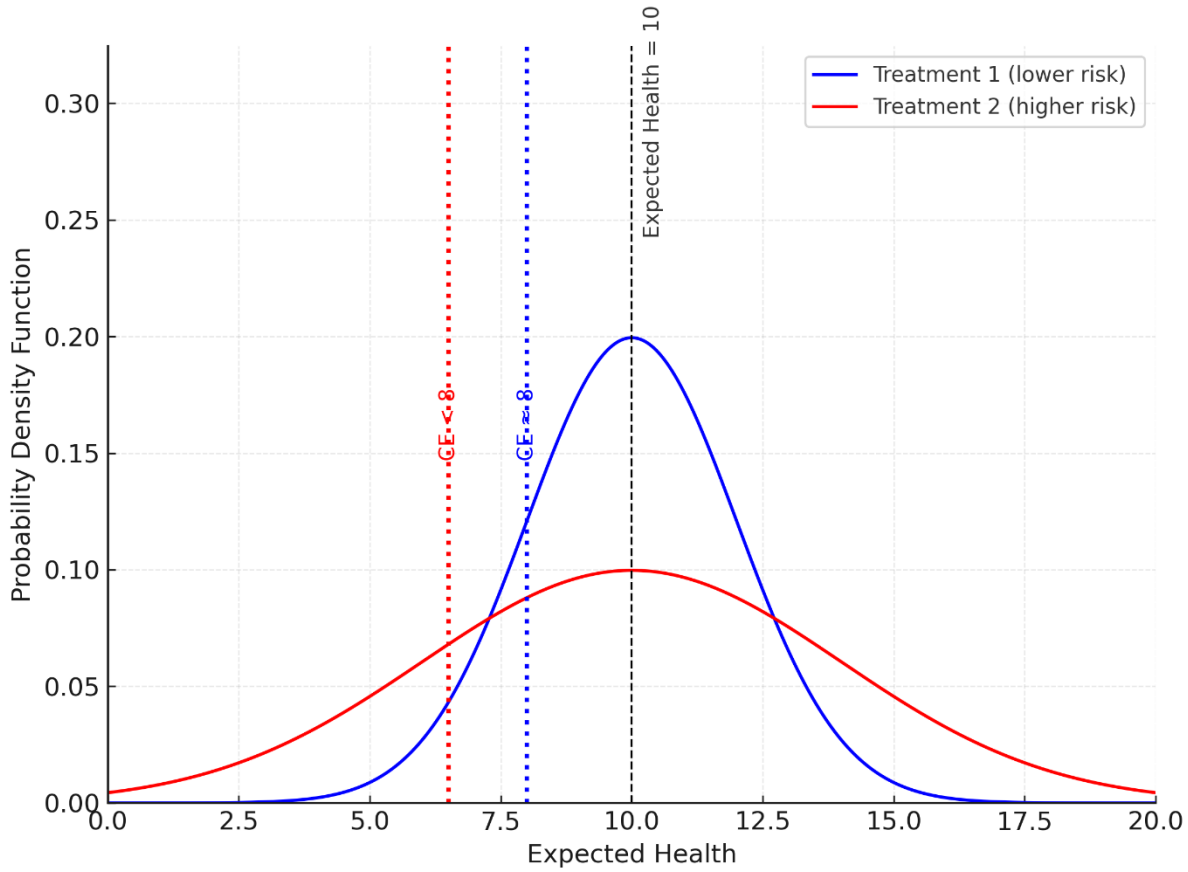

Figure 1 plots symmetric probability density functions of two treatments with the same expected health (here, at 10, measured along the horizontal axis on an arbitrary scale). Treatment 1 in blue has lower variation than Treatment 2 in red, indicating that it is lower risk. For a given risk averse individual, the certainty equivalent of Treatment 1 (shown at 8) is higher than that of Treatment 2, because risk aversion rewards the lower variation from Treatment 1.

Conventional economic evaluation (which uses expected health) does not distinguish between the health outcomes of these two treatments, but GCEA (which uses certainty equivalents) does.

