R E V I E W

Health Equity Considerations in Cost-Effectiveness Analysis: Insights from an Umbrella Review

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Abstract: Cost-effectiveness analyses (CEA) are important in healthcare decision-making and resource allocation; however, expanding the scope of CEAs beyond the traditional clinicoeconomic concepts to also include value elements such as health equity has attracted much interest in recent years. This umbrella review aimed to synthesize evidence on how equity concepts have been considered in modified types of CEAs. Publicly available articles in MEDLINE were searched on January 25, 2024, to identify systematic reviews (SLRs) published in English since 2013 that incorporate health equity considerations in CEAs. Title/abstract, full-text article screening and data extraction were conducted by a single reviewer and validated by a second reviewer. Results were qualitatively synthesized to identify common themes. Eight SLRs were included. Distributional CEAs (DCEA), equity-based weighting, extended CEA (ECEA), mathematical programming and multi-criteria decision analysis (MCDA) were the most discussed approaches. A lack of consensus on the best approach for incorporating health equity into CEAs was highlighted, as these approaches are not currently consistently used in decision-making. Important limitations included scarcity of robust data to inform health equity indices, bias associated with commonly used health outcome metrics and the challenge of accounting for additional contextual factors such as fairness and opportunity costs. Proposals to expand CEAs to address equity issues come with challenges due to data unavailability, methods complexity, and decision-makers unfamiliarity with these approaches. Our review indicates that extended and distributional CEAs can support decision-making by capturing the impact of inequity on the clinical and cost-effectiveness assessment of treatments, although future modeling should account for additional contextual factors such as fairness and opportunity costs. Recommendations for actions moving forward include standardization of data collection for outcomes related to equity and familiarity with methodologies to account for the complexities of integrating health equity considerations in CEAs.

Keywords: health technology assessment, health equity, cost-effectiveness analysis, value elements, umbrella review

Introduction

Cost-effectiveness analysis (CEA) is widely used as the foundation for assessments of new health technologies and has traditionally focused on the clinicoeconomic aspects of therapies, providing an objective assessment of the costs and benefits of a given intervention. Recently, there has been a movement to consider additional elements outside of the solely clinical or economic metrics and to incorporate social values into CEA. Elements that reflect the ability of therapies to provide hope to the patient (the value of hope), to extend a patient's life and therefore open possibilities for future treatments (real option value) and the value associated with scientific discoveries and their subsequent applicability (scientific spillover) are just some of the additional aspects of value that are promoted as valued additions to the traditional CEA model. There has been an explosion of publications referencing "additional" elements of value assessment from health technology assessment (HTA) bodies in recent years in response to demand from both the public and from reimbursement agencies alike to better capture the experiences of those from disparate populations.

The concept of additional elements of value in CEA has been discussed at length by the Professional Society for Health Economics and Outcomes Research (ISPOR) and spearheaded by the ISPOR Task Force. Their work is nicely summarized as the "Value Flower", which illustrates the elements essential to addressing CEAs in a full and

comprehensive manner.[1] While a consensus is growing regarding the need for additional elements of value in CEA, there remains a significant challenge in gaining consensus on exactly what those elements represent and how they should be incorporated into CEA most seamlessly. We have previously discussed this challenge elsewhere and summarized the dilemma in our "Value Puzzle" (Figure 1).[2] Among the keys identified in the Value Puzzle is the incorporation of health equity concepts in CEA, an important and emerging concept in health economics, but one that is rarely incorporated into current HTA policies.[3,4] Health equity is concerned with differences in health status between populations or groups that result from economic or social conditions[5–7] that are often considered unjust,[8] and differs from equality, which refers to the distribution of health based on a given metric.[5] Equality requires providing equal treatment for all, regardless of other challenges that a subgroup may face, whereas equity aims to level the playing field and provide care and resources such that all members of a population are able to achieve a desired endpoint (Figure 2).[5,9] The difference between the concepts is further illustrated when contrasting the individual nature of healthcare with the population focus of public health, ie, what may benefit an individual patient may not be in the best interest of the public, and vice versa.[5]

Several systematic literature reviews (SLRs) investigating the methods used to incorporate health equity concepts into CEA have been published in recent years. Chief among the goals of these reviews was to evaluate the methods used to incorporate health equity concerns, of which there are many. We previously outlined the various methods available to expand the CEA process in our review of additional elements of value in CEA,[2] each of which is represented in the current research into health equity inclusion. Common among the current SLRs – both regarding health equity and more broadly regarding elements of value – is the comment that traction on these methodologies has been somewhat slow due to unfamiliarity with the methods and a hesitation amongst those that perform the analyses to embrace new methods that may disturb the status quo.[2,3,10–12]

Given the amount of research effort that has been expended on this topic, we sought to perform an umbrella review of recent SLRs to consolidate information regarding the specific challenges, limitations and potential solutions to the broad incorporation of health equity concepts into CEA. In our umbrella review, we sought to systematically identify and synthesize evidence on how health equity concepts have been considered in modified types of CEAs and summarize the main methodological considerations, challenges and limitations.
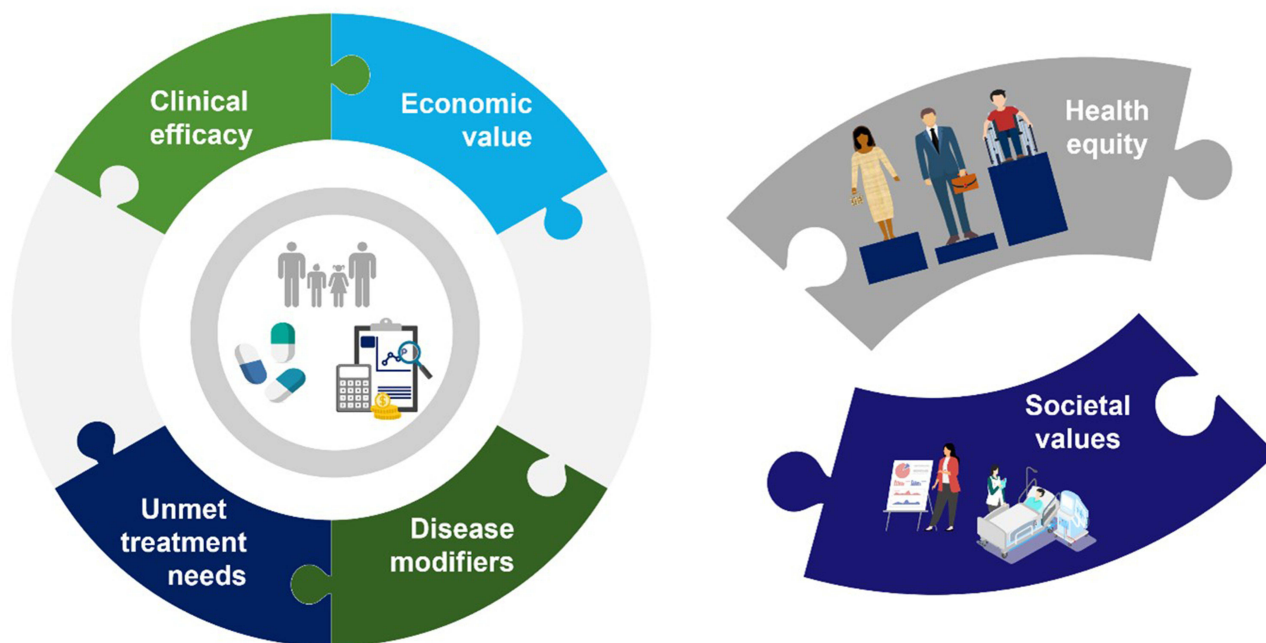

