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Hidden Costs: the ethics of cost-effectiveness analyses for health interventions in resource-limited settings

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Abstract

Cost-effectiveness analysis (CEA) is an increasingly appealing tool for evaluating and comparing health-related interventions in resource-limited settings. The goal is to inform decision-makers regarding the health benefits and associated costs of alternative interventions, helping guide allocation of limited resources by prioritizing interventions that offer the most health for the least money. Although only one component of a more complex decision-making process, CEAs influence the distribution of healthcare resources, directly influencing morbidity and mortality for the world's most vulnerable populations. However, CEA-associated measures are frequently setting-specific valuations, and CEA outcomes may violate ethical principles of equity and distributive justice. We examine the assumptions and analytical tools used in CEAs that may conflict with societal values. We then evaluate contextual features unique to resource-limited settings, including the source of health-state utilities and disability weights; implications of CEA thresholds in light of economic uncertainty; and the role of external donors. Finally, we explore opportunities to help align interpretation of CEA outcomes with values and budgetary constraints in resource-limited settings. The ethical implications of CEAs in resource-limited settings are vast. It is imperative that CEA outcome summary measures and implementation thresholds adequately reflect societal values and ethical priorities in resource-limited settings.

Keywords

cost-effectiveness analysis; ethics; resource-limited settings; equity

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Introduction

Cost-effectiveness analyses (CEA) have become an increasingly appealing and powerful tool for evaluating and comparing alternative health-related interventions (Dhaliwal, Duflo, Glennerster, & Tulloch, 2011; Eichler, Kong, Gerth, Mavros, & Jonsson, 2004; Jamison, Breman, & Measham, 2006). The purpose of CEAs is to provide information to decision-makers on the efficiency of different interventions for achieving a specific health outcome, helping guide allocation of finite resources and prioritize interventions that offer the most health for the least money (Gold, Siegel, Russell, & Weinstein, 1996; Jamison, Breman, ARMeasham, & et. al., 2006; WHO, 2005). The ethical complexity of incorporating costs into clinical decisions or healthcare policy have been explored in resource-rich settings (Brock, 2004; Pinkerton, Johnson-Masotti, Derse, & Layde, 2002; Williams, 1992); CEA outcomes may violate ethical principles of equity and distributive justice (Braveman & Gruskin, 2003; Mshana et al., 2007; Rawls, 1971; Whitehead, 1992). Despite growing interest in CEAs among researchers and policymakers (Baltussen, 2006), given poor baseline health, economic instability, and the role of external donors in driving allocation of scarce resources, the ethical incongruences of CEAs with societal values may be especially pertinent in resource-limited settings.

Ethics, broadly, are the values or ideals that we perceive as an appropriate standard or code to govern behavior and actions. Equity is one such value, emphasizing the quality of fairness within this larger code of ethics; distributive justice refers to the equitable distribution of scarce resources. Although the expectation is not that policymakers will make healthcare resource-allocation decisions based solely on the outcome of a CEA model, it is imperative that we appreciate the potential conflict between CEA outcomes and societal values as these models are incorporated into decision-making processes. Failure to do so may result in distribution of scarce dollars towards interventions that do not reflect priorities of implementing partners.

In this paper, we briefly review the basics of CEA modeling and its intended use. We then examine the assumptions and analytical tools used in CEAs that may conflict with societal values, including how currently applied CEA metrics may clash with values of equity and distributive justice. We then evaluate contextual features unique to resource-limited settings including the universality of health state utility or disability estimates and the challenge of establishing cost-effectiveness thresholds in light of economic uncertainty and given the role of external donors. Finally, we evaluate methodological opportunities to help align interpretation of CEA outcomes with objectives, values, and budgetary constraints for policymakers in resource-limited settings.

