Comment on the Draft Report by Health Economics Methods Advisory (HEMA):
Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies

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Comments and recommendations

We commend the HEMA authors for providing a well-structured and balanced review of approaches to incorporating novel value elements into economic evaluation. The report provides a clear and methodologically rigorous framework that avoids advocating a single predefined agenda. By anchoring all proposed extensions to the concept of opportunity cost and to the practical responsibilities of HTA organizations, the report provides a transparent and adaptable foundation for future decision-making. The following comments are intended to support and further strengthen the report's clarity and applicability, particularly for contexts such as the United States.

1. Emphasis on Opportunity Cost and the Misperception of Unlimited Budgets

Opportunity cost remains under-recognized in US value assessments of health interventions because of the system's decentralized, multi-payer structure, political resistance to explicit rationing of care, and a cultural emphasis on innovation and access over fiscal constraint [1], [2]. The HEMA report rightly stresses that opportunity costs are often overlooked yet implicitly present in nearly every coverage and pricing decision.

In the US, resources may appear more elastic because insurers can raise premiums, negotiate rebates, or shift costs to patients. This flexibility, however, hides the reality of finite resources and contributes to inefficiencies, resulting in wasteful spending, delayed or restricted access, and insurance disenrollment driven by rising costs. These are, in effect, opportunity costs expressed through economic and social consequences rather than explicit health trade-offs.

About one-third of the US population is insured through public programs, where budget limits over the short-term are binding and trade-offs unavoidable. In Medicaid, for instance, resource constraints shape access through mechanisms such as prior authorization, drug tiering, and eligibility limitations. From our group's own work with Colorado Medicaid over the past three years, we have seen these constraints firsthand [3], [4]. Decisions surrounding high-cost one-time therapies such as cell and gene therapies illustrate the practical tension between long-term value and short-term affordability. These therapies may

offer substantial lifetime benefits yet must be paid for within the current fiscal year's limited financial resources.

While the HEMA report does not focus on how budgets for public insurers are determined, it is vital to acknowledge that such budget constraints are real and pressing in the US as well. There is no coordinated public-sector mechanism to ensure that budgets expand in line with the introduction of all good-value therapies, regardless of whether their value is measured in QALYs or by other benefit metrics. As a result, public payers often must ration access, funding treatment only for subgroups of eligible patients or negotiating outcomes-based agreements to align payment more closely with realized value.

This reality underscores why the report's emphasis on opportunity cost is so important. Even in systems without formal budget caps, collective resource constraints dictate real trade-offs. We therefore strongly support the report's conclusion that opportunity cost must be treated as an evidential requirement in any framework used to assess value. Recognizing and quantifying these trade-offs, rather than assuming they do not exist, is essential for transparent, consistent, and defensible decision-making in both public and private insurance systems.

Recommendation:

The report should clearly show how the lack of a formal opportunity-cost framework affects practices, especially in the US. Even when budgets are flexible, trade-offs are a reality. In addition to the trade-offs identified in the HEMA report, such as increased premiums and loss of insurance, the reality of these trade-offs can be seen in other aspects of insurance benefit design like prior authorization or eligibility restrictions. Recognizing these as opportunity costs would make the report's case stronger, showing that opportunity cost is an essential, evidence-based part of all value frameworks, not just a theoretical one.

2. The Opportunity Cost of Neglecting Benefit Assessment in the US Public Domain

In the US, both the use of QALY as a measure of health benefit and the use of QALY-based thresholds is controversial in the public domain, and in some contexts, is explicitly prohibited. As a result, public payers responsible for allocating public funds, such as Medicaid and Medicare, are left without clear guidance on how to evaluate the value of new interventions as they enter the market.

Without an explicit framework, yet operating under clear budget constraints, public payers must make coverage and payment decisions in a largely ad hoc manner. These processes vary across states and programs and often rely on short-term budget pressures or political considerations rather than systematic assessments of health benefit relative to opportunity cost. This environment can easily lead to suboptimal resource allocation. In the absence of a transparent value framework and a defined benefit function, it is difficult to measure the magnitude of inefficiency that results and there is no empirical evidence suggesting that current approaches, which do not use QALYs, are more efficient in utilizing available resources compared to a structured framework.

Although political and ethical concerns have made the use of QALYs and CEA controversial in the US, the complete absence of a benchmark prevents efforts to improve upon it. Even if the traditional QALY framework is viewed as imperfect, it provides a transparent reference point against which alternative

methods can be evaluated, modified, or replaced. Without such a benchmark, new frameworks cannot be empirically tested for their ability to enhance fairness or better capture health benefits.

Recommendation:

The HEMA report rightly emphasizes that any modification or extension of the traditional approach to assessing value should be accompanied by a consistent opportunity-cost analysis. We would encourage the authors to extend this reasoning one step further: the absence of an explicit value framework (such as in the US public domain) also has its own opportunity cost. Continuing reliance on unstructured decision processes imposes hidden trade-offs, undermines transparency, and risks inequitable allocation of public resources. Recognizing this as an opportunity cost would reinforce the report's broader call for consistency in how benefits are defined and valued.

3. Clarification on Distinguishing Health Benefit Measurement from Societal Value Judgments

The HEMA report defines "in-scope" benefits broadly, as all outcomes that decision makers may seek to achieve through the use of limited resources, not only improvements in health. Within this broad framing, distinguishing between benefit measurement and benefit valuation could improve clarity for HTA organizations.

- **Benefit measures** capture the components of health that accrue to individuals as a result of an intervention (e.g., survival, quality of life, process utility).
- **Societal value judgments** determine how those benefits are valued across individuals or groups (e.g., by severity, inequality aversion, rarity).

Clarifying this distinction would help HTA bodies determine whether a proposed value element expands the scope of measurement or represents a normative weighting factor applied at the deliberative or threshold-setting stage. It would also support transparent ICER interpretation, prevent potential double counting, and clarify the link between such modifiers and their associated opportunity costs.

This distinction aligns with international practice. Many health systems now apply severity-adjusted cost-effectiveness thresholds to reflect a societal preference to prioritize patients in worse baseline health. Systems such as those in Norway, the Netherlands, Lithuania, Slovakia, Hungary and the United Kingdom use multiple thresholds or equity weights to account for disease severity and rarity [5].

Understanding this distinction is crucial for the consistent application of opportunity cost principles. Introducing severity weighting implies that resources are intentionally shifted toward those with worse baseline health, which generates an opportunity cost elsewhere in the system. Acknowledging and quantifying that trade-off aligns directly with the report's call for opportunity cost to be treated as an evidential requirement in any expanded value framework.

Additionally, the rationale for excluding scientific spillover is not entirely clear. Although it does not represent a direct benefit of a current product, it reflects a societal preference to reward innovation and knowledge generation represented by a current product [6]. In that sense, it could be considered as a societal value judgement, similar to equity-based modifiers, such as severity weighting. Clarifying whether

its exclusion is based on practical reasons (e.g., measurement challenges) or on normative grounds would enhance interpretability.

Recommendation:

Emphasizing the distinction between benefit measurement and benefit valuation would improve the practical clarity of the report for HTA organizations. Clarifying in Table 4 why certain elements, such as scientific spillover, are excluded—whether due to measurement challenges or normative scope—would further enhance transparency and ensure consistent interpretation of which elements expand the benefit measure and which represent societal value judgments applied at the deliberative stage.

References

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AbbVie Comments on the HEMA Draft Report:

"Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies"

Section 3 (Table 2): Summary of Principles Guiding Specific Benefit Inclusion in Economic Evaluations

1. Considering the accelerated development of many advanced therapies (particularly in oncology), as well as increasing pressures on payers and health systems, demonstrating the clinical and economic value of innovative medicines is crucial. As health systems around the world grapple with rising costs and increasing healthcare demands, current HE methods undeniably need to evolve to assist increasingly complex HTA decision-making.[1] Given the wealth of patient-level data and impressive advancements in digital and computer sciences, defining appropriate benefits and broadening the scope of economic evaluations for demonstrating the full value of innovative medicines is welcome. HTA innovation should thus foster appropriate patient-centric benefits and HE methods that are robust and fit-for-purpose to assess future health technologies.

2. In particular, the rationale for considering alternatives to the QALY (Box 2) should include a description of its limitations. These have been discussed in many methodological papers. For instance, how to explain that most HTA organizations using cost-utility analyses (CUAs) as reference case must systematically reanalyze all CUAs submitted? Having to invest resources to reanalyze CUA models suggests that HTA agencies must have little confidence in this method. Additionally, CUAs are not seen as being patient-centric[1] and appear to lack robustness and reliability since significantly different results are often derived from using slightly different assumptions selected by HTA agencies on a case-by-case basis. This reinforces the need to look for alternative and more robust methods, or at minimum, to consider additional evidence of value to reduce uncertainty and optimize critical resource allocation decisions. Consideration should thus be given to acknowledging current limitations and allowing for alternative or supplemental relevant HE approaches and more patient-centric health economic evidence to be considered for decision-making. For instance, rather than restricting HE evaluations to CUAs (as reference case), supplemental HE methodologies (with proper justification) would provide more than one single source of truth and perspectives to be considered for value assessment, contributing to reducing uncertainty and optimizing decisions. Since uncertainty represents a significant and recurrent challenge (as often mentioned in the HEMA report), where cost-effectiveness is used, there should be a clear discussion of sources of uncertainty and reimbursement pathways that allow these to be managed and resolved in a pragmatic manner over time not to delay patient access.

3. Importantly, HTA as a process should only consider economic value following the robust assessment of clinical and broader humanistic evidence from the patient`s perspective and other relevant stakeholders. Of note, under relevance (Table 2), "health" (and by extension patient experience) is defined as the key benefit of HTA organizations. It would thus appear

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[1] Value and Outcomes Spotlight: Measuring the Value: The QALY turns 50: What is its future? What has it achieved? Nov/Dec 2024; Vol 10(6): 1-6.

to be of paramount importance that patient "health outcomes" (efficacy, safety, and patient-reported outcomes rigorously and scientifically measured in registrational clinical trials) also be primarily and explicitly valued in the context of cost-effectiveness analyses (cost/clinical outcomes) either as standalone HE assessments, or as supplement to any reference case. Additionally, contrary to the QALY, patient health outcomes objectively measured in registrational trials fully reflect and integrate the "patient experience" (as referred to in the HEMA report p.9 – CDA-AMC). By extension, RWE and composite endpoints could also be considered as effectiveness criteria in classic cost-effectiveness assessments.

4. Regarding ICER thresholds, we submit that a broader and more flexible approach based on patient clinical outcomes and key value drivers be used when determining the acceptable value of new health technologies rather than using strict and arbitrary cost-effectiveness thresholds to guide reimbursement recommendations. Since an ICER threshold and willingness to pay refer to different concepts, a clear distinction should be made (willingness to pay representing an individual's maximum price one would pay for a good or service, while the ICER threshold is a societal benchmark used to determine if a new treatment is deemed cost-effective).

5. Under relevance (p.26): "decision makers who use HTA are typically assumed to be risk neutral with respect to each decision they make about individual heath technologies because the health of the populations they serve is only marginally impacted by each individual reimbursement". We submit that the assessment of evidence and estimation of overall benefits and costs (including beyond healthcare budgets) should be conducted independently from (and prior to) pricing and reimbursement decisions. Ultimately, the economic value should not dominate the clinical value but be equitably considered to reflect the full value of clinical innovation.

6. Overall, the proposed principles of relevant and opportunity costs are aligned with the current mandates of these organizations. However, it is important to note that there may be a status quo bias in the report, where categories that are already in place are given higher value and not compared to the same standards as the new categories proposed. There is not a great justification for the scope limitation on benefits only, when costs are a major part of the picture and influence healthcare systems' budget. In particular, the guiding principle of valuation based on the public perspective can lead to underestimation of the value.

Section 4 (Table 3): Additional value elements in scope

7. As previously stated, patient-centric clinical health outcomes rigorously measured in pivotal trials should be valued on their own merit in health economic evaluations (either as standalone or as supplement to CUAs) to truly reflect disease-specific clinical benefits and patient experience. Of note, where cost-effectiveness is used, the estimation of benefits and costs should be presented separately from relevant perspectives for each country.

8. Most elements are covered, though the specific scope of the document means that other categories are left out (e.g., productivity losses for caregivers). There also may be some missing elements: for example, it is excluding aggregate effects on populations' health and

the resources of the healthcare system (e.g., a treatment which affects millions and that removes the need for IV chair will free resources for other diseases, potentially having a benefit spillover, and vice versa, going from no IV chair to needing one could block). The impact on other health systems "bottle necks" should also be considered as part of the value assessment frameworks for new health technologies (e.g. impact on access to health services, reduction of long waiting list for specialists, and diagnostic or medical procedures in many countries).

9. The following value elements could be added: i) Long-term societal impact, especially in neuroscience, interventions that alter lifetime independence, societal participation, or intergenerational effects (e.g., pediatric/ophthalmic therapies) could be better captured. ii) Clearer positioning of caregiver and family wellbeing (for the same disease areas like NS and Eye Care) iii) Value of platform technologies: Platform technologies, or diagnostics, recognizing that a therapy may pave the way for future innovations or system efficiencies could be considered, though current framework excludes this.

10. Resources/delay therapy for other diseases. A deeper reflection on EQ-5D and its sensitivity to capture the multiple dimensions of health would be welcome. It is a bit contradictory when the report states that HTA bodies are risk neutral, but then it is clearly seen in their reports that they tend to be critical of uncertainty (given same expected value, they would advocate for the alternative with lower uncertainty, which is against the risk neutrality principle).

Section 4 (Table 4): Additional value elements out of scope

11. If we assume that the benefits-only focus is of interest, then the rationale can make sense. However, focusing on benefits-only may be limiting and short-sighted, particularly when opportunity costs are at the center of the report, and in a highly interconnected economy where healthcare budget is not a constant but a function of societal preferences, the economy (GDP growth, which depends on productivity), and taxes/available income for insurance premiums. By focusing only on benefits, HTA recommendations may create welfare losses to society.

12. From the lens of benefits only, rationale for exclusion seems plausible. However, the guidance can be quite misleading and create an impression that these costs are not relevant. It should become clearer from the paper what type of costs should be considered in the economic evaluation.

Section 5: Conclusions and Recommendations

13. Overall, the proposed recommendations appear overly complex and prescriptive for the broad HTA community. They should perhaps be simplified. Of note, HEMA might want to raise awareness on the need to broaden the scope of value assessment frameworks, and to evolve current methods through HTA innovation strategies that leverage patient-level data, reliable data sources, and robust HE methods to assess and capture the full value of innovative medicines for patients, health systems, and society. Notably, the report should address common limitations and allow supplemental methods that can incorporate patient-

centric benefits and health outcomes to ensure more consistent assessments of economic value to increase the reliability of the results, reduce uncertainty, and reflect real patient experience.

14. Given the framing limitations and the points already mentioned, the recommendations are consistent, though the points on productivity and on DCEA do not seem consistent. i) The point made against individual risk preferences is accurate and the focus should be on more granular benefit measures as well as individual risk assessments and preferences. In this sense, HTA bodies should be more aware of their implicit bias in terms of risk. ii) Productivity: To the extent that healthcare resources are paid with taxes or premiums, and these are derived from income, favoring younger populations (working age, or populations who would be able to work in the future) makes sense, as there is an opportunity cost of not doing so (less resources for health system). Furthermore, there are some diseases where the productivity dimension is hugely important, in some cases they can block economic development as a whole, which in turn limits healthcare budget and population health, so it does make a lot of sense to include this dimension. A clear example of this is malaria where a 10% decrease in prevalence has been associated with 0.3% increase in per capita income growth,[2] so there can be a huge opportunity cost of excluding this dimension of the analysis. Healthcare expenditure is highly dependent on income, which means considering productivity is on the remit of an HTA body which looks after health (since a part of the productivity benefit of a treatment will end up in higher available healthcare budget). iii) DCEA: in the dimension of relevance, for some reason the report does not put in context the impact of DCEA on decision making. When compared to other items, DCEA shows that the impact could be of second or third order in terms of relevance for health inequality (e.g., in Alzheimer's[3] with a 0.009% reduction in health inequality). Are medicines the right way to handle inequality in health? What is the opportunity cost of spending resources in these analyses or changing treatment decisions considering this instead of targeting highly effective, known interventions to reduce health inequality? (e.g., school meal programs)[4]

15. Disease modifiers: the report mentions that NICE does apply disease modifiers for rare diseases, but it does not evaluate this approach with the same criteria as it does to these other approaches. When it mentions " No additional benefits should be routinely incorporated into economic evaluation until there is an evidential basis to reflect them in opportunity costs." What evidence are these HTA bodies using to create these differences? Why are disease severity thresholds hard instead of soft (continuous)? Why is it optimal to do this but then the report questions including productivity gains because it may prioritize working age population (or future workers) over those that do not work? This is another example of status quo bias, where new benefits are not measured with the same standards as current ones.

Respectfully submitted on behalf of AbbVie, October 30th 2025.

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30 October 2025

ABPI consultation response to draft HEMA report "Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies"

Purpose and scope of the report

One of the stated aims of HEMA is to "Provide guidance and recommendations to the HTA community — this guidance may relate to the adoption of novel methods, modifications that might be required, uncertainties in the application of certain methods, and suggestions for further research."[1]

In several areas, the report appears to recommend standards that are not currently adopted by the HTA agencies involved in its development. For example, it proposes that if distributional cost-effectiveness analysis (DCEA) is used it should be used uniformly across all evaluations, which is not standard practice at NICE, where DCEA is recommended to be used only for evaluations where "clear evidence of a significant burden of health inequalities in the eligible population."[2]

While the effort to make "gold-standard" style recommendations is understandable, these do not appear rooted in the pragmatic reality of conducting HTA, even among those organisations whose methods are established and advanced. HTA agencies carrying out assessment have to carefully balance complexities and data uncertainties to reach decisions which impact patients. The recommendations in this report should be framed with this practical context in mind; otherwise, there is a risk of setting expectations that are too high, potentially discouraging agencies from adopting elements of value that are particularly relevant within their own jurisdictions.

The report makes reference to being "primarily developed" for or having a "focus [..] on the needs of" NICE, CDA-AMC and ICER. While using examples from these agencies to inform the output of the report is reasonable, this stated focus appears to be in tension with the aim of providing recommendations applicable to the wider HTA community. It also risks the HEMA outputs being perceived as the HTA bodies involved in the initiative setting standards directed at themselves and their potential future work programmes.

Grounding guidance in practical implementation

Many of the recommendations presented in the executive summary and conclusion adopt an overly rigid stance that lacks the nuance found in the main body of the report and do not adequately reflect the practical realities of conducting HTA. It is important that these recommendations are appropriately caveated to avoid setting an unnecessarily high bar for evolving HTA methods to include value elements that matter to patients, the public, and society.

As it stands, the report represents a missed opportunity to provide usable methodological guidance that would enable HTA agencies to appropriately capture important additional areas of value. It falls short of providing clear signposting of future research priorities for each topic, which would support the development of appropriate evidential standards. Additionally, whilst an evidence-based approach is important, a balance needs to be struck to ensure countries that use HTA are appropriately incentivising and rewarding innovation in healthcare interventions.

Appropriateness of principles

Principles 1 and 2 are appropriate considerations, though as noted elsewhere in this response, they may not always have been applied in a fair and reasonable fashion when assessing the appropriateness of including the additional elements of value that are the subject of this report.

The ABPI does not consider the third principle "Need to reflect any additional benefit in the assessment of opportunity costs" to be an appropriate principle to apply. The report is overly focussed on the authors' views that HTA decisions should solely be grounded in what the supposed opportunity cost is, rather than having a broader perspective about the added value of healthcare technologies beyond direct health-related benefits.

While the agencies discussed in detail in this report do explicitly consider opportunity costs, this is not universally true.[3] Moreover, even among these agencies, there is ongoing debate around the primacy of focussing on the (arguably unknown) opportunity cost of HTA decisions versus the need to be globally competitive and take a broader view of the positive impact of investing in medicines on society and economies. Existing HTA methods are unlikely to fully meet the evidentiary demands implied by this principle. Supply-side threshold estimates are subject to considerable uncertainty and critique,[4] making it problematic to impose a higher evidential standard on additional elements of value than on those already routinely considered. Attempting to find a different representation of the opportunity cost for each individual element of value is highly unlikely to be practical.

The generalisability of this principle is also questionable. Many HTA bodies use thresholds based on historical decisions, demand-side willingness to pay, or have no explicitly stated approach at all.[3] Although the report acknowledges the weak link between stated thresholds and opportunity costs, it does not explore the implications of this for the appropriateness of the principle itself.

We suggest Principle 3 is removed or at the very least reframed as just a consideration when assessing the pros and cons of HTA methods changes.

Implementation of modifiers *via* weighting

In reference to both severity and DCEA the report implies that a weighting of less than one is required to operationalise any modifiers. For example, the report states that "*HTA organizations still need to manage the implications for opportunity cost of attaching weights greater than one to gains for patients with severe disease as compared to weights less than one for gains for less severe disease*." While this is one potential approach to implementing modifiers, it does not reflect either their purpose or how they are used in practice by HTA bodies. For example, NICE does not weight QALYs for less severe conditions less than 1. Instead QALYs for moderately severe and very severe conditions are assigned weights of 1.2 and 1.7 respectively.[2] This is based on evidence suggesting a preference for the public to value QALYs more highly in severe conditions. While the report correctly points out that severity modifiers thresholds used by NICE do not have an empirical basis, part of the reason for this is that the NICE severity thresholds were explicitly designed to be "opportunity cost neutral" with respect to the previous "End of Life" modifier, As a result of this it is not clear that the severity modifier is fulfilling the purpose for which it is designed, and available evidence suggests that it is likely to undervalue treatments for more severe conditions compared with public preferences.[5]

Suggesting that modifiers must be implemented with weights less than one implies that no methodological evolution should allow greater value for some medicines without reducing it for

others. This is neither a view that is progressive nor aligned to government ambitions to improve access to medicines.

Including productivity as a value element

The framework implies that if productivity is to be considered in a decision-making framework, the opportunity costs associated with introducing technologies with a positive benefit on productivity must be considered. Specifically regarding England, the report states that *"Each lost QALY in opportunity cost is also associated with an average a net productivity effect of £11,600."*

It is unclear in the reference cited in the report[6] how the £11,600 figure has been derived. We also note a recent paper from NICE,[7] which states that "generating this type of evidence would be an enormously complex task because it is not feasible to directly analyse the displaced services themselves and additional advanced statistical analysis would be required. So far, studies have looked only at the forgone health of displaced services and even this has stimulated significant debate among researchers."

There appears to be a contradiction between NICE's stated position, which states that studies so far have only looked at the forgone health of displaced services and the report, which cites a specific productivity effect.

Local context and policy ambitions are also important to consider in any discussion on perspective. For example, in the UK economic inactivity results in lost revenue and increased health service costs, with around 3 million people economically inactive due to ill health.[8] Therefore, there is a strong focus on health interventions which improve productivity in the NHS 10-year plan.[9]

The report raises fairness concerns around the inclusion of productivity benefits, particularly the risk that prioritising working-age populations could lead to inequitable decisions. While this is an important consideration, it's worth noting that HTA agencies already make decisions that favour certain age groups and there are methods that can be applied using distributional weights to take into account equity considerations. For example, NICE applies greater flexibility in paediatric evaluations and uses a higher threshold in the HST programme, which predominantly benefits younger people. Additionally, considering the positive impacts of productivity benefits highlights the benefits of considering additional evidence of value, such as spillover effects, which may mitigate some of the concerns around inequity. For example, a health intervention that enables someone to return to work may also allow them to resume caregiving responsibilities, positively affecting non-working-age family members, such as children or elderly relatives. These indirect benefits are not currently captured in HTA processes but are highly relevant when considering the fairness of methods that appear to prioritise working-age individuals.

It could be argued that HTA agencies should have a broader remit of maximising social welfare, rather than purely maximising health. This goal is recognised to varying degrees by ICER (which includes a modified societal perspective), CDA-AMC (which has an ongoing pilot of a societal perspective) and NICE (which has the option of including a societal perspective as a non-reference case analysis in certain situations). Guidance on how productivity (or other wider societal benefits) could be most appropriately included in HTA evaluations and discussion of preferred methodologies, alongside their strengths and limitations would be a valuable addition to this report.

Use of Distributional Cost-Effectiveness Analysis (DCEA)

Recommendations around use of DCEA do not reflect current usage of DCEA by HTA bodies, are not supported by strong evidence and may conflict with public preferences. The report implies that if DCEA is used it should be used across all evaluations. This does not reflect the current usage of DCEA by agencies such as NICE, nor the practical limitation that sufficient evidence to conduct a DCEA is unlikely to be available across all indications. If the intent of the report was instead to state that use of DCEA should be symmetric (i.e. consider where a new technology may increase health inequalities rather than decrease it), we note that this is a normative decision and we are not aware of evidence suggesting that the public supports this application. Indeed, in the NICE Listens exercise on health inequalities[10] it is stated that "participants believed that by improving conditions and outcomes for most people, standards would gradually improve for all (including those who were more disadvantaged)." Where benefits came at the expense of reducing health inequalities, participants preferred to ensure there was no loss of life for the more disadvantaged groups and that alternative action was taken to improve their health outcomes and mitigate widening inequalities. This suggests an asymmetry in public preferences around health inequalities in that the public may support the introduction of technologies that increase health inequalities, providing they improve health outcomes for the population as a whole.

The recommendations in this report should not serve as an impediment to HTA agencies in implementing consideration of health inequalities in line with stated public preferences.

Lack of due consideration of or explanation of patient preferences and the patient experience

Some of the recommendations in the conclusions and executive summary could be misinterpreted by the lay-person as stating that "individual patient preferences" should not be used in HTA. These recommendations appear to be focused specifically on additional value elements included in measures like the GRACE-QALY but could be interpreted to extend to, for example, patient preference studies in individual therapy areas, which may highlight additional values of new therapies (for example, preferences for specific adverse event profiles, mechanism of action etc).

Similarly, the recommendation that "The deliberative process within HTA, which may consider potential additional benefits qualitatively, should not be used in a way that bypasses the consideration of opportunity costs" also appears to neglect to consider the patient experience of the HTA process and need for value judgements in decision making.

Some elements of the framework have been unreasonably applied

There are several examples of where the framework seems to have been applied based on the authors' interpretations of the studies currently available for informing the evidence base for each of the selected value elements.

For example when considering the relevance of the value of hope, the authors dismiss patient preferences for treatments that may offer a small chance of a greater improvement in health outcomes, stating: *"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"*

While such preferences may appear irrational to informed researchers it seems unreasonable to

dismiss them without careful consideration. As an analogy, it could be argued using similar logic that discounting, which is standard in the HTA process, should be excluded based on this framework as a preference for benefits occurring in the future could be interpreted as irrational. While there may be valid reasons for not including concepts such as value of hope, this example doesn't appear to provide strong evidence this value has no relevance and is potentially a misuse of the framework.

Similarly, when considering valuation for the value of hope the authors state that "it is the preferences of individuals assessing the benefits from available treatments for themselves that are proposed for inclusion" and that this differs from "the standard approach where it has been considered that health care decision makers seek the average preferences of the general population."

The report later cites a preference study[11] that aggregates a section of the general US population, this appears to be in line with the "standard approach" and principles of valuation as defined in the framework. While several valid limitations of the study are highlighted, it remains unclear how, in the context of the report framework, the principles of valuation used in the cited study differ from, for example, EQ-5D; where a representative sample of the general population state their individual preferences for health states which are then aggregated to provide an average population utility value.

In general, while several methodological limitations related to the value elements discussed in the report are valid, these have presented simply as evidence of the value element not aligning to the principles in the framework. A more valuable contribution would be a set of actionable research recommendations to support the inclusion of additional value elements, where appropriate for individual HTA bodies.

Spillover effects

The report notes that "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. […] The challenge has been more practical, however, in generating suitable evidence quantifying such spillovers and to ensure these are causally related to the interventions under evaluation."

While this is accurate to an extent, typically only the health benefits of direct caring is captured (if at all) and the impact on other members of the immediate family is not addressed. A more detailed consideration of these additional "non-routine" elements would be within the scope of the report and of value to the HTA community. As the authors note, evidence generation in these areas can be challenging. Recommendations of further potential research, or appropriate signposting to recommendations from the literature (for example Pennington 2023[12], Campbell 2024[13]), to act as an enabler for the collection and incorporation of evidence related to carer and wider family quality of life would be a valuable output. Furthermore, for healthcare systems as resource strained as the UK, it would be instructive to note that community spillover can include impacts such as waiting lists for care and return to the community. The example given of infectious diseases is valid and robust, but a more general non-communicable example could be provided as well.

Minor textual clarifications

Box 3 provides a useful visual explanation of the concepts under consideration. The text on the dotted lines on the figures is difficult to read, please move the text beside the lines.

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Response to the Draft Report of the HEMA: On the Value of Knowing
Bernarda Zamora and Louis Garrison

HEMA Page ES1 : process benefits (such as the value of knowing about disease from diagnostics): "process utility" benefits such as the value associated with information about future prognosis with no impact on health outcomes.
We present four arguments to show that the value of knowing has an effect on health outcomes per se, and also on the utility of health outcomes.

1. The concept of "process utility" assumed to be different from "outcome utility" is not standard. There is a difference between process and outcomes. Yet, the initial definition of utility from process was called "Procedural Utility". Regarding valuation of process, procedural utility has an effect on individuals' reported subjective well-being, which is the definition of utility [1]. HEMA states that the information from diagnostics does not affect the level of the health outcome, measured by QALYs. Even if accepting that life expectancy do not change, the concept of procedural utility is related to EQ-5D as defined by reported outcomes in subjective well-being.

2. The concept "peace of mind" is used as part of the "value of insurance". Citing again the concept of procedural utility as derived "from activities towards which people have an intrinsic attitude", as well as our work on Value of Knowing [2], the concept of "peace of mind" is linked to knowing the result of a diagnosis, independent of actions derived from the information. We have cited examples of positive willingness-to-pay for diagnostic information. Whether this is related to possible treatment, value, or planning, or an intrinsic attitude as "peace of mind", can be reflected.

