**Title:** Incorporating equity concerns in cost-effectiveness analyses: A systematic literature review

**Running title:** Incorporating equity concerns in cost-effectiveness analyses

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All authors contributed to the concept and design, drafting and critical revision of the manuscript. The acquisition of data and the provision of study materials was contributed to by TW and AML. Further, AS, AML and RMM provided supervision to TW throughout the manuscript development. AS assisted with attaining funding through TWs PhD grant and TW contributed to the analysis and interpretation of data alongside administrative support.

**Abstract**

**Word count:** 511

**Introduction**

The aim of this study is to review analytical methods that enable the incorporation of equity concerns within economic evaluation.

**Methods**

A systematic search of PubMed, Embase and EconLit was undertaken from database inception to February 2021. The search was designed to identify methodological approaches that are currently employed to evaluate health-related equity impacts in economic evaluation studies of health care interventions. Studies were eligible if they described or elaborated on a formal quantitative method used to integrate equity concerns within economic evaluation studies. Cost-utility, cost-effectiveness, cost-benefit, cost-minimisation and, cost-consequence analyses, as well as health technology appraisal and budget impact analysis, alongside any relevant literature reviews, were included. For each of the identified methods, summaries of the scope of equity considerations covered, the methods employed and their key attributes, data requirements, outcomes, and strengths and weaknesses were provided. A traffic light assessment of the practical suitability of each method was undertaken, alongside a worked example, applying the different methods to evaluate the same decision problem. Finally, the review summarises the typical trade-offs arising in cost-effectiveness analyses and discusses the extent to which the evaluation methods are able to capture these.

**Results**

In total, 68 studies were included in the review and methods could broadly be grouped into equity-based weighting (EBW) methods, extended cost-effectiveness analysis (ECEA), distributional cost-effectiveness analysis (DCEA), multi-criteria decision analysis (MCDA), and mathematical programming (MP). EBW and MP methods enable equity consideration through adjustment to incremental cost-effectiveness ratios, whilst equity considerations are represented through financial risk protection (FRP) outcomes in ECEA, social welfare functions (SWFs) in DCEA, and scoring/ranking systems in MCDA. The review identified potential concerns for EBW methods and MCDA with respect to data availability, and EBW methods and MP with respect to explicitly measuring changes in inequality. The only potential concern for ECEA relates to the use of FRP metrics which may not be relevant for all healthcare systems. In contrast, DCEA observed no significant

concerns but relies on the use of SWFs which may be unfamiliar to some audiences and requires societal preference elicitation. Consideration of typical cost-effectiveness and equity-related trade-offs highlighted the flexibility of most methods with respect to their ability to capture such trade-offs. Notable exceptions were trade-offs between quality of life and length of life, for which we find DCEA and ECEA unsuitable, and the assessment of lost opportunity costs, for which we find only DCEA and MP to be suitable. The worked example demonstrated that each method is designed with fundamentally different analytical objectives in mind.

**Conclusions**

The review emphasises that, not only are some approaches better suited to particular decision problems than others, but also that methods are subject to different practical requirements and that significantly different conclusions can be observed depending on the choice of method and the assumptions made. Further, to fully operationalise these frameworks, there remains a need to develop consensus over the motivation for equity assessment, which should necessarily be informed with stakeholder involvement. Future research of this topic should be a priority, particularly within the context of equity evaluation in health care policy decisions.

**Highlights**

We undertake a systematic search of relevant economic databases to identify methodological approaches that are currently employed to evaluate health-related equity impacts in economic evaluation studies of health care interventions.

The review adds to the published literature by systematically comparing the scope of equity considerations covered, alongside the methods, outcomes, data requirements, and strengths and weaknesses of each of the identified methods, with a focus on their practical application in economic evaluation of health care policy; a traffic light system is used to assess the suitability of each method for use in cost-effectiveness analysis and HTA.