CEA Basics

CEAs are a form of economic analysis in which interventions (e.g. drugs, devices, screening programs) are compared to each other in terms of both costs and outcomes. The primary outcomes for CEAs capture benefits incurred by interventions in terms of both health quantity (years of life) and health quality gains (reduced morbidity). The traditional metric of evaluation used in CEAs in resource-rich settings is the quality-adjusted life year (QALY)

–a composite measure that represents disease or disability burden associated with a given health state, ranging from 0 (death equivalent) to 1 (perfect health) (Drummond, Sculpher, Torrance, O'Brien, & Stoddart, 2005). Conversely, the disability-adjusted life year (DALY) is the preferred metric for use in resource-limited settings as it is based on disability weights derived from surveys administered internationally by the Global Burden of Disease, Injuries, and Risk Factors Study (GBD) (Salomon et al., 2012). Disability weights, quantified on a scale from 0 (full health) to 1 (death), are used to calculate years of life living with disability and combine with years of life lost due to disability to generate the DALY estimate, accounting for both disability and mortality (WHO, 2005).

Whether generating QALY or DALY estimates, the final summary measure in CEAs is frequently an incremental cost-effectiveness ratio (ICER), representing comparative benefits and costs between two comparators by linking survival, health-related quality of life, and resource consumption into a single unit. For the purposes of prioritizing interventions, ICERs can be compared to one another or to an *a priori* defined threshold of cost-effectiveness (WHO, 2005). Although just one component of a complicated decision-making process, CEA outcomes can be used to help justify expansion or elimination of health programs, with the overarching goal of optimizing the allocation of finite resources targeted towards population health improvement.

The setting-specific quality of CEA metrics

The "quality" component of the QALY is derived from utility surveys conducted almost exclusively in resource-rich settings. Truncated attainable health (i.e., persons not able to reach "perfect" health) and poorer baseline health complicate the extension of utility weights derived from resource-rich populations to resource-limited settings. If health status utility is considered only as it relates to attainable health, then health utility will necessarily differ between resource-rich and resource-limited settings (Bleichrodt, Herrero, & Pinto, 2002). Expectations of health and the value associated with health gains are different between resource-rich and resource-limited settings (Fryback & Lawrence, 1997; Ottersen, Mbilinyi, Maestad, & Norheim, 2008). Use of a common utility weight that does not consider differential life expectancy and health expectations may inappropriately categorize the utility decrement of an illness based on resource-rich setting values, distorting the potential benefit of interventions when applied to resource-limited settings (Fryback & Lawrence, 1997).

The DALY is able to avoid some of these biases and is thus preferred over the QALY for use in resource-limited contexts. Nonetheless, the DALY is still subject to setting-specific limitations. The ordinal rank of disability weights from the GBD may be relatively stable across countries (Salomon et al., 2012; Ustun et al., 1999), but the universality of their specific valuations has been debated (James & Foster, 1999; Jelsma, Chivaura, Mhundwa, De Weerdt, & de Cock, 2000). How an individual experiences disability depends on societal accommodation of persons with that disability such that functional status and social participation of two people with the same diagnosis may vary widely in different contexts (Mont, 2007). Setting-specific utility and disability weights are critical in order for CEA outcomes to accurately reflect health status values.

Concerns of Equity and Distributive Justice in CEA: is the QALY/DALY to blame?

Prioritization of health interventions based on DALY aversion may be at odds with societal values of equity. CEA-guided resource allocation relies on the assumption that resources should be distributed to maximize overall population health (*Making choices in health: WHO Guide to Cost-effectiveness Analysis*, 2003). This utilitarian approach of maximizing quality gains and averting disability has inherent tensions with the ethical principles of equity and distributive justice; maximizing population health could neglect particular societal preferences related to distribution of health benefits (Bitton & Eyal, 2011; Bobinac, van Exel, Rutten, & Brouwer, 2012; Mshana et al., 2007; Ottersen et al., 2008; Ubel, DeKay, Baron, & Asch, 1996; Ubel et al., 2000). Although derived from inverted scales of health utility and disability, the QALY and DALY may suffer similar ethical pitfalls in both resource-rich and resource-limited settings such that discussion of equity and distributive justice in CEAs can apply broadly to analyses based on either metric (Brock, 2004).