3. Value of knowing focuses on individual patients' preferences. HEMA states that this implies a normative position with no implications on societal aggregation or trade-offs to be considered in economic evaluation. Without the need to enter into whether introducing the value of knowing as individual (normative) preferences, a direct aggregation of the value of knowing is the uptake of diagnostics. The uptake of screening has been clearly linked to the value of knowing [3], or fear of knowing. As an aggregate effect, uptake should be considered in the economic evaluation of diagnostic programs.

4. Value of knowing and Value of Planning is included in NICE manual (NICE, 2023, page 41, paragraph 2.2.19).

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Re: HEMA Draft Report — Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies
October 2025

Introduction

the cancer collaborative welcomes the opportunity to comment on HEMA's draft report. Our submission is grounded in a national patient consultation initiative focused on modernizing patient engagement and value assessment within Canadian HTA frameworks. Over the last year, we have worked with patient groups, individuals with lived experience, and advocates across multiple therapeutic areas to co-develop recommendations for a more transparent, equitable, and patient-responsive HTA process.

The HEMA draft report represents an important contribution to the global conversation on evolving value assessment. We support the intent to ensure rigour, transparency, and relevance in determining which additional benefit elements should be incorporated into economic evaluation.

Our feedback reflects alignment with HEMA's principles, and highlights key areas where patient evidence and practical experience suggest the need for stronger ambition, clearer operational pathways, and earlier co-development with patient communities.

I. Alignment with HEMA's Three Tests for Additional Value Elements

1. Relevance to HTA Mandates

We agree with the requirement that additional value elements must fall within HTA bodies' responsibilities. However, patients emphasized that current definitions of "health benefit" are narrower than how value is experienced. For example, time to diagnosis, access to biomarker testing, functional ability, treatment burden, emotional wellbeing, and family impact meaningfully shape outcomes but remain insufficiently reflected in economic evaluation.

Modern definitions of value must recognize that health system stewardship includes avoiding preventable loss of function, inequity, and household-level harm, not only maximizing QALYs.

2. Measurability and Methodological Feasibility

We agree that inclusion should be contingent on robust and consistent measurement approaches. Patient groups, however, stressed that feasibility must not be conflated with maintaining the status quo. Emerging tools—including standardized patient-experience measures, qualitative

evidence frameworks, real-world evidence (RWE) infrastructure, and structured preference-elicitation methods—can support measurement today.

Patients emphasized that "lack of perfect data" is often cited as a barrier, while lack of structured guidance and incentives to generate such data is a more accurate limiting factor.

3. Opportunity Costs

We agree that trade-offs must be considered. Yet, opportunity cost analysis should incorporate societal and long-term health system consequences—including diagnostic delays, lost productivity, caregiver burden, and avoidable system strain—rather than limiting analysis to near-term system costs.

Failure to account for these costs may lead to decisions that appear efficient on paper but are misaligned with patient welfare and long-term system sustainability.

II. Response to HEMA's Four Benefit Categories

1. Risk Preferences and Uncertainty

HEMA concludes more research is needed before risk-related preferences can be included. Our consultations show patients consistently value the possibility of meaningful benefit, particularly in life-limiting conditions. Delaying inclusion risks undervaluing therapies where hope, optionality, and heterogenous benefit are central to decision-making.

Recommendation:
Develop interim methodological guidance and pilot preference-elicitation workstreams rather than deferring action.

2. Value of Information and Care Experience

HEMA cautions against double counting. We agree. However, current methods risk systematically under-counting:

- value of earlier diagnosis and avoided diagnostic delay,
- emotional and cognitive burden of uncertainty, and
- quality of care delivery.

These elements are not consistently reflected in QALYs or existing cost-effectiveness analyses.

Recommendation:
Define boundaries between clinical effect capture and experience-of-care elements, and develop guidance for structured integration of patient experience data.

3. Equity Considerations

We strongly support HEMA's emphasis on transparency, consistency, and definitional clarity. Our findings indicate that without operational mechanisms, equity risks becoming an aspirational principle rather than a functional criterion.

Recommendation:
Create a standardized equity impact framework that includes access to diagnostics, representativeness of evidence, and differences in time-to-access.

4. Burden on Patients, Families, and Society

We agree this domain requires careful handling to avoid unintended prioritization. However, patients stressed that economic and social burden is currently systematically undervalued, particularly in rare disease, cancer, and mental health.

Recommendation:
Establish methodological guidance for structured inclusion of caregiver burden, productivity, and ability to participate in life roles—supported by patient-generated data and post-market evidence.

III. Opportunities for Strengthening the Report

We respectfully recommend that HEMA:

1. Define a phased adoption pathway for new value elements rather than an open-ended research horizon.
2. Co-develop measurement and implementation guidance with patient communities, HTA agencies, economists, and health system leaders.
3. Support early and iterative patient involvement in defining benefit categories and evidence requirements.
4. Pilot test methods in real-world evaluations before finalizing recommendations.

Our consultations reveal that the patient community is ready to collaborate on methodological development. A structured partnership model would accelerate rigor and feasibility.

Conclusion

We value HEMA's leadership in advancing clarity and discipline in value assessment. To ensure decisions reflect public values, lived reality, and modern standards of equity, it is essential to move beyond conceptual acknowledgment toward clear operational guidance, demonstration projects, and co-development with patients.

the cancer collaborative stands ready to support this work through patient-driven evidence generation, methodology pilots, and collaborative design.

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Center for Innovation & Value Research

Response to the Draft Report of the Health Economics Methods Advisory (HEMA): "Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies

October 30, 2025

Dear Health Economics Methods Advisory Group,

The Center for Innovation & Value Research (Center) appreciates the opportunity to provide comments on the draft report, "Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies."

The Center is a 501(c)3, non-profit research organization committed to advancing the science, practice, and use of patient-centered health technology assessment (HTA) to support decisions that make healthcare more meaningful and equitable. Founded in 2017, the Center's membership includes researchers, patients, payers/purchasers, clinicians, and innovator stakeholder communities. The Center's work emphasizes collaboration and exploration of new solutions in pursuit of a U.S. learning healthcare system supported by patient-centered HTA and focused on high-quality, efficient, innovative, and accessible care for all people and communities.

We commend HEMA for its rigorous framing of relevance, valuation, and opportunity cost as guiding principles and for addressing the complex question of how to define benefits in economic evaluation. However, several aspects of the draft report could be strengthened to ensure its applicability to contemporary, patient-centered HTA practice in the United States.

Recommendations to Strengthen the HEMA Report

- **Elevate patients and caregivers from commenters to co-creators.**
  The report treats deliberation as an adjunct to quantitative analysis (Box 1) rather than a source of empirical insight. The Center's *Blueprint for Patient-Centered Value Research* demonstrates how patient advisors can co-develop benefit models, improving validity and societal relevance. Future iterations of this report should include patient advisory panels for methodological development, not just post hoc review.
- **Broaden what counts as "relevant" benefits.**
  The report focuses almost entirely on population-level health gains using a healthcare perspective, but patients define value much more broadly. HEMA should recognize patient-identified outcomes—such as treatment burden, mental health, ability to work or learn, and social connectedness—as part of what's relevant in assessing benefits. To ensure that decision-makers have comprehensive views of value, the use of a societal perspective alongside the healthcare sector perspective should also be encouraged. The Center's *Major Depressive Disorder* Value model is

one example where patients helped identify these broader outcomes as essential to understanding value.

- **Treat equity as a foundational principle, not a modifier.**
  Treating equity as just another "novel value element" underplays its centrality to HTA legitimacy. It should be built into the core principles of HTA—ensuring that benefits and burdens are not distributed unfairly across populations. Using frameworks such as the **Racial Equity and Policy (REAP)** framework would help HEMA systematically assess these impacts. While the report identifies equity as a key value element and notes NICE's use of equity modifiers in some select cases, U.S. HTA practices still lack standardized guidance. Given the complexity of healthcare systems and sociopolitical contexts, the final report should call for systematic testing of these methods across jurisdictions, particularly in populations historically underserved in the health system. (IVI & Sick Cells, *Finding Equity in Value*, 2022; Cookson et al., *Value in Health*, 2017).
- **Be explicit about who bears the opportunity costs.**
  Lack of evidence on opportunity costs should only be considered a temporary barrier to the inclusion of novel value elements. Opportunity cost has been estimated for use in traditional CEA and HTA; it should be possible to do the same for broader perspectives and cross-sector comparisons. In addition, opportunity costs are not neutral—when systems already underserve certain groups, traditional cost-effectiveness thresholds can reinforce inequity. HEMA could lead by exploring equity-weighted opportunity cost analyses or distributional cost-effectiveness analysis to make those trade-offs more visible (Asaria et al., *Social Science & Medicine*, 2016; IVI–Sick Cells, 2022).
- T**ransparency should be a core principle**.
  Transparency in HTA processes, methods, and communications are important, yet this topic is notably underrepresented throughout the report. Transparency, such as through open-source models, publicly accessible meetings, patient-friendly reports, and open access publications, are essential for patients and other stakeholders to trust and engage with the HTA process.
- **Do not over-emphasize concerns about double counting.**
  While there are legitimate concerns about double counting when including novel value elements, these concerns should not preclude exploration of their use. Research should be conducted into ways to parse value across these novel elements to reduce the risk of double counting. In the meantime, it should be acknowledged that excluding these elements may lead to the under-counting of benefits.
- **Acknowledge that evidence is more than numbers.**
  Patients' lived experience is evidence. HEMA should make space for qualitative and real-world data that show how treatments actually affect daily life. At the same time, deliberative processes must not bypass quantitative rigor. The report acknowledges this risk but provides limited guidance on how and when patient and caregiver voices should be meaningfully incorporated. Mixed-methods approaches can

connect these insights to quantitative models in a rigorous way (Perfetto et al., *Value in Health*, 2020; Linthicum et al., *Finding Equity in Value*, 2022).

- **Pilot, don't pause, novel value elements—especially for the era of precision medicine.**
  The report's call for restraint risks leaving HTA behind the science. HEMA should identify ways to pilot and test new value elements in real-world studies, particularly for cell and gene therapies and other precision treatments that challenge traditional population-based measures. Practical implementation and experimentation allow for rapid learning about the measurement and use of novel value elements in HTA and decision-making. The field should evolve through experimentation, not exclusion, to ensure HTA remains relevant to 21st-century innovation (Xie et al., *Pharmacoeconomics*, 2021; Innovation and Value Initiative, 2024).

By embedding patient partnership, equity, transparency, and methodological pluralism into its recommendations, HEMA can position itself as a leader in advancing global HTA methods that are not only scientifically rigorous but socially accountable. The Center would welcome collaboration on pilot initiatives and methodological testing to operationalize these principles in practice.

If you have any questions, please contact me at rick.chapman@valueresearch.org.

Regards,

Richard Chapman
Head of Research
On behalf of the Center for Innovation & Value Research

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Patient Advocacy Coalition Response to the HEMA Draft Report

Preface

This annotated commentary has been prepared by The CML Society of Canada as an evidence-based response to the Health Economics Methods Advisory (HEMA) Draft Report (October 2025). Its purpose is to ensure that patient-defined outcomes, Value-Based Healthcare (VBHC) principles, and real-world lived experiences are represented in the evolving methodologies guiding HTA decisions in Canada and internationally.

The analysis integrates economic, clinical, and ethical perspectives, aligning each section of the HEMA report with patient advocacy priorities. Direct quotations from the report are paired with commentary identifying potential areas of bias, omission, or misalignment with patient-centred care. Empirical evidence on long-term outcomes, capability, and the 'value of hope' is referenced to support each recommendation.

This document aims to establish a shared platform for patient organizations to:
- Influence HTA modernization through inclusion of VBHC outcomes (Capability, Comfort, Calm)
- Promote transparent deliberation processes involving structured patient input
- Ensure long-term and tail-benefit modeling for chronic and rare diseases
- Encourage equitable, data-driven decision-making across ICER, NICE, and CDA-AMC frameworks

A word on HEMA Contributing Authors: Background and Methodological Leanings

The HEMA report is authored by a distinguished panel of academic health economists, primarily affiliated with institutions shaping HTA policy globally. Their expertise adds technical rigor but also reflects a methodological bias toward efficiency and modeling coherence over patient heterogeneity. Below is a brief profile of each contributor and its implications for advocacy review:

- R. Brett McQueen, PhD – University of Colorado; pharmacoeconomics and HTA expert; payer-centric orientation.
- Allan Wailoo, PhD – University of Sheffield; Director, NICE Decision Support Unit; aligns with UK cost-effectiveness remits.
- Aki Tsuchiya, PhD – University of Sheffield; specialist in QALY valuation and social welfare; favors aggregate over individual preference.

- Lauren E. Cipriano, PhD – Ivey Business School; Canadian policy analyst; contributes system-level modeling expertise.
- Jason Robert Guertin, PhD – Université Laval; Canadian HTA expert with strong methodological rigor but limited VBHC emphasis.
- Denise Schmidler, PhD – Duke-Margolis Institute; payer engagement strategist; pragmatic but market-focused.
- Lotte Steuten, PhD – Office of Health Economics; promotes multi-criteria analysis and value frameworks; industry-aligned pragmatism.
- Sean D. Sullivan, PhD – University of Washington; pharmacoeconomics authority; adheres to classical cost-effectiveness foundations.
- Kednapa Thavorn, PhD – Ottawa Hospital Research Institute; specializes in real-world cost-effectiveness evaluation.
- Mark Sculpher, PhD – University of York; foundational architect of opportunity-cost theory in HTA; promotes symmetry across decisions.

Collectively, the authors' academic authority gives credibility to the report's technical framework. **However, the absence of patient advocates, ethicists, and VBHC implementers skews the analysis toward traditional efficiency-driven perspectives.**

Executive Summary Analysis

The Executive Summary outlines three guiding principles—Relevance, Valuation, and Opportunity Cost—each limiting innovation unless empirically justified. It discourages the addition of new value elements (risk attitudes, process value, equity) unless these can be symmetrically measured against opportunity cost. While methodologically sound, this approach restricts HTA evolution and risks sidelining patient experience.

Key Advocacy Flags

• Over-reliance on population-level QALY valuations excludes lived experience and patient diversity.

• The principle of 'opportunity cost symmetry' freezes innovation and disregards qualitative evidence.

• Equity is acknowledged but left optional, perpetuating structural inequity in access.

• VBHC and the 3Cs (Capability, Comfort, Calm) are absent from consideration.

• ICER's 3–5 year modeling horizon undercounts durable value in chronic and rare diseases.

1. Opportunity Cost and Resource Trade-offs

"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…"

Why flagged: This zero-sum framing ignores dynamic system value and improved long-term outcomes from remission or independence.

VBHC/ICER link: VBHC conflicts with this narrow definition by recognizing longitudinal benefits and system resilience.

• Fails to recognize VBHC's multidimensional definition of value (Capability, Comfort, Calm).

• Mentions ICER's evLY/QALY use but not modeling horizons; in CML, ICER's 3-year models undervalue long-term survival and remission.

Recommended advocacy action: We call for dynamic modeling of system savings and reinvested value over time.

In practice, this means that HTA models should not stop at measuring what a therapy costs today. They should also show what it *saves* the system tomorrow — and how those freed resources can buy new health gains for other patients. Over a lifetime horizon, this captures the real, evolving value of innovation.

2. Definition of Benefit (Population vs. Patient Perspective)

"Preferences of the public are typically used to measure health…"

Why flagged: Confirms the exclusion of patient preference data from QALY valuation, erasing lived experience.

VBHC/ICER link: VBHC redefines benefit around the patient's own goals and daily functionality.

Opportunity cost is treated purely in monetary terms, not in lost patient outcomes or delayed recovery.

• ICER's 3–5-year windows distort value for lifelong therapies, demand lifetime projections.

• VBHC advocates should emphasize that resource use should reflect total health system impact, not just budget-year snapshots

Recommended advocacy action: We recommend that HTA bodies incorporate **patient-derived utility values**—that is, health-state valuations directly elicited from patients living with the condition, rather than relying solely on public preference weights.

This can be achieved through the use of validated **patient-reported outcome instruments (PROMs)** and **direct preference elicitation** (e.g., time-trade-off or discrete-choice experiments with patient samples). Incorporating patient-derived utilities would improve the sensitivity of models to factors such as symptom fluctuation, fatigue, treatment burden, or functional independence—elements that general-population tariffs often overlook.

Where feasible, agencies should publish results **with and without patient-derived utilities** to show how lived-experience valuations alter incremental QALY and ICER results. This dual reporting would enhance transparency and better align HTA with Value-Based Healthcare principles of *Capability, Comfort, and Calm.*

3. Adaptation to Ill-Health

"It has been argued that a focus on individual patient utilities may not be appropriate because it penalizes a patient's adaptation to ill health."

Why flagged: This dismisses resilience as bias rather than capacity.

VBHC/ICER link: Contradicts VBHC's 'Capability' domain emphasizing function despite disease.

Relevance principle – must evolve with patient participation to redefine what matters.

• Valuation principle – averages erase heterogeneity, advocate for stratified patient preference data.

• Opportunity cost principle – should include long-term social and economic gains, not just short-run system displacements.

Recommended advocacy action:
We would like to see that adaptation not be framed as a methodological bias to be corrected, but as evidence of **empowerment and capability preservation**—key indicators of real-world value.

In HTA terms, adaptation reflects the patient's ability to maintain function, autonomy, and quality of life despite chronic illness or treatment side effects. This capacity should be modeled as a **positive outcome** rather than discounted as a "response shift."

HTA bodies should therefore consider incorporating **capability-based outcome measures** (such as the ICECAP-A or EQ Health and Wellbeing index) alongside HRQoL instruments. These tools capture patients' ability to "live well with disease," aligning with the *Capability* and *Comfort* dimensions of Value-Based Healthcare (VBHC).

Reporting both **traditional HRQoL** and **capability-adjusted results** would provide a fuller picture of health outcomes and prevent underestimation of therapies that improve patients' capacity for independent living and participation in daily life.

4. Risk Attitudes and Value of Hope

"Patients who are severely ill have a higher certainty equivalent for riskier treatment options… This could equally be termed 'desperation' rather than 'hope.'"

Why flagged: This language pathologizes hope, ignoring empirical data linking hope to survival, adherence, and psychosocial health.

VBHC/ICER link: VBHC recognizes hope as a measurable contributor to Comfort and Calm, central to real-world outcomes.

Risk attitudes – rejects inclusion of 'value of hope'; this neglects terminal and rare-disease realities.

• Process of care – minimizes psychological and informational value; VBHC treats reassurance as measurable benefit.

• Equity – optional, not mandated; VBHC requires systematic inclusion and reporting of equity impacts.

• Broad perspectives – productivity recognized only partially; caregiver outcomes should be formalized as secondary benefits.

Recommended advocacy action:
We call for the **structured integration of GRACE-style risk-adjusted cost-effectiveness analyses** in oncology and rare-disease HTA to capture the *Value of Hope*—patients' rational preference for treatments offering small probabilities of major benefit.

The GRACE framework extends standard QALY modeling by incorporating risk preferences into survival valuations. Applying this approach within existing HTA appraisals (e.g., for TKIs in CML, gene and immunotherapies) would reveal how recognizing hope and uncertainty tolerance influences incremental cost-effectiveness ratios.

Embedding such analyses within current evaluation processes—rather than limiting them to research "pilots"—would align HTA with VBHC's **Comfort** and **Calm** dimensions, recognizing that psychological well-being and confidence in care are measurable components of value.

5. Equity

"Such an approach is entirely focused on efficiency, while people often value equity, particularly in health."

Why flagged: Equity is treated as optional—this creates moral hazard within HTA decisions.

VBHC/ICER link: VBHC requires fairness and proportionality as integral to value definition.

Advance implementation instead of paralysis: require that HTA agencies integrate risk-preference, process-utility, and caregiver-impact measures into routine evaluations within 24 months.

• Request explicit modeling transparency: lifetime vs. short-term sensitivity results must be published.

• Encourage formal integration of VBHC outcomes into next HEMA cycle.

Recommended advocacy action:
We would like to see a **systematic application of equity weighting** in all HTA models, ensuring that cost-effectiveness thresholds reflect not only efficiency but also fairness across patient populations.

Equity weighting can be implemented using established frameworks such as **Distributional Cost-Effectiveness Analysis (DCEA)** or **equity-informed thresholds**, which assign greater weight to health gains in underserved, high-severity, or low-socioeconomic groups. These approaches are already under methodological review by NICE and CADTH, making their adoption both feasible and evidence based.

Applying explicit equity weights would prevent hidden biases that arise when aggregate averages obscure disparities in access or outcomes. Reporting both **unweighted** and **equity-adjusted** ICERs would improve transparency and enable decision-makers to see the distributional impact of resource allocation.

Cross-Cutting Concerns

The report reinforces a traditional QALY-based paradigm, **risking the entrenchment of static models** that undercount longitudinal and experiential forms of value central to patient outcomes. For chronic and rare diseases such as **CML**, where **durable remission, treatment-free intervals, and restored capability** define success, frameworks modeled on **short ICER-style horizons** and **strict opportunity-cost symmetry** systematically misprice benefit and create access barriers.

A modernized approach should incorporate **patient-derived utilities**, **risk-adjusted value (GRACE)**, and **dynamic modeling of system savings and reinvested value over time**,

ensuring that long-term health gains and real-world efficiencies are properly captured within HTA processes.

Value of Hope Addendum

The **Value of Hope (VoH)** represents the measurable utility patients assign to treatments that offer a **small probability of substantial or curative benefit**. Empirical work by Lakdawalla, Phelps, Corn, and others demonstrates that patients rationally value such *tail-risk* options, particularly in life-limiting diseases where even a modest chance of remission or cure transforms perceived well-being and decision-making.

In oncology and chronic conditions such as **CML**, hope is not merely psychological—it correlates with improved **treatment adherence, coping capacity, and engagement in care**, all of which generate measurable downstream value.

The **GRACE (Generalized Risk-Adjusted Cost-Effectiveness)** framework operationalizes this by adjusting conventional QALY weights to reflect **risk preference and outcome variability**, enabling structured inclusion of hope-based utility within HTA modeling **without double-counting quality of life**.

HTA bodies should move beyond research pilots to **integrate VoH-adjusted sensitivity analyses** within evaluations of **oncology and rare-disease therapies**, particularly those with positively skewed survival distributions (e.g., **TKIs in CML, cell and gene therapies, and immuno-oncology treatments**). Reporting results both **with and without VoH adjustments** would enhance transparency and demonstrate how accounting for risk preference alters incremental cost-effectiveness ratios (ICERs).

Recognizing the **Value of Hope** formally aligns HTA methodology with **Value-Based Healthcare's Comfort and Calm dimensions**, ensuring that the **psychological, behavioral, and motivational benefits** that sustain patients through treatment are no longer excluded from value assessment.

References

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COLORECTAL CANCER CANADA

Response to the Draft HEMA Guidance
October 30, 2025

Colorectal Cancer Canada is a national patient advocacy organization dedicated to ensuring equitable and timely access to effective cancer treatments, including clinical trials and precision medicine approaches. This submission reflects the lived experiences of colorectal cancer patients and caregivers and provides recommendations to strengthen the HEMA draft guidance so that it aligns with patient needs, supports innovation, and protects Canada's role in global oncology research.

We commend HEMA for taking on the complex and necessary work of modernizing health technology assessment (HTA) to reflect the evolving needs of patients. The report demonstrates thoughtful consideration of fairness, opportunity cost, and methodological rigour. We also greatly appreciate the decision to hold public consultation and invite patient and caregiver perspectives. We agree with the report's emphasis on consistency, transparency, and avoiding double-counting. These are essential for maintaining a credible and sustainable healthcare system.

Feedback #1: Precision Medicine Considerations

We share concerns expressed by other patient-led and multi-stakeholder groups that the current framework relies too heavily on traditional cost-effectiveness approaches, especially the QALY, which reflect population averages and may not fully capture the value delivered by precision medicine. This is particularly important in oncology, including colorectal cancer, where biomarker-defined patient populations are often small and heterogeneous, and treatments involve trade-offs related to toxicity, functional independence, emotional well-being, and reducing uncertainty. These factors are not only meaningful to patients but are also measurable and relevant to health system goals, meeting the framework's own criteria for relevance, measurability, and opportunity cost when appropriate structured methods are used. Precision medicine can provide additional value by offering clearer diagnosis, diagnostic certainty, emotional reassurance, avoidance of unnecessary toxicity, access to clinical trials, and support for dignity and autonomy in treatment decisions. These benefits are deeply personal, often time-sensitive, and not fully captured by QALY-based assessments. Without explicitly recognizing them, the framework risks underrepresenting what matters most to patients and may reinforce inequities in access for smaller or more diverse sub-populations.

Feedback #2: Patient-Centred Evidence

We recognize and support the report's emphasis on avoiding double-counting benefits. However, many patient-centred elements, particularly diagnostic certainty, peace of mind, the ability to maintain daily functioning and family roles, emotional

reassurance, and the lived experience of tolerability, are not currently captured in QALY-based metrics and therefore are not counted even once. These benefits are both relevant and measurable when collected through established approaches such as patient preference studies, validated patient-reported experience measures, and real-world data sources. For this reason, the final HEMA guidance should explicitly state that patient-generated evidence is not merely a supportive narrative context, but structured, decision-relevant evidence appropriate for consideration during HTA deliberation. For many colorectal cancer patients, especially those living with Stage IV disease, values such as quality of remaining time, predictability, mental well-being, and the ability to remain at home have significant weight in treatment decision-making. Incorporating patient-generated evidence directly into HTA deliberation ensures that the assessment process reflects lived reality rather than hypothetical average preferences.

Feedback #3: Dynamic View of Opportunity Costs

While the report emphasizes the importance of acknowledging opportunity cost, it largely treats opportunity cost as fixed. In reality, investments in precision diagnostics, biomarker infrastructure, clinical trials, and real-world data systems can generate long-term system efficiencies and future cost savings. Precision medicine reshapes clinical pathways in ways that may reduce downstream treatment intensity, avoid ineffective therapy, and support earlier intervention. HTA should be equipped to recognize innovation as a contributor to long-term system sustainability, rather than as a cost pressure to be minimized.

Feedback #4: Innovative Agreement Models

We encourage the final guidance to explicitly support adaptive access mechanisms such as conditional reimbursement, value-based agreements, managed access agreements, and iterative reassessment informed by real-world evidence. In oncology, where delays of even weeks can meaningfully affect patient outcomes, flexible access models are essential not only for timely care but also as an ethical imperative. Without these mechanisms, Canada risks slower access to emerging therapies, reduced participation in clinical trials, and a declining attractiveness as a launch market for biomarker-driven or precision medicines. These consequences would disproportionately affect patients with rare molecular subtypes or limited treatment options, further exacerbating inequities in access.

Conclusion

Colorectal Cancer Canada supports HEMA's goal of establishing a more transparent and consistent HTA framework that focuses on health benefits. To ensure it is both rigorous and compassionate, we recommend that the guidance explicitly integrate patient-generated evidence into decision-making, formally recognize the value of

diagnostic certainty and uncertainty reduction, adopt a dynamic and innovation-aware view of opportunity cost, and support adaptive reimbursement models that allow evidence to mature in real-world settings. We are committed to collaborating in the next stages of guidance development and to contributing patient-driven evidence and lived experience to ensure that the final framework supports timely, equitable, and patient-centred access to precision cancer care in Canada and globally.

Yours truly,

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Colorectal Cancer Canada

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October 24, 2025

Mark Sculpher, PhD
Working Group Chair
Health Economics Methods Advisory
c/o Institute for Clinical and Economic Review
14 Beacon Street, Suite 800
Boston, Massachusetts 02108 via e-mail to: public_comments@hemamethods.org

Re: "Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies," Draft Report

Dear Dr. Sculpher:

I write in response to the invitation from the Health Economics Methods Advisory ("HEMA") for public comments on the draft report issued on October 9, 2025 entitled "Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies." My comments will hereinafter refer to this document as the "Draft Report."

I. Introduction

My comments are offered in my capacity as the father to my fabulous 24-year-old daughter, who is living and thriving with the serious chronic disease known as cystic fibrosis ("CF"). I have for many years been active with the Cystic Fibrosis Foundation ("CFF") in the realms of public policy and fundraising. Since 2021 I have been a member of the New England Comparative Effectiveness Public Advisory Council (commonly known as the New England CEPAC), one of the three independent appraisal panels convened by the Institute for Clinical and Economic Review ("ICER") to deliberate on the findings and recommendations in ICER reports. My relationships with the CFF, the New England CEPAC, and ICER are provided here for information purposes only. I speak for none of those organizations and offer my comments solely as an individual.

In that capacity, I perceive keenly the urgency of getting Health Technology Assessment ("HTA") right. Over the course of my daughter's life, the median predicted survival age for a person born with CF has increased from 31 years to 61 years and beyond, the result of remarkable breakthroughs in the treatment of what was until fairly recently considered a fatal childhood disease. At the same time, my daughter's annual pharmacy bill has also grown to the point where it is now routinely in excess of $400,000 a year. This is unsustainable and, indeed, the high cost of CF drugs are, in my judgment, the single most significant threat to my daughter's longevity, success, and happiness.

For the reasons stated in the Draft Report, HEMA and its sponsoring organizations are wise to focus their initial research on the benefit side of the HTA benefit/cost analysis. As the Draft

Report acknowledges, there is growing acknowledgement of the need to credit benefits that are either difficult to quantify or, indeed, are simply beyond the scope of what can plausibly be included within the four corners of economic analysis. I and my colleagues on the New England CEPAC confront this reality every time we deliberate. As someone who serves on the New England CEPAC by virtue of the insights I contribute as a member of a disease community, I feel a particular responsibility to assure representatives of other disease communities that they have been heard, understood, and cared about as the proverbial 'dismal science' of economics is brought to bear on new drugs and other emerging technologies.

With this in mind, I would like to recommend certain improvements as the Draft Report matures into a final document. I lack the expertise to critique the exercise of anyone's expert judgment as an economist or healthcare profession. Rather, my suggested improvements are offered in hope of making the final edition of your report legible and persuasive when read by members of patient communities who are willing to engage in good faith with HTA experts. I appreciate the inclusion of a plain-language summary of the Draft Report but this should not become an excuse for allowing the report itself to become so prolix that only people with a PhD in economics can understand it.

II. Relevance as the First Guiding Principle

Section 3 of the Draft Report lays out three fundamental principles to guide whether a particular benefit warrants inclusion in an HTA rubric. The first principle – that "benefits must be relevant for the decision-making organization and for the decisions of interest" – is an example of analytical bootstrapping or, in colloquial terms, a self-licking ice cream cone. Essentially, this principle if taken literally reserves to HTA decisionmakers unbounded authority to determine which benefits are in scope and which are not.