We demonstrate that, not only are some approaches better suited to particular decision problems than others, but also that methods are subject to different practical requirements and may confer significantly different conclusions depending on the assumptions made.

## 1. Introduction

The World Health Organisation describes equity as "the absence of avoidable or remediable differences among groups of people, whether those groups are defined socially, economically, demographically, or geographically", and strongly advocates the reduction of health care inequities[1]. Importantly, health care inequities may be thought of as the unfair and avoidable differences in health status seen within and between regions or groups of people. Within this context, health care equity evaluation relates to the measurement of health-related outcomes and health care resource use distribution within a population, with the goal of establishing whether or not patients have equal opportunity to attain their full potential for health[2].

Social determinants of health such as level of education, income, and geographical location, are examples of unfair differences that contribute to health outcome variability. Globally, lower levels of education, income and living standards, are all factors associated with increased morbidity and mortality[3,4]. Over recent years, Western societies have seen a significant evolution in health care policy alongside substantial advancement of medical technologies. However, these improvements are not necessarily correlated with reductions in healthcare inequality. For example, the study by Mackenbach et al. (2016) suggests that, in Europe, whilst the absolute inequalities gap has narrowed, the relative inequality gap has widened, with 82% of the countries assessed demonstrating increased relative inequality in survival between the periods 1990-94 and 2005-09, in both men and women (i.e., whilst the differences in life expectancy between population subgroups has declined, the distribution of life expectancy within subgroups has become more unequal)[5]. Policies specifically employed to reduce these inequalities have commonly been focused outside of health care policy, aiming instead to address the underlying social causes. However, the introduction of specific health care policies, or the reimbursement of specific treatments, have the potential to inadvertently impact the distribution of health to the disadvantage of certain groups in society, and so their effects on equitable health distribution also need to be studied. An example of such an effect has consistently been observed amongst colorectal screening initiatives, where there exists substantial differences in screening uptake by socioeconomic status, with the least deprived observing significantly higher rates of uptake[6].

In Europe, healthcare systems are based on the Beveridge or Bismarck models (or an amalgamation of the two), with the former providing government-backed (single-payer) health care for all citizens, funded through general taxation, and the latter providing health care through both government-backed and private institutions, with

funding coming from employer and employee payments[i] [7,8]. In the majority of these countries, as in many others around the world, the (formal or informal) evaluation of new health care policies is typically based on principles of efficiency, where the health benefits of a particular policy or treatment are weighed against the costs of introducing that policy or treatment[9]. Those that are deemed cost-effective based on a particular threshold or formula are reimbursed, and those that are not deemed cost-effective are not reimbursed. However, there exist no formal analytical frameworks from which to assess the equity impacts of health care policy decisions, beyond general discussion by the groups appointed to design the policy guidelines at the relevant stages of evidence appraisal. With an increasingly heterogeneous patient population, alongside a treatment landscape that is moving further towards targeted medicine, the need to understand whether the introduction of a new health care policy is likely to increase or decrease existing health inequities is becoming increasingly important[10].

Sassi et al. (2001) were the first to systematically review equity measures for economic evaluation, adopting relatively broad search strategies and research objectives[11]. Eleven years later, the systematic review by Johri et al. (2012) explored whether cost-effectiveness analysis could integrate equity concerns into Health Technology Assessment (HTA) and identified two obstacles that have impeded their use in decision making to date: the multiplicity of equity components and values, and the lack of a widely accepted normative source on which to ground equity value choices[12]. Over subsequent years, Dukhanin et al. (2018) reviewed methodological solutions that could enable the integration of social justice concerns with economic evaluation, and Lal et al. (2018) reviewed equity measurement methods that could be used specifically in the context of public health policies[13,14]. Most recently however, Avancena et al. (2021) described applications of equity-informative cost-effectiveness analyses[15]. The study focused on exploring the applications and settings of the various methods and examined how the introduction of an equity dimension affected cost-effectiveness value outcomes, and subsequently, the favourability of the interventions under assessment and the conclusions of the comparison.