One distinction between the QALY and DALY is rooted in the ability of the DALY to apply age-based weights to life-years of similar quality (Murray & Lopez, 1996). By over-valuing the socially productive life-years, the age-weighted DALY has been criticized for assigning value to individuals for the societal and economic gains of others rather than for individual health benefit (Brock, 2004). Others maintain that age-weighting is necessarily equitable because every person has the potential to live through all ages, thereby leveling the weights over an individual lifetime and permitting age-based prioritization (Murray & Lopez, 1996; Tsuchiya, 1999). According to policymakers in many resource-limited settings, age, along with other considerations such as severity of disease, is often the main criterion when determining resource distribution (Baltussen, Stolk, Chisholm, & Aikins, 2006; Kapiriri, Arnesen, & Norheim, 2004; Kapiriri & Norheim, 2004; Ottersen et al., 2008).

While a distributive justice framework prioritizes resource allocation to the sickest persons in a society, irrespective of the likelihood and magnitude of expected improvement, a DALY-aversion approach prioritizes the sickest persons only if they are likely to achieve the greatest health gains (Nord, 2015; Ubel et al., 2000). For example, in terms of CEA calculus, a health intervention that provides disability reduction of 0.4 to 0 is equivalent to one that provides reduction from 0.9 to 0.5; both interventions reduce disability by 0.4. However, an egalitarian approach would prioritize the program that improved the status of a very sick person (disability weight 0.9 at baseline) to moderate health, over the program that improved a moderately sick person (disability weight 0.4 at baseline) to perfect health. This ‘realization of potential’ or ‘fair chances’ argument advocates that permanently disabled or chronically ill persons should have a fair chance of receiving health-improving interventions despite having truncated attainable health (Nord & Johansen, 2014; Nord, Pinto, Richardson, Menzel, & Ubel, 1999; Williams, 1997). Importantly, not all scenarios offer identical health gains; the scenario in which the choice is between disability reduction of 0.4 to 0 versus 0.9 to 0.6 complicates the fair chances argument. Selecting the intervention that prioritizes the very sick would do less good, thereby violating ethical principles of beneficence, but selecting the larger disability reduction for the healthier person violates principles of equity.

This conflict exemplifies that, ultimately, the sole objective of averting DALYs may not align with a society's valuation of the severely ill, or persons with chronic illness or disability (Pinkerton et al., 2002).

Analyses based on utility and disability weights, typically developed by health professionals and the non-disabled, may undervalue the years of life of the disabled or chronically ill and favor interventions that prevent or cure illness rather than enhance the lives of persons living with disabilities (Brock, 2004; Fox Rushby, 2002; Mont, 2007). A systematic review of HIV/AIDS interventions in Africa concluded that programs focused on preventing incident HIV infection are considerably more cost-effective than treatment and care for the already infected (Creese, Floyd, Alban, & Guinness, 2002). However, strictly utilitarian and human capital approaches to cost-effectiveness that ignore pre-existing heath inequities, disease-specific stigmatization, and socio-political priorities may perpetuate health disparities by valuing healthy privileged persons with higher social capital over already sick or disadvantaged groups (Pinkerton et al., 2002). This ethical consideration should demand particular attention when evaluating interventions in resource-limited settings.

Demonstrating the conflict with accepted societal norms, district and regional health planners in Tanzania prioritized interventions that supported persons with the lowest life expectancy over interventions that maximized the number of life-years (Ottersen et al., 2008). The strength of a society's concern for disease severity, or 'vertical equity', has been studied empirically by asking subjects how much more utility would have to be gained (or disability averted) for an intervention targeted at healthier individuals to be preferred over an intervention targeted at sicker individuals (Dolan, 1998; Nord, 2015; Nord & Johansen, 2014). Representing the point at which a society would permit less cost-effective interventions that address diseases of greater severity, this higher utility value demonstrates the conceptual divergence between CEA outcomes and the objective of distributive justice – a concept that must be considered when interpreting CEA models.

The ethically indifferent CEA thresholds

Cost-effectiveness thresholds are wrought with ethical conflicts. Thresholds define a dollar-per-QALY-gained or dollar-per-DALY-averted (i.e., ICER) cutoff of acceptability. Selecting an appropriate and defensible CEA threshold is challenging and cutoffs are often chosen arbitrarily (Hirth, Chernew, Miller, Fendrick, & Weissert, 2000). Although failure to achieve a cutoff does not automatically dismiss a program, understanding the limitations of how thresholds are established is relevant when incorporating the CEA outcome into the resource-allocation decision process.