From the perspective of transparency and legibility, it would be better if the "relevance" principle were rephrased so that the inquiry is not "is it relevant?" but, rather, "is it a health benefit?" or, even better, "is this benefit connected to health in some way?" If I am understanding the Draft Report correctly, the authors believe that benefits unrelated to health should simply not count even when such benefits contribute to overall utility or consumer welfare.

In my respectful opinion, this draws too bright a line. Although purple pills are prettier than white ones, aesthetic improvements of that sort should obviously not be considered a benefit for HTA purposes. But other benefits – for example, the easing of burdens taken up by patient caregivers – are, I respectfully suggest, sufficiently tethered to health outcomes to be relevant. I recommend changing the "relevance" criterion into two criteria: Health-relatedness and quantifiability. Benefits that have a demonstrable connection to health deserve to 'count' as long as they can be quantified. With respect to quantifiability I stress that "difficult to quantify" should not become a pretext for exclusion; in some cases, good-faith estimates – or reasonable inferences from available evidence -- should be deemed sufficient.

III. Hope as a Benefit for HTA Purposes

More significant, from my perspective as a member of the cystic fibrosis community in the U.S., is the treatment of Hope at pages 23 through 28 of the Draft Report.

Hope is a big deal here on Planet CF. Had I been born with cystic fibrosis in 1958, just 20 years after the disease was first identified, I would have been lucky to survive early childhood. How hopeless that would have seemed to my parents. But when my daughter was born 43 years later, in 2001, I was devastated to learn that the median predicted survival age for her CF birth cohort was just 31 years. But my daughter's caregivers emphatically and compellingly urged our family to embrace an attitude of hopefulness, predicting that progress toward a cure (or something very close to a cure) would continue.

That is *exactly* what has happened. As I have already noted, the median predicted survival age for today's cystic fibrosis birth cohort is not thirty-one years but *sixty*-one years and climbing. From the perspective of me as a first-time dad of a newly diagnosed baby with cystic fibrosis, the value of allowing myself to imagine then where we are today – as I am writing this letter, my daughter is working on her law school applications – was, though difficult to quantify and admittedly not infinite, something palpable and far north of zero.

Thus it is no coincidence that when the Cystic Fibrosis Foundation turned for the first time to a person living with CF to chair its board of trustees in 2022, the Foundation chose someone who has doggedly pursued hope as a subject of academic inquiry. Of her capstone project in pursuit of a masters degree at the University of Pennsylvania, CF Foundation Board Chair KC White reported survey results revealing that "people with CF saw the world as a better place, a more enticing place, and a more improvable place at statistically significant levels than the control group of the general population." Thus, she continued:

> these results depict a population for whom positive psychology could be an important and welcome resource. Optimism, hope, and positive primals all correlate with well-being. In people with CF, these positive views seem to be independent of health measures (FEV1), which may suggest that they are independent of circumstance and would therefore remain available at times of change, whether positive or negative. Positive interventions designed to enhance any of the three could increase flourishing and protect against depression. In addition, people with CF approach their disease both realistically and hopefully, with a strong sense of agency that is reflected in their adherence to often-burdensome treatment regimens. Positive interventions that build on this sense of agency could be important in helping people with CF to feel an internal sense of control about their future, while also offering pathways for a broader, more robust experience of flourishing than can be measured by both physical and mental health outcomes. These types of interventions could be beneficial for those living with chronic illness and the general population as well.[1]

[1] KC White, "A Land Called Hope: Assessing Positive Views in People Living with Cystic Fibrosis" (2022), available at www.mappmagazine.com/articles/a-land-called-hope. "FEV1" refers to forced expiratory volume over one second, the standard measure of pulmonary health in people with cystic fibrosis.

I am not here to suggest, and I am certain KC White would never claim, that people with cystic fibrosis have a greater claim on hope as a resource than do people who live with other life-shortening medical conditions. But I do respectfully contend that if the discussion of hope appearing in the Draft Report survives unedited into the final edition, many in the CF community will be offended and bewildered. They will not recognize the commodity, hope, that the Draft Report describes and, arguably, derides.

Some of what concerns me is superficial, but this matters. Repeatedly placing the word hope inside of quotation marks, implying skepticism, and repeatedly referring to "claims" about hope and its efficacy, reinforcing the skeptical tone, will not help the cause of HTA within a patient/family community that has been conditioned (largely via strategically deployed pharmaceutical company propaganda) to view established HTA methods (e.g., the use of the QALY metric) as morally dubious scheming to devalue the lives of disabled people and deprive suffering patients of needed medications.

People with CF, and likely people with other chronic illnesses as well, simply will not recognize the hope described in the Draft Report, which focuses on the risk-seeking preferences of patients. With reference in particular to page 23 of the Draft Report, I have no quibble with the notion, in economic terms, that there is positive utility associated with remote possibilities of successful outcomes, as can occur with gene therapies and other experimental treatments. (I lack the expertise to have an informed opinion about the related concept described at page 23 of prudence (referring to patients preferring certain treatments over comparators when they have a "right-skewed distribution of health benefits" as shown in the figure at page 24.) Rather, my objection has to do with the conclusion, at page 26, that hope is germane to HTA merely as a means of incorporating risk attitudes in HTA analysis. You are overlooking what drugs like Pulmozyme and Tobi gave my daughter and her family in my daughter's early years – reasons to believe that these medications, though far short of being curative, would prolong her life to an extent sufficient to allow her to be alive when the truly curative breakthroughs arrive.

In other words, while patients do sometimes take experimental drugs, and expect their health insurance to pay for them, as the medical equivalent of a Hail Mary pass in American football, hope as I understand it as a member of the CF community is also a quantifiable (or at least estimatable) amount of additional reasons to expect future advances and progress. This kind of hope may, as an analytical matter, require careful scrutiny so as to assure it is not double-counted via some other non-QALY benefit. And this type of hope may prove illusory, especially if the U.S. continues to abandon its historical role (particularly through the National Institutes of Health) as the leader in world progress toward a cure for cystic fibrosis and other illnesses. Nevertheless, hope as a concept deserves a full and respectful analysis in your assessment of benefits that require consideration in health technology assessment.

IV. Conclusion

Please know that the concerns expressed above are tended in a climate of respect and affection. Since early 2020 I have had the privilege of watching ICER at close enough range to have concluded that it is the finest nongovernmental organization I know, not just in healthcare but across all fields of endeavor. I was delighted to discover that ICER has teamed up with the respected HTA agencies in Canada and England to form HEMA. I hope – not as a risk-seeker

but as someone who knows what can emerge when smart people collaborate – that ultimately HEMA will advance the cause of health technology assessment by contributing lucidly described insights that have the ring of truth to them so as to overcome skepticism and hostility in patient/family communities and the policymakers who are attentive to those communities.

Thank you for considering my views.

Sincerely,

Donald M. Kreis

Comments on "Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies"

Dr. Doug Coyle

The HEMA report is well written and logical in the conclusions it reaches. The approach of focussing on the three underling principles of relevance, valuation and opportunity cost makes the conclusions reached consistent and clearly suggests any broadening of what economic evaluation considers with respect to the HTA process does not currently have the evidentiary basis for its justification.

The paper could benefit from explicitly stating that if a fundamental objective of a health care system is to increase the health of the population it serves then any consideration of wider issues such as the distribution of risk, non-health benefits, considerations of equity and broadening of the perspective **MUST** lead to a reduction in the health of the population. This does not preclude decision makers considering such additional concepts in decision making. It is not the place of a health economist to say what should not be considered when making a reimbursement decision. However, it is clear that if the purpose of economic evaluation is to ascertain whether the health of the population will increase or decrease if a new technology is reimbursed, inclusion of these concepts will make it impossible to determine this.

Although risk attitude both at the level of decision makers and patients may be important criteria for making decisions concerning reimbursement or for choosing which therapeutic option to take, the technical aspects of including risk attitude clearly have not been adequately addressed in the literature. Furthermore, if risk attitude was important and could be considered an additional criterion within the reimbursement process, then concerns over the increasing uncertainty within the clinical evidence base used to facilitate economic evaluation (e.g. the rise of non-randomised studies as a basis for product approval) could be addressed more deliberately. This would also require that good practice in terms of the specification and propagation of uncertainty within economic models and the technical validity of models used be further developed to ensure risk is adequately addressed.

Incorporating consideration of equity explicitly suggests hat efficiency in producing health is not the primary concern of the analysis. The incorrect notion of equity-efficiency trade-offs seriously hampers the literature in this area. It should be noted that there is a lack of consistency in the literature over whether equity relates to the condition a patient suffers or the patient themselves and that this leads to inconsistent application of equity principles and when applied can lead to repercussions which may not have been

expected.(Coyle, Health Economics Review 2024) Thus, although equity is a highly reasonable criterion to consider with respect to reimbursement decisions, further work is required to make sure it is adequately addressed. Economic evaluation is based on an explicit equity statement that a health gain or loss by any individual is of equal value. To adopt a different equity statement would need a degree of consensus which had not been achieved and would need to be explicitly considered with respect to opportunity costs.

Whether a decision maker should consider a broader perspective and non-health benefits within an economic evaluation is severely affected by the current lack of quality in determining these costs/benefits from a decision makers point of view. The standard of ascertaining indirect costs in economic evaluation is still weak and much work on improving this is required. Similar concerns relate to non-health related benefits. My fundamental concerns relate to how opportunity costs can be ascertained when such wider perspectives are included and how trade-offs between health benefits and non-health benefits and productivity can be made.

Thus, my conclusion on this report is that it adequately addresses the issues with respect to inclusion of issues such as the distribution of risk, non-health benefits, considerations of equity and broadening of the perspective and whether they should be included within an economic evaluation within the HTA process. I do feel all of these issues may be valid concerns for a decision maker to consider. However, I feel the inclusion of any of these within an economic evaluation is not justified and furthermore, more ork is required to develop good practices with respect to their inclusion as an additional factor to consider within the HTA process.

Dr. Eldon Spackman

Notes on HEMA Report

Pg 10 – "The principle: Need to reflect any additional benefit in the assessment of opportunity costs."

I would suggest: All benefits considered in the evaluation of a treatment should be accounted for when assessing opportunity costs.

I think this captures the principle more accurately and includes additional benefits too. Also, most jurisdictions don't have an empirical threshold already accounting for core benefits, which this statement suggests.

Pg 11 – "As Brouwer et al state, "in acting as agents for their clients, the public, we do not have to assume that decision-makers are acting as they think the principals whom they represent would act, but rather as they think they ought to act."24 In both tax-funded and insurance-based systems, arguments can be made that preferences of the public are relevant as a proxy for potential future patients or as a representation of collective views about what should be insured."

I suggest framing this paragraph to emphasize that decision-makers act with a remit to society rather than to individual preferences. This makes the point more broadly acceptable, especially to readers in US contexts, and aligns with the idea that public preferences can serve as a proxy for collective societal values or for potential future patients. It avoids language that might be interpreted as 'top-down' or overly government-driven while retaining the normative argument from Brouwer et al.

Pg 12 – "Economic evaluation is fundamentally concerned with measuring and valuing the benefits of alternative health care technologies and comparing these to their opportunity costs." I would add that the consideration of opportunity cost is what differentiates an economic evaluation from other types of evaluations that might measure benefits.

Pg 12 – "For example, in Canada HTA practice relies on conventional benchmarks (e.g., CAD $50,000 per QALY)."

It is not clear what this is an example of.

Pg12-13 – “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, and international estimates are also available.35-38 These are generally based on regression models using aggregate national or international data. As Pg 13 for much evidence used in HTA, current estimates of opportunity cost are subject to uncertainty and would be improved by additional data collection and further development in methods.”

I suggest moving this paragraph to a separate section and not mixing the principled issue of not ignoring the opportunity cost of additional benefits, and the practical issue of measuring an empirical CET.

The point of this paragraph is not very clear.

Pg 13 – “however, the latter should still be reflected in HTA decisions and available to support transparency. 39”

Suggest spelling out what is included in ‘latter’, I am not following.

Pg 13 – In the paragraph, “Although the link between the cost-effectiveness thresholds currently used by HTA organizations and evidence on opportunity cost is uncertain…”

You could be more clear that the same threshold can not represent different benefit functions. I would also simplify the productivity example. Maybe something like this is a bit simpler,

This risk is illustrated by research on the impact of adding productivity to NICE’s measure of benefit. A new intervention may increase productivity by improving the health of treated patients, and this can be valued in monetary terms. However, if the intervention increases NHS costs, it will reduce the health of other patients through opportunity costs, and their lost productivity must also be counted. If these losses are omitted, the analysis becomes incomplete and may mislead decision-makers. Previous work shows that for each QALY lost through opportunity costs of a NICE recommendation, there is an associated average net productivity loss of about £11,600.

Pg 14 – “using it as the basis of a cost-effectiveness threshold for the use of current health care funding is problematic.”

It would be really nice to have a clear explanation of the problems or a reference to an explanation.

Pg 29 – “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.”

Can the double negative be avoided?

Pg 30 – “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.”

I like this point, but it seems a bit dismissive as it is written.

Pg 30 – “As outlined previously, the policy objective of economic evaluation used in HTA by those organizations which are the focus of this report is to maximize population health using a benefit function with estimates of a treatment’s impact on length and aspects of HRQoL.”

This is contradicted by “Current HTA practice has already recognized the greater weight decision makers place 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,”

Pg 31 – it might be worth mentioning at some point that the recommendations for dealing with equity are separate from the measurement of benefit and could be applied to any measurement of benefit. It seems slightly different from the other issues being discussed which change the measurement of benefit. This is about the distribution of the benefit.

Pg 31 – “but this would not be politically viable”

I would remove this as I don’t believe it is necessarily always true.

Pg 32 – “defined as shortfall in expected lifetime QALYs”

Change to ‘defined as a shortfall in expected lifetime QALYs’

Pg 35 – “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.”

I would explicitly refer to the effects on ‘equity’ and highlight the challenge of balancing these two potentially competing desires.

Pg 36 – “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.”

This has serious implications for transparency and consistency between committees and overtime. This does not negate the necessity to make trade-offs but instead of explicit trade-offs as in the previous paragraph now trade-offs are made by whoever happens to be in the room at the time. I think the these concerns need to be discussed.

Pg 36 – Under Opportunity cost – is it true that including additional things like productivity in the benefit function, with some reasonable assumptions, would decrease the cost-effectiveness threshold? If so, this would be useful to discuss. Additionally, this might be a good section to discuss the trade-offs of spillover effects. Not only will there be opportunity costs to other patients but there may be opportunity costs to the patients being treated. In an extreme scenario a treatment might make a caregiver better off but the patient worse off. This could be in terms of health or productivity.

Pg 37 – "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."

I totally agree with this.

What does this mean for CDA that doesn't consider opportunity costs as they don't have a threshold?

Pg 37 – "Distributional cost-effectiveness analysis provides a framework for building distributional considerations into economic evaluation but, if used, needs to be used in all assessments."

This could be more general. All evaluations should be consistent in their assessment of benefits, even if a treatment has a negative value for an 'additional benefit'.

October 30, 2025

Dear HEMA group:

Below are suggestions from Thermo Fisher Scientific (Evidera^{TM}) for HEMA's consideration. Thank you for the opportunity to provide these comments.

The HEMA draft report (published on the 10th of September 2025) is a great initiative from three of the main health technology assessment (HTA) agencies (NICE in England, ICER in the USA and CDA-AMC in Canada). This represents a major attempt to consolidate their thinking on how health economic evaluations should be shaped in response to new value frameworks and the ongoing debates over what outcomes should be accounted for in HTA.

The report was much anticipated by many stakeholders, and it was expected to address this debate by providing a clear steer on three key aspects:

a) Clarify the normative foundations and establish a normative direction of travel.
b) Provide a pathway for including a broader set of value elements beyond the two covered by QALYs.
c) Offer pragmatic guidance on how agencies and analysts around the world might implement such expansion.

We find that the report effectively provides the authors' view of the normative foundations, but we believe it lacks depth on the other two expectations, providing largely abstract comments on how to test or pilot solutions to the problem.

Our main concern is the use of "opportunity costs" as a means to thwart expansion of the benefits considered. While opportunity cost is a theoretically well-grounded concept, it is poorly applicable in practice. At the health care system level, it is impossible to identify "the benefits forgone elsewhere resulting from the funding of more expensive interventions". Instead, agencies assume a "cost-effectiveness threshold" and use this as the shadow price of a QALY to determine if the value provided by the "more expensive intervention" is sufficient. This shadow price has proven to be exceedingly difficult to establish, in part because QALYs are a very artificial construct that is not "traded" in reality. In a large UK study, for example, it was found that the estimated shadow price varied more than one-thousand-fold across therapeutic areas, from a low of about £2,000/QALY for respiratory illness to nearly £3,000,000/QALY for maternal and infant interventions.

If decision makers are willing to presume the shadow price of a QALY based on little evidence, it is unclear why the shadow prices of non-QALY benefits cannot also be estimated. Indeed, given the advance in discrete choice methodology and other preference techniques, monetary valuations of whatever benefits are of interest should be on much more solid ground that the thresholds currently in use.

Moreover, the claim that “opportunity costs are the consequent reduction in those individuals’ health outcomes” is only valid for a system operating at full efficiency. If the system is inefficient, then the costs of the new intervention may be covered, partially or even fully, by reducing waste and withdrawing interventions that provide few benefits.

We look forward to the next draft of this report and hope that it addresses the practical approaches to reflecting broader value of health care interventions rather than holding to an entrenched theoretical position.

Health Economics Leadership, Thermo Fisher Scientific (Evidera™)

EviGen
Data-Driven | Practice-Proven

To:
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Email: info@icer.org

October 30, 2025

Subject: Public Comment on HEMA Report: *Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies*.

Dear Members of the HEMA Secretariat,

EviGen commends ICER, NICE, and CDA-AMC for their leadership in convening the Health Economics Methods Advisory (HEMA) group and for advancing this critical dialogue on the future of value assessment. The HEMA report highlights the growing tension between conceptual innovation in economic evaluation and the practical realities of implementation, adoption, and equitable impact.

At EviGen, our work centers on bridging this gap and ensuring that methodological progress in value assessment translates into decision frameworks that are feasible, credible, and equitable in real-world use. We strongly support HEMA's principles of relevance, valuation, and opportunity cost as foundational, yet believe an additional lens is needed: implementation feasibility. The inclusion of novel value elements such as risk attitudes, process benefits, and equity weights should not only be theoretically sound but also implementable within the resource, data, and operational constraints of HTA systems and payer decision environments.

We also encourage HTA bodies to incorporate equity as both a value element and an evaluability condition. As the WHO, CDC, and others have recently emphasized, monitoring inequities without corresponding evaluability frameworks risks widening the gap between evidence and action. Incorporating distributional cost-effectiveness analysis or severity weighting is important, but these methods must be embedded within processes that ensure learning, accountability, and stakeholder engagement, especially for underrepresented populations.

Finally, we echo HEMA's caution that novel benefit measures must be anchored in opportunity cost. However, opportunity cost itself should be contextualized by implementation outcomes such as reach, adoption, and sustainability. In practice, the real opportunity cost is not only what the system pays but also which populations never benefit when methods fail to translate to practice.

EviGen appreciates the opportunity to provide input and looks forward to continued dialogue on advancing methods that align scientific rigor with equitable implementation and real-world adoption.

With appreciation,

Larragem Raines
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From Testing to Targeted Treatments

1st DRAFT

A Collective Multi-stakeholder Response from the From Testing to Targeted Treatments (FT3) Program Project Groups on Value of Precision Medicine and PED in HTA

We commend the HEMA report for addressing the important topic of updating health technology assessment (HTA) and access decision-making methods and processes in light of the continuing evolution of the associated scientific progress. Acknowledging the complexities of these processes, the report rightly focuses on relevance and pragmatism in adapting HTA methodologies. We also appreciate the effort to carve out pathways for future change, emphasizing the importance of ongoing research to refine, expand, and incorporate novel value elements. This forward-thinking approach will be key in shaping more inclusive and effective healthcare systems that better meet the needs of diverse patient populations. FT3 greatly appreciates this step as well as the decision to invite and welcome public consultation. FT3 celebrates this step as well as the decision to opt for a public consultation. As a patient co-led, multi-stakeholder program, FT3 seeks to advance patient access to the right treatment at the right time, while acknowledging the need for sensible and realistic HTA to support a sustainable health-innovation ecosystem.

Closing the innovation-implementation gap will require more adaptive, real-world focused, and patient-sensitive HTA.

While the HEMA report provides a thorough analysis of current HTA practices, in our view it continues to rely too heavily on traditional cost-effectiveness analysis (CEA) based on the quality-adjusted life-year (QALY), reinforcing the status quo. We believe that these methods, though foundational, do not fully capture the value of innovations, especially those that enable personalized healthcare solutions, where considerations of uncertainty reduction, sub-populations, and real-world outcomes are essential. Given the significant progress made by the HTA bodies who commissioned the work in integrating patient-generated data and insights, the report's conclusions seemingly under-emphasizing the need for patient-centered evidence may lead to misconceptions for patient organizations aiming to submit to HTA processes.

Moreover, the report's approach to patient-centeredness appears less pronounced, underemphasizing the emotional, preference-based, and heterogeneous needs that are crucial in assessing the true value of innovative health technologies in the broad population. By emphasizing rigid evidence requirements in terms of the QALY metric and health sector focus, the report could unintentionally limit adaptive pathways that allow HTA systems and health systems to keep pace with scientific advancements. The assessment of the value of such innovations should reflect the diversity within patient populations as well as wider societal impacts, yet the current and proposed framework does not fully account for these aspects. Additionally, the report seems to underplay the dynamic nature of opportunity costs and the flexibility required within healthcare systems and broader state budgets. Investment in innovation, including infrastructure, often depends on the ability to adapt to changing needs and new evidence. A fixed-budget view of opportunity cost, as presented in the report, may not fully capture the reality that opportunity costs in healthcare are dynamic, with investments expanding when the social and health returns exceed the initial costs, allowing for greater (and at times more efficient) long-term value. HTA frameworks should reflect this adaptive,

investment-oriented approach to ensure they are responsive to the evolving needs of healthcare systems and society at large.

While the report thoughtfully engages with these issues, its focus on traditional short-term focused CEA methodology may inadvertently restrict the flexibility needed to advance HTA as a system that can genuinely support the evolution of healthcare to meet the demands of diverse patient populations.

We invite you to consider providing recommendations that help HTA capture the full societal value of innovative health technologies, ensuring health systems can offer the best care possible. This includes recognizing the preferences of sub-populations and creating pathways for HTA to evolve into a system shaper that drives meaningful change and equitable access to care in the entire health-innovation ecosystem.

The report's reliance on rigid HTA methodologies, fixed particularly on QALYs (and EQ-5D), risks under-counting benefits, such as the benefits of more personalized care outcomes, by downplaying the importance of capturing the heterogeneity of patient populations and their specific preferences (e.g. for reducing uncertainty). These methods, while valuable, have limitations in capturing the full value of innovative health technologies that address diverse patient needs. As such, there is a critical need for more flexible, patient-centered frameworks within HTA that can better reflect the true value of personalized precision approaches to the full population at risk, beyond what traditional measures can encompass. Not considering this may lead to worse population health outcomes by overlooking the true value that precision diagnostics and sub-population tailored treatments offer. For example, equity remains underemphasized and underdeveloped in HTA, but we concur that it should be a foundation, not an afterthought, for the core principles of HTA – ensuring that benefits and burdens are not distributed unfairly or inefficiently across populations. Given the complexity of healthcare systems and sociopolitical contexts, there is a need for more comprehensive systematic methodologies to support meaningful integration of equity and uncertainty-reducing considerations. Moreover, the focus on traditional metrics makes it difficult to incorporate valuable real-world data and patient-centered evidence, restricting HTA's ability to fully capture certainty-benefits, equity, and the value of knowing for health systems. The exclusion in HTA of the latter particularly risks undervaluing diagnostic tools that enable more efficient care rather than direct health gains. In personalized precision care, information itself contributes to value – not just treatment outcomes. Evidence indicates that diagnostics can reduce uncertainty, improve wellbeing, and therefore aligns with the report's key pennant of efficient resource use.

FT3's multi-stakeholder groups are concerned that some of the report's recommendations may inadvertently disincentivize innovation, especially in areas where sub-populations are targeted, by overlooking critical aspects of care such as sub-population preferences, certainty benefits, and the heterogeneity of treatment impact. These elements are essential for driving meaningful progress and should be appropriately recognized in the HTA process. While it is important to avoid double-counting benefits, particularly when assessing certainty and outcome benefits, this principle assumes that the first count, represented by the QALY framework, is comprehensive and unbiased. However, in practice, QALY-based measures, including EQ-5D and related health state elicitation methods, often fail to capture real-world patient experience, emotional wellbeing, and diversity in health preferences. Recognizing these limitations should not be seen as duplication, but rather as a necessary correction to ensure economic models reflect the lived experience of patients.

This group strongly encourages HTA to continue evolving towards a more flexible, patient-centered framework, which can safeguard methodological rigor while recognizing the full range of benefits innovation brings to patients, caregivers, and society. We are committed to demonstrating that balancing the avoidance of double-counting with an appropriate evaluation of unique patient-centered benefits can effectively lead to the integration of innovative health technologies into health systems, ultimately improving outcomes for all patients.

We recommend a broad, multidisciplinary collaboration to improve HTA guidance, ensuring it evolves in a way that is both responsive to emerging healthcare technologies and truly reflective of the diverse needs of patient populations.

While FT3 acknowledges and appreciates HEMA's efforts to address the necessary evolution of HTA, we believe there is an opportunity to take this a step further. We recommend involving a patient advisory board in the revision process, which would bring valuable patient-centered insights, enhancing the report's recommendations with more inclusivity and perspective.

As indicated throughout this response, by making HTA more adaptive to the rapidly changing health-innovation ecosystem and the fast pace of scientific progress, we can better meet the needs of patients. This could include pathways such as conditional approvals, managed access agreements, test beds, and pilot programs, which would allow HTA to gradually expand towards a more holistic, real-world-informed value assessment – especially for innovative technologies targeting sub-populations with limited conventional trial evidence. We are eager to engage in a dialogue to explore how to translate this need into actionable, real-world practices.

Ultimately, we strongly advocate for a collective, multidisciplinary approach to improve HTA guidance, drawing on diverse perspectives to better assess the societal value of health innovations. This collaborative approach will enable HTA to more effectively shape health systems and drive patient-centered innovations. FT3 stands ready to be a proactive partner in this effort. We have already begun gathering real-world examples of HTA's integration of novel value elements (see here) and are actively fostering multidisciplinary venues for cross-stakeholder dialogues to shape the future of value assessment, particularly for personalized healthcare solutions (e.g. see here).

Together, we can create a future where HTA supports fair, realistic, and patient-centered access to the right treatments at the right time. We look forward to joining forces and advancing these shared goals

Helena Harnik
Executive Director, From Testing to Targeted Treatments
On behalf of 30+ members from patient organizations; pharmaceutical, biotechnology, and diagnostics companies; academia; and medical professionals, in FT3's project groups on:
Value of Precision Medicine
Patient Experience Data in HTA

Health Economics Methods Advisory

Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies

DRAFT COMMENTS

HTAi RARE DISEASE INTEREST GROUP
Group 4: Economic Methods Working Group

Introduction

The Rare Disease Interest Group of Health Technology Assessment International is dedicated to sharing good practices in evidence generation for rare disease technologies (RDTs), fair assessment processes that take account of the feasibility of evidence generation and appraisal processes that take account of the burden of rare diseases on patients and society when determining value.

We would like to thank the authors of the draft report for providing an opportunity to provide our feedback as follows:

Comments on section "Relevance"

1. The report supports the perspective of the health care system which, whilst methodologically appropriate, will inadequately capture the full value of treatments for rare diseases. This approach risks excluding important societal benefits, such as improved productivity, reduced caregiver burden and enhanced social participation. These broader impacts can be substantial for rare disease patients and their families. Hence, decisions based on a narrow health system perspective are likely to undervalue treatments that have significant social and economic benefits and lead to further inequity for rare disease patients.
2. Whilst the authors recognise additional value elements – particularly inclusion of equity, value of knowing, family and caregiver spillovers – it is disappointing that there remains a lack of commitment to adopt a holistic societal perspective. Ignoring these dimensions could underestimate the true value of interventions that improve social welfare beyond direct health outcomes.
3. Alignment with societal priorities allows decision makers to capture benefits that matter to society, such as reducing inequalities or improving workforce participation.
4. Potential for overall efficiency: some interventions may slightly reduce health outcomes but generate large benefits elsewhere (e.g. economic growth or social stability), resulting in overall net gains for society.
5. The overall net gains for society may ultimately be available to provide additional resources which could then be reinvested to increase overall population health.
6. Ignoring these benefits may lead to suboptimal resource allocation from a macro economic and societal perspective.
7. We recommend to explicitly prioritize severity and early onset common in RDs and encourage HTA bodies to apply transparent severity/fair-innings modifiers to reflect large lifetime health shortfalls typical of paediatric and ultra-rare conditions [3,4].

8. Recognize “value of knowing” as especially important in RDs. For example, genetic confirmation enables the diagnosing physician to implement a myriad of management approaches, even in the absence of approved treatments such as earlier specialist care, coordinated services, carrier testing, and family planning. This value should be quantified and allowed for inclusion in the evaluation to ensure that rare disease patients are not disadvantaged by narrow benefit definitions [1,2,8].
9. Where generic instruments under-capture rare disease burden, allow dual measurement (disease-specific + generic) with validated mapping so rare disease benefits are visible and may be compared with other diseases in an appropriate and fair manner [1,2,8].