Figure 2: Two Treatments with a Symmetrical and an Asymmetrical Distribution

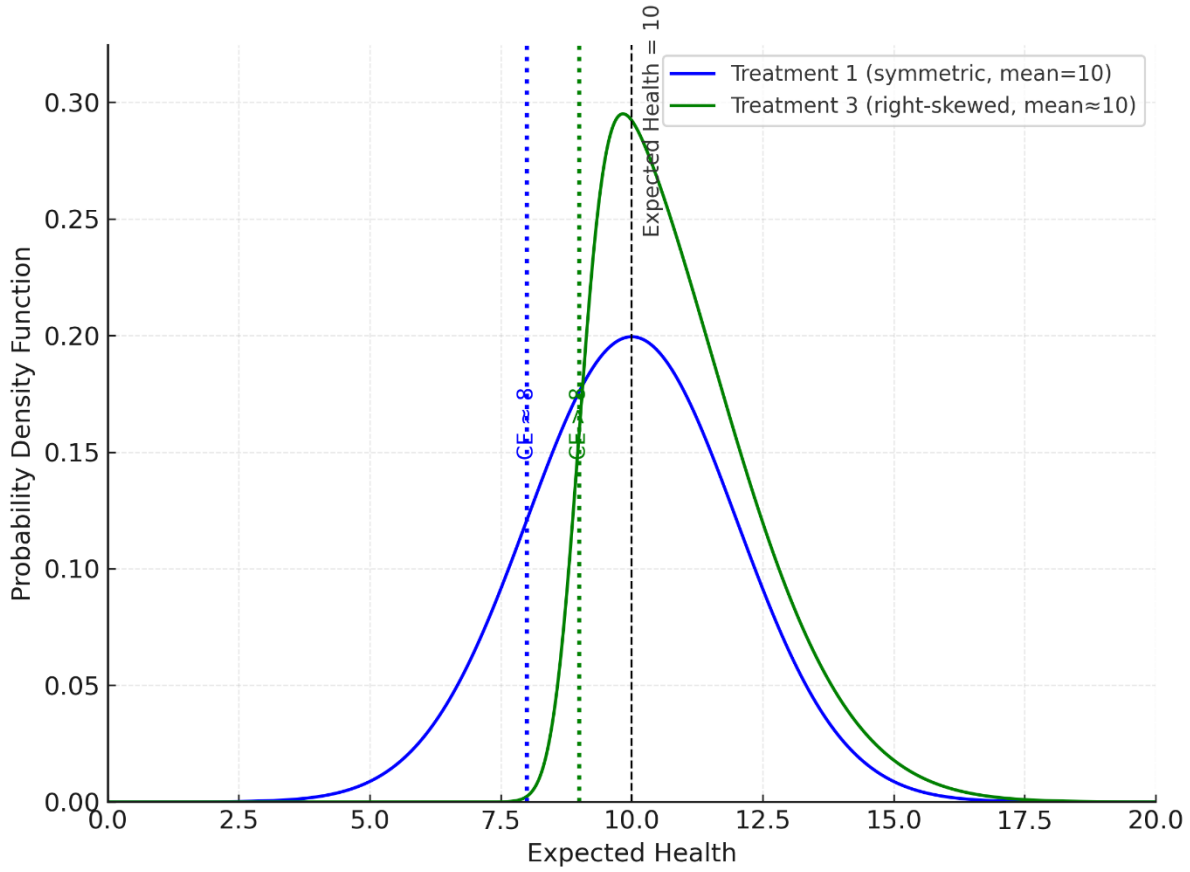

Figure 2 plots the probability density functions of two treatments with the same expected health (10) and the same level of variance. The one in blue is symmetrical and is identical to Treatment 1 in Figure 1. Treatment 3 in green is asymmetrical and is right-skewed – compared to Treatment 1, the probability density curve has a thinner left-hand tail, a fatter right-hand tail and a taller mode located to the left of the mean. The certainty equivalent of a risk averse and prudent individual for Treatment 3 is higher than 8 which is the certainty equivalent for Treatment 1, because the thinner left-hand tail represents lower chances of outcomes less than 8, while the fatter right-hand tail represents higher chances of better-than-average outcomes. GCEA based on certainty equivalents rewards Treatment 3 for its right-hand skew, relative to Treatment 1. However, as long as the individual is risk averse, the certainty equivalent of any distribution, by definition, remains smaller than the mean (10 for both treatments in this example).

These figures were developed using the above text as prompts with assistance from ChatGPT, an AI assistant created by OpenAI.

Relevance

The GRACE framework retains a view of health in terms of length of life and HRQoL at the heart of the assessment of benefits. However, it does still represent a potentially significant departure from standard economic evaluation because it seeks to incorporate risk attitudes towards the distribution of health outcomes. “Risk attitude” here refers to reflecting preferences individuals may have, although a variety of standpoints, even within this framework, can be identified (see the following section on “Valuation”).

It is important to be clear about the source and basis for claimed preferences, since decision makers are unlikely to want to reflect preferences that may be seen as irrational or groundless. As outlined above, the “value of hope” has differing explanations. The first is that, given two risky treatment options with the same expected health, patients who are severely ill have a higher certainty equivalent for the riskier treatment option than the one with less risk; that is, they are risk-seeking.[45] But such patient preferences may arise because patients assign a higher subjective probability to treatment success than is objectively warranted (and vice versa).[46] For example, there is evidence of optimism bias amongst patients enrolling into early phase oncology trials. This could equally be termed “desperation” rather than “hope” or seen as the application of subjective probabilities that are likely to result in disappointment or despair once treatment has been provided, and its effects become apparent. There are few health care settings where this is likely to be appropriate as an evidential basis for decision making.

The alternative explanation, where the value of hope stems from the concept of “prudence”, has different implications. In this situation, the value of a health distribution is determined not only by its expected value and variance, but also by its skew (see Box 2, Figure 2). Specifically, patients assign greater value to health gains from treatments that have long right-hand tails compared to treatments that have the same expected health gain and variance but have a symmetrical or a left-skew distribution, even though patients remain risk-averse. For a treatment with variable outcomes, taking risk-aversion into account leads to a lower certainty equivalent than the expected value of health. Taking the value of hope (or prudence) into account increases the certainty equivalent for right skewed distributions of health, partially, but not fully, offsetting the reductions due to risk aversion.

It may, in principle, be desirable to seek to align standard measures of health benefit more closely to the preferences held by individuals. The risk neutrality in preferences under standard methods, which GRACE seeks to relax, is one of many assumptions about preferences embedded in benefit measures used in economic evaluation for purposes of simplification (see following section on Valuation). A strong case is required to elevate the incorporation of risk attitudes above these other simplifications. Furthermore, measures with claimed theoretical superiority to standard approaches proposed in the past have encountered substantial practical challenges in valuation, restricting their usefulness.[47] The Healthy Year Equivalent (HYE) is one such example purported to overcome some of the theoretical limitations of standard measures by allowing for preferences about the profile of health. Use of the HYE was limited by practical complexities of measurement.

Valuation

In considering whether the proposed use of individuals' risk attitudes to their own health can be appropriately valued in economic evaluation, the normative question of whose preferences should count is an important consideration. As discussed in Section 3.2, standard economic evaluation for HTA uses community preferences regarding health. Conventional economic evaluation takes the normative position that assigns patients as the relevant source for describing and measuring health, but not for valuation. It is true that, in standard methods, there is often an over-reliance on crude tools for measuring health. These constrain the ability of patients to convey adequately the ways in which new health technologies benefit their health (although HTA bodies do have other processes in place to elicit these details from patient respondents). Although not the focus of this report, better methods of capturing and reflecting patient experience for economic evaluation would help to ensure community preferences are elicited for appropriate health impacts.

The proposed new methods for quantifying health benefits differ from this approach. In the context of what is referred to as the "value of hope" and the "value of reducing risk in health outcomes" in the GRACE framework, it is not community preferences but the preferences of individuals assessing for themselves the benefits from available treatments that are proposed for inclusion. For health care decision making at the individual patient level, these attitudes are critically important when choosing between a set of available treatment options but, for HTA decision making, the normative case for using community preferences has been accepted by HTA organizations.

In the context of the proposed additional benefit termed "the value of risk protection", the proposed source of preferences in the GRACE framework is different. Here it is argued that individuals gain peace of mind from having new health technologies covered in their insurance plan. It is the risk preferences of individuals (here assumed to be risk-averse) as purchasers of insurance that form the basis of the assertion that benefits differ from those captured in standard (risk-neutral) economic evaluation. There is likely to be substantial overlap between the preferences of the community and populations covered by health insurance. However, there is inconsistency in the sources proposed for those preferences elicited as part of suggested novel benefits relating to risk attitudes. There is not a single consistent position that advocates the use of patient preference. Furthermore, the definition of patient appears to fluctuate across the range of suggested novel benefits relating to risk attitudes. For those elements relying on the elicitation of patient risk preferences over their own health, the type of patient considered relevant needs clarification. Is it individuals with the health condition in question, those who have the condition currently and are candidates for the technology in question, or those who have experienced the relevant set of non-fatal health states, or some other group? Which groups constitute "patients" in the context of screening or diagnostics? These categories of "patient" are not identical to each other and have different implications for research methods, including the feasibility, burden, and cost of data collection. Indeed, there is a lack of clarity about this in the range of proposed elements of benefit which draw on the concept of incorporating risk preferences into assessments.