Figure 1 The "Value Puzzle" illustrates the existing aspects of traditional cost-effectiveness analyses (clinical efficacy, economic value, disease modifiers and unmet treatment needs) but also highlights the missing aspects of the current system, of which health equity is a key. How to best incorporate concepts of health equity into CEA remains a challenge for HTA agencies and decision makers. Reprinted from Muir JM, Radhakrishnan A, Freitag A, Ozer Stillman I, Sarri G. Reconstructing the value puzzle in health technology assessment: a pragmatic review to determine which modelling methods can account for additional value elements. *Front Pharmacol.* 2023;14:1197259. Creative Commons.[2]
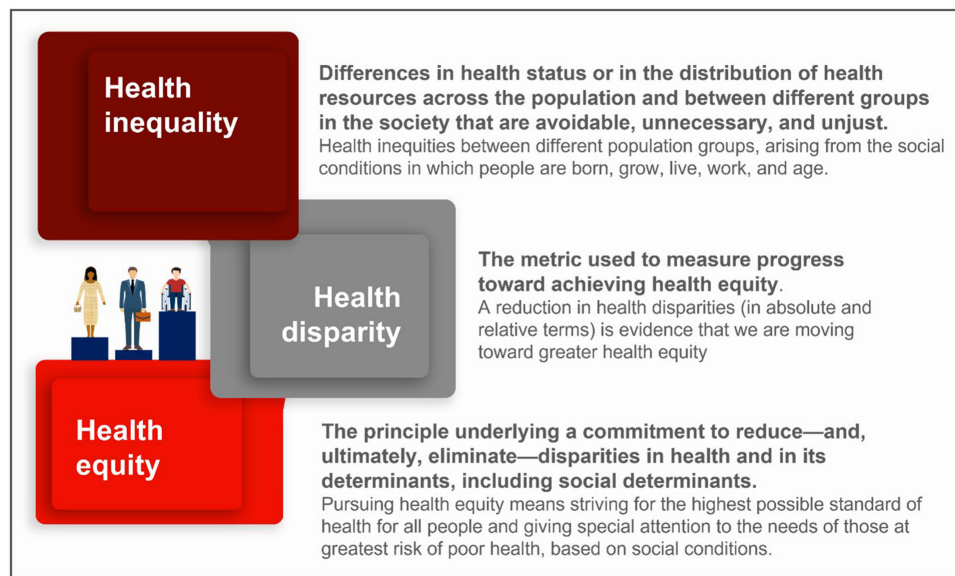
Figure 2 Health equity, health equality and health disparity are related but distinct concepts for decision makers when considering new health technologies.

Materials and Methods

To gather the latest information from the peer-reviewed literature, we performed an umbrella review (ie, a review of reviews) to compile evidence from SLRs. Our objective was to gather data on current and proposed methods for incorporating health equity into the economic analysis during HTA decision-making and to identify challenges associated with these efforts. Umbrella reviews are designed to aggregate evidence from numerous reviews to develop an accessible summary document but also to thematically examine the findings of SLRs and to provide guidance on a topic moving forward.[13,14]

Search Strategy and Eligibility Criteria

A targeted literature review guided by the Preferred Reporting Items for Overviews of Reviews (PRIOR) was conducted to identify SLRs reporting on the incorporation of health equity concepts in CEAs. We conducted a structured search of the MEDLINE (Ovid) and Embase databases for English-language, publicly available literature published between 2013 and January 25, 2024 (see Table S1). No geographic or jurisdictional limits were placed on the search. Keywords for our search included: "economic evaluation", "equity", "equality", "cost-effectiveness analysis" (and related variations), "cost utility analysis" (and related variations) and "incremental cost effectiveness ratio" or "ICER". We limited our search to systematic literature reviews only; narrative reviews, commentaries, editorials, grey literature sources and original research were not eligible for inclusion. Conference abstracts or posters were eligible for inclusion if they described findings from a systematic literature review and no published manuscript was available.

Screening and Data Extraction

Screening of titles/abstracts was carried out in the DistillerSR platform (Evidence Partners Incorporated; Ottawa, Canada) by a single reviewer with a second reviewer screening up to 15% of excluded articles as a quality check. The same approach was used for full-text screening.

Data extraction of included studies was carried out in a pre-specified template by a single reviewer and validated by a second reviewer. Data were extracted on publication characteristics, key themes, methodologies used to incorporate concepts of equity into CEA and limitations in existing CEA approaches. Eligible articles were evaluated based on the specific methodology for incorporating health equity concepts into CEA. Expected methodologies included (but were not limited to): modifications to the current CEA approach (modified CEA: mCEA), including specific methodologies such as distributional (DCEA) or extended (ECEA) CEA methodologies; structured approaches such as multi-criteria decision

analysis (MCDA); equity-focused methodologies including equity-based weighting and other approaches including mathematical programming (see Table 1).

