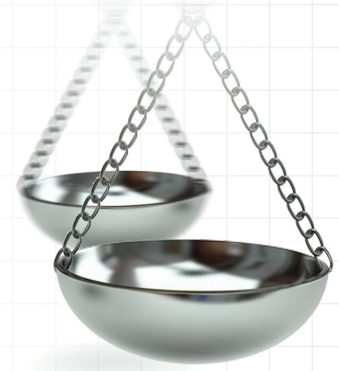




Generalized cost–effectiveness analysis: charting a path forward for measuring the societal value of medical technologies

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“The goal of GCEA is not to selectively highlight elements that make a treatment appear more favorable; rather, it aims to systematically and comprehensively capture societal value.”

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As we accelerate innovations in healthcare to meet critical unmet needs, understanding the full value of novel technologies is essential for balancing affordability and innovation. Many countries, particularly those with centralized health systems, have established formal health technology assessment (HTA) processes to guide coverage and reimbursement decisions. Although specific frameworks vary, cost–effectiveness analysis (CEA) is a key component. A notable example is the UK’s National Institute for Health and Care Excellence (NICE) using explicit cost-per-QALY thresholds to recommend coverage for new technologies within the National Health Service (NHS) [1,2].

In contrast, the US system is more market-based and lacks a centralized HTA agency. However, the Institute for Clinical and Economic Research (ICER), a research organization independent from the US government, has similarly adopted cost per QALY as a key metric for value and is increasingly influencing discussions and perceptions of healthcare value in the USA [3,4]. Particularly, ICER is developing special assessments to inform CMS Drug Price Negotiation [5].

While there is broad consensus that prices of healthcare should reflect the value they provide, the definition of value and its assessment remain active areas of research. Traditionally, CEAs have focused on narrowly defined clinical benefits and adverse events, occasionally considering impacts on productivity and caregiver burdens [6,7]. This limited perspective overlooks many important societal aspects influenced by healthcare interventions. Recently, significant progress has been made to broaden our understanding of the value of health care [8–12].

GCEA framework proposed in Shafrin *et al.*

Built on existing research, Shafrin *et al.* proposed the generalized cost–effectiveness analysis (GCEA) methodology to address key limitations of conventional CEAs and to provide a roadmap for value assessors and modelers to better account for costs and benefits of innovative healthcare technologies important to patients and caregivers from a societal perspective [13].

The GCEA methodology encompasses 15 ‘petals’ across four domains. The uncertainty domain captures how risk aversion and uncertainty in treatment outcomes impact value, including aspects such as outcome certainty, disease risk reduction and the value of knowing. The dynamics domain addresses factors like dynamic net health system costs, dynamic prevalence, societal discount rates, option value and scientific spillover, which enable a better evaluation of how value changes over time. The beneficiary domain reflects variations in value based on who benefits, incorporating patient-centered health improvement, equity, family and caregiver spillovers and community spillovers. The remaining value elements cover productivity, adherence and direct non-medical costs.

The paper also details the latest methodological advances to facilitate implementation of GCEA. Numerical examples illustrate how to account for risk aversion, outcome uncertainty and disease severity, as well as how to

employ a stacked cohort approach for incorporating dynamic net health system costs and prevalence. Acknowledging the limitations of available methods, data and the constraints of time and resources, the authors recommend that practitioners should strive to incorporate novel elements into scenario analyses or discussions of limitations, if it is impractical to include them in the base case. Additionally, the authors provide a checklist for modelers to assess whether specific value elements were incorporated in base-case analysis, sensitivity analysis, or omitted as less relevant, to facilitate transparency in reporting of GCEA.

Future areas of research

While GCEA can address key limitations of conventional CEA, several areas of future research should be prioritized to ensure widespread adoption.

To begin with, uncertainty is pervasive and must be thoroughly characterized in GCEA. For instance, the *ex ante* real option value relies on forecasting future treatment arrivals and their expected efficacy, both of which are highly uncertain. Future pricing trends and disease prevalence are also unpredictable and estimates of patient risk aversion add another layer of uncertainty. By omitting these value elements, results from conventional CEAs may seem more precise, but they can be grossly inaccurate. Quantifying and minimizing uncertainty in GCEA estimate allows us to confidently assess the true value of treatment.

In addition, the GCEA method does not fully tackle the challenge of double counting. Some novel value elements, such as the psychic value of knowing and the fear of contagion, may overlap with aspects already captured by conventional QALYs. For instance, cancer screening result can alleviate worry and improve mental wellbeing of individuals [14,15]. In this context, the value of knowing intersects with constructs like anxiety and depression, which are commonly included in utility-weight elicitation instruments such as EQ-5D [16]. Thus, including the value of knowing as a separate element from conventional QALYs risks double counting.

Furthermore, a key advancement in the GCEA framework is the consideration of how patient risk preferences influence value estimates. However, it remains unclear whose preferences should be elicited and applied. Similar to discussions in patient-preference research, further exploration is needed to determine whether to use preferences from the general population or those from individuals with specific diseases and its implications. Empirical evidence suggests that individual's risk preference is influenced by the level of risk as well as individual characteristics [17,18]. More research is necessary to identify the conditions under which treatments create value by reducing uncertainty in efficacy, as well as those scenarios where treatments provide value by offering hope – characterized by a long tail in the efficacy distribution and a larger standard deviation.

Looking ahead

A few decades after the first published CEAs, serious efforts are finally being made to address the limitations of conventional CEAs. Shafrin *et al.* consolidates past research on this topic and can serve as a practical guide for modelers and value assessors on capturing the societal value through GCEA.

While the list of value elements and considerations may seem overwhelming, practitioners can implement a few immediate and straightforward steps to enhance their value assessments. For instance, analyses should incorporate dynamic elements such as dynamic pricing, dynamic prevalence, option value and discount rate, as these are either already quantified or can be quantified. If certain elements are deemed irrelevant or impractical to include, this should be clearly stated in the reporting. The goal of GCEA is not to selectively highlight elements that make a treatment appear more favorable; rather, it aims to systematically and comprehensively capture societal value.

The GCEA framework and methodology will continue to evolve through rigorous research and broader application. Both producers and consumers of value assessment research should take a more proactive role in developing methods and data to operationalize and enhance GCEA. This will ensure that our value estimates more effectively inform the decision-making needs of various stakeholders.

Author contributions

Meng Li was responsible for all aspects of the paper.

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