In addition, in publicly funded systems, the magnitude of health care funding is determined via a political system that reflects the preferences of the general population, albeit imperfectly. The value to individuals of knowing they have health coverage, the extent of that coverage, and, in addition, the "caring externalities" from the coverage for others are all captured, in principle, through this system. The assessment of individual therapies using economic evaluation takes place as a distinct stage given prior decisions about the funding of other specific technologies.

The practical challenges to incorporating risk attitudes, even if considered desirable in principle, are substantial. Previous attempts to develop health measures claimed to be theoretically closer to preferences have failed to be adopted because of the complexity of eliciting the required values, balanced against the expected impact on decisions that draw on the results of economic evaluations. Decision makers and analysts require reliable and readily available "off-the shelf" estimates for use in economic evaluation.[48]

One study that has been advocated for use in practical applications of GRA-QALYs, Mulligan et al., attempted to elicit risk attitudes from individuals for health states (but not for survival).[8,49] This study recruited nationally (US) representative samples of community members rather than actual patients and conducted thought experiments based on hypothetical health scenarios using a simple one-dimensional scale of health states from 0 – 100, with all health scenarios lasting one year.[49] Participants were asked to consider, from the standpoint of a patient aged 40 years in a health state below full health, choices between a treatment with a certain health gain versus a risky health option that has two equal probability outcomes. Such choices are complex, and several simplifications and limitations are reported by the authors. Most notable among these is the need to simplify health to a single composite HRQoL 0-100 scale, although people may have different risk attitudes depending on the dimension of health.[49] One may also ask whether the 0-100 scale used satisfies interval scale properties necessary for the elicitation of risk attitudes, and whether participants could distinguish between, for example, health states rated 21, 24, 27, or 29 on this scale to answer the choices meaningfully.

The issue is further complicated by Mulligan et al.'s finding that the US general population utility function for health is S-shaped: risk-seeking in very poor health, which becomes more risk-averse as health increases, with an inflection point around 0.485 on a 0-1 scale.[49] This implies that the greatest marginal benefit in terms of GRA-QALYs (or the value of hope) comes not from states with the most severe health scores, but with those around the center of the range of possible scores.

Few other relevant studies have been conducted. Attema et al. provide an example of work conducted using a sample (n=500) of the community in the Netherlands, and found risk aversion across the HRQoL range, rather than the S-shape found in Mulligan et al.[50] The work of Mulligan et al. would require replication and extension in different populations for use in other jurisdictions (where relevant), validation of the findings and consideration of issues such as the relevant population for each purported element of benefit (for example, whether patient samples are also needed), further consideration of attitudes in the face of losses versus gains and, potentially, the development of multi-attribute descriptions of health but without rendering these experiments infeasible for respondents. Moreover, given the empirical evidence suggesting that

utility function over their own survival may also be S-shaped, the implications of non-constant marginal utility over life years (and possible interaction with HRQoL) need to be explicitly considered.[51]

The extent to which the incorporation of risk preferences would change estimates of benefit and impact decision-making has yet to be established. Expansion of the emerging evidence base is required to enable an informed assessment that balances real-world impact versus additional practical complexity.[52,53]

Opportunity Costs

In principle, opportunity costs could be estimated to reflect risk preferences and to be consistent with a measure of benefit like GRA-QALYs. However, such research would need to reflect clear methods to measure and value these outcomes more generally.

Summary

Valuation of health benefits using community preferences incorporates both current patients and potential future patients, as well as consumers and potential consumers of health insurance. New proposed elements of benefit variously advocate the incorporation of risk attitudes from patients and/or from people with health insurance. Standard methods of economic evaluation place patients at the center of the assessment of benefits by measuring the impact on patient self-reported health. However, the normative position that the value of health benefits should be based on community preferences has been adopted by HTA agencies, consistent with the remits of their funders. It is a position that has been reviewed over time and is consistent with the recommendations of others, including the 2nd Panel on the Cost-Effectiveness of Health and Medicine. Simultaneously incorporating patient preferences, including those relating to risk, lacks a coherent normative basis and is not recommended.

Health state valuation methods make many simplifying assumptions, in addition to risk neutrality, which means they cannot claim to represent pure preferences or utilities. These include assumptions regarding independence of the assessment of HRQoL from survival duration, additivity over time, and constant proportional trade-off. There have been several attempts over the years to bring a simple preference weighted measured of lifetime health gain closer to individual preferences or utilities. Despite meeting some theoretical criteria, their practical implementation has been limited because new preference studies would have to be designed for each new intervention, and the elicitation methods were potentially challenging and burdensome to recipients. These challenges would be further magnified if the preferences of patients, who would differ according to the health technology being assessed, were required.

Similar issues exist with the use of GRA-QALYs regarding routine practical implementation in HTA studies. Furthermore, key studies - such as Mulligan et al.'s quantification of risk attitudes - need extension and validation. Extensions include the assessment of risk attitudes to survival and/or health states. Although such methods are not ready for "prime time" in HTA, further research on extending the measure of lifetime health gain to reflect preferences more fully,

including but not necessarily limited to risk attitudes, may be warranted. This should, however, take into account the emerging evidence on the extent to which such developments would materially affect decisions.[53]

Recommendations

- A clear normative and practical case for routinely incorporating risk preferences into a measure of lifetime health gain is necessary. This needs to consider both the theoretical merit of doing so and the importance of reflecting risk attitudes compared with other aspects of preferences that are simplified in standard methods.

- The practical case for routinely incorporating risk preferences into a measure of lifetime health gain should consider: whose preferences should be elicited; over which aspects of health they should apply; the need to produce robust evidence for the relevant jurisdictions; and whether such developments would significantly affect HTA decisions.

- HTA organizations that have adopted a normative position to use average community preferences to define benefits for economic evaluation should be aware that simultaneously incorporating aspects of current patients' preferences would be a departure from and inconsistent with this view.

4.3. Benefits from the Process of Care and the Value of Knowing

A further category of benefit which is not routinely included in economic evaluation for HTA relates to aspects of the process of health care which, despite not generating a change in health outcomes, might be something over which individuals have preferences. One example of this, taken from the ISPOR Value Flower, is the "value of knowing". The context for this putative benefit is diagnostics which provide information to make judgments regarding a person's disease or condition. The information they provide impacts decisions about clinical management, and changes in treatment decisions may in turn lead to changes in health outcomes and costs which should be captured in conventional economic evaluation. The putative benefit of the value of knowing is predicated on the idea that, separately, patients may derive benefit from the information diagnostics provide aside from its instrumental value in promoting changes to decisions that promote health for the patient themselves or for others. This could include, for example, enhanced opportunities to make personal and family plans. In some cases, this information may cause disbenefits where, for example, the knowledge of the condition causes distress, there is no effective treatment, or the information is incorrect.