Comments on section “Valuation”

1. The report places substantial emphasis on using the QALY approach to guide resource allocation even though not all three HTA bodies represented have the authority or funding responsibility to implement these decisions. This raises a critical question: why do HTA bodies without direct financial accountability consider QALY the preferred assessment method, despite its well-known limitations? Moreover, even when funding is provided, QALY-based decisions fail to capture a full societal perspective thereby denying taxpayers and the public the transparency and assurance that scarce resources are being optimally allocated.
2. Efficient resource allocation is only possible when decisions are guided by a comprehensive societal perspective that encompasses all sectors, including health, education, transport, and productivity. The QALY-based approach, while valuable within healthcare, is inherently limited: it captures only health-related outcomes and excludes broader social and economic benefits, making cross-sector comparisons impossible.
3. The report does not fully recognise the role of suitable alternatives to the traditional QALY approach, including recently methods such as the GRACE approach, while we believe that alternative methods warrants further exploration.
4. Another approach which may be considered is cost–benefit analysis (CBA) in those situations where a significant proportion of the benefits cannot be adequately captured with traditional QALY approaches. This flexibility in methods is appropriate and relevant particularly for rare diseases. CBA enables policymakers to directly compare the value of interventions across sectors, thereby promoting more transparent, equitable, and economically sound decision-making that can also be more easily understood by the public.
5. A variety of evidence should be considered to reach HTA decisions. I also think it is important to recognise that HTA bodies do not operate in silos and are impacted by broader government policies. Hence methods that allow them to demonstrate the value of investment in rare disease treatments vs other areas of government policy could be a useful option.
6. Where the QALY approach is used, we recommend including evidence on patient preferences, caregiver/family HRQoL RDs, reflecting the profound family impact and patient input in decision making [1,2]. This has the potential to lead to improve HTA decisions and improve HTA process [9].
7. In terms of clinical evidence, we support structured use of surrogates when hard outcomes are not feasible, with predefined validation plans and reassessment triggers; this avoids systematically penalizing RDs for practical evidence constraints [1,8].

8. We recommend the recognition of "transformative" outcomes. For example, in the case of gene/cellular therapies with durable responders, there is a need to ensure that RD therapies with long-term potential are not undervalued at launch [1,8].
9. We recommend the use age-appropriate pediatric instruments/tariffs and report within-family correlation checks so child benefits and caregiver impacts are captured rather than diluted [1,2,8].

Comments on section "Opportunity cost"

1. Decision thresholds are frequently shaped more by budget constraints and political considerations than by true economic opportunity costs. Many thresholds are not publicly disclosed, and even when they are, they often fail to reflect up-to-date, accurate estimates of opportunity cost due to opaque or outdated methodologies. This lack of transparency undermines the credibility of HTA decision and hampers evidence-based, efficient allocation of resources.
2. The crucial role of deliberative processes for rare diseases is played down in favour of a strict opportunity cost framework, which does not take into consideration the challenges associated with rare disease evidence generation.
3. Variations in HTA decision thresholds across countries can result in inconsistent access to treatments. Hence, rare disease patients may receive life-saving treatments in one country but be denied the same care elsewhere. While economically understandable at a macro level, these disparities point to a critical need for transparency and improved equitable patient outcomes. For rare disease patients, who are typically represent a tightly knit international, such inconsistencies are deeply frustrating and highlight the need for transparent decision-making with a full and detailed consideration of the rare disease patient perspective.
4. Whilst the report advocates for transparency and inclusion of opportunity costs, the specific methods for how this can be done in a fair and equitable manner that does not penalize rare diseases or indeed any other patients, requires further clarification.
5. The issue of double counting of health benefits particularly with regards to quality of life is raised several times. However, from the perspective of measuring rare disease quality of life, the methods and measures currently in place are more likely to result in an under measurement of the true humanistic and economic impact. Therefore, we strongly recommend the use of all available methods, including disease-specific measures in addition to generic measures as well as a stronger focus on individual patient experiences captured through other methods.
6. We encourage the implementation of managed access for innovative treatments for rare diseases with evidence development with predefined outcomes and re-assessment rules so patients can access promising therapies without further [5–8].
7. Because small RD cohorts can create budget volatility, we recommend to consider marginal health trade-offs at the program level rather than "per-patient cost" that systematically disadvantage RDs [5–7].

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October 30, 2025

Response to Health Economics Methods Advisory (HEMA) Group's Draft Report on Defining appropriate benefits for economic evaluation of health care technologies.

Innovative Medicines Canada & BIOTECanada are the primary associations representing the innovative medicines industry in Canada. We thank HEMA for the opportunity to provide feedback on the current consultation for their draft report on *Defining appropriate benefits for economic evaluation of health care technologies.* Upon reviewing the draft report, we acknowledge and appreciate the work of HEMA in providing a targeted review of "novel value elements" that could be included in economic evaluations for Health Technology Assessment (HTA). We hope that the final report will include a practical framework that can be adapted to various contextual realities to facilitate adoption by interested HTA stakeholders. Our considerations preserve its methodological intent while preventing unintended structural bias against safety-led innovation, rare diseases, and long-term system value. The goal is not to weaken rigor, but to ensure rigor does not unintentionally become rigidity.

The innovative medicines industry appreciates the continued effort to include additional value elements within health technology assessments such as the value of hope. We are encouraged to see HTA organizations aim to evaluate and integrate these broader impacts within economic evaluations. We encourage HEMA to provide implementable guidance on how to move forward with these elements for reimbursement advice. We highlight the following important considerations, specifically as they pertain to processes for implementation and the current reimbursement landscape in Canada.

Important Considerations for Implementation

1. **Practical steps to Implementation and Applicability to the Canadian Reimbursement Landscape**

There are considerable advantages to enhancing the breath of an economic evaluation and including additional elements of value. For example, the inclusion of broader dimensions of treatment impact, particularly for rare diseases and areas of high unmet need, is especially pertinent, as therapeutic benefits may extend beyond direct health outcomes to encompass increased productivity for the patients and their caregivers. Guidance with actionable steps to move this important work forward is needed. The innovative medicines industry appreciates HEMA's acknowledgement that "some variation in methods across organizations is necessary — it reflects local preferences and priorities. There is also significant value in evaluating new methods as an international community before they are considered for local implementation." We

also appreciate the coordinated effort of the three HTA organizations to establish HEMA though we note that the implementation of these recommendations may differ among the three countries.

The innovative medicines industry highlights the work Canada's Drug Agency (CDA-AMC) has done to date to include additional elements such as societal perspectives as part of their economic evaluations. With respect to the current HEMA recommendations, it is important to continue to value innovation in the context of an evolving landscape of therapeutics that are increasingly personalized and/or treating rare disease populations. Furthermore, consideration should be given, in the context of the HEMA recommendations, of the regulatory and HTA trends that have emphasized the importance of timely access for patients to innovative therapies, through conditional approvals with post-market learnings (e.g., time limited reviews) and new HTA processes seeking to shorten review timeframes (e.g., Target Zero, PACES).

We recognize the importance of including broader economic and societal impacts, such as productivity improvements, reduced caregiver burden and decreased reliance on expensive institutional care, to enable access to innovations designed to enhance workforce participation or enable treatment in a community setting. Many new innovative therapies improve patient quality of life by reducing toxicity, travel time, and hospitalization costs, thereby also improving economic resilience.

Practical applications should also consider administrative burden and feasibility. There are a number of elements that are discussed in the recommendations for which more work is required to implement in Canada (i.e., severity weighting, DCEA). For example, the report states that, if used, (i) distributional cost-effectiveness should be used in **all** assessments and, (ii) if broadening the perspective of economic evaluation to include benefits to the wider economy or other sectors is considered consistent with decision makers' remits, additional evidence requirements **must** be considered.

If adopted these recommendation risks requiring equity frameworks for all situations, not just situations where they are most relevant, and could create administrative burden and deter adoption. A potential next focus for HEMA could be to identify the methods gaps which could be addressed.

2. Reflection on the Use of Opportunity Costs

It is important to acknowledge that while opportunity costs underpin economic evaluations, the use of this in actual practice for decision making is less standardized. Often decision makers will want to understand the potential benefits that could be associated with innovative medicines, understanding that evidence is evolving and there may be associated uncertainty.

We note that **it is not practical to require the quantification of opportunity costs for each value element added to the economic evaluation**. While opportunity costs are a grounding theory of performing economic evaluations, the exact opportunity cost per value element is difficult to quantify, especially as these value elements cover benefits spanning multiple sectors and domains. Considering additional relevant benefits while capturing and identifying opportunity costs is challenging, and more importantly, there may be inherent future value associated with each opportunity cost. These opportunity gains are not captured as optimally as they could be in current economic evaluations.

Requiring symmetrical opportunity costs for every benefit creates an unreasonable evidentiary barrier given current trial design. This requirement focus may have the unintended consequence of discouraging innovation by failing to adequately capture the value that innovative treatments create. If applied rigidly, the recommendation requiring symmetrical opportunity costs before including novel benefits may favor established comparators with associated population data and penalize new or high-innovation therapies. where economic impact is real but not fully measurable. This would constrain innovation and under-value key attributes of novel therapies, particularly those with improved safety, patient and caregiver convenience, and care quality benefits.

3. Valuing Patient Centricity

Patient preferences and experiences are a significant input into the economic evaluation across HTA agencies as demonstrated by formal policy practices. The current language used for the principles in **the draft report is not reflective of the importance of patient value and reported outcomes.** For example, noting "benefits must be aggregated (valued) appropriately and consistently with average preferences of the general population rather than preferences of specific individuals" may be interpreted to mean that individual patient preferences or experiences are not to be included in economic evaluations of health technologies. This deviates from international efforts to include the patient voice in all HTA components and deliberative frameworks. For example, Canada includes a patient input process to integrate patient perspectives in reimbursement recommendations. Furthermore, "additional benefits should be relevant to the responsibilities, objectives, and decisions of the HTA organization" removes patient-centeredness entirely from the core function of the HTA organization's mandate, which is to provide recommendations for reimbursement decisions which ultimately affect patients.

We recognize significant gains have been made by HTA to include patients and have them participate in the process. As a result, it is better understood which outcomes are important for patients and through this, we have the opportunity to work together with the patient community to understand how to incorporate these preferences into the HTA and deliberative processes.

The report states that "HTA organizations that have adopted a normative position to use average public preferences to define benefits for economic evaluation should not simultaneously incorporate individual patient preferences, as this lacks a coherent normative basis." This recommendation makes equity conditional on uniform implementation which is not practical in a broad health care system. The standard normative position embraced by most HTA organizations is to reflect trade-offs using average preferences of a representative sample of public preferences in the organization's jurisdiction. If adopted, this could undervalue treatments that target small subgroups, such as rare and ultra-rare diseases and biomarker-driven oncology. These diseases need to be considered as a unique case – especially when the diseases themselves are so impactful on mortality and morbidity. This recommendation could undervalue incremental, but meaningful safety improvements that hold critical value for patients and their caregivers. For example, patient-centric treatments, such as those treatments that can preserve fertility, may offer high value for specific patients, but could appear less cost-effective because their benefits don't scale to population averages even though they have potential to transform individual lives.

Especially in the cases where there are no disease treatments available such as for many rare diseases, individual risk preferences should be considered differently given the gravity of the diseases and impact on patients and caregivers. In the case of rare-diseases, the equity perspective of HTA should go beyond the socio-economic framework to address lower health-baseline equity for these patients.

The report also states that "if specific benefits associated with the process of care are to be included in economic evaluation, further research is necessary to ensure there is no overlap with routinely used health-related quality of life measures." This recommendation intends to prevent double counting of benefits but may unintentionally undervalue improvements that enhance care experience. Delaying recognition of process of care benefits may discourage incremental innovation that improves treatment safety, patient care quality, and convenience.

4. Importance of Qualitative Deliberative Processes

The innovative medicines industry acknowledges the work that Canada's Drug Agency (CDA-AMC) has made on its deliberative framework, specifically, bringing diverse perspectives and elements for discussion, and trying to bring different elements consistently for discussion. Within this deliberative framework, it may be challenging to quantify these important elements. The deliberative process itself is essential to a robust, inclusive and impartial HTA as it brings scientific evidence together with contextual and experiential forms of evidence, experiences and values. **The lack of methodology to incorporate novel elements of value in the economic analysis currently underscores the importance of considering them in the deliberative process.**

The innovative medicines industry recognizes the need for quantitative analysis; however, qualitative elements are equally valuable and are needed for decision making. These elements should continue to be considered for effective decision making and their usefulness within the reimbursement process should not be understated.

The innovative medicines industry is encouraged with the continued efforts of HEMA to provide independent and critical guidance on new methods and processes for economic evaluation. The methods and processes should continue to value innovation and novel ways of working together. HTA organizations have a significant role in providing recommendations for drug reimbursement systems. Highlighting actionable steps for the implementation of these recommendations, using existing methods or filling in the knowledge gaps, is necessary to ensure faster access to innovative treatments that are valuable and needed for patients.

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October 29, 2025

Dear HEMA Group:

ISPOR – the professional society for health economics and outcomes research - is pleased to respond on behalf of its membership to your consultation entitled "Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies."

ISPOR is a scientific and educational society with many of its members engaged in evaluating health technologies, including pharmaceuticals, medical devices, public health measures, and other interventions. We have a large membership living and working in 110 countries globally, across a range of disciplines, including health economics, epidemiology, public health, pharmaceutical administration, psychology, statistics, medicine, and more, from a variety of stakeholder perspectives, such as the life sciences industry, academia, research organizations, payers, patient groups, government, and health technology assessment bodies. The research and educational offerings presented at our conferences and in our journals are relevant to many of the issues and questions raised in this request for information.

The response to this consultation was led by the ISPOR Science and Health Policy Initiatives Team. Comments were solicited from the ISPOR Health Science Policy Council, ISPOR Corporate Partners, and the ISPOR Health Equity Research Special Interest Group. The attached document provides a summary based on their comments. We hope they prove useful.

ISPOR would be happy to answer any questions about our response, to serve as a partner, or to participate in any follow-up consultations on the relevant program items mentioned within the report.

Sincerely,

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Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies

ISPOR commends the Health Economics Methods Advisory (HEMA) group for developing this draft report on "Defining Appropriate Benefits for Economic Evaluation of Health Technologies." Understanding what constitutes "appropriate benefits" is foundational to determining if a technology provides value for money. While the answer will depend on many factors including perspective and decision context, we appreciate this important first step taken by HEMA.

The document is clear, thoughtfully organized, and provides an initial analytical framework that holds promise for methodological consistency across health technology assessments (HTA). As HEMA evolves and given the pressing need for transportability of HTA assessments along with harmonization of methods, ISPOR recommends that HEMA establishes a living, cross-country methods reference case—supported by UK, US, and Canadian policies and practices—to promote clarity, comparability, and transparency across jurisdictions. With time, it might even be possible to enlarge the membership of HEMA to include other leading HTA bodies representing other economic, social, geographic and cultural domains (HAS, TLV, IQWiG, PBAC, and others), further strengthening the robustness of the methods discussed.

The tone of the document at present feels cautious, leaving the reader with important considerations about health benefits but with no strong direction. The breadth of topics covered also feels overly ambitious; a deeper dive into each of these through a series of more focused reports might be a better way to address these methods rather than a single, revised report. In particular, the title of the report, "appropriate benefits", is perhaps too vague. In a health economics context, "benefits" is understood to represent health gains derived from a technology or healthcare intervention compared to an alternative (standard or care or no intervention). Further, these gains should be meaningful to patients (and society at large), measurable, attributable to the intervention and comparable across interventions and disease areas. "Appropriateness" is in the eye of the decision maker and their respective priorities and budgets. Assuming that "appropriateness" in this report refers to appropriateness in NICE, ICER, and CDA-AMC evaluations, the report should more clearly explain how this was determined. What criteria of a given health benefit render it "appropriate"?

In addition to the points raised above, the report would be strengthened with a deeper exploration of the need for harmonization of real-world evidence (RWE) and artificial intelligence (AI) policies and practices across jurisdictions. Finally, the challenging topic of perspective would benefit from a fresh opinion from HEMA; though historical guidance recommends the societal perspective, there

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are data and methodological challenges associated with it. It is acknowledged that the list of topics stated here goes beyond the intent of this inaugural report but could prompt thinking about where to focus HEMA's efforts moving ahead.

Our review of the report itself was abbreviated due to the short turn-around time—which challenged ISPOR's standard operating procedure of inviting members to comment. Consequently, we highlight a few specific areas where further refinement could enhance its scientific rigor and relevance:

- First, we appreciate reference to the ISPOR Special Task Force on Value Assessment Frameworks in the draft and emphasize that while the quality-adjusted life year (QALY) remains an important starting point for measuring value, it has well-documented limitations. The QALY alone does not sufficiently capture dimensions such as the value of reducing uncertainty, improving equity, or incorporating broader impacts. The task force's deliberations also underscored meaningful philosophical and methodological differences in how welfarism is interpreted in the US versus the UK context. While the draft appropriately reflects the UK National Health Service's reliance on the QALY, it is important to note that the US government prohibits its use in federal decision making. Given that HEMA represents three HTA bodies operating across distinct policy environments, ISPOR encourages a more thorough discussion of QALY alternatives (GRACE, evLYG, and others mentioned). ISPOR notes that cost per disability-adjusted life year (DALY) averted has not been adopted by the more mature HTA bodies—and comes with its own methodological challenges—but is perhaps less contentious than the QALY. Though both QALYs and DALYs focus on morbidity and mortality, ISPOR suggests a deeper dive into DALYs averted given its established connectivity to global health (eg, the World Health Organization Global Burden of Disease Study) and would be interested in connecting members to HEMA to support a review or project on this topic.

- In addition, regarding the QALY, its use as an outcome measure should be stated. For example, decision-analytic modeling along with the use of QALY is an important (and still underused) tool for the benefit-harm analyses to inform clinical guideline development, where costs are often not considered, and decisions are made based on the benefit-harm balance alone.

- ISPOR also suggests that the final HEMA report includes greater detail on expanded value measures such as caregiver burden and productivity. Neither of the latter measures are new; there is a significant body of literature on each of them which could inform which methods should be

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used. ISPOR also notes that HTA bodies are increasingly interested in measuring the environmental impact of interventions. This is a relatively nascent area of the science which ISPOR is working to develop. Together, these expanded value measures are consistent with our Strategic Plan 2030 theme of whole health, an approach that emphasizes person-centered outcomes and quality of life beyond clinical endpoints to collectively achieve health of societies. Understanding the benefits beyond direct health gains is especially useful in value-based pricing contexts.

- Regarding the issue of preferences, sound emphasis on public preferences is well-established for HTA, but evaluations should also consider patient preferences. There is a strong case in the economics literature that a social welfare function can be based on a weighted average of individual preferences, using essentially the same conditions that QALY use is based on. In addition, it would be useful to provide case examples on how to mitigate double counting of benefits given that both these preference types are important.

- ISPOR appreciates the section on opportunity costs given that healthcare systems, globally, are significantly resource constrained. From a measurement standpoint, the methods here are not standardized but fundamental questions such as 1. “Whose resources are being used?” 2. “What are those resources?” could be addressed by HTA. Another more challenging question related to opportunity costs is “What alternative health benefits could have been achieved if those resources were used elsewhere in the system?”, though that could reasonably be considered to be outside the scope of HTA (ie, in the realm of payers or healthcare delivery system). As a relatively straightforward starting point, it is reasonable that a system-level cost of treatment be included in HTA evaluations. This measure would indicate the total cost of care to deliver the treatment in the system, including the intervention itself as well as human and non-human resources such as supplies and transportation.

- Many of the detailed comments ISPOR received pertained to the disconnect between the report and patients. ISPOR emphasizes that HTA must be rooted in the realities of patients, caregivers, and the health systems that serve them. The impact of HTA on policy and practice will only be realized when assessments reflect lived experiences. In low- and middle-income countries, for example, value extends beyond incremental cost-effectiveness ratios. It includes patient trust, continuity of care, and the capacity of health systems to deliver new technologies without overburdening providers. A new technology is “appropriate” only when it strengthens the continuum of care, promotes engagement and trust, and

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empowers providers to deliver value-based, Whole Health-oriented care with dignity.

- We appreciate mentioning the importance of patient and citizen preferences when making HTA decisions as the patient voice is critical to making decisions that are best for the population and to understand the quality-of-life tradeoffs that patients are willing to accept. At the same time, there is concern that the approach to including patients may be too rigid and can exclude patient-level heterogeneity. For example, the discussion of risk attitudes (pp ES2–ES3) highlights the tension between population averages and individual preferences. We recommend encouraging HTA bodies to pilot hybrid approaches where patient-derived utilities supplement public preferences, while maintaining comparability.

Given ISPOR's strong membership base of HEOR professionals along with our commitment to furthering science, we hope that HEMA's final report more clearly identifies where more research is needed to inform the methods to assess health benefits. We welcome a more expansive discussion about the comments ISPOR received as well as our current scientific initiatives and where they might help to inform HEMA's efforts. We also welcome discussion with HEMA on priority gaps in the methods that ISPOR, through its 20,000 members in over 110 countries, can help to address. Finally, we urge HEMA to consider the role that ISPOR might play in providing a forum for debates and discussions on methods.

We acknowledge the ISPOR Health Science and Policy Council members for their help assembling these comments, and ISPOR staff Laura Pizzi, Mitch Higashi, Ana Amaris, and Kelly Lenahan.

Minding the gap between CEA traditionalists and novel element proponents

Joshua T Cohen and Peter J Neumann

December 4, 2025

A field still in flux

If Rip Van Winkle[1] had fallen asleep in 1976 after reading one of the first published health care cost-effectiveness analyses – and who hasn't at times nodded off while reading these papers – and awakened today, he might conclude that the field has become an extraordinary success. Well over a thousand peer-reviewed studies are now published each year,[2] the methodology underpins drug price negotiations in several countries,[3] and even in the United States, the Institute for Clinical and Economic Review relies on cost-effectiveness analysis to make price recommendations for pharmaceuticals.[4]

Yet there is discord. Advocacy groups have labeled the quality-adjusted life year (QALY) – the field's foundational measure – as unethical.[5] The US government has substantially restricted its use.[6] And a 2018 Special Task Force convened by the International Society for Pharmacoeconomics and Outcomes Research concluded that traditional cost-per-QALY cost-effectiveness analysis (CEA) omits important elements of value.[7]

Is traditional CEA far off the mark?

Some prior investigations have taken a "bottom-up" approach, estimating how much value so-called novel elements might represent.[8-10] Those assessments necessarily depend on assumptions about the parameters that feed their calculations. Our recent analysis[11] instead adopted a "top-down" approach that treats the market as the ultimate arbiter of value. We asked whether traditional CEA judged drugs that ultimately succeeded in the market to be good value. We found that for about half of the drugs with annual worldwide sales of at least $500 million, conventional CEAs deemed their cost-effectiveness ratios unacceptable. *In other words, traditional CEA missed half of the successes.*

To be sure, the inconsistency between the market and CEA might have other explanations. As our paper notes in part: "(1) some CEAs use list prices rather than the actual net prices after discounts and rebates paid in the marketplace; (2) a drug's unfavorable cost-effectiveness may reflect its initial indication … while its market success may reflect subsequent indications; (3) the initial CEA projection may reflect a drug's initial formulation …" Finally, our paper points out that "whether 'market success' is an accurate indicator of value is contestable given … possible market failures…" That is, perhaps [we are] "'overpaying' for many drugs, reimbursing at amounts exceeding true value."

However, the mounting evidence from earlier bottom-up analyses, together with the strong signal from our top-down approach, suggests that traditional CEA may be inadequate. Although limited data constrain the full implementation of novel value elements, we nonetheless recommend sensitivity analyses to illustrate what a 'base-case' traditional CEA may be overlooking.

Sensitivity analysis won't save us

I might ordinarily end this commentary here. But sensitivity analysis will not reconcile the opposing camps in our field. Some CEA traditionalists have moved somewhat. For example, the UK's National Institute for Health and Care Excellence (NICE) has adopted severity modifiers to account for the value of addressing severe conditions.[12]

But novel element "proponents" have called for more, such as incorporating dynamic pricing,[13] which our analysis and other work suggest can often be important.[10,11] The authors of the Generalized Risk Aversion Cost Effectiveness (GRACE) framework also advocate a shift away from maximizing average health per se and toward a focus on individual preferences that explicitly accounts for risk aversion. The debate over the recent Health Economics Methods Advisory (HEMA) report exemplifies this ongoing battle.[14,15]

Ongoing argument has undoubtedly helped the field advance, but it is not clear that the current conflict is as constructive as it could be. Here are some ideas that might help going forward.

To the CEA traditionalists

The debate over how we assess value and which elements belong in that assessment is healthy. But it would be helpful to avoid the effective sidelining of elements that many people clearly care about – such as equity, community-level benefits, and scientific spillovers – by assigning them, from the outset (page 2, Box 1) to qualitative deliberation only.[15] Quantification is admittedly difficult but treating these elements as beyond the scope of quantitative analysis risks undermining the perceived relevance of the framework.

Similarly, the principle that "benefits must be relevant for the decision-making organization"[15] is reasonable, and it is understandable that HTA bodies want to stay within what they see as their remit. But setting aside the primacy of individual preferences – the microeconomics "gold standard" for assessing whether resource allocation improves welfare – requires a more substantial justification than HEMA provides. Table 2 asserts that benefits are relevant only if they "reflect the statutory, legal or other authorities of the decision-making organization…".[15] From HEMA's presentation, it is not obvious that existing statutes compel this conclusion. Even if they did, framing relevance solely in terms of institutional mandates makes it appear that HEMA is prioritizing what HTA organizations say they care about over the concerns and preferences of citizens. Once again, that stance risks undercutting the relevance of the enterprise.

To the novel element proponents

Bringing theoretical rigor to the debate is valuable: it grounds novel value elements in well-established principles, sharpens their definitions, helps prevent double counting, and lays the foundation for quantifying impacts. But while theoretical rigor can prove propositions, it neither explains nor persuades on its own. The arguments in the rebuttal to the HEMA report would be more effective if they first laid out the intuitive story in plain language and then relegated the heavier theoretical machinery (e.g., Harsanyi's theorem[14]) to an appendix or supplement. In addition, while the rebuttal offers seven reasons for rejecting the HEMA report, it is not clear that it systematically addresses all of HEMA's specific critiques of frameworks like GRACE. A more effective strategy would be to follow the HEMA report's own structure and respond point by point, explaining what is wrong with each element in turn.

To everyone

Greater openness – especially around simulation models – would help build trust.[16] The issue is not simply the potential for programming errors. Rather, we should all make it possible for others to interrogate our models, including exploring how conclusions might change under alternative assumptions or scenarios that the original authors did not consider in their sensitivity analyses.

Better documentation of cited material would also help. Instead of merely listing the source from which an estimate is drawn, we should describe – perhaps in a supplement – precisely where it comes from within that source and how we manipulated or transformed the values we retrieved. That level of transparency allows readers to independently interrogate the basis for our assumptions, rather than having to trust that we did something reasonable.

The hope

There is no doubt that differences will persist. But by setting aside unnecessary burdens – such as catering to the stated needs of HTA organizations, by directly engaging each other's arguments rather than trying to overwhelm with theory, and by "showing our work," we can narrow these disagreements to genuine debates about the underlying science. In doing so, we can also build credibility with the audience that matters – the people whose health and lives we aim to benefit, not just our fellow health economists.

Statement on use of large language models

The authors used ChatGPT v 5.1 to assist in the review of cited sources, suggest a title, suggest section headings, and refine wording.

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First, great to see this work as it represents a good synthesis of current topics and recent advances that are important to consider for contemporary economic evaluation. Kudos to the group for this work.

The document refers to the HTAs commissioning the work; are the guidelines meant for them, or also for other HTAs? Is this meant to extend beyond the HTAs represented in the HEMA? I was unclear on that.

Agree that a generic benefit function allows comparability. Good discussion of QALY and alternatives, as well as individual vs. public preferences/utilities, and double counting as a basis for all that follows in the report.

Wanted to clarify the point about adherence not being in scope – if measures of effectiveness (RW or RCT) themselves should pick up on adherence effects, there is no need to count it separately, otherwise it's double counting. If this is what is meant, that is appropriate.

Good discussion of risk attitudes and GRACE; appropriate that a specific framework is not recommended by HEMA in this discussion.

Regarding the use of DCEA: the rationale for needing to use this in all assessments (or none) was unclear. It is possible that using these methods may produce results that are difficult to interpret/implement or run counter to preferences for equity improvements. However, these are very data intensive analyses and it may not be reasonable to perform robust equity informative evaluations in all cases. This requirement may hold back advancement in equity in cases where it matters, and could preclude possible gains by disadvantaged groups. Given that value of information (VOI) tools exist, it may be reasonable to require an approach that uses VOI to determine which evaluations would be impacted with equity analysis, or use a triage approach to determine in which cases would equity analyses be important.

The overall recommendation that evidence on opportunity costs is important to support use of additional benefits. But what is the threshold for that evidence? Spillover effects, caregiver impacts, and productivity in particular have quite a bit of evidence and are a priority for many stakeholders. Can this evidence be used outside of modeling inputs as part of context or deliberation? This should be more clearly guided.

Regarding value flower element inclusion: true that we need strong evidence to incorporate additional benefits. However, we have progressed beyond needing perfect

information and have tools for uncertainty. I might suggest that there be some consideration of when would evidence meet the threshold for inclusion, and are there acceptable tools to use when the data are close, but not quite there, to ascertain what elements are in that zone? In places felt like there was a disconnect between the recommendations around evidence/data availability and techniques we have like VOI and EVPI – is there a role for these when there is not strong data on opportunity costs?

Minor comment on the executive summary –it was long enough that it would benefit from an outline or roadmap for the reader.

HEMA: Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies
Comments from Katherine Payne, 12 December 2025

I have been asked to review this report using three criteria: clarity; relevance to US HTA; recommendations. I am a health economist based in the UK. I am not well placed to comment on 'relevance to US HTA'. In this document, I have written comments as I read the HEMA report. There are not in order of importance. I apologise for this lack of organisation but I was very limited on time to read and comment on this report.

Clarity: are there inconsistencies across sections or terminology that should be addressed? Are there areas where the definitions of benefits for economic evaluation may need further elaboration?

I think the focus on HTA needs to be made clearer with a supporting definition that describes what 'technology' includes. The reason for this comment is the UK National Screening Committee currently draws heavily on the NICE Methods Guide; although just starting the process of developing their own Methods Guide for Generating Economic Evidence for the UKNSC. The UKNSC sits within the Department of Health and Social Care and when producing economic evidence rely on NICE methods. But as the UKNSC produces recommendations for government ministers they are also asked to provide evidence using elements of The Treasury Green Book. This may include using a different discount rate and ICER threshold but also in some instance attaching a measure to wider elements of value eg. Productivity. Being clear what the 'T' in HTA covers in each jurisdiction is therefore important.