Results

Study Eligibility

The database searches returned 283 records and after removing duplicates and applying publication and language limitations, 129 unique records were screened at the title/abstract level. Twelve reviews underwent full-text review, and 8 reviews were ultimately included in our umbrella review. Figure 3 summarizes the literature selection procedure.

Description of Included Publications

The 8 SLRs included in our review represent a total of 289 studies (205 unique publications) and 6 unique methodologies, which included: DCEA (7 articles[5,8,15–19]), ECEA (6 articles[5,15–19]), MCDA (5 articles[9,15–18]), equity-based weighting (3 articles[5,16,18]), mathematical programming (2 articles[16,18]) and stratified CEA (1 article[18]) (Table 2). The majority of included articles discussed a number of methodologies, with only 2 articles focused specifically on 1 methodology (DCEA[8] and MCDA[9]). Several demographic or socioeconomic topics were included to define "equity criteria" in the included studies and included age (discussed in 5 articles[8,9,15–17]), gender/sex (4 articles[5,8,15,17]), socioeconomic status (4 articles[8,15–17]), geography (3 articles[8,15,17]), race/ethnicity (2 articles[8,15]), disease severity (2 articles[15,16]) and social justice (1 article[18]). Among the included articles, one focused on the concept of health equity in low- and middle-income countries (LMICs),[17] one summarized economic analyses that included health equity as part of public health policies[5] and one focused exclusively on European HTAs.[9] One study[19] was an update of a previously published review.[16] The approaches discussed in the eligible articles can be broadly categorized as to whether direct approaches in CEAs were employed or recommended (eg, equity weighting or DCEA) or whether a more indirect approach was taken/recommended (eg, expanded MCDA). Direct approaches were those that incorporated considerations

Table 1 Summary of Direct and Indirect Approaches to Incorporating Equity in CEA

Modelling Approach			Description
Direct Approaches[a]	**Modified CEA**	Distributional CEA	Focuses on the distributions of health effects (health gains/disease burden) associated with health care interventions at both population (societal) and subgroup (eg, sex, race/ethnicity) levels as well as the distribution of health opportunity costs per equity-relevant sociodemographic variables and per disease categories. Decision-making considers the trade-offs between improving total population health and reducing unfair health inequality.
		Extended CEA	Assesses the distribution of both health benefits and financial risk protection benefits and considers financial benefits of policies considering out-of-pocket payments in certain geographies
		Stratified CEA	Cost-effectiveness results are stratified by population group and variability between these groups is then considered
	Equity-based weighting		Proposes to assign weights to value outcomes based on equity criteria that consider fairness for subpopulations within the evaluated cohort.
	Mathematical programming		Mathematical programming can be used to create an "outcome maximization framework" that incorporates any constraints imposed by considerations of fairness. The economic analysis is then conducted with and without the constraints and the trade-off between efficiency and the constraints is calculated as part of the CEA.
Indirect Approach[b]	**MCDA**		Involves a structured and rational decision-making approach informed by evidence on multiple criteria that uses quantitative scores to choose, rank, select options

Notes: [a]Direct approaches incorporate considerations of health equity into the cost-effectiveness analysis, [b]Indirect approaches assess health equity considerations in parallel with the cost-effectiveness analysis.
Abbreviations: MCDA, multi-criteria decision analysis; CEA, cost-effectiveness analysis.

MEDLINE/ search
(n=129)

Title screening
(n=129)

Excluded (n=110)
- Clinical guideline (n=2)
- Disease- or condition-specific article (n=84)
- Economic focus (n=14)
- Incorrect topic (n=3)
- Paediatric population (n=7)

Abstract screening
(n=19)

Excluded (n=7)
- Disease- or condition-specific article (n=2)
- Economic focus (n=2)
- Incomplete results (n=1)
- No equity-specific methods discussed (n=2)

Full-text screening
(n=12)

Excluded (n=4)
- Economic focus (n=1)
- Insufficient information (n=1)
- No equity-specific methods discussed (n=2)
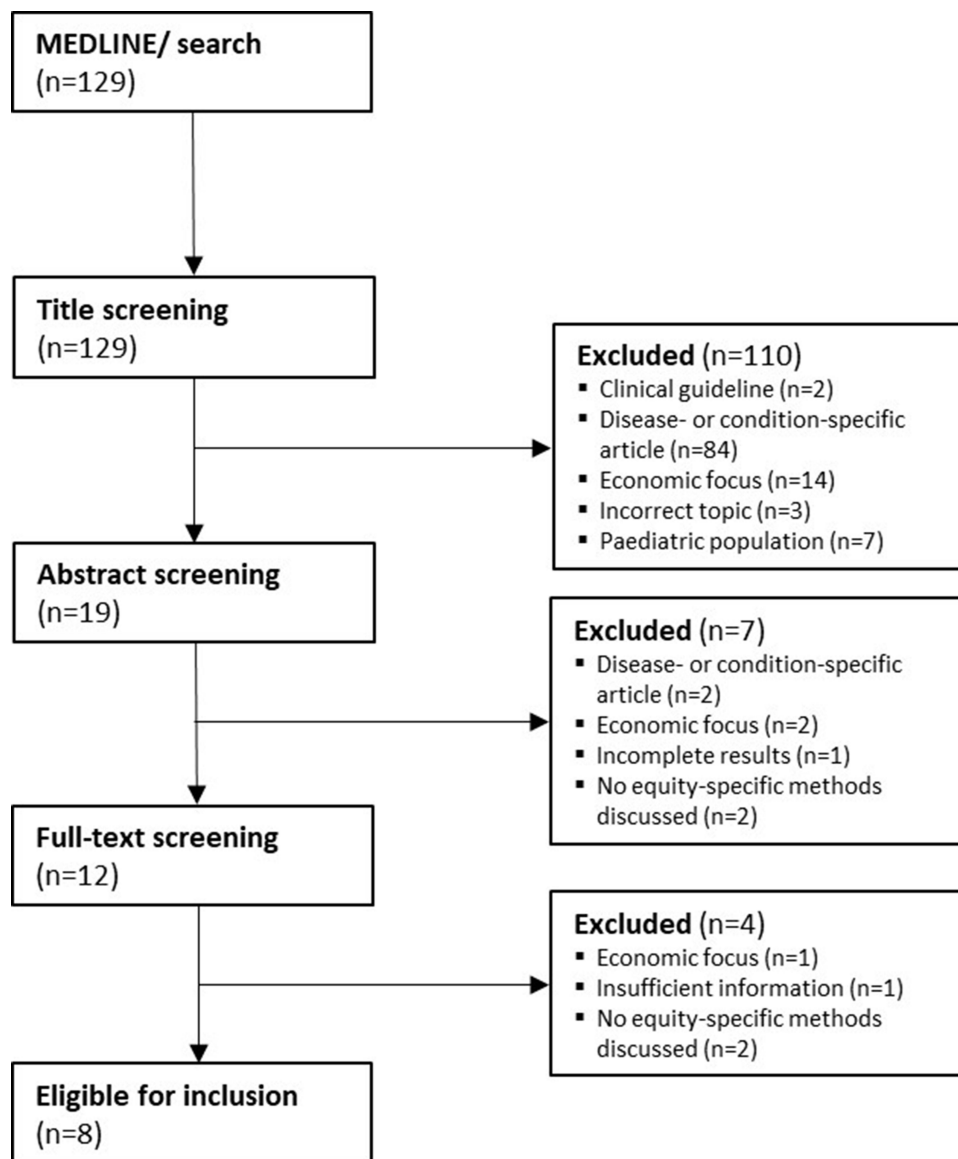
Eligible for inclusion
(n=8)