Other examples of the concept of process benefits or process utility have been discussed in the economic evaluation methods literature over many years. Researchers have estimated the process utility conferred on individuals by a range of factors such as the mode of treatment delivery (e.g., oral versus injection), waiting times, continuity of care, and the degree of

information given to patients about treatment options. Methods such as willingness to pay and discrete choice experiments have been used to quantify process utility relative to other attributes such as health outcomes.[54,55] Donaldson and Shackley examined what they termed "reassurance value" arising from knowledge of a test, in the context of antenatal screening for cystic fibrosis.[56]

Relevance

There may be relatively few situations where the impact of a component that is considered part of the process of care is not associated with measurable impacts on HRQoL. Other examples might be seen as good practice in delivery standards that should be universally required for all health care services (for example, the provision of sufficient information to patients to allow informed decision making, the communication style of clinicians, or distance to travel) rather than characteristics distinguishing options to be considered in HTA.

The inclusion of "pure" process benefits is likely to be contentious in resource-constrained systems because the implications for resource allocation decisions reflected in HTA would be that some degree of health gain can, in principle, be sacrificed to promote process benefits. At the extreme, this could lead to the funding of some interventions - for example a diagnostic for a condition that has no available treatment - which has no positive health gain at all.

Valuation

The distinction between the process of care and health outcomes can be blurred. Needle phobia, for example, can cause measurable impacts on discomfort, anxiety, and usual activities for prolonged periods and, therefore, could be captured, at least partially, through standard measures of HRQoL. Broader aspects of HRQoL have been developed that more explicitly incorporate factors that overlap with those that could be considered part of the process of care. For example, the EQ-HWB-9 instrument includes items such as "having control over day-to-day life", although interestingly, items more specifically related to care, such as "independence in decision making" and "feeling valued and respected", that were considered as preliminary themes, do not appear in the final EQ-HWB-9 instrument.[57] The ICECAP instruments include domains such as independence, choice, and preparation (in the palliative care setting).[57,58] Although not in scope for this report, this development of more sensitive instruments for assessing HRQoL may be seen as part of the improvement of methods that respond to the need to capture process benefits in a more generalizable manner than in many of the studies of process utility itself, which tend to be setting-specific.

In any case, there is a challenge to avoid double counting of these aspects of benefit that may already be captured, albeit imperfectly, in existing HRQoL measures.

Opportunity Costs

The feasibility of ensuring that the extent of these process benefits is reflected in the measure of opportunity cost depends in part on the methods that are adopted to capture these non-health

benefits. For example, a process utility study might give an estimate of the relative value respondents place on process components versus health gains, but such estimates are very context-specific and tend not to be generalizable to other disease areas or technology types, making it problematic to measure process benefits forgone from displaced services.

Summary

Distinguishing what is formally considered a health benefit from a "process" benefit of a health care intervention can be challenging conceptually and in terms of measurement. Before extending the measure of benefit used in economic evaluation to include these process effects, it would be important to understand whether they are (at least partially) included in existing measures of HRQoL used routinely in studies. If these are not covered, consideration should be given to more sensitive forms of measurement of HRQoL rather than add-on forms of valuation. The suggested benefit labeled the "value of knowing" opens up the stark choice to decision makers about whether health benefits could legitimately be forgone to promote such "benefits".

Recommendations

- Before considering whether specific benefits associated with the process of care (e.g., the value of knowing about disease prognosis) should be included in economic evaluation, further research is necessary to ensure these effects are not already being captured in HRQoL measures, or this could not be achieved with the use or development of more sensitive measures.

4.4. Equity

As stated previously, the main policy objective of economic evaluation used in HTA by those organizations that are the focus of this report is to enhance population health using a benefit function with estimates of a treatment's impact on survival duration and aspects of HRQoL. Such an approach is entirely focused on efficiency, while people often value equity, particularly in health. The term "equity" used in the ISPOR Value Flower has been very general. Recent literature on equity in HTA has aimed to incorporate such values by applying various weights to health gains in economic evaluation.[59] One example of this is to consider different types of unfair inequality and how that might be reflected in economic evaluation.[8] While the text below refers to health, the argument is generic and is not restricted to any particular benefit measure relevant to health care.

Various measures of health outcomes are positively correlated with socioeconomic status, demonstrating a socioeconomic gradient in health. This persists in many populations, is often recognized as being caused by societal mechanisms largely beyond individuals' control, and is typically regarded as unjust, unfair, and inequitable.[60] A reduction in the socioeconomic gradient of health may be considered a good outcome and, if so, this should be reflected in the value of the health gain given to the socioeconomically disadvantaged. The benefit function may

capture this through two distinct mechanisms: an aversion to the inequality in health per se (in other words, reducing a health inequality is good, regardless of who benefits from this); and/or a dislike of the socioeconomic inequality per se (in other words, the extra health gain should be given to the socioeconomically disadvantaged, even if their baseline health is no worse than the population average). These are not mutually exclusive and can be combined.

It is important to emphasize that individuals' preferences for their own health are distinct from equity considerations over population health. More specifically, priority for those with low health based on individual preferences for their own health cannot be used to derive priority for those with low health because of normative distributional preferences across the health of different individuals in society. Notwithstanding this, after noting the qualitative and deliberative manner in which HTA organizations have considered equity, Mulligan et al. state that, based on neoclassical economics, "empirically measured utility over HRQoL could be used to support a more principled microeconomic approach to the analysis of welfare and inequality" (p.22).[49] Indeed, individual utility over HRQoL can inform who would gain the most utility from the extra HRQoL gain. But note that this does not capture the shape of the benefit function or normative distributional preferences.

The benefit function used in economic evaluation for HTA by the three HTA organizations is a function of health, and it is agnostic about the level of utility people derive from their own health. In its simplest additive form, it does not distinguish between a unit of lifetime health gain accruing to individuals from different socioeconomic groups and is therefore distribution-neutral. The implied equity stance is that everybody's health is treated the same. This can be extended in two ways, both of which rely on normative social preferences.

The first extension is to allow for inequality aversion – this is, where health-related social benefit is increasing in population health but can also be decreasing in health inequality. Under inequality *aversion*, as the relative importance given to health inequality increases, the extra health benefit would improve health-related social benefit more if it was given to those with worse health. (In theory, a benefit function could be inequality *seeking*, so that it is increasing in population health and increasing in health inequality) Degrees of inequality aversion can be captured by an inequality aversion parameter elicited from members of the community using surveys designed to elicit normative social preferences (as opposed to individual preferences for own health).[61-63]

Whereas the benefit function for conventional economic evaluation is *symmetric* – the social benefit of this distribution is insensitive to any correlation between socioeconomic status and levels of health, the second proposed extension to the benefit function is to allow for asymmetry – such that the health of different population subgroups is given different weightings, because of who they are rather than because of their health. On the one hand, if the benefit function is asymmetric in favor of the socioeconomically disadvantaged, then health-related social benefit will improve more if extra health benefits are given to them, not because they have worse health but because of their socioeconomic status (for instance, because prioritizing those in socioeconomic deprivation is a matter of social justice). It is also possible that the benefit function is asymmetric in favor of the socioeconomically advantaged: then health-related social

benefit will improve more if extra health benefits are given to them, notwithstanding their already better health, because of their socioeconomic status (for instance, because they will be more productive and make more tax contributions by being healthy). Degrees of asymmetry can be captured by an asymmetry weight.