The report focusses on 'benefits' but economic evaluations should also identify and measure and value the harms associated with a technology. Using the term 'benefits' may mean that 'harms' are overlooked. Would consequences be a more inclusive term?

Related to this. I do not think it is correct to conflate measures of the 'consequence' of an intervention with the delivery 'process' of an intervention. Within the executive summary; attitudes is also introduced as an element of value. This is not correct.

The executive summary confusingly uses the terms equity and inequality to refer to the same thing which are two distinct concepts: …equity considerations (e.g., consideration of health inequalities). This should be corrected.

The report refers to economic evaluation but makes no reference to the vehicle for generating evidence to feed into the evaluation. I believe that most HTA agencies rely on model-based economic evaluation? Is this correct? If so, this has a bearing on how the evidence for different elements of value can be measured and valued and subsequently used in the model-based economic evaluation. The challenges in generating data to populate a model-based economic evaluation are different to designing and conducting a trial-based economic evaluation. I think the term 'modelling' is first used on p19 but remained un-defined.

It is important from the outset to be clear which budget is being spent and informed by the HTA. This is implicit at the moment. It is also crucial to be clear that the relevant jurisdiction using the HTA views the budget for healthcare alongside other aspects of society (education, environment, employment etc) ie. Is their scope for transferability between budgets? In the UK – although the perspective is health and social care – because funds are not transferable between these two aspects often it is the health budget that is the focus for a HTA (hence health maximisation).

Table 1 should include which budget is being informed? And the type of health care system (public/private). The relevant model of health care provision and relevant budget for the US only becomes apparent on p13.

The first para in section two could also explain how out of the three HTA agencies which have a fixed budget and which do not. The text on p7 contains this but it is incredibly dense and hard to follow as written. Hard to follow in the sense of 'so what' for valuing benefits in an economic evaluation.

This phrase is confusing '… although running time-limited deficits may be possible in some instances'. What does this mean? Specifically.

In general, the Tables as presented are not easy to read as they simply have long sections of text under one column. Adding more columns with clear headings and breaking up the text would make it easier for the reader to assimilate and understand what (important) information is being presented.

Some core concepts eg. 'supply-side' are not defined when first used in this report. For example, supply-side is included in a table but not defined until much later.

In general, the executive summary (and some aspects of the report) mixes up: fundamental principles (which budget); normative positions; definition (identification), measurement and valuation of consequences, process and attitudes; value judgements. I think more structure would be helpful.

The report does not make it clear how the Q in the QALY is quantified. Some of the criticisms of the QALY are not because of the concept or construct but down to how the Q is measured. These are not mentioned. The critique of the QALY should be more clearly presented with a structure around: fundamental principles of using the QALY (assumed desire to maximise health); how to identify, measure and value the Q; how to use the Q-adjustment in decision-making and the assumptions made (eg. A QALY gained is the same for everyone).

Relevance to US HTA: a note that we are planning a "Box 3" on differences between the US and other countries related to the benefit function. This may include an overview of legislation on the QALY. Your insights here would be especially valuable.

I am not in a position to comment on this.

Recommendations: are the recommendations helpful regardless of whether you agree or disagree with them? Are there additional recommendations that may be helpful?

The whole report seems to be underpinned by the ISPOR value flower, which although an important summary of different elements of value, it does miss other key concepts that are in the wider health economics literature (one example being capability). This is important because some of these other elements are consistent with extra-welfarism and do have measurement tools.

The value flower is also not informative because it does not distinguish between 'elements' that can be identified, measured and valued and those that cannot. It simply places a list featuring as 'petals' around a core that says 'value'. Confusingly some of these petals also have value in the description.

The report says '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…'. This is the fundamental issue with the report. It fails to recognise the extant literature on valuing (wider) consequences in economic evaluation and how to include process .

Using the phrase 'non-health benefits' is neither useful nor helpful. It does not recognise the importance of harms. Using non-health is shorthand for non-QALY as measured using the EQ5D valued using public preferences. More careful definition of including consequences (benefits and harms) moving beyond the QALY as currently defined, valued and used is required.

October 30th, 2025

Subject: Response to Health Economics Methods Advisory (HEMA) Group's Draft Report on "Defining appropriate benefits for economic evaluation of health care technologies"

We thank HEMA for the opportunity to provide feedback on the current consultation for their draft report on "Defining appropriate benefits for economic evaluation of health care technologies". This consultation process represents a valuable opportunity for dialogue and constructive engagement between all interested parties, including industry.

As a global research-intensive biopharmaceutical company, we recognize the importance and relevance of evolving HTA methods and practices. We appreciate that HEMA has taken this critical first step to more holistically describe and incorporate additional considerations when assessing value of innovations in economic evaluations. We commend HEMA for advancing thoughtful approaches to health economics evaluation that align with recent developments in the field, such as incorporating individual risk preferences into benefit calculations and considering broader economic impacts beyond those restricted to the health care system.

The establishment of a structured framework for evaluating additional benefits reflects recent research that expands the definition of value which represents significant progress towards modernizing HTA practices. Where possible, harmonization and standardization of methods for robust value demonstration in HTA is welcomed for efficiency and consistency. However, variability is also expected and therefore flexibility will remain paramount for local contextualization. As such, we appreciate HEMA's recognition that "some variation in methods across organizations is necessary - it reflects local preferences and priorities," as this acknowledges the diverse healthcare ecosystems in which innovative medicines operate. This balanced approach should create opportunities for scientifically rigorous methodological innovation at a global scale while maintaining contextual flexibility for application around the world.

We encourage HEMA to ensure that the final report includes a robust and practical framework that is adaptable to various contextual realities. We recommend that HEMA articulates its recommendations with clarity and precision, ensuring they are easy to interpret and implement. We also recommend adding best practice examples in the final report to contextualize the framework and make it more practical. This will facilitate consistent and efficient adoption by all HTA stakeholders.

We look forward to the publication of the final report, and to HEMA's ongoing contributions to advancing HTA methodologies. As an industry stakeholder, we remain committed to open dialogue and collaboration in pursuit of our shared common goal: ensuring that the value of scientific innovation gets recognized through a more holistic economic evaluation that would

include not only benefits to patients, but also to their families, caregivers and the overall economy. We welcome future research recommendations on aforementioned topics.

Sincerely,

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Feedback on “Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies”

Dr Mike Paulden, School of Public Health, University of Alberta

The following is feedback on the HEMA report titled “Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies”.[1]

I offer this feedback as an academic health economist who has published papers on several topics relevant to the report, including the measurement of health opportunity costs, the valuation of health benefits, and distributional cost-effectiveness analysis, and who has actively engaged in policy debates on these topics in all three countries (Canada, UK and the US).

My feedback will focus on three areas of this report:

1. Clarity
2. Relevance to HTA in each country
3. Recommendations

Clarity

Overall the report is clearly written, and I believe the authors have done a good job of explaining their reasoning to an informed audience. I did not spot any major errors, omissions or inconsistencies within the report.

The core principles adopted by HEMA in this report are as follows:

1. “Relevance: additional benefits should be relevant to the responsibilities, objectives and decisions of the HTA organization.
2. Valuation: benefits must be aggregated (valued) appropriately and consistently with average preferences of the general population rather than preferences of specific individuals, and avoid double-counting.
3. Opportunity cost: any additional benefits need to be reflected in the benefits forgone elsewhere resulting from the funding of more expensive interventions.”

These are very reasonable principles. However, there is a minor inconsistency between this wording (taken from the executive summary) and that used to summarize each principle in the first column of Table 1. For example, “consistency” in the valuation of benefits has been dropped from the first column of Table 1 (although it appears in the second column). I

recommend fixing this, because “consistency” in the valuation of benefits is vital for supporting HEMA’s recommendations later in the report.

I also recommend that HEMA considers adding “... using methods that are feasible to implement in real world practice”, or similar words, to the 2nd principle considering the valuation of benefits. HEMA’s recommendations must be implementable by HTA agencies in real-world practice, which precludes HEMA from recommending approaches that may be theoretically desirable but infeasible to implement.

Finally, I recommend that HEMA considers whether creating a plain language summary of the report would be of value for a lay audience. Many of the topics considered are complex, and it is important that stakeholders without expertise in health economics are able to engage with HEMA’s reasoning around these topics.

Relevance to HTA in each country

Each of the principles articulated above is relevant and appropriate for HTA conducted in each of the three countries (Canada, UK and the US).

That said, the first principle requires that HEMA carefully considers the legal restrictions against the use of the QALY in the US, and the implications for HTA conducted by ICER and other organizations. I recommend adding a Box 3 to deal with this. In considering these legal restrictions on the use of QALYs, I also recommend that HEMA emphasizes the problems with alternatives to the QALY such as the evLYG and HYT.[2]

Recommendations

I broadly agree with the recommendations in this report. In particular, I agree that the GRACE framework should not be recommended at this time for use by NICE, CDA or ICER.

In addition to the reasons given by HEMA, I would add that GRACE is currently infeasible to consistently and equitably implement in practice. This is because GRACE relies upon the consideration of individual preferences, yet many of the individuals impacted by a recommendation by NICE, CDA or ICER are not identifiable at the time that the recommendation is made. This includes the individuals who bear the opportunity cost of a recommendation to reimburse a medicine - these individuals are determined later by reallocation decisions made by administrators within the public health care system or private insurance plan in question. It is therefore not feasible for NICE, CDA or ICER to take into account the individual preferences of all patients impacted by any specific recommendation. While it may be possible to consider individual preferences for a *subset* of the patients affected by the recommendation (specifically those patients who receive the medicine), considering *only*

these individual preferences would be inequitable and inconsistent. I recommend that the text on “Opportunity Costs” on p.28 be expanded to make this clear.

It is also concerning to see the dismissive response from the authors of GRACE and the ISPOR ‘Value Flower’ to HEMA’s considerations around the opportunity cost of reimbursing medicines.[3] The authors of these frameworks make the erroneous argument that because the NHS budget increases over time, and temporarily increased in response to the COVID-19 pandemic, it follows that the NHS budget can expand within a budgetary cycle to accommodate any additional costs of new medicines recommended by NICE. This is incorrect - the NHS budget does not increase (even temporarily) following a routine recommendation by NICE to reimburse a medicine, and any resulting incremental costs fall upon this budget, displacing other health care services. While the authors of GRACE and the ISPOR ‘Value Flower' may argue that this *should* not be the case, the reality is that, in practice, NICE and other HTA agencies face budget constraints, and HEMA’s recommendations must reflect this. In my opinion, HEMA should not recommend that NICE, CDA or ICER use GRACE, or additional elements within the ISPOR ‘Value Flower', until these frameworks are adapted to take into account the real-world opportunity costs associated with reimbursing medicines.

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Submission to Canada's Drug Agency, HEMA Working Group
Delivered via email: **public_comments@hemamethods.org**
Re: **Health Economics Methods Advisory Group Releases Draft Report: Assessing Treatment Benefits in Health Technology Assessment Decision-Making**
Submitted by: MS Canada
Date: October 30, 2025

MS Canada appreciates the opportunity to comment on the draft guidance, "Guidance to Help HTA Organizations Assess Whether Additional or Alternative Benefit Measures Should Be Incorporated into the Benefit Function Used for Economic Evaluation."

As Canada's national organization supporting more than 90,000 people living with multiple sclerosis (MS), MS Canada brings the lived-experience perspective of those navigating a chronic, progressive and unpredictable disease.

Our work is guided by a central goal: that people living with MS have access to the right treatment at the right time, and that affordability, equity, and lived experience are foundational to decision-making in Canada's health system.

MS Canada strongly supports the report's recognition that treatment benefits extend beyond traditional measures such as QALYs and its focus on achieving greater consistency and transparency in HTA.

Due process and stakeholder engagement

HTA organizations should only apply principles that have undergone transparent stakeholder consultation and are supported by evidence. MS Canada recommends that people living with, and affected by MS, clinicians (and where applicable industry representatives) be engaged before new benefit-assessment principles are adopted.

Lived experience must be central

MS Canada supports the recommendation to build a stronger evidence base for benefit measures. We also believe it's essential to develop a framework that reflects both population-level perspectives and the lived experience of people living with MS.

Population-level data inform system priorities, while individual experience provides depth, context, and relevance to the highly heterogeneous disease journey of people living with MS. Relying solely on population averages risks oversimplifying MS a disease marked by significant variability in symptoms, progression, and treatment response.

The concept of ‘the right medication at the right time’ is central. HTA frameworks must establish structured pathways that integrate both quantitative population health data and qualitative lived-experience insights, recognizing that each offers distinct and essential value.

Equity and access must be core principles

MS Canada encourages a clear, consistent approach to applying equity modifiers, like severity. We encourage a consistent, transparent approach that reflects both clinical evidence and the lived experience of people affected by MS.

Canadians living with MS already face unequal access to care due to geographic, social, and financial barriers. Rural and remote communities, provincial reimbursement differences, and interruptions to employment or insurance coverage all impact timely access to treatment and care.

For a progressive disease like MS, time matters. Delayed or restricted access to effective therapies can result in irreversible disability. HTA decisions must embed equity as a core principle, accounting for urgency of treatment, geographic variability, and differing needs of the MS community.

Opportunity cost, affordability, and real-world value

Willingness-to-pay models don’t reflect the financial realities of Canadians living with MS, who already face significant out-of-pocket expenses for costly therapies, assistive technologies, and mobility supports. Affordability should not be mistaken for value.

While financial accountability is important, too much focus on opportunity cost risks overlooking benefits that are difficult to measure such as maintaining employment, reducing caregiver burden, and preserving independence. HTA frameworks should adopt a balanced approach that reflects both health and social system constraints and the impact on those with lived experience.

Recognizing broader societal and cross-sector benefit

The draft report acknowledges that evaluating productivity and cross-sectoral benefits such as education, employment, and social participation requires further research and sector-specific data. Yet for people living with MS, these broader outcomes are central to overall health and well-being. The ability to remain employed, support a family, and participate in community activities directly contributes to both individual quality of life and the broader social and economic value. When these factors are overlooked, there is a real risk of undervaluing therapies that help sustain independence and reduce long-term costs to health and social systems.

MS Canada

HTA organizations must develop robust evidence frameworks for these broader impacts rather than exclude them until complete data is available. Recognizing these benefits will lead to more equitable and holistic value assessments that align with the realities of people living with MS.

We call on HTA organizations to:

- Apply only principles established through transparent stakeholder consultation;
- Integrate both population-level and lived experience perspectives;
- Embed equity as a core principle across all assessments;
- Recognize affordability challenges and avoid equating willingness-to-pay with value;
- Balance opportunity-cost analyses with meaningful, real-world outcomes; and
- Invest in evidence frameworks that capture broader societal benefits.

MS Canada supports the Health Economics Methods Advisory working group focus on advancing a more comprehensive approach to assessing treatment benefits, including outcomes that matter most to those living with and affected by MS.

Sincerely,

Jennifer McDonell
Director, MS Information and Resources
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I provide below two comments on the draft report from NICE colleagues in technical, methods-focused roles.

1. The report states that “cost savings by the introduction of a new technology is not considered a direct benefit here but can generate benefits by freeing up resources for the management of other patients”. This assumes any time saved is diverted to provide care elsewhere, rather than reduce staff workload (or allow them to do continuing professional development, etc.), or provided ‘add on clinics’ are removed (i.e. removing excess demand could mean that clinics are more able to regularly run at their intended (rather than maximum) capacity). Helping staff/reducing burden on staff is a point that is flagged as a primary benefit of some healthtech, which (perhaps very) indirectly can benefit patient’s health, but could be useful to expand here, or include explicitly as something not considered/out of scope, if this is the case.

2. It would be helpful for the report to distinguish between value elements and value assessment methods. For example, discount rate is labelled as a value element (albeit one that that was considered out of scope), whereas we would normally this about discount rate as a methods choice.

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October 30, 2025

RE: NPC's Comments on the HEMA Group's Draft Report
Submitted electronically to public_comments@hemamethods.org

Dear HEMA Working Group,

The National Pharmaceutical Council (NPC) appreciates the opportunity to submit comments on the Health Economics Methods Advisory (HEMA) group's draft report titled "Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies."

Below, we describe concerns about the framing and content in this draft report, as well as recommendations for addressing some of its limitations. Our primary concern is that, although this report purports to be about broadening the benefits captured in health technology assessments (HTA), in practice, it establishes barriers to the inclusion of comprehensive benefits to patients and society and reinforces the continued use of potentially harmful status quo methods.

The draft report represents a missed opportunity to advance evidence-based, patient-focused HTA methods, and we offer these comments in the spirit of rectifying this shortcoming in the revised report. NPC's key concerns and associated recommendations for this report include:

I. **The proposed principles reinforce existing HTA practices and often assume the status quo as the gold standard.**
   - NPC recommends that the authors take a holistic approach to value — namely, that prior to deliberating on the value of a medicine, one must first measure all impacts to patients and society.

II. **The proposed "opportunity cost" principle is not operational within the U.S. healthcare system and relies on weak evidence.**
   - NPC recommends the use of multi-stakeholder deliberation and patient preferences, which better capture the patient voice and are more reflective of U.S. priorities.

III. **Economic evaluations must be viewed as a tool, not a rule.**
   - NPC recommends that, given economic models and HTA practices require both science and judgment and are often not validated, the authors must acknowledge both qualitative and quantitative uncertainty in the process and findings, and view them as one of many inputs to achieve value in health.

I. The proposed principles reinforce existing HTA practices and often assume the status quo as the gold standard.

Although presented as an exploration of opportunities to broaden the benefits considered in HTA, the draft report relies heavily on the standard normative positions of three HTA bodies (CDA-AMC, ICER, and NICE) to define the role and remit of HTA to inform recommendations about which benefits should be considered in economic evaluations. This approach presents multiple concerns.

First, **the U.S. does not have an authoritative HTA body or remit**. The authors acknowledge that the report focuses on the needs of HEMA's three Secretariat HTA organizations. However, the recommendations and principles may more appropriately align with the Canadian and English healthcare systems than with the U.S. system. The report assumes HTA organizations have a formal remit to maximize population health within a constrained budget and warns that adding "wider benefits" (e.g., productivity) is only appropriate if decision-makers are accountable for cross-sector trade-offs and can model matching opportunity costs. This framing may better reflect the role of NICE and CDA-AMC, which have centralized remits to maximize health from a supposed "fixed-budget" perspective.

Conversely, there is no government-backed HTA body in the U.S. ICER's remit and methods are established through its own governance processes, and its assessments are intended to be one of many resources that inform, not dictate, payer decision-making. In the U.S., healthcare decision-making is decentralized across multiple types of payers (e.g., Medicare, Medicaid, health plans, PBMs, employers) whose priorities differ from those of nationalized health systems (e.g., profit, member retention, employee productivity, etc.). This reduces both the demand and the political feasibility of establishing a single national HTA body in the U.S.

Second, **the report does not recognize the limitations and potential harms associated with current HTA methods.**

Reliance on a "fixed budget" perspective. The report's emphasis on the "fixed budget" perspective effectively assumes a short time horizon (e.g., annual) and that healthcare spending is appropriately allocated and therefore fixed within and across domains and cannot rise to support or reward new healthcare innovations. This stance is misaligned with the structure of the U.S. health system and should be questioned within any system for multiple reasons.

Applying a "fixed-budget" perspective prioritizes short-term affordability and risks underestimating long-term treatment value. This view of healthcare resource allocation disregards evidence that historical investment in healthcare has generated substantial social and economic returns through improved survival, quality of life, and productivity, creating lasting value rather than crowding out other effective care. For example, empirical research has found that increased healthcare spending in the U.S. has been a significant source of value creation for top diseases associated with disability and mortality.[1,2]

A "fixed-budget" perspective also risks weakening incentives for industry investment and innovation in areas of greatest unmet need.[3] Notably, in the UK, rising manufacturer rebate rates for pharmaceuticals under the Voluntary Scheme for Branded Medicines, Pricing, Access and Growth (VPAG) have coincided with high-profile exits from major life sciences firms and declines in late-stage clinical trial activity.[4,5]

Inclusion of a narrow perspective and limited set of benefits. Current value assessment methods rely heavily on clinical trial data and often exclude data related to patient-reported benefits, treatment burden, and adherence from the benefit function. These can each have a significant effect on patient outcomes and cost. For example, HTA methods typically do not capture measures of treatment burden, even though it often ranks as a top priority for patients, particularly for those with chronic conditions or treatments affecting older populations.[6-10] Patients also place high importance on how their treatments affect caregiver burden, especially in the case of rare childhood diseases and those affecting the elderly.[11-13] Additionally, patients living with severe and/or progressive conditions often consider the insurance value of treatments, recognizing that a treatment may provide protection from future physical and financial risk for themselves and their families.[14,15] Despite rigorous theoretical and mathematical foundations for including additional dimensions of value, the recommendations and principles in this report reinforce the use of existing HTA methods which assess a narrow set of treatment benefits.

Logical inconsistencies. In the plain language summary, the authors caution against incorporating measures of "burden on patients, their families, and the wider economy" in economic evaluations as "including these factors could shift priorities in ways that help some patient groups more than others." However, cost-effectiveness methods already do this. For example, costs vary by age and differentially affect results for two treatments that extend life by the same amount but are used in different age groups. It is therefore a flaw in logic to reject the inclusion of broader benefits in HTA because they may reallocate priority, when existing HTA methods already do so.

Prioritization of population versus patient preferences. The authors argue that valuation of treatment benefit must reflect average population preferences versus individual patient preferences. Population-level analyses do not account for patients' clinical heterogeneity or the variability of treatment benefit, and applying this principle in economic evaluation results in HTA analyses that mute or silence patient preferences and limit the patient voice.[16] This approach does not align with the multi-payer U.S. system or U.S. culture where the consumer/patient voice is a valued component of care delivery. Moreover, U.S. federal law prohibits the use of the Quality-Adjusted Life Year (QALY) in determining coverage or payment decisions in Medicare and other federal programs.

The report's recommendations also **discourage the application of innovative HTA methods that capture a more comprehensive view of value to patients and society.** The report's recommendations anchor on population-level preferences and capturing opportunity cost, a

perspective that naturally disadvantages innovative HTA methods like the Generalized Risk-Adjusted Cost-Effectiveness (GRACE) model and the Generalized Cost-Effectiveness Analysis (GCEA) framework, which are built on patient-level risk attitudes and willingness to pay. This framing privileges existing HTA norms and methods and dismisses mature research efforts to advance more patient-centered value assessment.

The authors conclude, "No additional benefits should be routinely incorporated into economic evaluation until there is an evidential basis to reflect them in opportunity costs." In practice, applying this recommendation could stall methodological development and progress aimed at measuring the benefits that matter to patients and employers, and result in value assessment determinations that reflect an even narrower view of the benefits medicines provide to patients and society. Moreover, the paper's recommendations are inconsistent with recent efforts by HTA bodies to make their assessments more comprehensive and patient-centered, particularly in capturing productivity effects, reflecting the societal perspective, and accounting for disease severity. This raises concerns that the recommendations could reverse recent progress by HTA bodies (e.g., NICE's introduction of a severity modifier)[17] and pull HTA practices backward toward narrower methods.

As stated in the plain language summary, HTA recommendations "directly impact the availability of treatment and how much some patients will have to pay out of pocket." HTA recommendations also have downstream implications for research and development. Given these stakes, it is important to get these decisions right. Applying a holistic approach to assessing value by systematically cataloging direct and indirect benefits and evaluating them against trade-offs would result in more comprehensive assessments that better align with the U.S. health system.

NPC recommends that the authors take a holistic approach to value — namely, that prior to deliberating on the value of a medicine, one must first measure all impacts to patients and society.

II. The proposed "opportunity cost" principle is not operational within the U.S. healthcare system and relies on weak evidence.

Although the draft report is supposed to focus on defining and expanding the benefits (not costs) considered in HTA, opportunity costs play a primary role in the report and its recommended principles, which suggest inclusion of any additional benefits must also be measured as opportunity costs. This argument has numerous limitations.

First, there is **limited evidence to support an opportunity cost-based threshold.** Research examining opportunity cost approaches to cost-effectiveness analysis and threshold development identifies substantial methodological and data limitations.[18,19] Sampson et al. caution that credible causal links between spending and health outcomes are difficult to isolate and that high-quality data on morbidity outcomes associated with healthcare interventions are lacking, posing a

significant challenge to rigorously estimating health opportunity costs. Moreover, the authors of this report explicitly recognize the lack of strong scientific justification for this approach, stating that "current estimates of opportunity cost are subject to uncertainty and would be improved by additional data collection and further development in methods."

Additionally, the authors cite Vanness et al.[20] to support the inclusion of opportunity costs in the U.S. However, this is a single simulation study that is not representative of all Americans and is subject to numerous limitations. Simply put, this study does not support strong evidence of a cause and effect.

An opportunity cost approach ties HTA determinations to the current marginal productivity of spending. In practice, HTA bodies predominantly focus their evaluations on prescription drugs, which often deliver substantial health gains and long-term cost offsets relative to other healthcare interventions.[21,22] This disproportionate review of biopharmaceutical innovations effectively penalizes the very interventions with the strongest historical return on population health.

Given the significant methodological and operational limitations associated with the opportunity cost approach, it is inappropriate for the authors to require routine inclusion of new benefit elements to be contingent on matching opportunity cost evidence.

Second, **calls for evidence on additional benefits should be consistent with good practices in economic evaluation, and not set to a higher standard.** Cost-effectiveness analyses synthesize evidence from a wide range of studies and sources, and these data are incorporated into a model alongside assumptions to produce a finding. Models commonly rely on inputs supported by indirect, imperfect, or limited evidence (e.g., surrogate endpoints, long-term survival extrapolation, treatment discontinuation, etc.), which can materially influence the model's result, and consequently, an HTA body's value determination. Current economic evaluations are often noisy, and a model's output can rarely be fully tested against observations and dynamic evidence. However, by making the inclusion of novel benefits contingent upon measuring opportunity costs, the authors are holding new benefit elements to a higher evidentiary bar than other frequently used model inputs and model assumptions. This inconsistent approach to evidence favors status quo HTA methods.

Third, this **principle does not give sufficient consideration to the unique characteristics of the U.S. healthcare system, limiting its relevance and applicability.**

The U.S. has a decentralized, multi-payer health system, and there are many different priorities and perspectives that inform decision-making on healthcare coverage and resource allocation. Differences in benefit design, covered populations, provider contracts, and member churn, among other factors, mean the consequences of funding a healthcare technology are not uniform across payers. Accordingly, U.S.-focused value assessment frameworks and HTA methods tend to rely on multi-stakeholder, deliberative, consensus-oriented processes.[23,24]

The U.S. prioritizes patient autonomy and access. The authors express significant caution about bringing patient risk attitudes (e.g., "value of hope" or "insurance value") into the benefit function and emphasize measurement challenges. This perspective conflicts with the U.S. private insurance market where arguments about individual risk and autonomy are salient. In the U.S., patient-centeredness is an important component of healthcare decision-making, and payers, particularly employers, prioritize value elements related to patient quality of life and productivity.[25] However, according to the report, consideration of such elements must be contingent upon accounting for opportunity costs, despite the lack of routine methods to support such analysis.

NPC recommends the use of multi-stakeholder deliberation and patient preferences, which better capture the patient voice and are more reflective of U.S. priorities.

III. Economic evaluations must be viewed as a tool, not a rule.

Economic evaluations must be viewed as a tool, not a rule, for multiple reasons.

First, **HTA methods involve both quantitative and qualitative uncertainty.** HTA methods are helpful scientific tools that must be used with scientific integrity and context-sensitive judgment. Assessing treatment benefit is complex; economic evaluations incorporate elements of both science and opinion and are often highly sensitive to model inputs. Despite this, model outputs are rarely tested against observed and dynamic evidence, raising concerns about the validity of the findings. Given these limitations, economic evaluations should be used as one of many tools to inform decision-making.

Second, **a single approach cannot sufficiently reflect diverse values and constraints.** There is no consensus on the structure or components of "value,"[26] and thus value assessment must rely on a multi-stakeholder deliberative process that reflects diverse patient needs, societal benefits and costs, and considerations of health system sustainability. This sentiment is echoed by numerous U.S.-focused best practices for value assessment, including guidance from NPC,[27] the Center for Innovation for Value and Research,[28] and ISPOR,[29] among others, which embrace a plurality of value assessment methods rather than relying on a one-size-fits-all approach. Notably, themes widely emphasized across U.S.-focused best practices, including the emphasis on patient-centered outcomes, heterogeneity in treatment effects and preferences, and the inclusion of broader impacts (e.g., productivity effects and caregiver spillover), are met with skepticism and caution throughout this report.

Third, **the application of inappropriate HTA methods can harm patient access to medicines.** Patients in the U.S. have historically enjoyed broader and faster access to new healthcare innovations compared with patients in countries that use cost-effectiveness thresholds to determine prices or coverage.[30] The U.S. health system affords patients and their providers greater ability to make informed, collaborative, and individualized treatment decisions that

reflect their individual preferences and clinical needs. However, HTA methods that tether coverage and reimbursement to a single cost-effectiveness threshold risk undermining patients' access today and eroding incentives for future research and development in areas of unmet need. The authors' recommendation to use "average public preferences to define benefits for economic evaluation" runs contrary to U.S. patient and clinician goals related to autonomy in treatment selection and access to multiple treatment options, which support optimal treatment for individual patients. These concerns underscore yet another reason why HTA methods must be a tool, not a rule, to inform decision-making.

NPC recommends that, given economic models and HTA practices require both science and judgment and are often not validated, the authors must acknowledge both qualitative and quantitative uncertainty in the process and findings, and view them as one of many inputs to achieve value in health.

***

NPC serves patients and society with policy-relevant research on the value of patient access to innovative medicines and the importance of scientific advancement.[31] We envision a world where advances in medicine are accessible to patients, valued by society, and sustainably reimbursed by payers to ensure continued innovation. We have deep experience conducting research and disseminating information about the critical issues of evidence, innovation and the value of medicines for patients and society.[32] Our research helps inform important healthcare policy debates and promotes optimal patient outcomes through evidence-based approaches.

We appreciate this opportunity to provide input on the HEMA group's draft report. NPC's continued engagement with ICER and the HEMA group reflects our commitment to the critical dialogue necessary to ensure the development of high-quality health economic methods and value assessment tools that help patients, physicians, payers, and others make informed decisions about all aspects of healthcare.