Figure 3 PRISMA diagram detailing literature search results and subsequent review process.

of fairness or equity into the analysis, as opposed to indirect approaches, where these considerations were evaluated in alongside the economic analysis.[18]

Methodological Challenges

The included SLRs identified several methodological barriers to the full and easy incorporation of equity concepts into CEA. Among these are ethical considerations, the proper selection of criteria and/or variables for meaningful measurement, methods for relating and interpreting inequity measures and how to manage inherent biases that may exist when using parameters specific to certain groups.

Dukhanin et al [18] discussed the concept of ethical considerations in depth in their study. Ethical considerations tend to reflect the challenge in determining what criteria are ethically important to address in CEA, and determining what ethical commitments are required. Several studies in their review[4,20,21] discuss difficulties relating to the multiplicity and conceptual complexity of these ethical considerations.[18] These concerns are discussed in the context of the challenges of establishing a normative basis for social justice considerations and the disconnect between how ethicists and

Table 2 Summary of Eligible Articles

Author(s)	Included Studies (n)	Study Aim(s)	Economic Evaluation Approaches Discussed	Equity Criteria Discussed	Main Themes and Conclusions
Patikorn 2023[19]	52	To gain a better understanding of when ECEA and DCEA analyses should be conducted to provide policymakers with relevant and meaningful evidence	ECEA, DCEA	NR	Three key characteristics were identified which indicated when equity-informative CEAs should be conducted: (1) the existence of health inequity in health systems, (2) local stakeholders' awareness of the need to address health inequity, and (3) effectiveness of health interventions in reducing health inequity
Steijger 2023[8]	18	To identify empirical studies on DCEA in healthcare and outline the challenges and limitations	DCEA	Age, SES, gender/sex, geography, race/ethnicity	In-depth analysis of the usefulness of DCEA showed that the availability of data, unfamiliarity with the methodology among policymakers and the difficulties in estimating differences between socioeconomic groups are significant challenges. Conclusions: the main aims going forward should be to improve data availability for future studies, including: linking and expanding databases, enriching existing registries, supporting new DCEA efforts and strengthening national information systems.
D'Ausilio 2022[9]	28	To determine how and in what European countries "equity" has been included in HTAs beyond the standard CEA approaches	MCDA	Age	The inclusion of equity concepts is recommended in both CEA and preventative programs, especially in areas such as cardiovascular medicine, oncology, diabetes, vaccination and falls. Conclusion: despite a societal preference for reducing inequalities in health, the current economic evidence rarely specifies equity in the evaluation of HTAs. Methodological challenges regarding establishing equity weighting, how to apply these weights and a general lack of consensus are barriers to broad incorporation of equity into CEA.
Ward 2022[16]	68	To review analytical methods that enable the incorporation of equity concerns within economic evaluation	DCEA, ECEA, EBW, MCDA, MP	Age, SES, disease severity	This comparative study suggests that equity evaluation methods can be broadly characterized as either modifying the current evaluative approaches to include preference weights or specifically measuring the impact of a healthcare policy decision on health outcomes across equity-specific strata. Conclusions: EBW methods are likely the most intuitive and flexible approach to address the former while DCEA is most suitable to address the latter.

Yang 2022[17]	12	To investigate how much health inequalities have been considered in economic evaluation of health interventions in LMICs, and what demographic or socioeconomic characteristics were used to define equity relevant subgroups	DCEA, ECEA, MCDA	Age, SES, gender/ sex, geography	Focusing on vaccination programs and cervical cancer screening in LMICs, the use of wealth quintiles or household income as strata for economic analyses, although these variables are fluid and can be unpredictable, weakening the value of estimates of distributional effects of a given intervention. Conclusions: equity concerns have begun to be incorporated into policy-makers' decisions, with the efforts in LMICs largely focused on vaccination and women's health. A variety of methods have been utilized in these efforts.
Avancena 2021[15]	54	To catalog and describe published applications of equity informative CEAs	DCEA, ECEA, MCDA	Age, SES, gender/ sex, geography, race/ethnicity, disease severity	An audit of currently utilized methods found that equity impact analysis (with and without equity weighting) was most commonly utilized. A base-case cost-effectiveness model found that when distributional effects were incorporated into the analysis, 78% of studies found that the value associated with intervention in question increased. Conclusions: while the number of equity-informative CEAs is increasing, the methods used are highly variable and questions remain regarding the appropriate use of equity-informative CEAs, although the inclusion of equity concepts seems to have the ability to shift the value of interventions.
Dukhanin 2018[18]	26	To describe methodological solutions suitable for integrating social justice concerns into economic evaluation and describe the challenges that those solutions face	DCEA, ECEA, EBW, MCDA, MP, stratified CEA	Social justice	In reviewing several methodologies, challenges were identified. Determining a normative base for evaluations, determining the relative importance of criteria, combining criteria appropriately and evaluating trade-offs were identified as the most pressing challenges. Conclusions: while viable options for incorporating social justice concepts into CEA exist, the associated challenges must first be addressed prior to widespread incorporation of any of these methods into CEA.