Relevance

The above framework applied to economic evaluation has been the theoretical basis of Distributional Cost-Effectiveness Analysis (DCEA).[64-66] DCEA takes health, measured in terms of lifetime health gain as the benefit, and can include two types of weights. “Indirect equity weights” are a function of inequality aversion and background health distribution, while “direct equity weights” are fixed weights applied to specific subpopulations independently of their levels of health.

The application of indirect equity weights to reflect inequality in health may be within the remit of health care systems. For instance, the concept of “fair innings” weights is an example of indirect equity weights and penalizes inequality in expected lifetime health gain.[67] The fair innings argument assumes that there is a reference level of lifetime health (“a fair innings”) that everybody is entitled to, so that health gain to different people can be given fair innings weights based on the level of their expected lifetime health relative to this reference. Health gain to those who are unlikely to achieve the fair innings will be weighted above 1, while health gain to those who are likely to achieve (or have already achieved) the fair innings will be weighted below 1. This is a form of severity weighting where severity is defined as a shortfall in expected lifetime health gain relative to the fair innings.

The application of direct equity weights is more contentious. Because direct equity weights apply independently of the background health distribution, it amounts to using the health care system to correct for social injustices (e.g., income inequality) or to penalize socially undesirable behavior (e.g., smoking). Whether these lie within the remit of the health care decision maker may be debatable.

Some HTA practices already place greater weight on improvements to populations with worse baseline health as compared to the population average. For example, NICE has explicitly incorporated “modifier” weights for severity in its decisions, defining it in terms of shortfalls in prospective lifetime health gain given current age (albeit currently with no empirical basis to do so). However, it has stopped short of including approaches such as DCEA with indirect inequality aversion weights across social characteristics as routine in the reference case analysis.[68,69] ICER does not formally incorporate severity weighting into economic evaluations, relying instead on a panel of voting members to deliberate on the value of drugs through the lens of “special ethical priorities” which may include severity. Recent additions to inform deliberation include presentation to voting panel members on the proportional shortfall of the condition in reference to other conditions.[18] Similarly, CDA-AMC does not currently have formal modifiers for severity, although a small number of drugs have gone through a reimbursement process using severity weighting but the weights and the process for determining the weights was not reported.[70]

NICE has also introduced modifiers for drugs for rare diseases ("highly specialized technologies").[69] However, the weighting is designed as an increasing function of the size of health gain, rather than gradations of the rarity of the condition (or of poor baseline health that is often associated with very rare conditions), and it is unclear what equity consideration it is designed to address. The two NICE modifiers (severity and rarity) cannot be applied together to a given intervention.

Valuation

The value of the fixed extra health gain to any group of patients in worse baseline health relative to the value of the same health gain to another group of patients in better baseline health depends on the specification of the relevant benefit function and its parameter values. This is ultimately a matter of interpersonal distributional justice and, as such, they cannot be based on how individuals value their own health.

There is a growing literature eliciting distributional preferences from the community to estimate the parameters of the benefit function.[61,62] Most empirical studies elicit aversion to health inequality across socioeconomic groups but, as aversion to other types of health inequality are explored, there will be a risk of double-counting. For example, people may regard health inequality across urban, rural, and very remote areas as unfair. But if regional health inequality aversion parameters and socioeconomic health inequality aversion parameters are elicited separately are both included in a DCEA, this is likely to involve some double counting, given the likely correlations between the two factors.

Opportunity Costs

If decisions about the funding of new interventions include equity weights which reflect social preferences regarding aversion to inequality, then this should also apply to resource allocation in health more generally, hence it should be reflected in the estimates of benefit forgone when new interventions limit available funding for other activities. Research has been undertaken in the UK suggesting that NHS expenditure changes generate greater health impacts for the most socioeconomically deprived, giving some indication that the opportunity cost of more costly new interventions could increase inequalities.[71,72] However, other research, focusing only on NHS hospital expenditure, suggests there is a neutral effect of expenditure on inequality.[73] This is an area in which more research is needed.

One consideration is whether DCEA, if used at all in economic evaluation for HTA, needs to be used consistently or could be used selectively. NICE now allows companies submitting evidence to the technology appraisal process to determine when they produce DCEA evidence to quantify the impact of an intervention on health inequality (although they reject full DCEAs that apply different weights across social groups).[69] However, there is a strong argument that, if used at all, DCEA should be implemented consistently to consider interventions that increase as well as reduce inequalities. Furthermore, these methods should be used routinely whatever the impact on inequalities of the technology under evaluation. A reasonable exception might be where it can be shown empirically that the health opportunity costs are neutral with respect to

the distribution of benefits (for example, through estimates of marginal productivity on the distributional effects of health system expenditure).

HTA organizations should acknowledge that there are limitations on any approach that weights or does not weight health outcomes; and this may have implications for decision making around coverage, funding, and reimbursement. Inadvertently, applying weights larger than 1 to the benefits of certain new technologies with the aim of reducing unfair health inequalities may actually increase unfair health inequalities elsewhere through the health forgone due to displaced or unfunded services resulting from the additional cost of the new technologies. This might apply, for example, if the selected benefit is obtained by a small fraction of the prioritized group at the expense of everyone, including the majority of that prioritized group. Different definitions of equity may be in conflict with each other. Upweighting severe conditions may aggravate the socioeconomic gradient in health, directly or indirectly via the health forgone due to displacement.

Summary

Calls for economic evaluation to reflect "equity" (variously defined) have been common in the literature. However, defining exactly what constitutes fairness in resource allocation over which there is broad consensus is challenging, mirroring the enduring practical barriers to quantifying health-related social welfare. The use of the preferences of the community to define social values with respect to equity has and can be used in HTA, but decision makers need to determine the relevant concept(s) of equity to which these preferences relate – e.g., baseline health, lifetime health and/or social disadvantage.

If equity considerations are important in the context of the evaluation of new technologies, they must apply more generally in resource allocation; consequently, they must be reflected in valuing the health forgone when additional funding is allocated to specific new interventions rather than existing services or other new investments. If adopted, the application of equity weighting (or the implementation of DCEA) should be symmetrical and consider interventions that increase as well as reduce inequalities. Furthermore, these methods should be used routinely whatever the impact on inequalities of the technology under evaluation. A reasonable exception might be where it can be shown empirically that the health opportunity costs are neutral with respect to the distribution of benefits (for example, through estimates of marginal productivity on the distributional effects of health system expenditure).