Sincerely,

John Michael O'Brien
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Response to HEMA Draft Report Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies

Amanda Cole, Patricia Cubi-Molla, Martina Garau, Matthias Hofer, Chris Sampson, Chris Skedgel, Office of Health Economics.

Note: This response is supported by Lotte Steuten, Deputy Chief Executive at the Office of Health Economics. While Lotte contributed to the HEMA report during early drafting, she has requested to be removed as an author of the report. The views expressed in the response below align with her professional stance.

Introduction

We welcome the establishment of the HEMA group and its ambition to assess best practices and provide actionable guidance to HTA agencies. This has the potential to drive and support harmonisation of methods and identify areas where further methodological advance is required. However, we find that this first output falls short of supporting HTA agencies and the broader stakeholder community in meaningfully exploring the inclusion of broader benefits in HTA decision-making.

The report offers a framework based on three 'principles': relevance, valuation, and opportunity cost. It is crucial to ground a methodological exercise in coherent normative principles. However, on examination, the authors' characterisation of these principles conflates descriptive statements about current practice, methodological constraints, and genuine value judgments. We find that the report's claims about what benefits *should* be considered in HTA are grounded primarily in support for current practice. As a consequence, the report exhibits significant status quo bias, ultimately reinforcing existing limitations instead of identifying opportunities for innovation and practical implementation guidance.

We identify four core concerns that warrant a substantial revision of the report's approach if it is to positively influence HTA decision-making.

1. The Report Is Conservative and Narrowly Focused

The report's framing of relevance is overly constrained by current institutional mandates, which often do not explicitly include broader value elements. This framing risks circular reasoning: because HTA agencies do not currently consider certain benefits, they are deemed irrelevant. We argue that this approach is not only limiting but potentially counterproductive. Excluding broader value elements, such as value of time (often, but not exclusively, productivity), caregiver burdens, and effects on sectors like education and the environment, can lead to suboptimal or even the misallocation of resources (Cubi-Molla et al., 2021). In this respect, we highlight the report's equity-based criticism of the consideration of "productivity", which suggests that such consideration could unfairly prioritise higher-income individuals. Within this narrow framing, we agree with their criticism: considering "economic potential" in resource allocation *could* prioritise people based on income rather than need. Yet excluding "productivity" does not eliminate this risk — it simply obscures it by asking decision-makers to ignore a relevant consideration. Moreover, this critique

sidesteps the practical alternative of valuing people's *time* at a population-wide rate (e.g., a national average wage) rather than by their *income*.

A core issue with the HEMA report is its reliance on extra-welfarism, which in theory promises a broader evaluative space beyond individual utility, but in practice often narrows the focus to health alone. As Coast (2009) argues, for example, this shift has not enriched the evaluative framework but instead constrained it. We note that, in principle, extra-welfarism offers a flexible framework which can include sources of value beyond health (Culyer, 1990; Sampson, 2016).

Focusing solely on 'health' is also not pragmatic in countries such as the UK, where health is closely interwoven with social care, and there is a continuing shift of patient care from hospital to community settings — the latter being primarily aimed at promoting individual well-being (Care Act 2014). As Brouwer (2019) highlights, deliberately limiting the scope of value in HTA means decision-makers remain unaware of the broader consequences of their choices.

While the debate around extra-welfarism is well-established in the literature, the report appears to adopt the framework in a way that serves primarily to preserve existing HTA practices, particularly in the UK. This selective application risks reinforcing the status quo rather than enabling progress toward a more inclusive and responsive approach to value assessment.

In light of these critiques, we argue that relevance in HTA should not be constrained by a narrow conceptualisation of health maximisation. Instead, it should be guided by a broader conception of societal well-being informed by empirical evidence and alignment with public policy goals.

Moreover, several HTA bodies are already moving beyond narrow definitions of health benefit. For example, Canada's Drug Agency (CDA-AMC) is piloting the inclusion of a societal perspective in its evaluations, and agencies, such as the Dutch ZiN, have a longer tradition in including wider effects (Geuzinge et al., 2025). In the same spirit, OHE has engaged with HTA agencies in the Asia-Pacific area to explore current implementation of a social perspective in HTA and next steps to integrate it more consistently (Theakston et al., 2025). These developments reflect a growing recognition that HTA must evolve to remain aligned with societal preferences and policy priorities.

Finally, the report also misses an opportunity to engage with recent evidence and policy debate. For instance, a recent UK report by ONS and NHS England on NHS waiting lists and economic productivity (Batrakova et al., 2025) underscores the importance of integrating health and economic impacts into health decision-making. By failing to acknowledge these shifts, the report risks reinforcing a disconnect between HTA practice and broader government objectives.

2. The Report Draws an Unhelpful Distinction Between "Public" and "Individual" Preferences

The authors of the HEMA report note that HTA adopts a normative position that value should be assessed on the basis of (ex ante) *public* preferences, distinct from (ex post) *patient* preferences. We do not challenge this normative position, although we do argue for a greater role for the Patient Voice in HTA to improve HTA processes, among other reasons (Kumar et al., 2024).

We find that the authors conflate the normative position for public over patient preferences with the idea that value must be assessed on the basis of "average public preferences" that are somehow distinct from "individual preferences." We see this in Table 2, where they state, "current approaches … in general value benefits to reflect the *average preferences of the general population* in the relevant jurisdiction rather than *preferences of specific individuals*." They discuss this again, where they note, "…standard economic evaluation for HTA focuses on the *average preferences of the public* regarding health. This is not consistent with the preferences and risk attitudes that *individuals* hold over their own health as patients or consumers."

We are unclear how the authors view the "average preferences of the public" as fundamentally distinct from an aggregation of individual preferences. The authors appear to accept, for example, that national tariffs for EQ-5D health states represent 'average public preferences', without seeming to accept that these are an aggregation of *individual* preferences. Furthermore, Mulhern et al. (2013) found that almost 90% of all respondents to a series of health state valuation exercises imagined themselves living in the different health states they were valuing, suggesting the distinction between public and individual preferences is blurrier than the authors present. If nothing else, the word 'specific' in "preferences of *specific* individuals" is carrying a heavy load in the authors' conception of this distinction.

Similarly, we find the authors seek to imply that any "individual" preferences must necessarily represent "patient" preferences, by unnecessarily using terms such as "individual patients" and "individual preferences of the patients" when discussing concepts such as value of hope and preferences over severity. There is nothing in those concepts that requires preferences from individuals *in* a particular health state (patients) as opposed to individuals *imagining* themselves in that health state. They misrepresent these concepts as somehow requiring individual *patient* preferences and, therefore, inconsistent with the normative foundations of HTA. We find this inappropriate.

3. The Report Misrepresents the Role of Opportunity Cost in Resource Allocation

Resources are limited and using them one way precludes other uses: opportunity costs exist. This is a truism. However, the report slides from this descriptive observation to the normative claim that opportunity costs "need to be reflected" in decisions, and that the need to measure opportunity costs may preclude the consideration of certain outcomes. This position is supported by several misrepresentations of the role of opportunity cost in resource allocation in health care.

First, opportunity cost is not a dominant part of the quantitative inputs that support resource allocation decisions in HTA. Although many agencies use a threshold, evidence on

displacement of funding or service provision is seldom considered beyond the immediate substitution effects of a technology. Very few HTA agencies employ an explicit cost-effectiveness threshold, and outcomes associated with new technologies are universally considered incrementally by comparison to alternative treatment strategies. The primacy of opportunity costs in the HEMA report does not reflect current practice, and nor do the authors provide normative justification for this position.

Second, the infeasibility of measuring opportunity costs does not preclude the consideration of benefits. HTA does not involve simple unidimensional optimisation problems, and health systems operate with a diverse set of objectives. HTA agencies – and health care decision-makers more broadly – routinely consider a wide range of outcomes that may not be rationalised into a linear optimisation problem. To ignore outcomes that are of value to patients and the public, and within the scope and remit of the health care system, on the grounds of evidence limitations, would be a neglect of duty by HTA agencies.

Third, we do not recognise the availability of marginal productivity or health displacement estimates that the HEMA report implies. In some jurisdictions, research has estimated the marginal cost of producing QALYs. However, the validity of these estimates and their relevance to decision-making have been widely challenged (Sampson et al., 2022). None of these estimates forms the basis of a cost-effectiveness threshold used by an HTA agency. Despite the lack of evidence relating to the displacement of QALYs in health systems, we do not exclude (and the HEMA authors do not suggest that we exclude) QALYs from decision-making. Thus, the report applies this 'principle' inconsistently to different outcomes that may be considered in HTA. We note that Section 4.5 on 'Broadening the Perspective of Economic Evaluation' misses the opportunity to provide actionable guidance. The authors examine whether including outcomes beyond health (e.g. education, environment) meets the three principles of relevance, valuation, and opportunity cost, concluding that this broader scope is "debatable", "feasible", but "underdeveloped". While this is an appropriate reflection of the current evidence base, the section offers limited discussion on how such challenges could be addressed in practice.

In addition, excluding the societal discount rate as "out of scope" seems inconsistent with the section's intent. Discounting has clear implications for valuing long-term and cross-sectoral outcomes and could help connect health and other policy domains. A more integrated approach would explore resource allocation across sectors using coherent welfare metrics and consistent valuation frameworks, to reduce the risk of inefficient allocation when health outcomes are valued differently across government sectors (see, for example, Cubi-Molla et al., 2021). Such an approach is becoming increasingly relevant, for example, through the inclusion of environmental impacts in HTA, and health co-benefits in environmental-related policies (MacClancy et al., 2025)

4. The Report Is Short-Sighted and Ignores the Changing Nature of Health Care

Health care systems are dynamic and must continuously adapt to evolving disease patterns and shifting public attitudes toward health (Hays, 2023). The HEMA falls short in engaging with these urgent and emerging challenges, such as those highlighted in the NHS Long Term

Plan (e.g. the transition from hospital to community care, the adoption of digital technologies, and a stronger emphasis on prevention). In this context, the evaluation of interventions should be seen as an opportunity to recognise value beyond the traditional health care perspective, particularly in addressing challenges that require multi-sectoral responses. For instance, interventions targeting large-scale public health and societal issues such as obesity (Mott and Hussain, 2025) and Alzheimer's disease (Theakston et al., 2025) require more systemic approaches to generate broader, long-term benefits such as caregiver relief, productivity gains, and reduced social care costs.

Furthermore, the HEMA report does not mention the word "incentive" even once. While the central function of an HTA body is to assess the value of current health care investments, its methods and (indirect) impact on pricing also shape the incentives that drive R&D investment and future innovation (Lakdawalla, 2018; Shaikh, Del Giudice and Kourouklis, 2021; Acemoglu and Linn, 2004; Dubois et al., 2015). From a social perspective, the optimal balance is at the point where access to existing innovation is maximised in the present without compromising incentives for R&D investment in future innovation (Danzon, Towse and Mestre-Ferrandiz, 2015). OHE research highlights that a dynamically efficient price balances patient access *today* with the rewards that encourage R&D *tomorrow* (Bell et al., 2023). Overlooking this second dimension is a missed opportunity. If we aim to advance as a society, we must make clear what we value—and in doing so, invite the innovation that can realise it.

Conclusion

In this response, we have critically examined the HEMA draft report and identified four major concerns: its conservative and narrow framing of relevance, its unhelpful distinction between "public" and "individual" preference, its misrepresentation of opportunity cost in resource allocation, and its failure to engage with the evolving nature of innovation in health care. Collectively, these issues reflect a short-sighted approach that risks reinforcing the status quo rather than enabling meaningful progress in HTA methodology and practice.

OHE has produced a substantial body of research supporting the inclusion of broader value elements in HTA and developed practical frameworks to support their systematic integration in decision-making (e.g. El Banhawi et al., (2025); Theakston et al., (2025); El Banhawi et al., (2024); Brassel et al., (2023)). We believe HTA agencies should be encouraged to expand their remit where justified by evidence and methodological developments, rather than constrained by existing paradigms.

To move the debate forward, we need practical methods and implementation strategies. We therefore call for a collaborative process to build consensus on best practices and initiate pilots that test broader value frameworks in real-world HTA settings. This is essential to ensure that HTA evolves in step with societal needs, policy priorities, and the future of health care innovation.

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Title: The Value of Patient-Centered and Curative Therapies: A Personal Perspective from a Family Navigating ADA SCID

Submitted by: Paola Andrea Fernandez de Soto AbdulRahin - Parent and Advocate for ADA SCID. Board member for ImmUnity Canada, NRBDO and Parent partner for Rarekids-CAN.

Date: October 29th 2025

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1. Introduction

I am submitting this comment as a parent and advocate for children living with rare genetic conditions, particularly those with Primary Immunodeficiencies such as ADA Severe Combined Immunodeficiency (ADA SCID). My son, Jakob, was diagnosed ten days after birth. Without early intervention, children with this condition face life-threatening complications and a severely reduced lifespan of 2 years.

Our family's journey highlights the **limitations of traditional economic evaluation frameworks**, which often fail to capture the full spectrum of benefits that new therapies such as gene therapy can provide. This submission illustrates the value of considering **patient-centered, societal and equity-related benefits** in health technology assessment (HTA), supported by data from the **National Rare Blood Disorder Organization (NRBDO, 2025)**.

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2. Context and Unmet Need

Jakob's diagnosis coincided with the implementation of newborn screening for ADA SCID in Alberta around July 2019. He was immediately placed on a series of interventions, including:

- **Immunoglobulin (IVIG) therapy**: weekly infusions to provide antibodies he cannot produce.
- **Enzyme replacement therapy (ERT)**: thrice weekly injections serving as a bridge treatment, each one of them with a cost of around 12000.00 per shot. This process part of the special medication program from the government.
- **Bone Marrow match search**: Global search with the help of Canadian Blood Services and Swab the World.
- **Application to the Out of Country Committee**: Access denied 2 time to take this child to Italy where there was a treatment called Strimvellis (Gene Therapy) and the only curative option available at the time.

The financial, emotional and logistical burden on families is enormous. For gene therapy abroad, our family was asked to provide costs exceeding $1.5 million CAD, in addition to travel, accommodation, and ongoing care if we wanted to take him to Italy. Desperation to save the life of our child drove us to create marketing campaigns to raise funds and compromised my

personal health due to stress, facing then in January 2021 a cancer diagnosis, chemotherapy and radiation.

Almost 5 years later on July 19th 2024, Jakob was included in a clinical trial-Gene Therapy for ADA SCID developed by Dr. Donald Kohn in California at UCLA, making him the first Canadian child under the new vector to receive this treatment and showing full reconstitution of his immune system up to today.

Supporting Evidence: NRBDO (2025) reports that families of children with rare blood and immune disorders often face substantial financial burden, with 70% of families incurring out-of-pocket expenses exceeding $50,000 annually and many forced to fundraise or travel internationally for treatment.

Beyond direct medical costs, families experience significant indirect impacts: parental work disruption, missed educational opportunities for the child, social isolation and ongoing psychological trauma. Traditional cost-effectiveness analyses rarely capture these profound, real-world effects.

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3. Assessment of Proposed Additional Benefits

a) Reflecting Individual Patients' Attitudes to Risk
Families navigating rare, high-risk conditions confront life-or-death decisions under uncertainty. Choosing between bone marrow transplantation, enzyme therapy or traveling abroad for gene therapy involved balancing survival probability, treatment toxicity, and long-term outcomes. Accounting for patient and caregiver **risk tolerance** highlights a dimension of value that standard models often ignore.

b) Widening the Perspective to Include Societal and Productivity Impacts
Caregiving responsibilities are extensive; parents frequently reduce work hours or leave employment entirely, resulting in lost income and societal productivity. NRBDO (2025) indicates that over 65% of caregivers report significant work disruption due to medical caregiving responsibilities. Other societal impacts include:

- Reduced hospitalizations, government costs and clinic visits with curative therapy.
- Improved parental work participation and family functioning.
- Enhanced quality of life and psychosocial development for the child.

c) Capturing Equity Implications
Access to life-saving therapies is deeply inequitable; availability depends on geography, financial means and proximity to clinical trials. NRBDO (2025) highlights that families in rural or low-income settings face substantial barriers to accessing specialized treatments, underscoring the need for **explicit consideration of equity in HTA**.

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4. Recommendations

1. **Include patient-centered, societal benefits and cost-efficiency in HTA evaluations**
    - Quantitative and qualitative methods should measure outcomes such as quality of life, caregiver burden, and educational and social development.
2. **Recognize opportunity costs of delayed or inaccessible curative therapy**
    - Early gene therapy reduces long-term medical costs, prevents irreversible complications, and improves life expectancy.
3. **Incorporate equity considerations explicitly**
    - Evaluate the impact of treatment availability across regions, income levels, and rare disease populations to ensure fair access.
4. **Support inclusion of risk preference and decision uncertainty**
    - Families make high-stakes choices under uncertainty; reflecting this in evaluations provides a more comprehensive understanding of value.

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5. Conclusion

Jakob's journey demonstrates that **traditional economic evaluations alone cannot capture the full value of transformative therapies** for rare and life-threatening conditions. Integrating patient-centered, societal and equity-related benefits in HTA aligns with HEMA's principles of relevance, methodological feasibility and opportunity cost assessment.

NRBDO data reinforce the urgent need to incorporate these broader dimensions of value, ensuring families like ours are supported and patients have equitable access to life-saving interventions.

References / Supporting Data (Appendices)

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3. NRBDO. (2025). *Impact of Rare Disease on Families and Caregivers in Canada*. National Rare Blood Disorder Organization.
4. Canadian Blood Services & Swab the World. Global donor registry data for bone marrow matching.
5. Internal family data on treatment costs and hospital visits (2019–2025).

October 29, 2025

Dear Members of the HEMA Group,

On behalf of Patient Focused Medicines Development (PFMD), we acknowledge the effort behind the development of this draft report, which examines potential extensions to benefit definitions within economic evaluation. We thank the HEMA group for providing the opportunity for public input on the draft report through this public consultation.

At a moment when health systems face mounting pressures related to sustainability and resilience, we recognize the importance and responsibility of your collective effort to reflect on evolving concepts of value. PFMD supports the forward-looking initiative taken on by this group. It is particularly encouraging to see three major HTA bodies—NICE, CDA-AMC, and ICER—openly reflecting and collaborating on areas where traditional approaches may not fully account for real-world benefits and where new evidence is still needed. PFMD believes there is significant opportunity to enhance the integration of these evolving value concepts into decision-making processes and welcomes the opportunity to contribute to this important discussion.

PFMD Comments and Recommendations

1. Reconciling Public Preferences with Patient-Centred Progress

The draft report emphasizes that economic evaluations typically reflect the preferences of the general public rather than those of individual patient communities. It states that most HTA bodies "see benefit in terms of the health of the populations for which their systems are responsible," distinguishing this from "individual patient preferences and choices."

While PFMD recognizes this normative position, it is important to note that all three HEMA organizations have made meaningful progress in patient inclusion across deliberative processes in recent years. Examples include:

- CDA-AMC's introduction of **lived experience presentations** in deliberative meetings where patients share their perspective on living with their condition, the drug under review, and the outcomes that matter most to them.[1]

- ICER's **Patient Council** to advise on patient engagement strategy, outreach, and process for input into drug reviews and broader initiatives.[2]

[1] https://www.cda-amc.ca/news/formulary-management-expert-committee-transitions-pilot-permanent-expert-committee

[2] https://icer.org/news-insights/press-releases/icer-launches-a-patient-council-to-amplify-the-patienprovidingt-voice-in-value-assessment/offering

- NICE's **longstanding leadership in involving the patient community** in guidance development, including providing feedback on guidances, contributing to methods, offering lay perspectives, and supporting equality initiatives.[3]

The draft report's prioritization of public-preference frameworks in economic evaluation may be incongruent with these organizational advances toward patient-centricity. We respectfully suggest that the final report reconsider the emphasis on public preference and better align with systemic efforts to integrate patient perspectives into decision-making, ensuring that patient-centred approaches are not sidelined in favour of generalized preferences.

Furthermore, while the draft report emphasizes public-preference inputs in economic evaluation, it does not reflect increasing evidence in the literature of the impact of patient engagement on economic evaluation methodologies and models. We kindly direct the authors to the following examples for consideration:

- An individual-based Markov model was constructed using guidance from a stakeholder advisory board (SAB), a patient Delphi panel, and published literature to evaluate direct-acting antivirals (DAAs) compared to no treatment for hepatitis C virus.[4]
- Analysis of approaches to develop methods for including family carer outcomes in economic evaluation.[5]
- Protocol for using the nominal group technique to elicit stakeholder input in the development of an early economic evaluation model of CAR T-cell therapy for adults with relapsed or refractory B-cell acute lymphoblastic leukemia. [6]
- Expanding cost and benefit considerations through patient input in early economic evaluation of CAR T-cell therapy for adults with relapsed or refractory B-cell acute lymphoblastic leukemia.[7]

We strongly recommend the authors include remarks and preliminary guidance on mechanisms for engaging patients in economic evaluation as part of the final report. Explicitly acknowledging the complementarity between public preference and patient input in economic evaluation would

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[3] https://www.nice.org.uk/get-involved/people-and-communities/patient-and-public-involvement-policy

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[5] Al-Janabi, H., Coles, J., Copping, J., Dhanji, N., McLoughlin, C., Murphy, J., & Nicholls, J. (2021) include. Patient and Public Involvement (PPI) in Health Economics Methodology Research: Reflections and Recommendations. *The patient*, *14*(4), 421–427. https://doi.org/10.1007/s40271-020-00445-4

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[7] Wilson, M., Thavorn, K., Hawrysh, T., Graham, I. D., Atkins, H., Kekre, N., Coyle, D., Lalu, M. M., Fergusson, D. A., Chan, K. K. W., Ollendorf, D. A., & Presseau, J. (2022). Engaging Patients and Caregivers in an Early Health Economic Evaluation: Discerning Treatment Value Based on Lived Experience. *PharmacoEconomics*, *40*(11), 1119–1130. https://doi.org/10.1007/s40273-022-01180-4

significantly strengthen the report and reinforce the trajectory toward mature, patient-informed, evidence-based decision-making.

2. Importance of Transparency Between Economic Evaluation and Deliberation

The draft report acknowledges that its focus is on concepts related to economic evaluations and reflects that many novel value considerations are addressed outside the economic model through the deliberation process. However, the report does not yet provide guidance on:

- How divergent conclusions between economic evaluation and deliberative insights should be reconciled;
- How deliberative inputs—including patient experience—inform final recommendations.

Across our community, patients and therapy developers have expressed uncertainty about the weight assigned to deliberative evidence relative to economic findings. There is concern that patient-informed value elements—if addressed only during deliberation—may lack visibility and influence compared to quantified model inputs.

We therefore recommend the final report:

- Recognize the need for transparency in how deliberative inputs shape final decisions;
- Identify reconciliation of economic and deliberative outcomes as a priority for future methodological exploration.

This would strengthen trust in HTA processes and support patient and public understanding of how balanced recommendations are formed.

3. Guidance on Integrating Patient Experience Data (PED) into Economic Evaluation

While the draft focuses primarily on traditional benefit measures such as QALYs, PFMD believes the report would benefit from recognizing how PED, when scientifically robust and designed and contextualized with patients, can inform components of economic evaluation (i.e., HRQoL, adherence assumptions, utility weights, and caregiver burden).

Including brief guidance or pointing to future work on how PED can support mainstream evidence requirements and how it may contribute to quantifying benefit within traditional economic model inputs would provide practical value to evidence generators and HTA applicants.

4. Collaboration Opportunity to Develop a Resource on PED in HTA

To support greater clarity on how PED can inform HTA, PFMD is currently co-developing a tool to map how PED can meaningfully contribute to evidence-based healthcare decision-making. The tool, called the HTA PED Navigator, was first introduced at a workshop at HTAi 2025. To date, we have received input from more than 40 stakeholders, including HTA representatives, patient organizations, industry professionals, and researchers, from various regions. It builds on our existing framework (the Global PED Navigator), methodically developed through multistakeholder collaborations from around the world.[8]

We would be pleased to collaborate with HEMA-affiliated organizations to refine this tool and explore how it might support future guidance development. In particular, exploring how to align PED with key components of HTA, such as QALYs and PICOs, where feasible. If there is interest in this opportunity, please reach out to my colleague Hayley Chapman, Executive Director - Operations (hayley@thesynergist.org), who would be pleased to provide more details.

We are grateful for the opportunity to provide input and reaffirm our commitment to constructive collaboration. Ensuring that the benefits of new health technologies are understood not only in terms of population health outcomes but also through the lived experiences of patients and caregivers is essential for fair, sustainable, and trusted decision-making.

We look forward to continued dialogue.

Sincerely,

Derick Mitchell,

Executive Director, PFMD

[8] Willgoss, T., Escontrias, O.A., Scrafton, C. *et al.* Co-creation of the Global Patient Experience Data Navigator: a multi-stakeholder initiative to ensure the patient voice is represented in health decision-making. *Res Involv Engagem* 9, 92 (2023). https://doi.org/10.1186/s40900-023-00503-9

Oct 30th, 2025

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Dear HEMA writing group,

I enjoyed reading this draft and agreed upon most of the main recommendations. I have some comments about Table 4. In the US, the administrative burden coming from step therapy (per the insurance requirement) has increased (Ref). Hospitals have been hiring the utilization specialists and team members focusing on pre-authorization, for which the cost will eventually transfer to the patients in some form. This perspective may be worth mentioning in Table 4.

(Ref) Sachs RE, Kyle MA. Step Therapy's Balancing Act – Protecting Patients while Addressing High Drug Prices. N Engl J Med. 2022 Mar 10;386(10):901-904. doi: 10.1056/NEJMp2117582. Epub 2022 Mar 5. PMID: 35245014; PMCID: PMC9067323.

Sincerely,

Perry Kuo

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Commentary Submission on the Draft Report: Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies

I am pleased to submit this commentary in response to the Health Economics Methods Advisory (HEMA) group's draft report, *Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies* I commend the HEMA group, for undertaking this critical and necessary work to bring intellectual discipline and methodological rigor to the expanding discussion of value in Health Technology Assessment (HTA).

The report's unwavering commitment to the Opportunity Cost Principle, that additional benefits cannot be routinely incorporated into quantitative economic evaluation without an evidential basis to reflect them symmetrically in costs forgone elsewhere, provides a crucial foundation for fiscally responsible resource allocation.

However, based on this review, which integrates the findings of the Generalized Cost-Effectiveness Analysis (GCEA) framework and research on health equity and adaptive systems, I propose that the report's rigid application of quantitative principles creates structural tension points that threaten the simultaneous pursuit of equity, transformative innovation, and global relevance.

Sincerelly,
Dr. Ramiro Gilardino

Type of comment: Individual
Region: Commentaries are on a global scope, beyond the remit of this report. i

The HEMA group report (report), *Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies*, is a methodologically rigorous document that seeks to impose necessary discipline on the expanding discussion of "broader value" by focusing intently on the standards of quantitative economic evaluation. Its primary objective is to ensure that any new value element can be coherently measured and validated within the calculation of opportunity cost. While this emphasis on intellectual coherence and budget accountability is essential, its rigid quantitative focus creates specific barriers to integrating complex societal goals, leading to the following points of constructive criticism:

1. The report explicitly separates its focus on quantitative economic evaluation from the wider HTA process, which includes a qualitative deliberative step to consider contextual and social factors.

- By demanding that benefits be valued consistently using the average preferences of the general public, the report effectively relegates essential, but difficult-to-quantify, elements, such as deep patient-centered experiences, process value, and specific aspects of equity, to the non-quantitative deliberative phase.
- The report then restricts the power of this deliberation by recommending that it "should not be used in a way that bypasses the consideration of opportunity costs". This mandate means that the quantitative conclusion on cost, based on average public preference, can unilaterally override the ethical, contextual, or social value derived from in-depth patient and citizen perspectives gathered during deliberation.

I would argue for the formal integration of tools like Multi-Criteria Decision Analysis (MCDA). MCDA is a structured, deliberative mechanism designed to transparently weigh the quantified economic outputs (like those from GCEA) against the crucial social criteria (such as unmet medical need, severity, or the reduction in uncertainty) that are derived from patient and stakeholder input, but which resist standardization by quantitative economic models alone.[1,2]

2. The core constraint of the report is its opportunity cost principle, which is defined as an *evidential requirement*: no additional benefits can be routinely incorporated until there is data to reflect them symmetrically in the benefits forgone elsewhere in the health system.

- This static, present-focused quantitative requirement creates a structural conflict, for example for curative, one-time therapies (such as Gene Therapies). These interventions incur high, front-loaded costs but produce dynamic, long-term, non-

health benefits (e.g., decades of productivity gains and the elimination of future care and caregiver costs).

- The approach (as stated in the report) struggles to capture value elements that accrue over decades, such as those formalized in the GCEA Dynamics Category, specifically Option Value (the benefit of keeping a patient alive until a future cure is available) and Scientific Spillovers (the knowledge generated for future R&D).[3] (Cite). Employing valuation strictly to the immediate cost of displaced care, the report implicitly undervalues transformative innovation, risking suboptimal allocation signals to innovators. [4]

It forces HTA bodies into a complex policy choice: either fundamentally re-evaluate the system's opportunity cost threshold (a highly contentious task) or mathematically decrease the Incremental Cost-Effectiveness Ratio of the product via modifiers (like severity weights).[5,6] The report should highlight that GCEA offers a more holistic quantitative approach to measure these dynamic benefits that HEMA's principles currently restrict.[3.]

3. While the report acknowledges the need to address equity (e.g., severity weighting and Distributional Cost-Effectiveness Analysis, or DCEA), its quantitative stringency conflicts with the current reality of data limitations.