(*Continued*)

Table 2 (Continued).

Author(s)	Included Studies (n)	Study Aim(s)	Economic Evaluation Approaches Discussed	Equity Criteria Discussed	Main Themes and Conclusions
Lal 2018[5]	31	To assess current approaches to inclusion of equity in economic analysis of public health interventions and to recommend best approaches and future directions	DCEA, ECEA, EBW	Gender/sex	An examination of cost-effectiveness using socioeconomic position to stratify patients found that a major weakness is the reliance on disaggregated data and the lack of guidance regarding interpretation of size differences in inequality that were noted. Conclusions: as the use of economic evaluations to investigate health inequality is a relatively new field, more work is required before the interpretation of findings can be broadly accepted and applied.

Abbreviations: DCEA, distributional cost-effectiveness analysis; NR, not reported; SES, socioeconomic status; HTA, health technology assessment; CEA, cost-effectiveness analysis; MCDA, multi-criteria decision analysis; ECEA, extended cost-effectiveness analysis; EBW, equity-based weighting; MP, mathematical programming; LMICs, low- to middle-income countries.

economists differentially prioritize public health, ie, there is little guidance on how to reconcile what is "good" for public health from an ethical standpoint with what may make economic sense. The authors argue that, without a consensus basis for the starting point, there will be ongoing difficulty in determining how to incorporate social justice concerns most effectively into priority setting.[18]

Accompanying the questions surrounding the appropriate starting point for policymakers and other stakeholders is the challenge of identifying which variables are most appropriate to be considered as "equity criteria" to identify equity concerns for a targeted population and how to combine them accurately and meaningfully. The sheer number of potential variables and the general novelty of the associated concepts present practical challenges to researchers, as does the challenge of combining data from several broad sources, which may lead to a loss of information (ie, due to excessive "noise") or a watering-down of results, such that the information gathered may not be meaningful for these assessments.[18] Indeed, in their review, Lal et al[5] note that a main weakness of current efforts is that, in studies with two or more interventions, there is often a reliance on disaggregated data. The counterpoint, however, suggests that incorporating more variables allows for a more nuanced perspective.[8] Steijger et al[8] have noted an additional challenge, noting that in low- and middle-income countries (LMICs), data collection is often accomplished through surveys administered in irregular time intervals, which presents challenges in comparing the data with that collected from other countries but also threatens to render the data inconsistent and out of date once it is ready for analysis. These authors also note that the differences in the ease of collection of relevant data in LMICs compared with higher income countries can lead to invalid or meaningless comparisons, which further marginalizes patients in LMICs. This is an excellent example of the challenges of establishing uniform data collection and the impact that variability can have on vulnerable populations. Yang et al[17] also identified this as a potentially important factor and have advocated for the introduction of a stable measure that would be useful in LMICs but also in richer countries as well. In their review, they suggest that DCEA methods, which utilize a single measure to show trade-offs between equity and cost-effectiveness, may provide a solution to this problem, as it represents a method to create uniformity in health equity analyses.

The third methodological challenge facing stakeholders is determining the best methodology to employ to increase wider adoption of equity considerations in healthcare decision-making. The included SLRs advocate for a number of different methodologies, each with their own benefits and drawbacks. As Ward et al[16] note, all methods have different requirements for anticipated trade-offs between equity and efficiency, with some (eg, DCEA, MP) explicitly capturing the trade-offs as opportunity costs, whereas others (eg, ECEA) are not flexible enough to adequately capture general social preferences. The observation is, however, that populations tend to be willing to engage in these trade-offs and exchange efficiency for equity – a change from the largely utilitarian approach of the traditional CEA, which remains objective.[15] Weighting is emerging as a preferred method for addressing these trade-offs, with different weights assigned to variables based on societal acceptance and tolerance. Despite this, Avancena et al[15] note that consensus on the best methods for estimating weights remains elusive, with variations focused on the patients themselves ("person trade-off"), society ("benefit trade-off") or a combination of both. As Dukhanin observed, all proposed methods have their own design for trade-offs, with each method sacrificing a component of the other, further complicating the search for consensus.[18] Equity-based weighting is suggested as a viable method, as it uses a direct trade-off between efficiency and weighting criteria and quantifies the result in cost-effectiveness units, making it directly applicable for decision-making.[18] DCEA has likewise been suggested as the preferred method,[8] as it is the only one that can compare interventions' impact on health equity through a full range of scenarios. Regardless of methodology, social value judgements are required to balance inequality with tolerance levels. The question thus is: how much is a society willing to give up to seek health equity across different groups in the society?

A final methodological challenge exists in the interpretation of inequity measures in metrics such as morbidity or mortality. Ward et al[16] note that lower levels of education, income and living standards are associated with increased morbidity/mortality,[22,23] while Lal et al[5] observed that the lower life expectancy and higher comorbidities in lower income groups often result in lower health gains than those noted in a higher income population when the same intervention is applied, and have potentially higher ICERs when these factors are calculated as part of a CEA. The sum of these observations is that, as morbidity and mortality are tied to socioeconomic position in the modelling of health outcomes, decision makers must remember that the use of subgroup-specific parameters such as lower life expectancy

and higher morbidity rates may result in the cost-effectiveness of a given intervention being inconsistent when applied to different subpopulations. Finally, the issue of bias can be added to this discussion. As noted previously, Steijger et al[8] highlighted that the sometimes-sporadic collection of data observed in LMICs can lead to further SEP-related bias in predictions, especially when data is missing (ie, not collected). Further, they caution against the potential bias created when the uptake of new treatments is increased in disadvantaged groups, in which case the existing utilization will effectively underestimate the benefits to health inequity.

Operational Challenges

Operationally, the incorporation of health equity concepts in decision-making requires processes to allow consistently and reliably measure data, meaningfully incorporating factors surrounding healthcare funding and opportunity costs and determining the most appropriate parameters for measurement in economic studies.