Even if an intervention meets a cost-effectiveness threshold, the ICER value does not necessarily reflect the bottom-line expense associated with implementation; a cost-effective intervention for a highly prevalent disease could exceed the entire budget, whereas a less cost-effective intervention that exclusively targets a subpopulation (i.e., pregnant women) may be financially feasible. Ultimately, choosing the more cost-effective intervention may not be compatible with health budgets (Birch & Gafni, 2006; Sendi & Briggs, 2001).

Decision rules using willingness to pay (WTP) per QALY/DALY may provide additional flexibility compared to defining a single ICER value threshold. WTP allows decision-makers to consider the decision context and incorporate societal value-of-life preferences. WTP assigns a monetary value to a package of health goods or benefits. Determining the WTP is frequently based on preference elicitation methods that employ hypothetical scenarios asked of the general population or policymakers. Unfortunately, much like the health state utilities and disability weights, preference elicitation exercises are often limited to surveys from resource-rich settings and may not reflect WTP in resource-limited settings.(Shillcutt, Walker, Goodman, & Mills, 2009)

The wealth of the surveyed population substantially influences the projected WTP. WTP increases with wealth, but this increase is not proportional, highlighting complexities in preference formation (Dolan, Metcalfe, Munro, & Christensen, 2008; Shillcutt et al., 2009). In fact, the value of health is often positively correlated with the current state of health within a population (King, Tsevat, & Roberts, 2004). Together, these observations imply that in worse states of health, commonly experienced by populations in resource-limited settings, health may hold less value than in wealthier and healthier countries. Essentially, this relationship produces a lower WTP per QALY gained / DALY averted in populations with lower baseline health. As health, and possibly even health literacy increase, so too will the setting-specific WTP thresholds.

The WHO advocates decision criteria based on regional gross domestic product (GDP) as an alternative to WTP thresholds. According to the CHOICE guidelines (*CHOosing Interventions that are Cost-Effective*), there are three categories of cost-effectiveness based on GDP: highly cost-effective are interventions that cost less than per capita GDP; cost-effective are interventions that are between one and three times per capita GDP; and interventions that cost more than three times per capita GDP are not considered cost-effective (WHO, 2005). This method is based in economic definitions of regional affordability, defining ceiling ICERs according to national productivity. However, the approach may violate notions of equity and ignore valuable contributions individuals make beyond livelihood.

GDP estimates from resource-limited settings are notoriously inaccurate, due primarily to the challenges of unrecorded economic activity and economic instability that may selectively inhibit production of goods and services, driving down GDP approximations (Jerven, 2013). Use of GDP thresholds may mask intra-region variation. The WHO region classification that groups countries based on estimates of burden of disease may not capture all relevant country-level realities, generating state-specific cost-effectiveness ceiling ratios that ignore variation between countries within a given WHO region, and fortifying inequalities in health between nearby but financially diverse settings. For example, per capita GDP in South Africa is estimated as 11,300 US dollars compared to 900 US dollars in nearby Malawi (*The World Factbook*, 2013); however, both are within WHO African region E, with an associated per capita GDP threshold of $2,154. In practice, regional GDP estimates may conceal country-specific economic complexities, and may create an artificially high (or artificially low) threshold for acceptability (Jerven, 2013). Ultimately, the approach may undercut access to interventions for economically unstable regions where GDP is unpredictable and

may be measured as artificially low. Comparing new interventions to already accepted interventions may be a more acceptable approach than the GDP comparison. However, this too is problematic as the choice of comparators can influence whether a program appears cost-effective or not (Johannesson & Meltzer, 1998).