Recommendations

- HTA organizations should provide a clear normative basis and measurement approach when applying "modifiers" (e.g., for severity) as an expression of equity considerations.

- Distributional cost-effectiveness analysis provides a framework for building distributional considerations into economic evaluation. If HTA organizations consider its use relevant to their responsibilities, this should relate to technologies which may increase as well as

reduce inequalities, and opportunity costs should always reflect any impact of additional expenditure on inequalities.

4.5. Broadening the Perspective of Economic Evaluation

Some proposed additional "novel value" elements may imply a broadening of the perspective of economic evaluation, beyond a focus on health-related benefits and costs falling on the health care system. One element of the ISPOR Value Flower proposes analyses considering "spillovers" to caregivers and family of the costs and health effects of interventions. Another is the dynamic effects of infectious diseases on future cohorts of individuals other than those who are subject to, for example, initial treatments for or vaccination against those diseases (this is called "community spillover" in the GCEA framework). Considering spillovers to such individuals in terms of *costs* falling on individuals (patients, carers, family) would require a widening of the cost perspectives used by some HTA organizations, including NICE and CDA-AMC. However, reflecting the spillover effects in terms of *health effects* of interventions is, in principle, *already part* of recommended methods for economic evaluation by HTA organizations such as NICE. In other words, once decisions are taken by HTA organizations about an appropriate benefit function to support their decisions, there is no issue in principle about counting intervention effects on such benefits regardless of who they fall on. The challenge has been more practical, however, in generating suitable evidence quantifying such spillovers and ensuring these are causally related to the interventions under evaluation. Regardless of practical challenges in parameterizing these inputs, the health impacts of caregiving should be included in the analysis with uncertainty in the estimates suitably expressed.

In thinking about the appropriate benefit function for economic evaluation in HTA, there have long been debates about whether benefits beyond those generally associated with the remit of health systems should be incorporated. A prominent example is the impact of interventions on productivity, and this has also been part of the ISPOR Value Flower. This can be understood as the causal effects of treatments and other interventions, typically because of improved health for those receiving interventions or through spillovers, on the value of what individuals contribute, or produce, net of the amount they use or consume. There is an extensive literature on how such effects can be measured, covering, for example, implications for absenteeism, presenteeism, and early retirement, but also considering informal work such as childcare.[27,74,75] Much has also been written about how productivity can be quantified in monetary terms or through the measure of lifetime health gain.[13] Despite extensive research, productivity is not formally considered by many HTA organizations, including NICE. Currently, CDA-AMC is piloting the use of a broader perspective in some evaluations.[76] ICER includes productivity effects in its "modified societal perspective" scenario analyses where data are available, and has recently introduced an "indirect" approach to modeling productivity and caregiver impacts during periods of life extension based on a published algorithm liking HRQOL to time-use data.[77]

A key challenge with combining costs falling on health care and productivity effects expressed in monetary terms is that the opportunity costs of changes in productivity are quite different from

changes in health expenditure. In other words, when net productivity is expressed in monetary terms as an offset to the incremental health care cost of a new intervention, this ignores the fact that there is no offsetting effect on health system resources, at least not directly and immediately. For example, estimating that the health benefits of a new technology could also generate $1 million productivity benefit net of consumption does not result in the value of that productivity gain being added to health care financial envelope to be spent directly on services. There are strong arguments, therefore, to express productivity effects (and any other broader impacts) separately from health care system costs rather than to assume every cost or effect that can be expressed in monetary terms are exchangeable with each other.[78]

Broadening the perspective of economic evaluation through the benefit function could also consider several other consequences of interventions. These can be seen as the implications of interventions and policies for the benefits that decision makers who are responsible for resource allocation in other sectors consider part of their objectives or remits. Examples include the impact of public health policies on criminal justice objectives and the effects of medical interventions for children's mental health or neurodevelopmental conditions on educational outcomes. The consequences of the production of health care on a country's carbon footprint are another example which has recently been considered by HTA organizations, although these effects may more appropriately be seen as a choice of perspective in costs rather than benefits.

As for other aspects of economic evaluation, there are evidential challenges to extend benefits to include productivity and other consequences of health to wider social value attributes. Quantifying the effects of interventions on productivity and other outcomes outside health could involve collecting data in prospective or retrospective studies alongside traditional health outcomes. Research has been undertaken on standardized ways to measure, for example, productive activities and work participation.[79,80] Standardized ways of collecting potentially relevant outcomes in, say, education and criminal justice are less well developed. An alternative to directly quantifying the effects of interventions on these types of benefits is to estimate how they change as health outcomes vary. This would also need to consider other characteristics of the recipients of interventions, such as age, sex, and clinical diagnosis. This indirect approach was used in the work undertaken in the UK on net production.[81,82] Below we discuss the evidential requirements to quantity wider effects on opportunity costs.

Relevance

While this range of consequences of changes in health for these wider social value attributes for some subgroups of the population may be important to broader policy objectives, their relevance to the remit of health care systems would need careful consideration. In general, it would be expected that policy-makers in health care are held accountable for the quality and access of health services and health outcomes for patients and the population, rather than impacts on the broader economy or meeting the objectives of other sectors like education. Furthermore, broadening the benefit function in HTA to encompass the *implications* of improvements in health for other social objectives would suggest some prioritization of those subgroups of the population who are the focus of those objectives. The most obvious example is that, if enhancing productivity net of consumption were to become part of the benefit function

informing HTA decisions, this would effectively prioritize the working age population who, on average, generate more net production, even allowing for informal work activities. This is likely to raise challenges for health systems in terms of the fairness of their objectives and decisions, given that this would amount effectively to maximizing productivity-weighted health. However, it would also be understandable that health systems drawing on funding from government could be expected to promote the latter's wider objectives, although this should be considered with full information on relevant trade-offs.

Valuation

Expanding economic evaluation to include these non-health social value attributes has been undertaken in many published studies and is used by some HTA organizations. Typically, however, this has been implemented by monetizing these extended benefits and including them as if they were costs or savings. This is problematic, as explained above, for productivity: mixing resource costs and monetized (dis)benefits is inconsistent with the aim of economic evaluation in HTA to support decisions about how to enhance health benefits from resources available to the system. An alternative approach to incorporating these wider benefits would be to represent them directly in the benefit function. This would use some measure of preference from a relevant group to express trade-offs between health outcomes and, for example, gains in productivity or education outcomes. In effect, this requires HTA organizations to be transparent about how they set the "rate of exchange" in the value of health against these other broader objectives.