Accurate data measurement related to health equity to be incorporated in decision-making is a complication of the relative newness of the field and a lack of consensus regarding which of several scales is most appropriate. Among the 18 primary studies included in the review by Steijger et al,[8] 8 different scales were used. These scales included the Atkinson index, Gini index, Kolm index and Theil index, plus indices based on the equally distributed equivalent, the slope index of inequality and the relative index of inequality.[8] Of these scales, usage ranged from 44.4% at the maximum to 5.6% at the minimum. Reviews by Lal,[5] Ward[16] and Yang[17] similarly reported the use of one or several of these equity indices, of which the Atkinson index was the most reported in Ward's review,[16] along with the slope index. The fact that these scales were used in widely varying numbers across 4 reviews (which include 129 studies) underscores the lack of consensus or consistency when collecting such data. The consequent difficulty in completing a meaningful analysis with this widely varying data remains a barrier to expanded incorporation of equity measures in CEA and one that will require a concerted effort from researchers to reach consensus.

Differing approaches to healthcare funding structures have led to concerns with respect to opportunity costs and the trade-offs related to resource allocation. Avancena et al observed this in their review, suggesting that most equity-informative CEA methodologies fail to consider the distribution of healthcare opportunity costs.[15] They noted that some healthcare initiatives or treatments may be displaced by higher spending that results from weighing outcomes among the terminally ill or severely sick. Dukhanin et al[18] similarly observed difficulties with the current methodologies when it comes to addressing opportunity costs. They found that both direct and indirect approaches must address the trade-offs to be considered in the face of scarce healthcare resources. They surmise that those who may benefit from a given intervention may be more easily identifiable than those who may bear the opportunity cost itself. They also caution that the opportunity costs themselves may differ when considered through economic or social justice lenses. Ward et al[16] addressed these concerns directly in their review and determined that DCEA and EBW were the methods most able to capture the trade-offs associated with the measurement of opportunity costs. They did mention, though, that other methodologies did not preclude the incorporation of opportunity costs into their methodologies. Regardless, Avancena et al highlighted the importance of this issue in noting that widening health inequities inevitably impose negative consequences on society,[15] with research suggesting that health inequities may be responsible for hundreds of billions in excess medical care and lost productivity.[24,25]

Perhaps, the biggest operational challenge to incorporating health equity into CEA is not the lack of consistent measurement scales or adequate funding trade-offs but is the lack of consensus on the most appropriate parameters for research studies, as those studies are the main drivers of change. The use of weighting is the central factor for consideration in this context, as establishing weighting methodologies often depends on context-specific value judgements, thus complicating the objective goals of CEAs. Avancena,[15] Dukhanin,[18] Lal[5] and D'Ausilio[9] all specifically found that consensus amongst researchers on the most appropriate weighting methods was elusive, with multiple weighting methods used in the studies in their respective reviews, with Dukhanin et al[18] citing several authors who underscored the lack of a comprehensive and high-quality evidence base necessary to define accurate measurements.[20,21,26–29] Avancena et al[15] noted at least 3 different methods for calculating QALY weights and broadly characterized methods as concerned with either "person trade-offs", "benefits trade-offs" or "conjoint analysis". Dukhanin et al catalogued several approaches to weighting.[18] In their review, they discuss Bleichrodt et al,[30] who

proposed a rank-dependent QALY model where groups or individuals are assigned a rank or weight in the evaluation of their QALY profile. Baeten et al[31] suggested assigning extra weights for those worst-off, which would enable comparisons at the level of disadvantaged populations. Finally, Dukhanin et al[18] echoed concerns initially voiced by Bleichrodt et al[30] over the trade-off between generalizability and practical applicability when choosing weighting strategies, as weights are particularly dependent on value judgements that may be context specific.[31,32] Ward et al[16] examined the issue of weighting in different methods in their review and found that there were concerns – especially for EBW and MCDA – that much research is still required and that the consensus extends beyond the best weighting methods to use to the actual methods to elicit this information. They cite the example that while consensus exists for some factors, such as the societal preference for greater weight for health gains amongst younger populations and those with more severe illness, the actual size of the weights used for these populations differ significantly across studies.[33,34] As Ward concludes, such differences allude to the difficulties in generalizing and estimating societal preferences that will "remain valid across an array of important healthcare evaluation factors, such as the evaluation setting, the disease area, and the type of intervention being evaluated, notwithstanding the ever-evolving state of social opinion".[16] Clearly, significant challenges remain.

Potential Solutions

Several solutions to the discussed challenges were offered by the authors of the reviews in our umbrella review, many of which are direct attempts at addressing the drawbacks identified in the various reviews and include explicitly quantifying health equity criteria and their relative importance; considering all options for willingness-to-pay thresholds, trade-offs, multiple sets of parameters and opportunity costs; considering the implementation of specific methodologies (eg, MCDA, ECEA) due to their potential benefits; and devising methods for addressing the general uncertainty of incorporating equity into CEA. While none of these solutions can be considered a failsafe, they represent a positive step in the process. The majority of authors in our review identified the need for explicit, quantifiable criteria (eg, weighting). Dukhanin et al, in contrasting direct and indirect methodologies, note a distinction between these two categories in that direct methods would require explicit quantification of social justice considerations, which would be incorporated into any economic analysis.[18] This is presented as potentially superior to indirect methods where, although variables would need to be specific and quantified, their inclusion after an economic analysis may not be optimal. In contrast, methods such as DCEA, which uses a single measure to evaluate trade-offs can be useful and a valuable way to facilitate transparency and consistency.[17] Lal et al[5] underscore this point when referencing a study by Asaria et al,[35] who state that transparency about value judgements and the use of sensitivity analyses to evaluate alternate scenarios represent a desired methodological approach.