Even regionally-adjusted GDP estimates ignore the role that external donors play in driving health programming implementation (Shiffman, 2006). Health programs and interventions in resource-limited settings are frequently sponsored by donor agencies with their own disease- or population-specific objectives (Kapiriri et al., 2004; Kapiriri & Norheim, 2004; Kapiriri, Robberstad, & Frithjof Norheim, 2003; Lasry, Carter, & Zaric, 2011; Reichenbach, 2002). For example, from 2003 through 2012, the Global Fund disbursed nearly $550 million to Malawi for HIV-related activities (*Global Fund Disbursements by Region, Country and Grant Agreement (in USD equivalents)*, 2012). This enormous influx of funds earmarked for HIV creates two parallel systems that Ministry of Health officials need to evaluate – HIV-related interventions and non-HIV related interventions. Cost-effectiveness thresholds that fail to consider the role of donors create a false paradigm for evaluating and comparing interventions. The role of external donors is also relevant when considering the decision-making autonomy. For example, money reserved for HIV prevention efforts cannot be spent on unrelated health programs even if they are evaluated as being more cost-effective. Relevant to earlier arguments regarding ethical challenges of CEA-focused decisions, earmarked funds may or may not adhere to the ethical principles of prioritizing the severely ill. It is important to consider spending restrictions, be they due to budget constraints or donor agencies, when evaluating the utility of CEAs and how they influence resource allocation in resource-limited settings.

Interpreting CEA outcomes in resource-limited settings - proposed solutions to inequity

As CEA studies gain traction in driving resource-allocation and priority setting in resource-limited settings, a thorough evaluation of the ethical implications of how these model outcomes are interpreted is warranted (Jamison, Breman, ARMeasham, et al., 2006; *Making choices in health: WHO Guide to Cost-effectiveness Analysis*, 2003; WHO, 2005). We have explored concerns of distributive justice and equity that may be imperfectly captured in CEA outcomes. We also considered how CEA thresholds create controversial cutoffs that may not account for the economic and funding environment in which resource-allocation decisions are made in resource-limited settings. Issues including maximum attainable health, the limited applicability of utility values of health established in resource-rich settings or the debated universality of disability weights, and the role of external donors in driving funding allocation are a few of the elements that complicate interpretation of CEA outcomes in resource-limited settings.

The relevance of CEAs in contributing to resource-allocation decisions may hinge on explicitly integrating equity concerns into the methods, associated outcomes, and the ultimate decision to implement an intervention (Sassi, Archard, & Le Grand, 2001).

Researchers have proposed several methodological approaches to incorporate societal considerations of equity and other ethical shortcomings into CEAs.

1. Cost Value Analysis

Finally, cost value analysis adjusts results from cost-effectiveness analyses to reflect society-specific degrees of concern for prioritization of disability or disease severity (Nord, 2015). In a QALY-based analysis this is done by compressing mild to moderate utility states towards the upper end of the utility scale such that individual gains for the sick are preferred over gains for the comparatively healthy. This methodology could be applied to DALY-based analyses for application in resource-limited settings by compressing disability weights at the lower end of the scale to overvalue the aversion of more severe disability. A setting-specific severity gradient adjustment can generate a graded willingness to pay per QALY or DALY that may better represent distinct socio-political priorities.

2. Equity Weights and Social Welfare Function

Severity preferences and health-potential considerations may be addressed in CEAs by the use of equity weights and social welfare functions (Nord et al 1999, Pinkerton 2002) (Bleichrodt, 1997; Ubel et al., 2000). In this approach, researchers must analyze the strength of a society's preference for health equity to inform weighting of interventions that benefit particular groups over others (Dolan, 1998; Wagstaff, 1991). There is no consensus regarding which distribution concerns should be incorporated into health intervention prioritization (Bobinac et al., 2012). The Guidance for Priority Setting in Health Care (GPS-Health) proposes a checklist of criteria to be considered for equitable priority setting of interventions that aim to maximize health, minimize inequities, and protect against prohibitive costs of illness including: severity of disease, realization of potential, past health loss, socioeconomic status, geographical area of living, gender, race, ethnicity, religion, sexual orientation, economic productivity, care for others, and catastrophic health expenditures (Norheim et al., 2014). Unfortunately, it is difficult to elicit stable preferences, complicating implementation of equity-weighted QALYs or DALYs for inclusion in CEAs (Johri & Norheim, 2012).