Another way to handle these wider benefits in HTA is to present them separately from the measure of health benefits. This disaggregated approach to implementing a broader perspective has been called cross-sectoral economic evaluation. It effectively works from the principle that decisions made in the health care sector will focus on health-related benefits but recognizes that other public organizations and sectors of the economy have different benefit functions (even if not formally defined) which reflect their remits and responsibilities. The same logic can apply to the wider costs/savings associated with those sectors. The "impact inventory" was developed by the Second Panel on Cost Effectiveness in Health and Medicine and can be used to support this approach to implementing a broader perspective in economic evaluation.[27] The impact inventory was extended by Walker et al. to include distributional considerations and opportunity costs[78] and applied in several studies.[83] From a decision-making perspective, this *extended impact inventory* can support wider discussions between decision makers across different areas of policy about making some resource allocation decisions jointly, although ultimately the need to quantify trade-offs cannot be avoided in most decisions.

Opportunity Costs

As for all other potential additions to benefit functions in economic evaluation for HTA, if such benefits are relevant to those new interventions which are subject to HTA, they are potentially relevant to those interventions and services from which resources are taken to fund the new technologies. So, a widening of the benefit function needs to be reflected in the measure of opportunity cost. In principle, empirical estimates of opportunity costs with these wider benefits

are feasible. Indeed, some work has been undertaken on this. Claxton et al., quantified the net production associated with the health opportunity cost of NICE's appraisal decisions.[34] This area of research is, however, still developing with recent evidence on causal links between health expenditure and productivity.[84] It would benefit from further improvement in methods and data, and needs to be extended if these broader measures of benefit were to be routinely adopted in HTA.

An important question is how much difference formally considering wider benefits might make to decisions. For some types of population-level interventions and policies – for example, workforce interventions to address obesity or community-based initiatives to tackle illegal drug use – the impacts beyond health could be considerable even allowing for opportunity costs. Whether this applies to most pharmaceutical interventions may be more debatable but can, of course, be assessed empirically.

Summary

The view that it is right for economic evaluation to consider benefits that fall outside of health and extend to other sectors of the economy is widely held and understandable. Some broader effects that have been discussed in the literature, such as spillovers to carers and families in terms of health, are already part of standard methods. When it comes to including a wider set of impacts, such as productivity or impacts on other sectors like education, the challenge is to specify how health gain should be traded off against other socially valuable attributes of interventions and in terms of opportunity costs. Although the widely used term "societal perspective" implies there is one way to aggregate across health and wider effects, this is not the case, and agreeing on a transparent and widely accepted set of weights to be used consistently in decision making is likely to be a challenge. However, enumerating and quantifying these wider effects and their opportunity costs in economic evaluation using an "impact inventory", even if these are not formally traded off against each other in the context of decisions, may aid transparency and inform wider policy considerations if these are significant.

Recommendations

- The generation of improved empirical evidence of spillover health impacts on carers and other family members should be encouraged.
- If broadening the perspective of economic evaluation to include benefits to the wider economy (e.g., productivity) or other sectors (e.g., education) is considered consistent with decision makers' remits, additional evidence requirements must be considered (e.g., opportunity costs by sector and trade-offs between different outcomes relevant to each sector).
- HTA organizations should consider the routine use of "impact inventories" to understand and enhance transparency regarding any significant broader impacts of health technologies, but this should also quantify opportunity costs for relevant outcomes.

5. Discussion

The HEMA Working Group, which provides the authorship of this report, was selected by the three sponsoring HTA organizations to provide independent advice on methods issues facing those organizations in their use of economic evaluation. Its membership has been drawn from the countries in which those organizations are based. The report reflects the views of the authors based on their experience in the fields, published literature, and feedback on earlier drafts, and no attempt has been made to reflect or develop a consensus across the health economics community. While the group has focused on NICE, ICER, and CDA-AMC, it is hoped that the report will be helpful to other HTA organizations that use economic evaluation routinely, other decision-making bodies internationally, and to practitioners in economic evaluation.

This first HEMA report has taken on a topical issue that has been broadly termed "novel value elements". The term has become all-encompassing and includes a range of suggestions about how economic evaluation could be undertaken differently. To make the development of the report tractable given the available time and resourcing, the agreed scope was to focus on those "novel value elements" which constitute proposed additional *benefits*. The rationale for this was that such benefits represent the largest proportion of value elements as defined in the "ISPOR Flower". Beyond recent proposals, there has been debate in the field over many years about whether a focus on health outcomes was sufficient for economic evaluation. Decisions about which value elements should be considered in the report to be consistent with its scope need to consider whether they are separate from the specification of the benefit function. For example, if economic evaluation for HTA routinely considered risk preferences and productivity in its benefit function, the cases which have been described for option pricing and scientific spillovers would be unchanged; as such, the latter methods' developments are not considered in scope for this report.

Reflection was needed regarding whether some proposed adaptations to economic evaluation methods might be considered costs (hence out of scope) or benefits. For example, the productivity effect of interventions can be expressed in monetary terms and might be considered a (negative) "cost." The principle was used that, for the purposes of this report, "costs" represent the financial value of the use of a real resource directly to generate health benefit. This is not the case for productivity effects, which were thus considered potential benefits and included in the report.

In thinking about appropriate benefit measures for economic evaluation, HTA organizations may be concerned about the quality of the evidence that would be provided to inform their decisions. Here, quality would be determined by factors like relevance to the jurisdictions in which decisions are taken and the appropriateness of the estimation methods used. Together with the size of the sample from which the relevant benefit is estimated, these quality considerations will directly impact the degree of uncertainty in the results of an economic evaluation. Of course, uncertainty is a feature of most evidence used in analyses, including the estimated treatment effects of interventions and their impacts on patients' health.[85] However, methods to quantify

uncertainty and integrate across all sources of evidence are available and routinely used in economic evaluation.[86,87] The expectation that estimated benefits will be subject to considerable uncertainty is not, therefore, a good reason to exclude the benefit from studies when there are compelling reasons (as considered in this report) to include them.

The issue of uncertainty in estimating benefits should not be conflated with the practicality of methods used in their measurement, including implications for measurement cost and the burden placed on patients or others. For some proposed new benefits, there are alternative options available for their quantification. This would be true, for example, for the estimation of non-health effects of medical technologies such as productivity and impacts on other sectors. For some other suggested benefits, however, there are potential estimation challenges in terms of costs or burden on recipients. For example, defining methods to elicit individuals' risk preferences across a full range of health states representing HRQoL and survival prospects would be complex, and the reliability and validity of responses may be questionable. The same applies to eliciting other types of preferences that could, in principle, enhance measures of expected health gain. If a normative position is taken that such preferences should be elicited from patients who have the disease for which the intervention under evaluation is indicated, cost and complexity issues arise from the need to undertake studies over many indications. If the additional benefit measures are considered important to include in economic evaluation – that is, they meet the relevance and valuation principles proposed in this report – further research may identify tractable ways of enhancing their practical implementation. Until this is achieved, however, it is entirely reasonable for HTA organizations to decide that their adoption is not yet appropriate. The decision becomes more challenging when there is reason to think that such methods could have significant effects on resource allocation decisions, in which case trade-offs between practicality and relevance become more finely balanced, and necessary research becomes a higher priority. The principles of value of information analysis may be helpful in addressing these trade-offs.