- DCEA, requires robust, standardized data, including sociodemographic variables, geographic information, and empirically derived preferences for inequality aversion. (cite) The report stress that by mandating that DCEA, if used, "needs to be used in all assessments". HEMA sets a rigorous quantitative standard that is currently infeasible for many systems due to these foundational data deficits.
- HEMA notes that existing empirical research on individual risk attitudes suggests priority for health gains is sometimes given to conditions in the center of the health range, not necessarily the most severe health states. Focusing on eliciting individual risk attitudes for quantitative inclusion, the report risks conflicting with the clear societal preference expressed through deliberation and policy (e.g., NICE's severity modifier) to prioritize patients based on low baseline health or high unmet need, a key equity goal. [7,8]

4. The report is focused primarily on three jurisdictions, NICE (England), CDA-AMC (Canada), and ICER (USA), one of which (ICER) does not have a formal government

mandate to set reimbursement policy. While it is strongly disclosed that the scope of this report is for these three institutions, it should consider that:

- Because established HTA bodies are frequently models for emerging HTA systems[9], HEMA's highly restrictive principles, especially the demand for detailed, symmetric opportunity cost evidence, create an unattainable standard for regions constrained by limited financial resources, human expertise, and data infrastructure.[10]
- Emerging HTAs require flexible, adaptive tools (such as the Managed Entry Agreements), to fund promising technologies under uncertainty while gathering real-world evidence.[11] HEMA's insistence on quantitative evidence upfront for *routine incorporation* risks slowing the adoption of adaptive pathways and hindering the development of agile, "Living HTA" systems that rely on continuous data updating rather than static, initial assessments [12]

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Critique of McQueen et al. 'Defining appropriate benefits for Economic Evaluation of Health Technologies'

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5th December 2025

Summary

Overall the report provides a very valuable contribution adding three essential criteria which must be satisfied before adding new dimensions of value to the benefits accrued to health care interventions. We particularly welcome the clarity around 'symmetry': any additional dimension on one side of the equation must also be added to the estimate of the opportunity cost to prevent 'QALY stuffing'.

This report is a timely response and critique to a number of the concepts discussed in the 'ISPOR value flower' paper. In these reviewers' opinion that paper does not provide a sound basis on which to adopt policy changes, and, if the consequences are improperly thought through, could be a basis simply for justifying excessive drug prices at the expense of those bearing the opportunity cost, rather than assisting in the economic problem of allocation of scarce resources. The report provides this much-needed thinking. Perhaps an additional criterion reimbursement agencies should consider is whether the benefit of explicitly including additional elements exceeds the cost in terms of increasingly complex modelling and associated scope for gaming and manipulation it affords.

Our critique begins with some general thoughts about the issues the report covers, followed by point by point.

General comments on concepts

- Broadening cost and benefits perspective

Conceptually this is appealing: any good or service (or element thereof) for which an agent has a positive willingness to pay (or rather, willingness to give up something else for) has value. A societal perspective attempts to encompass this, and is indeed adopted in some reimbursement agencies, most notably the Netherlands. However, the broader the perspective, the less concrete the data and the greater the scope for gaming. There are also potential ethical concerns; as discussed in the report, including lost earnings and tax revenue lead to some problematic implications. If included does that mean we value the lives of higher earners greater than that of low earners (and the economically inactive at zero)? The alternative would be to value all time foregone at a shadow price, but should this be based on (mean or median) wages or some measure of human capital? The values implied vary wildly, allowing scope for gaming.

- Symmetry

These reviewers wholeheartedly agree with the importance of symmetry as expressed in the report. It may be worth including an example illustrating it. For example, in the UK, the NICE

manual states the threshold is intended to represent the health opportunity cost, that is the current mean cost of generating a QALY in the NHS, which it estimates at somewhere between £20,000 to £30,000. At the time this was not empirically based. Subsequent research placed the cost somewhat below this (eg £5,000 to £10,000 [Martin et al. 2021], with the most recent estimate pertaining to 2016/17 data estimating £6000 per QALY, [Martin et al. 2023]). Our understanding of the data behind these figures is that they represent the health opportunity cost for a single patient.

For mathematical simplicity, suppose that it costs £20,000 to generate a QALY for a patient in the NHS. Pennington et al. (2025) estimated that for every 0.1 improvement in health utility gained by a patient, a carer's QoL improves by 0.012. If this was typical across all diseases, then this means that for every QALY accrued to a patient, there is (at least) 0.12 QALYs accrued to others. Including these extra beneficiaries means the cost of the NHS to generate a QALY is therefore £20,000/1.12 = £17,860. So, the threshold must be modified downwards if carers and other beneficiaries are taken into consideration. Other work looking at the impact of social care spending found that for every £1000 spent increased carer utility by 0.3 (Longo et al. 2025). These reviewers understand work is underway estimating this for NHS spend. It may be worth noting that NICE committees already have scope for inclusion of broader benefits (eg carers) qualitatively: the threshold can be increased to account for where a treatment has a particularly beneficial effect on carers, but this informal approach opens opportunities for gaming.

- Reflecting patients' attitudes to risk

Again care must be taken to include this element on both sides of the equation. Investing in a new pharmaceutical is a risky investment whose risk is borne by patients bearing the opportunity cost of the decision.

- Value of innovation

It is unclear whether the role of a health system is to promote innovation, as well as health of the population. Most governments have business departments dedicated to this, separate from the health system. If a health system wishes to promote innovation for its own sake, then it must be clear about the trade offs – how many QALYs/patient lives is the system willing to forego to promote innovation? Is innovation valuable for its own sake or for its ability to deliver future health gains? If the latter, then the net present value of QALYs gained needs to be considered (that is, the negative impact on human health in the present vs the future gain). This is in danger of leading down a rabbit hole so innovation may be better considered through an equity lens – eg allowing a premium for the first treatment for a disease (not necessarily first in class when there are other treatments already available). Care must be taken to identify gaming by industry though, eg. salami slicing disease definitions to claim novelty.

- Benefits unrelated to change in health outcomes

The petals of the value flower this relates to are value of hope and option value. These are excluded from consideration in this report (although value of hope is partially addressed in the section on individual risk attitudes), but we consider it important to address these in future work. The value of hope is a very difficult concept to tie down. As a general rule, elements of value (and thus preferences relating to them) should be complete, transitive, continuous and independent (axia of expected utility, Von Neumann & Morgenstern 1953). Hope is presumably derived from the effectiveness of a treatment, and thus is not independent. However, if hope is

considered an independent element then other sources of hope such as prayer and kind words from well wishers (or perhaps more scientifically, a placebo) become relevant comparators in the decision space. This would not be an advisable route and is the tactic by which 'cure-all' patent medicines were sold in the 19th Century. It is important that the modern pharmaceutical industry is not seen in such light.

Point-by-point comments

ES1L1: may be worth explicitly stating that this means giving less weight to others (weightings used by NICE have increased the willingness to pay threshold for some groups, but with no consequent reduction in the threshold for others, which ignores the fundamental economic problem (finite resources) and is the key (sole?) reason for the existence of reimbursement agencies, i.e. principle 3 on pES1).

ES1, principle 3: As per comment above, it may be worth explicitly stating within the text that if there was no opportunity cost to decisions there would be no need for reimbursement agencies.

ES2, Para 3 ("we expand on our principles…"): the authors are right to acknowledge the conflict between maximising population health and reliance on patient preferences (even though at first glance it is 'obvious' that patient preferences are key). In any normative framework, preferences are fundamental. The issue is *whose* preferences – our concern is that a lot of the discussion of patient preferences focuses on the preferences of patients with the disease in question. This is only half of the story- the preferences of those bearing the opportunity cost of the decision also need incorporating. This is the main argument in favour of basing decisions on public rather than patient preferences (e.g. the MVH algorithm used by NICE to value the EQ5D is based on a general population survey). Another argument is the adaptation of patients to their health state – an example a colleague used was that a paraplegic may subjectively value their own health state very highly, yet as a society are we indifferent to whether or not people have limbs?.

ES2, last para ("proposals regarding new…"): This is crucial (and we realise eloquently crystallises the points made above!).

ES3, para 2, reference to fair innings: The choice to use life years in favour of lives saved implies acceptance of the fair innings arguments (and places greater value on the lives of the young over the old).

ES3, para 2: may be worth covering the most common application of DCEA to date in here i.e. weighting according to socioeconomic status.

ES4, bullet 1: may be worth noting in the report that insurance companies can 'simply' pass on the opportunity cost through higher premiums. This doesn't eliminate opportunity cost, it just shifts it from the insurer to insured who then have to decide what to give up to pay for the increased premium (or to give up the insurance).

ES4, bullet 2: we agree with this.

ES4, bullet 6 (value of information): perhaps label this as 'value of knowing' as risks being confused with value of information analysis (an approach to measuring the return on investment from research). The value of knowing also needs to be valued in terms of the

opportunity cost: what is the rate of exchange between knowledge of disease progress vs QALYs foregone to other patients?

ES4, bullet 6 (value of knowing): one of the most common themes raised for this idea is that knowledge could influence decisions for others outside of the patient i.e. knowledge of a genetic mutation could lead to testing and treatment in the wider family and/or decisions related to family planning. We don't see anything in here which covers benefits from knowledge leading to actual health gains to others which would appear to be the most reasonable part of this to consider in existing frameworks.

ES4, last bullet (broadening perspective): key element here is that these dimensions must be included in a modified threshold, to avoid 'QALY stuffing' or the equivalent on the cost side to achieve an ICER below the threshold.

P2, para 1, definition of benefit: important clarification separating out cost savings from the definition well made.

P2, Box1, paragraph 2, "movement away from economic evaluation into broader decision process": Economic evaluation at its core is a question of "what do we get, and what do we have to give up to get it": if (our valuation of) what we get exceeds (our valuation of) what we give up, then we say yes, otherwise no. As such there can be nothing more to the decision (note the "our valuation of" represents utility in the classical economics sense and so would include whatever equity weightings were attached to the outcomes).

Perhaps it would be better to reframe the idea of 'moving away from economic evaluation' in terms of 'the scope of costs and outcomes in the analysis not being comprehensive', some of which are likely unquantifiable, therefore necessitating discussion. The danger from framing this as 'moving away from economic evaluation' is that consideration of opportunity cost gets lost. It may be worth noting that no analysis can ever be 'complete', hence only advises a decision, rather than making it. An economic analysis such as cost utility analysis is a model of the decision process and therefore a simplification of reality.

P2, Box1, final paragraph. It's not clear where prioritisation fits in here. The ISPOR working group report referenced is talking about prioritisation of topics for assessment. The discussion around contextual factors and value conflicts e.g. in Box 5 and 6 of the manuscript may be more relevant.

P3, final paragraph, focus on length and quality of life: An important aspect is that the broader the definition of benefits (and costs), the fluffier and less easy to measure and value they are. This opens up opportunities for gaming. The methods for measuring and valuing length and quality of life are fairly well established, albeit far from perfect.

Table 1. It would be helpful to be clearer on how ICER reports influence decision making by insurance bodies.

P4, Box 2. We're not certain where the best place to mention this is (possibly here) but there does appear to be increased interest in moving beyond valuation of only health benefits. The development of the EQ-HWB is a critical development in that field. It's worth nodding to somewhere in this report.

P7, para 1: limited funds also apply to private insurance based systems. As per our comment above though, the adoption decision can be more easily shifted to individuals by increasing

premiums and allowing them to decide whether or not to purchase insurance. Of course, this is not without implications for the health of individuals and society.

P7, the discussion here focuses on constraints in England and covers Canada to some extent but is not clear on how the US sits within this.

P10, "Need to reflect any additional benefit" and "Any additional benefit should be reflected not just…": Suggest edit to 'dimension of benefit' (assuming we've understood the point here).

P11, para 1: The key point here which I think needs stating is that using individual utilities only leads to a utility- (or welfare-) maximising resource allocation where that individual also bears the opportunity cost. If someone else bears it, then the decision for the individual will always be a 'yes' at the expense of others which will lead to market failure (i.e. a non-Pareto optimal allocation of resources). Any system that pools risk (i.e. any insurance programme or state funding) separates the beneficiary from those bearing the opportunity cost. Hence the need for some overall decision maker representing some aggregate of societal preferences to ensure a 'fair' allocation of resources.

P11-13, sect 3.2 in general: clearly articulated argument in favour of use of public preferences over patients!

P12, sect 3.3: The argument for symmetry is utterly fundamental and well made to prevent QALY stuffing (eg by inclusion of QALYs of carers, family etc) as we state above.

P12, penultimate line, empirical estimates of the threshold: These estimates represent the 'average' cost per QALY gained at the margin. For an intervention to be net health-increasing it only needs to be more efficient than what it replaces. In the absence of an explicit disinvestment policy, this mean is probably appropriate. One way to put the cat amongst the pigeons though would be for the manufacturer of the new product to suggest what less efficient service should be cut back to pay the incremental cost…

P13, paragraph 2 & 3: May be worth stating here that NICE explicitly states that the threshold is meant to represent the health opportunity cost in its manual. As stated above, further issue with productivity cost estimates is the implication that it values the lives of those with higher salaries greater than those with lower or those out of the job market, which likely conflicts with social preferences. Of course this can be solved by applying a constant shadow price equivalent to some representative annual salary.

P13, paragraph 3: In reality the English system is more complicated than this as the VPAG caps drug spend on top of the application of NICE's threshold (rebates were substantial this year) which means that the real ICER's once these discounts are considered are quite a bit lower than the NICE thresholds would imply. If we're bringing in the literature on what the productivity in the NHS implies the threshold should be it would be remiss not to discuss this as well.

P13: It would be good to cover Canada more explicitly in here.

P14: may be worth explicitly stating that the implication of the demand side threshold is that (in the UK case) taxes would have to rise after every NICE decision to adopt a new treatment, which would be a rather chaotic approach to macroeconomic policy.

P16: risk attitudes. As stated at the top of this review, our main concern with all these elements is that they are not independent of effectiveness of the treatment in question, so risk double

counting. Combined with the need for symmetry as well articulated in section 2, this simply complicates the quantitative analysis without leading to much benefit.

P17: Process utility. The process of care surely can have a direct impact on HRQoL through impact on mental health (anxiety / depression etc....) This would be able to be included in standard methods of valuation and may be important in some disease areas (avoiding very traumatic procedures with high rates of post treatment PTSD for example). The way this is worded (and in earlier discussion) doesn't make fully clear that there can be direct health impact from process related to treatment.

P17: Family and Caregiver Spillovers. It would be good to address bereavement in here as well as this is frequently argued for by manufacturers.

P19: out of scope elements: I know this is not covered in the report but dynamic pricing is extremely problematic. Patent protection allows a monopolist to charge a monopoly price, i.e. taking all (or most) of the consumer surplus as revenue. In this case consumer surplus is measured in foregone health, so there is zero net health benefit during the patent protected period. Only on patent expiry – and an associated price drop – is there a positive impact on net health. Incorporating dynamic pricing ensures the monopolist is able to claim all the consumer surplus even beyond patent expiry, thus ensuring zero net health benefit from their product for all time. Option value is also highly problematic, in particular attempts to include this have focused on the value of the option to benefit from a future, as yet undeveloped treatment, but not the obligation for the payer to pay for it. I would highly recommend a follow-up report considering these issues.

Sect 4.2 - risk attitudes: The key issue with incorporating risk is again symmetry – risk aversion would need including in the measurement of opportunity cost and it is unclear how this could be measured meaningfully. It may be worth referring to the Arrow-Lind hypothesis arguing that public sector decision making should be risk-neutral.

Diminishing marginal utility to QALYs could only really be considered at a societal rather than individual level. Armed with some average measure of diminishing marginal returns to a QALY would then give a value for the optimal mix of, say, hip replacements to cancer drugs, rather than a corner solution suggesting we should exhaust demand for hip replacements before moving on to cancer drugs.

P32, paragraph 2: As I stated above, the decision to quantity life-years gained rather than lives saved already incorporates a bias towards the young which may (imperfectly) accommodate the fair innings argument. Including further weightings could risk double counting.

Page 32: Are there no equity weight considerations applied at all in US / Canadian HTA?

P33, opportunity costs: Some of my comments above about symmetry are covered in the text here so may be ignored. A comment re the impact of NHS expenditure: a founding principle of the NHS was that care should be delivered according to need rather than ability to pay, which implies the rich should be treated the same as the poor. Weighting the health gains of the most socioeconomically deprived higher than those of the least likely conflicts with this, but nevertheless is probably in keeping with societal preferences.

P35, valuation: Didn't South Korea reasonably recently stop requiring a societal perspective due to evidential challenges?

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October 30, 2025

To: Health Economics Methods Advisory Group

Re: Hoffmann-La Roche Ltd. Response to Draft Report: Assessing Treatment Benefits in Health Technology Assessment Decision-Making

Thank you for the opportunity to respond to the Health Economics Methods Advisory (HEMA) draft report, *Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies,* which explores the incorporation of additional value elements into the measure of benefits in economic evaluations for health technology assessment (HTA).

Roche appreciates the collaboration between the three leading HTA institutions and the engagement with patients, academics, and industry. This shared commitment is vital for enabling patient access to innovative therapies.

At Roche, we strongly support broadening the definition of 'value' beyond the traditional elements of direct costs and health outcomes (i.e. quality-adjusted life years) to more accurately capture the impact of treatments on patients and their families, the healthcare system, and society as a whole. We are actively collaborating with HTA agencies and scientific societies and conducting research to advance this, focusing on critical topics such as broader societal perspectives, addressing health inequities, care closer to home, and quantifying caregiving impacts.

Recognizing that this report represents HEMA's proposed framework in examining new methods and processes, we offer several considerations to ensure HEMA's efforts can produce evidence-based, relevant recommendations that reflect how HTA is conducted and used in real world practice.

1. A Pragmatic Approach to Novel Value Elements and Implementation

We believe the primary focus of this report, and future work in this area, should be on providing pragmatic, actionable guidance for how HTA bodies can more effectively consider novel value elements. HTA methodology is inherently complex, and economic evaluation is just one component within a broader, deliberative process (including both quantitative and qualitative inputs). For agencies using economic modeling, the most meaningful insights come not from deterministic results, but from scenario and sensitivity analyses that explore uncertainty. These approaches provide a natural mechanism to test and evolve methods in a structured, transparent way.

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Our concern is that the report's conclusions and recommendations risk being interpreted as overly prescriptive, which could inadvertently stifle the very innovation it seeks to guide. In practice, most health economics advances—from probabilistic modeling to patient preference integration—have evolved through incremental testing following an identified need for new methods. A rigid, restrictive framework discourages this progress, reinforces a status quo with known shortcomings, and ultimately fails to promote methodological advances that support the evolving needs of HTA decision-making.

Therefore, we recommend the report identify concrete entry points within the HTA workflow to incorporate novel value elements that stakeholders deem relevant. This guidance should outline practical conditions for their inclusion, suggestions for alternative approaches to address limitations in the evidence, and allow for testing and learning, especially in cases of high unmet need or significant equity implications.

Furthermore, by explicitly identifying future research priorities, HEMA can create a clear path for evaluating and incorporating novel value elements novel value elements that stakeholders deem relevant for their respective markets. HTA needs to reflect the full range of benefits that matter to patients, the healthcare system and society, and HEMA is uniquely positioned to lead this methodological evolution through structured, pragmatic guidance.

2. The Universality of Principles and Adaptability of Different Healthcare Systems

The application of economic evaluations varies significantly across the globe, a reality recognized in HEMA's stated goal to 'intentionally include individuals with a diversity of research experience, viewpoints and geographic locations.' The report's principles, however, appear focused on a single, normative view of opportunity cost, particularly in its emphasis on Principle 3. This approach is at odds with the reality of global HTA: the three sponsoring agencies themselves have different mandates and approaches to opportunity cost, and HTA bodies worldwide operate within unique health systems. This focus does not reflect the fact that many systems do not use fixed thresholds, relying instead on methods like post-HTA pricing negotiations or contextual deliberation. By anchoring to this single theory, the report imposes a high evidential standard that stifles the inclusion of novel value elements and limits the consideration of benefits beyond direct health gains.

Therefore, we recommend HEMA's work reflect this diversity. Instead of a single standard, HEMA should focus on generating methodological and research guidance that encourages adaptable methods. This guidance should support countries in adapting principles to their own contexts—testing, validating, and refining new approaches over time. HEMA should also promote capacity-building to strengthen the use of local data and address evidence gaps. Ultimately, the principles themselves should be reframed to allow for this flexibility, ensuring HEMA's outputs are both globally relevant and locally implementable.

3. Patient-Inclusivity in HTA

There is an important and growing movement in HTA toward becoming more patient-inclusive, with HTA bodies globally giving more weight to patient experiences, preferences, and caregiver impacts. As patients become more involved in HTA deliberations, integrating their values is critical. HEMA aims to consider what is truly valuable to patients by including patient representatives on the steering committee. The HEMA report, however, offers little practical guidance on how to better integrate these patient perspectives. Its strong methodological recommendations—anchored in normative economic positions—appear at odds with this practical trend. This risks a disconnect from current HTA practice and could be misinterpreted as dismissing individual preferences, which runs counter to the significant efforts made to incorporate patients into the HTA process.

To bridge this gap, we suggest that HEMA should place a stronger, more explicit emphasis on patient and caregiver engagement in shaping its methodological guidance. This includes directly involving patient representatives in refining the value framework to ensure it reflects real, lived experiences. It also means ensuring the report's recommendations do not imply that individual patient preferences or broader value elements are secondary or irrelevant to the benefit function. Furthermore, HEMA should promote the co-development of methodological pilots with patient groups. This would allow patient-relevant value elements to be tested, documented, and appropriately incorporated into HTA, ensuring the framework maintains methodological rigor while fully resonating with what matters to patients and caregivers.

In summary, we believe that this report provides a foundation for evolving economic evaluations in HTA, identifying key principles that will shape future work on novel value elements. To build on this foundation and accelerate its impact, we see clear opportunities to refine the recommendations, ensuring they are practical, adaptable, and patient-inclusive.

Sincerely,

HOFFMANN-LA ROCHE LIMITED

Submission to Health Economics Methods Advisory Committee

Draft Report October 2025: Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies

This submission is being presented on behalf of Save Your Skin Foundation, a national patient organization dedicated to the fight against non-melanoma skin cancers, melanoma, and ocular melanoma.

Comfort with Risk

We agree with the report that some individual patients are more willing to take more of a risk than other patients. Many factors will impact this decision, not the least of which are the severity of the disease, its impact on quality of life, stage of disease, and social and economic determinants of health.

Targeted therapies and personalized medicines definitely pose a challenge for HTA bodies, but these organizations making critical decisions must find methods that better reflect modern approaches to development of bespoke therapies because they are highly effective for patient populations. Development of targeted therapies and personalized medicines have been funded by federal and provincial governments, are being understood by regulatory authorities, and have informed Health Canada through strategic foresight and horizon scanning activities in various reports.[1,2] Together, these activities suggest that HTA must also evolve with evolving science and regulations. Strategies that include valuing and implementing real world evidence, surrogate endpoints, and genomic and genetic testing are within the scope of HTA and CDA is recommended to more broadly consider the changing landscape of drug development and what kinds of data can be collected as new and emerging therapies are developed.

In the interim, individual patients should be placed in a clinical trial setting to continue to receive the drug. These data will provide additional information about the utility of this drug, which, over time, will build sufficient evidence to make a more informed decision about reimbursement for specific population groups.

The Value of Information and Quality Care

We agree that there should not be double counting in the HTA process. This is an area where the fairness and health equity lens discussed below should be applied.

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1 The biodigital convergence: Cross-cutting policy implications

2 What we heard: A summary of scanning and consultations on what's next for health product regulation - Canada.ca

Fairness and Health Equity

Fairness and equity should not be excluded from decision-making. The reasons given in the report simply do not hold.

In Canada, Health Canada has developed a list of factors that implicate health outcomes and that could surely be a starting point.[3,4] Ontario has developed a Resource Guide and Framework for implementing health equity.[5] British Columbia and Alberta also provide useful papers on this topic.[6,7] Together, these federal and provincial initiatives designed to identify and measure social determinants of health indicate that these may be considered by each jurisdiction, therefore is no "average patient" and the "general population" that is referred to does not accurately reflect the fabric of Canadian society without consideration for these factors in HTA.

While there may be a perception that the CDA is "neutral" if it does not consider social determinants of health, another perspective is that CDA ignores the inequities that exist in healthcare systems – and society – despite significant evidence.[8]

Consistent application across all treatments and conditions is within the capability of HTA bodies.

The Burden on Patients, their Families and the Wider Economy

This a very problematic decision for the people living in Canada that our organization represents because we know that the burdens are significant. A study by the Canadian Cancer Society, and informed by ICES, evaluated the financial toxicity factor for cancer patients and found that the average patient must pay $33,000 for out-of-pocket for expenses.[9] Of note that this is for "average" cancer patients. Social determinants of health data show that the "average" cancer patient can be described differently depending on what kind of cancer you have, age, race, etc. It is clear that there is a greater impact on health outcomes – and productivity - for those patients who have less access to pay for out-of-pocket expenses based on lower socioeconomic status.

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[3] Health determinants | Statistics Canada

[4] Social determinants of health and health inequalities - Canada.ca

[5] Resource Guide to Ontario Health's Social Determinants of Health Framework

[6] B.C. Social Determinants of Health Value Set - Province of British Columbia

[7] Interactive health data | Alberta.ca

[8] Key Health Inequalities in Canada: A National Portrait – Executive Summary - Canada.ca

[9] Counting the true cost of cancer: How ICES data helped power a landmark report | ICES

Furthermore, the costs carried by patients would certainly have an impact on their productivity. Productivity losses due to illness have been estimated by food safety regulatory economists that may provide additional models for CDA to consider in the future.[10,11,12]

We are surprised to see the conclusion that that including these priorities might favour working age patients over retirees and children. These is no evidence to support this supposition. The impact of looking after a retiree or child is surely equally onerous and caregiving is estimated to result in a loss of $1.3B productivity loss per year in Canada.[13] Patients have been requesting that HTA processes include this factor for some time. The potential for time missed from work or school, financial strain and impact on productivity are significant.

As noted in the document on page 34, there have been several studies to monetize the value of absenteeism, presenteeism, early retirement and childcare. Surely, the COVID pandemic revealed that the Canadian economy needs healthy people to be working. Healthy working people provide the finances required to support health care systems in Canada, which benefit from federal and provincial investments in research and development. While challenging to measure for each product that is assessed by HTA, CDA is recommended to learn from Innovation, Science and Economic Development (ISED) about how scientific spillovers can be measured and develop a model that includes the contributions of domestically developed or manufactured products and their contributions to the Canadian economy.

Innovative regulatory mechanisms in the UK allow for questions about HTA to be included earlier in the development of a health product or medical device.[14,15] A similar mechanism exists in Canada, and is yet untested.[16] As regulatory systems evolve, so too much HTA because the types of evidence required for clinical trials, and the design of clinical trials, is evolving away from the gold standard randomized controlled trials, in many cases, opening the landscape to opportunities to more precisely regulate, and generate evidence to support safe and effective use of innovative therapies in more precise patient populations.

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10 Examination of Methods to Estimate Productivity Losses in an Economic Evaluation: Using Foodborne Illness as a Case Study | PharmacoEconomics

11 Annual Cost of Illness and Quality-Adjusted Life Year Losses in the United States Due to 14 Foodborne Pathogens - ScienceDirect

12 Socioeconomic Costs of Food-Borne Disease Using the Cost-of-Illness Model: Applying the QALY Method.

13 Canadian Caregivers are at a Breaking Point – Canadian Centre for Caregiving Excellence

14 : Innovative Licensing and Access Pathway (ILAP) - GOV.UK

15 The Innovative Devices Access Pathway (IDAP) - GOV.UK

16 Advanced therapeutic products (ATPs) - Canada.ca

It is easy for HTA to get further input from patients and the public through a number of processes including surveys, webinars, focus groups, town hall meetings, to name a few. As the CDA considers costs and benefits related to a drug, health technology, and health system decisions, we trust that these activities are grounded in the current and evolving landscape of scientific advancements, including evolving methods of HTA, such as broadening how *value* is considered.

We were pleased to see that CDA is piloting the use of a broader perspective in its evaluations and we agree entirely that it should be consistently applied across all treatments. This would also be consistent with issues of fairness and health equity.

Overarching Comments

1. Patients must be consulted more broadly including underrepresented populations must be consulted specifically on this document before it is finalized. It is very dense and complex and meaningful plain language and a plain language interpretation is needed.
2. Indigenous population led consultation must be undertaken following the principles of their way of knowing and OCAP Principles (find source).
3. The federal, provincial, and territorial governments that fund the CDA are also responsible for health research (through higher education) and the domestic life sciences sector, including the delivery of health care. National and sub-national investments in health innovation are celebrated, however poor adoption in Canada is noteworthy and the CDA plays a key role in this system.[17]
4. CDA will be seen by stakeholders as doing their job effectively if additional factors outlined above are integrated into its decision-making framework.

Recommendations

1. Individual patients should be placed in a clinical trial setting to continue to receive innovative therapies. These data will provide additional information about the utility of these interventions, which, over time, will build sufficient evidence to make a more informed decision about reimbursement for specific population groups.
2. Indigeneity and race have been identified as a social determinants of health and must be included.
3. Equity and fairness must be included in decision making. HTA must bring interested parties to assist in develop the component.
4. HTA should begin processes to obtain patient and public input about whether these shifts are acceptable. Should they be deemed to be, HTA countries not already doing so should widen their cost perspectives to include these as a factors in HTA deliberation frameworks.
5. CDA to review Canadian data sources for health information related to population and patient stratification to better model current and evolving demographic trends and identify factors that can be used in HTA.

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[17] Innovation paradox - The Globe and Mail

USC Schaeffer

Leonard D. Schaeffer Center
for Health Policy & Economics

Response to the Draft Report of the Health Economics Methods Advisory (HEMA): "Defining Appropriate Benefits for Economic Evaluation of Health Care Technologies"*

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[*] The views expressed in this document represent those of the authors, and not the views of the Schaeffer Center for Health Policy and Economics, the University of Southern California, the CHOICE Institute, the University of Washington, FTI Consulting, or the University of Rochester.

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Overview

Healthcare resource allocation should serve the needs of the individual people in a society who benefited from it and paid for it, not the needs of health technology assessment bodies or payers who are entrusted to manage those resources on individuals' behalf. This intuitive observation rests on a bedrock principle of economics, namely that society's values mirror what individuals in that society value. Yet, by mischaracterizing and misapplying basic economic principles, the Health Economics Methods Advisory (HEMA) draft report instead reaches the opposite conclusion. The same errors in logic lead HEMA to reject novel elements of healthcare value, which are explicitly designed to align healthcare value assessment with what individuals value. The so-called "novel" value elements derive from almost a century of settled economic theory and empirical analysis; in contrast, HEMA advocates an *ad hoc* approach riddled with internal inconsistencies and disregard for the well-being of the people whom healthcare systems serve.