3. Mathematical Modeling

Mathematical programming can compare opportunity costs associated with alternative policies and health interventions/programs (Cleary, Mooney, & McIntyre, 2010). The goal of this methodology is to maximize health gains while incorporating equity constraints that can ensure prioritization of specific populations. While attempting to represent the equity/efficiency tradeoffs associated with alternative health resource allocation options to optimize equity and efficiency, such modeling is limited by the challenges in quantifying the opportunity costs associated with competing equity constraints. Quantifying these costs will be critical to future research efforts, and is addressed in part by the rank-ordered approach of multi-criteria decision analysis.

4. Multi-Criteria Decision Analysis

Multi-criteria decision analysis may be a promising approach to quantify and weight potentially competing priorities of efficiency (i.e., cost-effectiveness) and equity (Baltussen & Niessen, 2006; Baltussen et al., 2006; Johri & Norheim, 2012). This method overlays a conceptual framework on complex decisions as a means to establish preferences between options, applying criteria for priority setting based on individual preferences. By doing so, multi-criteria decision analysis tools explicitly consider local values and judgments, creating a rank-ordering of program priorities. Multi-criteria decision analysis and formal economic evaluations using ICERs are distinct from one another in that multi-criteria decision analysis incorporates mathematical modeling of existing evidence that devises priority setting and weights with consideration of opportunity costs and recognition of fixed budgets, through techniques such as program budgeting and marginal analysis (Thokala, 2011). Multi-criteria decision analysis has been used successfully in the health resource allocation process of resource-limited settings (Jehu-Appiah et al., 2008). However, there are important limitations to multi-criteria decision analysis, most notably that the preference ranking method may not address the feasibility or complexity of a given intervention. To date, evaluations of multi-decision criteria have focused on elements that are amenable to quantification, including cost-effectiveness and disease severity (Baltussen et al., 2006; Jehu-Appiah et al., 2008).

The objective of these approaches is to rectify the disconnect between CEA outcomes and societal preferences by combining the complexity of implicit decision criteria (i.e. values of equity and distributive justice) with the concrete health status and cost criteria of CEA models. In the absence of universal utility or disability weights or severity adjustment factors, researchers and policymakers can employ these methods to generate setting-specific interpretations of cost-effectiveness results, informing difficult resource allocation decisions. Unfortunately, adjusting for equity in a utilitarian model by applying weights to one individual or group will unavoidably detract from another; existing methodological accommodations do not account for the opportunity costs associated with resource allocation in the context of finite funds. Explicitly addressing these tradeoffs will be a critical next step in CEA design and outcome evaluation. One objective of future research should focus on end-user application of CEA outcomes – adapting the often-sought universality of models to permit utilization by policy makers. Next steps for equity weights may include an extension of GPS that considers the health disability as well as the system- and population-specific priorities in terms of disease burden and the characteristics of the social groups that a given intervention targets (Norheim et al., 2014). Eventually, these priorities could be assigned weights based on a given community or country's *a priori* values, with subsequent integration into models. Multi-criteria decision analyses may establish tools that translate CEA outcomes to robust estimates of costs and coverage to establish scalability and feasibility of the rank-ordered cost-effective interventions. Ultimately, these methodological advances could permit intervention implementation – transforming the desirable "universal" CEA outcomes that focus on comparability and uniformity, to setting-specific appropriate applications.

The ethical implications of CEAs in resource-limited settings are vast. While many considerations may overlap with resource-rich settings, ethical shortcomings of CEAs particular to more resource-limited settings and the methodological interventions needed to address them require ongoing discussion. Although only one component of a larger, more complex decision-making process, CEAs stand to influence the distribution of healthcare resources that directly influence morbidity and mortality for the world's most vulnerable populations. Alongside cost-effectiveness, considerations of equity, feasibility, and affordability are all essential dimensions of the resource-allocation decision making process (Johri & Norheim, 2012). CEAs stand to make meaningful contributions to the much-needed efficiency gains in healthcare. However, communities will incur substantial, albeit hidden, costs if policymakers and researchers fail to consider the economic and societal ramifications associated with allocating scarce resources in a manner that does not reflect the ethics and priorities of implementing partners.

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