This report has put considerable emphasis on the importance of all measures of benefit being appropriately reflected in opportunity costs. Given all collectively funded health systems are constrained in their ability to increase expenditures, and these constraints are not instantly eased or budgets adjusted if a new technology meets a threshold of value defined in terms of willingness to pay estimates, any failure to reflect opportunity costs can lead to a misallocation of resources in terms of forgone aggregate benefits across the population. In other words, without including evidence on opportunity costs in an economic evaluation, the analysis is not really doing its job. This principle applies to existing measures of benefit focused on lifetime health gain as much as any additional benefits. The extent to which HTA organizations are currently appropriately considering opportunity costs – whether in determining a cost-effectiveness threshold or as a separate and explicit measure – should be considered. Adding new benefits without symmetrical consideration of opportunity costs risks exacerbating resource misallocation. Empirical estimates of health systems' marginal productivities exist[34,84,88] – at least in terms of lifetime health gain but increasingly for other attributes of social value – which can be used to represent opportunity costs in HTA. Like all other evidence used in economic evaluation, they can be improved through research in better methods and improved data.

Many researchers working in economic evaluation are enthusiastic to extend the methods used in these analyses in various ways, and this is reflected in initiatives such as those producing the ISPOR Value Flower. Some may, therefore, consider the report conservative and focused on the status quo, although it has recommended consideration of some extensions to methods and identified relevant priorities for research. One counter-argument would highlight the report's clarity about the importance of reflecting opportunity costs, the routine use of which in HTA is questionable. More generally, whether to include additional measures of benefit is a normative issue, not one to be settled by technical or empirical considerations. The economics applied to evaluation in health has predominantly adopted an "extra-welfarist" or "non-welfarist" view that decision makers and the legitimate authorities they represent should determine the objectives underlying resource allocation given the remits or types of authority they have been given and makes these organizations the legitimate arbiters of an appropriate benefit function on HTA.

The literature on "novel value elements" can understate inevitable trade-offs when benefits other than health outcomes are included in economic evaluation. The facts of constrained funding and consequent opportunity costs when new and more costly technologies are adopted means those trade-offs are unavoidable, and the political implications can be complex. For example, the report draws attention to the fact that bringing productivity net of consumption into economic evaluation would mean decisions are based on some forms of productivity-weighted health. Regardless of how it is done, bringing equity into analyses will inevitably lead to some reduction in overall health gain at the population level. There are numerous ways in which these extensions to benefit could be operationalized, but a social consensus on whether any would be appropriate would be unlikely.

The importance of "patient-centeredness" in HTA is often emphasized, but its relevance to economic evaluation should be clarified.[89,90] One aspect of this is how lifetime health gain is quantified. There is debate in the literature about whether the preferences that weigh different aspects of health into a single measure for economic evaluation should come from patients with the disease or from the community. In addressing this normative question, however, it should be emphasized that the community *includes* current and past patients and effectively consists of potential future patients. A second consideration is that the evidence on the measurement of health outcomes from interventions is centered on those patients with the condition in question. This reflects their involvement in the clinical trials from which the effects of treatments are estimated, including the completion of relevant instruments to measure their HRQoL, which are key sources of information for economic evaluation. It also covers their involvement in helping to design these instruments and address any limitations in how they capture the patient health experience, as well as their increasing levels of involvement in specific HTA appraisals, including scoping, review, deliberation, and other components. A third aspect represents a further reason why quantification of opportunity costs is central to economic evaluation. The patients of concern in the decisions informed by economic evaluation are not just those with the potential to benefit from the new technology but also includes those whose services are unfunded or displaced and hence stand to experience the disbenefits of the funding of the new technology. HTA can have no claim to patient centeredness unless it treats these two broad types of patients equally.

6. Recommendations

In this section, we list recommendations made in this report. The first three of these are drawn from Section 3 which sets out the principles we consider relevant when HTA organizations consider adding to the benefit function used in economic evaluation. The remainder comes from Section 4 that looks at specific proposals for additional benefits.

1. When considering additional measures of benefit for economic evaluation, HTA organizations should assess these against the guiding principles of relevance, valuation, and opportunity cost outlined in this report.

2. No additional benefits should be routinely incorporated into economic evaluation until there is an evidential basis to reflect them in opportunity costs. This is essential to ensure comparability and consistency in decision-making, and to avoid inappropriate resource allocation.

3. The deliberative process within HTA may consider potential additional benefits qualitatively, but it should not be used in a way that bypasses the consideration of opportunity costs. HTA organizations should consider how the design of their processes, including any pre-specification, supports transparent and consistent consideration of opportunity costs.

4. A clear normative and practical case for routinely incorporating risk preferences into a measure of lifetime health gain is necessary. This needs to consider both the theoretical merit of doing so and the importance of reflecting risk attitudes compared with other aspects of preferences that are simplified in standard methods.

5. The practical case for routinely incorporating risk preferences into a measure of lifetime health gain should consider: whose preferences should be elicited; over which aspects of health they should apply; the need to produce robust evidence for the relevant jurisdictions; and whether such developments would significantly affect HTA decisions.

6. HTA organizations that have adopted a normative position to use community preferences to define benefits for economic evaluation should be aware that simultaneously incorporating aspects of patients' preferences would be a departure from and inconsistent with this view.

7. Before considering whether specific benefits associated with the process of care (e.g., the value of knowing about disease prognosis) should be included in economic evaluation, further research is necessary to ensure these effects are not already being captured in HRQoL measures, or this could not be achieved with the use or development of more sensitive HRQoL measures.

8. HTA organizations should provide a clear normative basis and measurement approach when applying "modifiers" (e.g., for severity) as an expression of equity considerations.

9. Distributional cost-effectiveness analysis provides a framework for building distributional considerations into economic evaluation. If HTA organizations consider its use relevant to their responsibilities, this should relate to technologies which may increase as well as reduce inequalities, and opportunity costs should always reflect any impact of additional expenditure on inequalities.

10. The generation of improved empirical evidence of spillover health impacts on carers and other family members should be encouraged.

11. If broadening the perspective of economic evaluation to include benefits to the wider economy (e.g., productivity) or other sectors (e.g., education) is considered consistent with decision makers' remits, additional evidence requirements must be considered (e.g., opportunity costs by sector and trade-offs between different outcomes relevant to each sector).

12. HTA organizations should consider the routine use of "impact inventories" to understand and enhance transparency regarding any significant broader impacts of health technologies, but this should also quantify opportunity costs for relevant outcomes.

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