HEMA offers a full-throated defense of an increasingly indefensible status quo, built around analysis of the QALY. Nowhere in their manuscript do they grapple with, or even mention, that the Inflation Reduction Act of 2022 prohibited the use of QALYs in decision making by American public payers. Nor do they acknowledge that alternatives such as Generalized Risk-Adjusted Cost-Effectiveness (GRACE) provide a legally compliant path forward [1], a considerable advantage over standard QALYs. While HEMA treats the political processes that determine the level of healthcare spending in national health systems as "reflect[ing] the preferences of the general population," (p. 27) it fails even to remark upon the preferences reflected by the US political processes that prohibited the QALY.

HEMA Ignores Both Empirical Objections to the QALY and Empirical Advantages of Novel Approaches

Summary: While HEMA argues that QALYs are strongly supported, they hold no special status and are, in fact, often rejected by the public and healthcare decision makers. HEMA also fails to mention numerous extant empirical objections to the QALY, all of which imply that it systematically fails to account for key aspects of individual preferences. At the same time, HEMA dismisses alternatives to the QALY by noting that "none has demonstrated empirical evidence that they align with either public or patient preferences" (Box 2). This assertion is undermined by a growing evidence base on more generally applicable value approaches, such as Generalized Risk-Adjusted Cost-Effectiveness (GRACE) [2]. However, even if it were correct, the right answer would be to call for further research on the topic given the clear limitations of the QALY, not to insist on maintaining a flawed *status quo*.

Analysis: HEMA's argument presumes in part that QALYs are strongly supported by empirical evidence of all kinds. On the contrary, QALY recommendations are often rejected by the public [3, 4]. Even healthcare decision makers, whom HEMA focuses on

representing, do not routinely find QALYs decisive [5, 6]. Generally, concerns arise when the less well-off are forsaken for marginal gains by the well-off [7]. Approaches like GRACE can address such issues, whereas QALYs cannot.

Other empirical evidence further conflicts with the QALY. For instance, its fundamental theory implies that, if QALYs are measured correctly, consumers would exhibit risk-neutrality over them. This would imply the absence of any disease severity premium, when in fact empirical evidence demonstrates that such a premium exists among consumers [8, 9] and even among payers [10, 11]. HTA bodies have explicitly incorporated disease severity premiums [12], as HEMA acknowledges. For example, the UK Cancer Drugs Fund [13, 14], and the use of *ad hoc* "Absolute Shortfall" and "Proportional Shortfall" adjustments [12] reflect the empirical shortcomings of QALY-based analyses.

HEMA itself makes arguments that undermine the empirical validity of the QALY. In their attempt to rebut the "value of hope," they assert that patients may overestimate the probability that a treatment will be successful (p. 26). Such systematically incorrect expectations would fall outside the framework of standard QALYs, a point that HEMA fails to appreciate. Indeed, such "optimism" or "pessimism" biases are captured in Prospect Theory [15], which readily comports with GRACE [16] and provides another reason to favor more general, novel approaches and disfavor standard QALYs.

In dismissing alternatives to the QALY, HEMA also overlooks empirical evidence that measures novel value elements in consumer preferences. Studies have documented the presence of nonzero value of hope [17, 18], nonzero option-value [19], and non-risk-neutral preferences over health outcomes [16, 20]. Theoretically, QALYs result from applying highly restrictive assumptions about preferences to the more general GRACE framework, which accommodates novel value elements like the value of hope and insurance value [21]. Generality is always preferred to restrictiveness, all else equal; therefore, it is up to the defenders of the QALY to justify its necessary restrictions by ruling out the presence or usefulness of novel value elements. Moreover, QALY's no longer represent the only feasible approach to value assessment. GRACE estimation is now feasible using only the inputs native to a traditional QALY-based analysis along with recent estimates of individual preferences over risky health outcomes [16].

HEMA Dismisses Patient-Centered Decision Making by Misunderstanding the Normative Basis of Economics

Summary: Centering value assessment on the preferences of individuals, rather than HTA bodies, is not only possible but also essential for ensuring alignment between collective decision making and the well-being of society's individual members.

Analysis: HEMA misunderstands the theoretical basis for its own preferred approach, the QALY, and its relationship to modern welfare economics. Two passages from the HEMA report illustrate this theoretical confusion.

> *Most HTA … see benefit in terms of the health of the populations for which their health systems are responsible. This is notably different from the ideas underlying some novel value elements which relate to individual benefits expressed as patients' preferences and choices*. [p. ES2]

> *Inevitably, the specification of a benefit function will be contested – both its constituent parts and the weights - and a social consensus will be impossible. This is consistent with the long-recognized understanding in economics of the impossibility of deriving a "social welfare function" from the preferences of individuals. [p. 3]*

The first passage reveals HEMA's problematic choice to focus on what HTA bodies view as beneficial, rather than on what individual patients view as beneficial. In the second, they attempt to justify this view by asserting that social decision making cannot be coherently based on individual preferences. Not only is this latter argument incorrect, but HEMA also appears unaware that the very assumptions underlying the QALY framework they embrace also undermine the supposedly "long-recognized" impossibility result they reference.

Although they do not provide a citation, we assume they are alluding to Kenneth Arrow's "Impossibility Theorem" [22] when arguing that social welfare cannot be built upon individual preferences.[1] Yet, less than five years after Arrow published his theorem, John Harsanyi, another Nobel Laureate economist, proved mathematically that social welfare functions *can* indeed be coherently built as weighted averages of consumer preferences, so long as utility levels can be compared across people [24]. (Arrow' explicitly assumed away the possibility of interpersonal utility comparison to enable his proof.[2]) Significantly, QALY-based decision making *requires* that utility be comparable across people [25], adding a layer of irony to HEMA's mistaken assertion about "impossibility." Indeed, such interpersonal comparisons remain central to economic valuations of all kinds, and the conditions for comparability are empirically reasonable: for example, if everyone assigns the same value to full health and the same value to death—conditions fundamental to HTA—then utilities will be comparable across people [26]. Arrow himself relied on interpersonal utility comparisons in his later work on health economics [27].

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[1] Arrow makes clear that his proof requires collective decision making to be limited only to rank-order voting of some sort. Yet, modern welfare theory has further demonstrated that this "long-recognized" impossibility result also fails when societies use alternatives to rank-ordered voting, such as majority judgement [23].

[2] Arrow's own restatement of his theorem makes this plain [22, p. 342] (emphasis ours): "*If we exclude the possibility of interpersonal comparisons of utility*, then the only methods of passing from individual tastes to social preferences which will be satisfactory and which will be defined for a wide range of sets of individual orderings are either imposed or dictatorial."

HEMA's focus on the QALY internally contradicts its claim that social decisions cannot be derived from individual preferences. This represents a fundamental error. By abandoning individual preferences, HEMA shifts decision making towards technocrats and away from patients, both current and future. Harsanyi showed that any social welfare function that departs from a weighted average of individual utilities fails to protect the rights and preferences of individuals [24]. Specifically, Harsanyi noted that only a weighted average of utilities respects the "Pareto principle," which ensures that collective decisions always at least favor policies that make every individual better or no worse off.

In contrast, the GRACE framework [2, 21, 28] and numerous other novel value elements [17, 29, 30] begin with the well-established economic principle that social welfare derives from individual welfare and can be readily measured through interpersonal comparisons of utility. Indeed, the foundational theory of the QALY itself assumes that QALYs should be based on individual preferences [25, 31], a topic we revisit below.

HEMA Misunderstands and Overemphasizes Opportunity Costs in Healthcare Resource-Allocation

Summary: It has long been shown that, like any other investment, health spending should be undertaken whenever the rate of return is sufficiently high. HEMA disregards this principle and instead baselessly assumes that healthcare spending levels are fixed and that spending on new health technologies always comes at the expense of other health technologies. This assumption is no more correct than asserting that opening a new semiconductor factory provides no additive benefit and necessitates closing an existing one. The historical record makes clear that healthcare budgets are not set in stone. They result from public and private choices about how to allocate resources across healthcare and non-healthcare uses. As such, health technology assessment should focus on ensuring that health investments are made whenever the benefits to individual members of society exceed the direct costs to society and foregone otherwise. These criteria do not depend on the sunk costs embedded in prior healthcare spending decisions.

Analysis: To illustrate the flaws in their logic, we begin by noting HEMA's claim:

> *All health care systems funded collectively, whether via taxation or insurance, impose opportunity costs when they devote additional resources to new medical technologies and other interventions. This is because those additional resources are inevitably taken from interventions and services which could have benefited other patients, and the opportunity costs are the consequent reduction in those individuals' health outcomes.*

This is incorrect. As the economist Michael Grossman established more than fifty years ago, consumer spending on good health can best be thought of as an investment, featuring

upfront outlays of time and money and downstream returns in the form of good health and its attendant value [32]. As with any other investment problem, a health intervention should be paid for if its monetized stream of benefits exceeds its direct costs. If the marginal value of healthcare spending rises, so should the amount of money spent on it. HEMA ignores this fundamental economic principle, and in doing so, erroneously instructs the entire field of health economics on the purported necessity of "giving due consideration to opportunity costs" (p. ES2) in the theory of value assessment.

Moreover, from a purely empirical point of view, healthcare spending is not fixed, certainly not in the long-run. This point is obvious in the US, but it is even true in "national health" countries like the UK. The British National Health System (BNHS) budget increased by an average of 2.3 percent per year (in 2023-24 prices) from 1956 through 2022 (https://www.kingsfund.org.uk/insight-and-analysis/data-and-charts/nhs-budget-nutshell). This led to a 4.5-fold increase in real spending for the BNHS over that period. Growth was somewhat higher when Labour controlled the Parliament and lower when Conservative governments had control, but increases occurred regularly. Over the same period, the British population increased from 42 million to 69 million, so real per-capita spending nearly tripled. The BNHS response to the pandemic also undermines the "opportunity cost" logic. Facing the threat of COVID, BNHS temporarily boosted its spending by more than 20%.

This also means that, even in the BNHS, "additional resources" are not inevitably taken from other patient-benefitting services, despite the historically incorrect assertion by HEMA. Additional spending may indeed be financed through increased BNHS budgets that reduce British consumers' ability to buy other goods and services. The tradeoff between improved health and non-health consumption is clearly present, and economic logic dictates that health investments make sense if they produce value that exceeds the cost of the monetary resources invested.

HEMA Ignores the Well-Being of Future Generations of Patients

Summary: When reimbursement reflects patient preferences, innovators accrue financial rewards by serving patients. By weakening the link between measured value and patient preferences, HEMA muddies these pricing signals to innovators and encourages innovation that serves HTA bodies, not current and future generations of patients. This error could have global consequences.

Analysis: The health economist Joseph Newhouse once remarked that "the patent system is an effort to approximate a dynamically efficient price"--in other words, one that produces the optimal amount of innovation globally [33]. HEMA's approach fails to produce a dynamically efficient price and thus distorts medical innovation, harming all patients, both current and future.

The economic literature makes plain that innovation becomes efficient when a technology's price depends on the value it produces for individual members of society, current and future [34, 35]. When prices instead reflect value to HTA bodies, firms will innovate to serve HTA bodies rather than patients. This corruption of innovation incentives harms the well-being of future generations of patients, who are denied a stake in decisions that affect their health and life expectancy.

This point also highlights a deep and troubling incentive problem inherent in HEMA's approach. Neither HTA bodies, nor governments, nor private firms pay for medical technology. People do, in the form of insurance premiums, taxes, and out-of-pocket payments. Thus, HEMA's approach would have individual people pay to serve the preferences of HTA bodies. Instead, the HTA process ought to represent the preferences of individuals, not diverge from them. Pricing new technologies according to the value accrued by individual patients ensures efficient incentives for innovators. Put more plainly, since innovators will focus on earning the highest reward for their efforts [36-39], society should align those rewards with the needs, values, and preferences of the individual people that pay for medical technology and receive its benefits.

This issue spans international borders. New medical innovations benefit people all over the world. At the same time, the US market produces an outsized impact on innovation incentives, accounting for at least two-thirds of global pharmaceutical profits [40]. Thus, getting US prices wrong harms people all over the world. For example, prior research demonstrates that importing European pricing policies into the US market would reduce longevity for Europeans almost as much as it would for Americans, even though only American policy would be changing [41].

HEMA Misunderstands Risk in Value Assessment and Unjustifiably Dismisses Risk-Related Novel Value Elements

Summary: HEMA asserts that HTA bodies should disregard health risks when making decisions. This assertion violates both economic theory and the common sense of all the human beings who worry about the risk and uncertainty associated with disease and poor health. Because of this faulty assumption, HEMA fails to refute novel alternatives to the QALY that properly account for the way individuals perceive and respond to health risks.

Analysis: HEMA argues for the dismissal of novel value elements related to risk—e.g., the "value of hope," "insurance value," and the GRACE framework. Their argument rests on another theoretical error: HEMA argues that healthcare decision makers ought not to care about risk—in economic parlance, HEMA assumes they are "risk-neutral." However, maintaining the presumption of "risk-neutrality" conflicts both with the theory of the QALY

that HEMA appears to embrace and with economic principles concerning the analysis of societal welfare.

Specifically, HEMA appears to confuse the concept of risk-neutrality over QALYs with risk-neutrality over health outcomes. This confusion undermines HEMA's dismissal of GRACE and all related novel value elements that capture patient risk preferences. Specifically, HEMA's unequivocal defense of traditional methods is contradicted by foundational theoretical work on the QALY, which explicitly notes that individuals may have non–risk-neutral preferences over underlying health benefits [25, equation (3a)], a point echoed in subsequent work [31, equation (4)].

As these and numerous other works make clear, one important purpose of the QALY is *to account for risk preferences over health improvements*. If in fact these risk preferences are fully accounted for, only then will preferences become risk-neutral over the QALY itself. Risk-neutrality over QALYs is entirely different from and does not imply risk-neutrality over health benefits, a critical distinction that gets lost in HEMA's misreading of the QALY literature.

Using this flawed logic, HEMA attempts to dispute that risk preferences should be accounted for in health technology assessment. Yet, the theory of the QALY on which they themselves rely has long settled this dispute in favor of the opposite conclusion: risk preferences over health benefits must be accounted for. This is settled theory, not a novel proposition requiring confirmation.

HEMA's reasoning also rests on an implausible assumption about aggregate health outcomes. For instance, HEMA asserts:

> *Decision makers who use HTA are typically assumed to be risk neutral with respect to each decision they make about individual health technologies because the health of the populations they serve is only marginally impacted by each individual reimbursement decision*.

Here, HEMA advocates abandoning person-centered economic analysis in favor of HTA-centered analysis. Implicitly, they assume that losses to one patient can be offset by gains to others, so long as aggregate population health improves. This framing treats health as if it were a divisible, transferable asset in a collective portfolio. Obviously, however, patients cannot redeem the survival or well-being of others to compensate for their own loss. Each person bears the consequences of uncertain health outcomes directly, and the ethical legitimacy of HTA cannot rest on the presumption that individual harms are acceptable so long as population averages improve.

What then is the incentive to preserve risk-neutrality at such high cost to patients? One possibility is that not everyone agrees with their colleagues on which methods should guide HTA. Risk-neutrality glosses over these disputes, seemingly permitting a wide array of methods for measuring "utility." Risk-neutrality offers a broad and welcoming tent for HTA

researchers. However, we find it troubling that the assumption of risk-neutrality appears to aid researchers more than it does patients.

HEMA's Conclusions Rest on an Undefined and Inconsistent Concept of "Group" Preferences

Summary: In place of focusing on individual preferences, HEMA advocates for a fuzzy and ill-defined concept of "average" group preferences. This approach runs roughshod over clinical and preference diversity in a population of patients. Imagine a society where two-thirds of people with a disease benefit more from a blue pill, but the other third benefit more from a red pill. "Average" preferences would seek a single rank-ordering – everyone gets the blue pill, everyone gets the red pill, or perhaps they all get a "purple" pill. Clearly, these "average" preferences efface individual diversity and harm large minorities of patients.

Analysis: Curiously, HEMA asserts the principle that "benefits must be aggregated (valued) appropriately and consistently with average preferences of the general population rather than preferences of specific individuals" (p. ES1). "[A]verage preferences of the general population" are never precisely defined, but to the best of our ability to interpret the term, it appears fundamentally inconsistent either with the rational allocation of resources or with HEMA's exclusion of individual preferences.

If the term "average preferences" corresponds simply to an average of individual utility functions, then HEMA would implicitly be accepting the principle that individual consumer preferences reign supreme, contrary to their assertions elsewhere. Let us assume they are not embedding such a fundamental contradiction. Instead, we presume that they have in mind some concept of a group preference ordering distinct from a linear combination of individual preferences. However, Harsanyi proved that the only way to create a rational and Pareto-consistent preference structure for a group is to use a weighted average of individual preferences [24]. The only way we can see to make sense of "average preferences of the general population" is thus to compute weighted averages of individual preferences, precisely what HEMA incorrectly advises against.

HEMA Lacks Any Budgetary Basis for Excluding Consumer and Patient Preferences in Valuation

Summary: In this response, we have shown that HEMA lacks any basis in economic theory for excluding patient and consumer preferences in value assessment. They also lack a pragmatic or budgetary basis for this assumption, because health economists can now use GRACE to conduct patient-centered value assessment without needing to expand healthcare budgets. Prior research on GRACE reveals that QALY-based modeling has spent too little on severe disease, but *too much* on milder illness, and that on balance,

recentering value assessment on patient preferences saves about the same on mild disease treatment as it spends on severe diseases [42].

Analysis: Recent analysis of the GRACE framework —which incorporates patient preferences for health states and addresses discriminatory aspects of traditional cost-effectiveness analysis—demonstrates this infirmity in QALY-based allocations. When GRACE was applied to 69 pharmaceuticals previously evaluated by ICER, it increased value-based prices for treatments of severe diseases while decreasing prices for treatments of mild conditions [42]. The net result was a mere 2% aggregate increase in total spending, with resources redistributed toward more severe, less prevalent illnesses that patients value more highly and away from mild diseases that traditional QALYs over-reimburse. (If desired, strict budget-neutrality could be ensured with a trivial reduction in the willingness-to-pay threshold.)

This finding fundamentally challenges the zero-sum narrative that constrains health technology assessment. Rather than creating an inexorable budget expansion, methods that incorporate patient perspectives can identify where traditional cost-effectiveness analysis undervalues treatments (severe disease) and overvalues others (mild disease). The budget-neutral redistribution demonstrates that person-centered value assessment need not come at the expense of fiscal responsibility—it simply allocates resources more efficiently according to how patients themselves value health improvements.

Summary

Economic thought rests squarely on individual liberty and respect for the diversity of individual preferences. HEMA focuses not on this broad arc that bends toward human freedom, but instead on the defense of a QALY-based *status quo* that has outlived its usefulness. Economics rigorously and thoughtfully centers welfare on the people that inhabit a society, not on technocrats or regulators. It is long past time for economic evaluation in healthcare to follow suit.

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Endnotes

Endnote 1

If Rip Van Winkle[1] had fallen asleep in 1976 after reading one of the first published health care cost-effectiveness analyses – and who hasn't at times nodded off while reading these papers…

> (**Ref #1**) From Wikipedia: " 'Rip Van Winkle' is a short story by the American author Washington Irving, first published in 1819. It follows a Dutch-American villager in colonial America named Rip Van Winkle who meets mysterious Dutchmen, imbibes their strong liquor and falls deeply asleep in the Catskill Mountains. He awakes 20 years later to a very changed world, having missed the American Revolution."

Endnote 2

Well over a thousand peer-reviewed studies are now published each year,[2]…

> (**Ref #2**) Neumann (2025) notes that "… new data from the Tufts Cost-Effectiveness Analysis (CEA) Registry shows that the number of English-language, published cost/QALY articles continues to rise, reaching 1300 new studies in 2023…". See also Figure 1 from Neumann (2024).

Endnote 3

… the methodology underpins drug price negotiations in several countries,[3]

> (**Ref #3**): Wouterse et al. (2023) states, "Several countries use economic evaluations routinely in their decision-making process, mostly for pharmaceuticals. A CEA is integrated in healthcare decision making to assess the eligibility of funding of pharmaceuticals in countries such as Australia (Pharmaceutical Benefits Advisory Committee), Canada (Canadian Agency for Drugs and Technologies in Health), Poland (Agency for Health Technology Assessment and Tariff System), The Netherlands (National Healthcare Institute), Sweden (Dental and Pharmaceutical Benefits Agency) and the UK (National Institute for Health and Care Excellence). These all pertain to decisions in the context of a collectively financed healthcare system made by public institutions."

Endnote 4

… even in the United States, the Institute for Clinical and Economic Review relies on cost-effectiveness analysis to make price recommendations for pharmaceuticals.[4]

> (**Ref #4**) Goss Sawhney and Thakur (2023) state that "In the United States, the Institute for Clinical and Economic Review (ICER), a nonprofit, nongovernmental organization, has increasingly become the predominant independent price assessor, offering 'rigorous, transparent evidence reports' from the 'US health care system perspective.' An ICER 'value assessment' has two substantial sub-assessments: a comparativeness clinical effectiveness assessment and a long-term cost-effectiveness assessment."

Endnote 5

Yet there is discord. Advocacy groups have labeled the quality-adjusted life year (QALY) – the field's foundational measure – as unethical.[5]

> (**Ref #5**) The Partnership to Improve Patient Care (PIPC) letter (2025) is signed by nearly 100 organizations and states, "It is critical to remain committed to our shared goal of preventing discrimination against people with disabilities and chronic conditions by condemning policies that would rely on the Quality-Adjusted Life Year (QALY) or similar average metrics that fail to account for those who are not average."

Endnote 6

The US government has substantially restricted its use.[6]

> (**Ref #6**) Neumann and Weinstein (2010) write, "The recently enacted Patient Protection and Affordable Care Act (ACA) created a Patient-Centered Outcomes Research Institute (PCORI) to conduct comparative-effectiveness research (CER) but prohibited this institute from developing or using cost-per-QALY thresholds." Not being allowed to compare cost-effectiveness ratios to benchmarks and hence not being able to classify cost-effectiveness ratios as representing "favorable" or "unfavorable" value greatly limits their usefulness for the purpose of allocating resources.

Endnote 7

And a 2018 Special Task Force convened by the International Society for Pharmacoeconomics and Outcomes Research concluded that traditional cost-per-QALY cost-effectiveness analysis (CEA) omits important elements of value.[7]

> (**Ref #7**) Lakdawalla et al. (2018) state, "QALYs and costs often form the basis of value assessments based on CEA, and as noted earlier, this is labeled CUA. Nevertheless, QALYs capture only a subset of benefits that may be produced by a health care intervention. This framework neglects numerous alternative aspects of benefits that should also be considered." The article's Table 1 details the missing elements.

Endnote 8

Some prior critiques have taken a "bottom-up" approach, estimating how much value so-called novel elements might represent.[8-10]

> (**Ref #8**) Graf et al. (2025) investigated the impact on cost-effectiveness ratios for sickle cell disease treatments of accounting for risk aversion, as characterized in the GRACE (Generalized Risk-Adjusted Cost-Effectiveness) framework. They state in the abstract, "Implementing the GRACE framework resulted in a 6% reduction in both direct and societal incremental cost-effectiveness ratios for lovo-cel and exa-cel, demonstrating a decrease from $192 651 and $161 816 to $182 036 and $152 900 per quality-adjusted life year, respectively. Additionally, willingness-to-pay thresholds increased by approximately 50%, reflecting a higher valuation of treatments under GRACE. GRACE-adjusted estimates suggest that lovo-cel and exa-cel are cost-effective from both direct payer and societal perspectives."
>
> (**Ref #9**) Ma et al. (2022) investigated the impact of incorporating "broader value elements (eg, patient and caregiver time, spillover health effects, productivity)" on cost-effectiveness estimates for two case studies: a vaccine to for human papillomavirus (HPV) and for combined modality treatment (CMT) for early-stage Hodgkin's lymphoma (ESHL). They state in the abstract, "Including each broader value element made cost-effectiveness progressively more favorable, with HPV vaccination becoming cost-saving … when the analysis incorporated productivity costs. For CMT versus chemotherapy alone in patients with ESHL … Including all elements made this treatment's net monetary benefits (the sum of its averted resource costs and the net value of its health impacts) less favorable, even as the contribution from CMT's near-term health benefits grew."
>
> (**Ref #10**) Whittington et al. (2025) investigated the impact of dynamic pricing, comparing cost-effectiveness ratios with and without accounting for this factor. They state in the abstract, "The static cost-effectiveness estimate was less favorable than the dynamic estimate for a chronically administered drug by between 82% (case 1) and 62% (case 2), and for a 1-time drug by between 34% (case 3) and 27% (case 4)."

Endnote 9

Our recent analysis[11] instead adopted a "top-down" approach that treats the market as the ultimate arbiter of value. We asked whether traditional CEA judged drugs that ultimately succeeded in the market to be good value. We found that for about half of the drugs with annual worldwide sales of at least $500 million, conventional CEAs deemed their cost-effectiveness ratios unacceptable. In other words, traditional CEA missed half of the successes.

> (**Ref #11**) Cohen et al. (2025) write, "Our first analysis found that half of commercially successful drugs in our sample had unfavorable published CE ratios, with some ratios exceeding the common benchmark of $150,000 per QALY by more than an order of magnitude."

Endnote 10

For example, the UK's National Institute for Health and Care Excellence (NICE) has adopted severity modifiers to account for the value of addressing severe conditions.[12]

> (**Ref #12**) Njoroge et al. 2024) write, "The NICE's methods and processes for technology appraisal (TA) updated in 2022 and adopted in 2023 incorporates a QALY weighting multiplier for disease severity…. Under the revised methods, the severity of the condition is considered in terms of both the absolute and proportional QALY shortfall associated with a disease (see Box 1) with specific criteria applied to determine whether a severity modifier is appropriate."

Endnote 11

But novel element "proponents" have called for more, such as incorporating dynamic pricing,[13] which our analysis and other work suggest is often important.[10,11]

> (**Ref #13**) Ramagopalan et al. (2024) write, "It is noteworthy that the vast majority of published pharmaceutical cost-effectiveness analyses do not make any assumptions about future reductions in drug prices following the loss of a drug's exclusivity. This omission distorts results by misrepresenting total drug costs and not reflecting real-world conditions... incorporating genericization will allow society to better use CEA when evaluating a drug's costs and benefits over timeframes that matter to governments and individuals..."
>
> (**Ref #10**) Whittington et al. (2025) investigated the impact of dynamic pricing, comparing cost-effectiveness ratios with and without accounting for this factor. They state in the abstract, "The static cost-effectiveness estimate was less favorable than the dynamic estimate for a chronically administered drug by between 82% (case 1) and 62% (case 2), and for a 1-time drug by between 34% (case 3) and 27% (case 4)."
>
> (**Ref #11**) Cohen et al. (2025) write, "We found that dynamic pricing drives the most substantial CE ratio improvements, achieving … changes often far exceeding the impact of other novel elements. The exploratory analysis found dynamic pricing to be influential across all case study drugs…"

Endnote 12

The debate over the recent Health Economics Methods Advisory (HEMA) report exemplifies this ongoing battle.[14,15]

> (**Ref #15**) McQueen et al. (2025) explain in the Executive Summary, "This report sets out and then applies a set of principles to guide HTA organizations in considering whether and how to incorporate a subset of these suggested 'novel value elements'…" They argue first that, "Most HTA bodies … see benefit in terms of the health of the populations for which their health systems are responsible. This is notably different from the ideas underlying some novel value elements which relate to individual benefits expressed as patients' preferences and choices… The second principle relates to how to aggregate benefits across individuals … The standard normative position by HTA organizations … is to reflect trade-offs using the average preferences of a representative sample of public preferences … in contrast with the implied normative position of some of the novel value elements which focus on individual patients' preferences."

Finally, McQueen et al. argue, “Proposals regarding new value elements often do not give due consideration to opportunity costs.”

(**Ref #14**): Chen et al. (2025) summarize their position as follows: “While HEMA argues that QALYs are strongly supported, they hold no special status and are, in fact, often rejected by the public and healthcare decision makers. HEMA also fails to mention numerous extant empirical objections to the QALY, all of which imply that it systematically fails to account for key aspects of individual preferences. At the same time, HEMA dismisses alternatives to the QALY by noting that "none has demonstrated empirical evidence that they align with either public or patient preferences" (Box 2). This assertion is undermined by a growing evidence base on more generally applicable value approaches, such as Generalized Risk-Adjusted Cost-Effectiveness (GRACE) [2]. However, even if it were correct, the right answer would be to call for further research on the topic given the clear limitations of the QALY, not to insist on maintaining a flawed status quo.”

Endnote 13

… it would be helpful to avoid the effective sidelining of elements that many people clearly care about – such as equity, community-level benefits, and scientific spillovers – by assigning them, from the outset (page 2, Box 1) to qualitative deliberation only.[15]

(**ref #15**): McQueen et al. (2025), Box 1 states, “The focus of this report is quantitative economic evaluation to inform decisions… This report was largely focused on quantified benefits … leaving out contextual factors… in actual health care priority setting, any benefits that … cannot be quantified … are moved to a deliberative step. Indeed, constructs such as equity … and community-level benefits are often considered in HTA deliberation. Some have suggested that additional value elements such as “scientific spillovers” should be discussed in deliberation.”

Endnote 14

“…the principle that “benefits must be relevant for the decision-making organization”[15]…

(ref #15): McQueen et al. (2025). See Table 2, row 1, left column.

Endnote 15

Table 2 asserts that benefits are relevant only if they “reflect the statutory, legal or other authorities of the decision-making organization…”.[15]

(**ref #15**): McQueen et al. (2025). See Table 2, row 1, second column from left.

Endnote 16

The arguments in the rebuttal to the HEMA report would be more effective if they first laid out the intuitive story in plain language and then relegated the heavier theoretical machinery (e.g., Harsanyi’s theorem[14]) to an appendix or supplement.

(**ref #14**) – Chen et al. (2025). See pages 3 and 4.

Endnote 17

Greater openness – especially around simulation models – would help build trust.[16]

(**ref #16**) Cohen and Wong (2017) argue that, “Open model publication bolsters credibility by allowing others to assess independently whether alternative, plausible assumptions substantially alter model projections. If those projections change little, the model’s conclusions are robust,… [openly published computer code] would also stimulate exploration of alternative structural assumptions or additional benefit or harm considerations, thereby enhancing credibility (or not) of the original findings.”