Avancena et al expand on the concept of specific, quantifiable metrics by suggesting that the adoption of concrete thresholds for metrics such as cost-effectiveness.[15] Specifically, they suggest that thresholds be determined based on criteria that are important and relevant to decision makers. They cite the example that in the United Kingdom, a higher threshold is used for interventions at end of life or for rare conditions such as congenital anomalies, where treatments may be more expensive due to the small market and/or high investment costs.[15,36] They further cite The Netherlands, where three severity-based thresholds based on "proportional shortfall" principles are used to determine cost-effectiveness.[37,38]

Of the several methodologies evaluated in the reviews, the various authors made several recommendations. Yang et al[17] recommended ECEA and DCEA to decision makers (especially those in LMICs), as both are fundamentally based on the traditional CEA approach but extend the methods by applying social inequality aversion preference metrics after estimation of costs and benefits for a given subgroup. Dukhanin et al[18] likewise found benefit in ECEA methods, while Patikorn et al[19] identified three key characteristics that identify when to conduct equity-informative CEAs: the existence of health inequity within health systems; the awareness of local stakeholders to the need to address health inequity, and when analyzing the effectiveness of health interventions in reducing health inequity. While Dukhanin et al[18] acknowledge that ECEA methods have thus far been limited to objective criteria only (income quintile, geographic location, sex, ethnicity, etc).,[3,39] they suggest the fact that the definition and selection of subgroups depends largely on equity and distributional issues proposed by analysts,[39] suggests that ECEA could easily be adopted as a methodology with a suitable potential benefit.[18] Avancena

et al[15] conversely recommend MCDA methods as a valid tool for "working around" the inherent limitations of traditional CEAs, particularly when considering elements such as equity.[1,40,41] Dukhanin et al[18] echo this recommendation, although they qualify their comments that measurement is crucial for direct methods but also for variations of MCDA such as quantitative MCDA. Their central comment is that while all methods require some type of data source, direct methods and quantitative MCDA should be held to standards more in line with the rigors associated with traditional CEA methods.

Discussion

Health equity – the pursuit of elimination of differences in health status between populations or groups that result from economic or social conditions – represents an important element of CEA that has historically received insufficient attention from decision makers. Despite this lack of full integration into CEA, much work has been completed on potential methods for and elements important to the incorporation of concepts such as health equity into CEA. We completed an umbrella review of previous SLRs examining the inclusion of health equity concepts in CEA to catalogue the challenges and limitations of the current climate and to encapsulate the barriers that remain in place today. We identified several methodological and operational challenges to the incorporation of health equity into current CEA approaches and summarized several potential solutions offered by various authors. While barriers remain – predominantly the hesitation from the community when it comes to upending the current methodologies and infrastructure in the name of progress – there is much to be optimistic about regarding the future of CEA.

Our review of reviews identified the main challenges facing those who aim to include health equity concerns in CEA, which can be summarized broadly into three questions: 1) where to start? 2) what to measure? and 3) how to measure it? The first question reflects the need for a common, normative baseline to serve as a starting point in any analysis. As discussed, this baseline is rooted in ethical considerations, ie, which criteria are ethically important to address as part of a CEA? A normative basis on which to base CEA represents an ideal circumstance and one that may in fact be elusive, given that different societies value different criteria. Baltussen & Niessen[41] describe the challenge in this, as even in a circumstance where a base framework is agreed upon, translating that into a meaningful set of criteria is very difficult. Dukhanin et al[18] note that a framework composed of too few criteria will not be exhaustive and will risk ignoring important variables, whereas too many criteria risk overly complicating the analysis and creating overlap.[4] As such, the main challenge for researchers and policymakers is to reach a consensus on which factors are important to include in a baseline, and how to modify those factors when applying them to different jurisdictions (with different sets of societal values) in a way that allows for a population-appropriate approach to CEA but one that can be reasonably compared across different jurisdictions. Unfortunately, there is little guidance on how to determine what is "good" for public health from an ethical perspective while still making sense from an economic perspective. One suggestion is to use the modified versions of the current CEA approach that are used for the analysis to also provide a normative baseline.[18] For example, DCEA methods could be used to create inequality quantiles and use those quantiles to create estimates of opportunity costs and outcome impact. This of course relies on the ability to adequately identify these quantiles in different populations. Similarly, stratified CEA methods have been suggested, where the stratification would be defined based on the population in question and used to consider the cost-effectiveness of an intervention in separate analyses.[18] These seem to be reasonable approaches, although they still require a consensus on which method(s) are most appropriate and valid, and there still exists the discrepancies created by having different methodologies provide the baseline, ie, this does not solve the problem of variable baselines and only threatens to increase heterogeneity by having different "starting points" for analyses. Clearly, there is much work to be done to identify a broadly acceptable baseline that adequately incorporates health equity concerns. As such, an ongoing and concerted effort from stakeholders will be required to see this goal come to fruition.

Assuming that a consensus could be reached on what to use as the normative basis for equity-conscious CEA, the next challenge for analysts and decision makers is to determine exactly what to measure. Specifically, there are questions regarding which variables to consider as part of CEAs and how to accurately measure these variables. Cheng et al[42] suggest that current barriers to more equitable HTA development are highlighted by gaps in existing data, specifically a lack of data to better measure heterogeneity in different patient populations and lack of transparency and interoperability in existing data sources. The issue of how to measure data was raised as a concern by Steijger et al[8] who, in their

review of LMICs, noted that data collection in these countries is often intermittent and inconsistent with respect to intervals between rounds of data collection. As such, there is a concern that data is out of date before it can be fully analyzed, which renders that data essentially worthless in the context of larger comparisons. Furthermore, data in these environments is often collected via surveys, which presents challenges in comparing that data with data from other counties that may be collected in a more objective manner.[8] Populations in LMICs, while already at a disadvantage due to their socioeconomic challenges, are further marginalized by the lack of a meaningful comparison to higher income countries. As such, those in greater need, instead of receiving disproportionate assistance – a key of the health equity concept itself – are at a greater disadvantage and could potentially fall further behind. The question becomes: are the rich getting richer while the poor get poorer? If so, that is the antithesis of health equity.

Which variables are used in these theoretical comparisons represents another important component of the "what to measure" question. To properly address health equity imbalances, one must first establish metrics for determining health status, in order to determine who may actually be at risk of unequal distribution of healthcare. The question becomes one of metrics. Are metrics such as household income or socioeconomic position (SEP) the most relevant for establishing criteria or strata in an analysis? Are demographic statistics more relevant as strata? Avancena et al[15] identified over 25 variables that could be used to help stratify populations, including demographics, perspectives, specific metrics and types of equity analysis available. Lal et al[5] took a more direct approach, using SEP as their main qualifier and evaluating equity concerns on that basis. Others promote weighting as the most viable option for measuring change and effect.[5,9,15,18] Again, consensus proves elusive in this as well, as while there may be agreement that equity-based weighting of factors is an appropriate approach, there is little to no agreement on what metrics to which weights should be assigned, or how those weights should be assigned. Some authors have suggested a rank-dependent approach to the QALY, where groups are ranked prior to QALY calculation and analysis.[30] Others suggest weighting based on socio-economic factors, such that those who are socioeconomically disadvantaged may receive proportional treatment in an analysis. The trade-off between generalizability and practicality when choosing weighting variables remains, however, as many weighting decisions are based on context-specific value judgements that can differ based on societal preference.[31,32] Despite these societal differences, there is general agreement that younger populations and those with more severe illness should receive preferential weighting, although this represents another area where there is conceptual consensus but not practical consensus. Societies agree on who among them may require preferential treatment but rarely agree on the degree of this preferential treatment. In general, the parameters and the data granularity to be measured for inclusion in DCEA will depend on several factors such as the equity concern, disease type, healthcare system and geography.[43]

Should HTA stakeholders one day agree on a baseline and on metrics, there remains the challenge of determining exactly how to measure these factors. Our review included recommendations for both direct and indirect methods for incorporation of equity concerns into CEA although, as with the other factors in this topic, there is little to no consensus. While objective methods such as mathematical programming receive some attention[16,18] and equity-based weighting is associated with challenges outlined above, modified versions of the traditional CEA methods and well-known methods such as MCDA receive the bulk of the attention. The latter has been proposed by several authors,[15,18] although there are drawbacks to that approach that are limiting. In a previous review,[2] we examined which of the current methods were best suited to broadly incorporate expanded concepts of value in CEA (of which health equity is central tenet) and found that while MCDA methods are regularly recommended, they have gained little traction, in part due to its overly mechanistic nature[44,45] and its tendency to ignore opportunity costs.[44,46,47] Conversely, modified CEA methods – as a general concept – have gained traction, due mainly to their similarity to current methods and the relative ease with which they can be incorporated into current approaches. As we commented on previously,[2] mCEA methods continue to be in favor with HTA agencies mainly out of convenience and due to a lack of a proven, viable alternative. In addition, the infrastructure in place and decades of published precedent make for an environment where fundamental change, while potentially necessary, is difficult to enact. Among the mCEA methods, ECEA is most easily able to incorporate objective demographic criteria that would allow for the creation of subgroups based on relevant socioeconomic variables. ECEA has been suggested as the method most likely to successfully incorporate expanded value definitions[48] and two of the reviews in our review likewise promoted its use to address health equity concerns,[17,18] as it is well suited to incorporate

equity and distributional variables.[39] Previous real-life equity informed DCEAs demonstrated how extended assessment frameworks evaluating additional value elements for new technologies can provide a more comprehensive valuation of their impact (eg faricimab in diabetic macular oedema from a UK societal perspective,[49] prevention and control strategies for rheumatic fever and heart disease in India,[50] gene therapy equity in sickle cell disease in the United States[51]).

The ongoing challenge, however, is the buy-in from stakeholders, which remains elusive. The mere fact that our review of reviews identified 5 different methodologies that have received significant support as viable options reflects the lack of consensus on this matter and underscores the difficulties in bringing all stakeholders together under an agreed-upon umbrella. The ISPOR Task Force has led the way in advocating for methods to incorporate expanded concepts of value in CEA and will likely need to continue this work to include the specific concept of health equity. However, other organizations such as ICER have recommended again using quantitative equity-informative economic evaluation and propose the use of deliberative processes to understand structural aspects of the health systems that should be addressed to ensure disparities are not worsened by the introduction of new technologies. With continued research in this area and ongoing dialogue between patients, clinicians and decision makers, the movement towards understanding the impact of health equity considerations in the assessment of new technologies will advance. The development of ECHTA (checklist to guide equity considerations in HTA) is a right step towards this direction.[52] For it to be successful, however, will require a concerted effort and buy-in from all relevant stakeholders. A continued lack of buy-in, however, threatens to widen the gap between those who have and those who have not by perpetuating the marginalization of certain groups in HTA decision-making.

Our study is not without limitations. We excluded any articles that focused on a specific disease, condition or treatment intervention, as our intention was to provide a broad overview of the concepts surrounding health equity in HTA. A consequence of this could be that we inadvertently excluded articles that may have provided relevant information; however, given that we are reviewing the topic from a conceptual perspective, we feel that excluding disease-specific articles was appropriate. We also limited our review to systematic reviews published since 2013. We felt that an umbrella review was the best approach to gather and examine what we anticipated to be a broad range of evidence. The exclusion of original research may be interpreted as a limitation; however, we felt that including systematic reviews provided us with an opportunity to include a greater volume of original research, as each review itself collected data generated from original research. Similarly, the potentially variability in criteria used by each systematic review included in our study may be criticized as introducing heterogeneity into our review; however, the goal of our umbrella review was to gather as much evidence as possible and provide a conceptual interpretation of this data. Gathering systematic reviews that each used a systematic approach to eligibility – regardless of the differences or similarities in those criteria – provide a comprehensive pool of data and information and helps us to meet our goal of a broad, conceptual summary of the current evidence.

Conclusions

Our review of reviews examined concepts discussing the incorporation of health equity concerns into CEA methods. We found much work on this topic but sparingly little consensus on the many areas of consideration. Establishing a normative baseline for defining and measuring equity concerns and collection of equity-relevant data will not only improve the evidence base for equity-informed CEA but also encourage calls for greater availability and accessibility of healthcare data across a wider patient group representation. Real-world data has a key role in shaping knowledge around health equity considerations. Likewise, while several methodologies have been recommended, there is no consensus on the approach that best incorporates health equity factors into CEA in a reproducible way for decision-making across technologies and disease areas. Modified CEA methods are currently at the forefront of these methodological recommendations; however, this is likely due to their similarities to the current CEA methodologies. Much work is required to continue the research in this important area and a substantial effort by all stakeholders involved will be required to see this topic move forward.

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