The objectives of this study are to identify and summarise the methodological approaches that are currently employed to evaluate health-related equity impacts in economic evaluation studies of health care interventions, focusing on their practical suitability for use in economic evaluation of health care policy, and the systematic comparison of the scope of equity considerations covered, alongside the methods, outcomes, data requirements, and strengths and weaknesses of each of the identified methods.

[i] Typically, unemployed citizens or those in poverty cannot pay and receive limited healthcare coverage; exceptions exist where governments opt to fund healthcare for those in impoverished circumstances.

## 2. Methods

### *2.1. Search strategy*

The review has been conducted according to the PRISMA-P (Preferred Reporting Items for Systematic reviews and Meta-Analyses Protocols) guidelines[16]. Systematic multi-string search strategies were developed using a combination of text words and index terms in line with eligibility criteria to retrieve studies from published literature. Searches were performed in PubMed (Medline), Embase and EconLit from database inception to February 2021. The review protocol was registered online with PROSPERO where further details may be found[17]. A summary of the search strategies can be found in **Supplemental Appendix A**.

The search was designed to identify methodological approaches that are currently employed to evaluate health-related equity impacts in economic evaluation studies of health care interventions. Studies were eligible if they described or elaborated on a formal quantitative method used to integrate equity concerns within economic evaluation studies. Cost-utility, cost-effectiveness, cost-benefit, cost-minimisation and, cost-consequence analyses, as well as health technology appraisal and budget impact analysis, alongside any methodological studies describing these types of analysis were included. Literature reviews were also considered if they met the eligibility criteria. Eligibility criteria were developed based on five previously published literature reviews with similar search strategy themes[11-15]. An overview of each of the previously published literature reviews can be found in **Supplemental Appendix B**. Analyses which only presented results stratified by relevant equity strata (akin to subgroup analysis) were excluded. Editorials, case studies, letters, conference abstracts, phase I and phase II clinical trials, newspaper articles, book sections, patient and expert opinion or commentary, social media and papers describing adaptations of existing economic models (unless the adaptation relates to the incorporation of equity considerations) were excluded.

Titles and abstracts of the identified studies were screened by one reviewer and checked for accuracy by a second reviewer. Those that did not meet eligibility criteria were excluded. Subsequently, all data were extracted using a standardised data extraction template in Microsoft Excel. Data were extracted by one reviewer and checked for accuracy and completeness by a second reviewer. Any discrepancies between reviewers were resolved by consensus or referral to a third reviewer.

### *2.2. Review framework*

For each of the identified methods, information pertinent to the following review components was extracted and summarised:

A. An overview of each method (including summary of the scope of equity considerations covered, methods employed and their key attributes, data requirements, outcomes, and strengths and weaknesses);
B. A traffic light assessment of the practical suitability of each method for use in economic evaluation studies and HTA;
C. An illustration of the typical trade-offs observed in cost-effectiveness analyses, and discussion around the ability of the identified methods to accommodate equity considerations arising from these trade-offs.

We describe each of the review components in more detail below.

*A. Overview of methods*

We initially summarise the methods and measures used to capture inequity of health status or outcomes and resource use. In a similar vein to Williams et al. (1997), we choose to focus on the assessment of health outcomes, as opposed to equity in process or allocation of health care resources[18]. In this sense, the equitable distribution of resource or health care access are considered as precursors to achieving equitable distribution of outcomes and, given equitable distribution of outcomes is a goal of most healthcare systems, this is where we focus our assessment. Importantly, and with this in mind, when we refer to assessment of the extent to which equitable outcome distribution is achieved, this is considered within the context of patients' having equal opportunity to attain their full potential health. We report on the scope of equity considerations covered, alongside the methods, outcomes, data requirements, and strengths and weaknesses of each method. In this context, health status or outcomes are typically measured by primary clinical effectiveness measures (e.g., mortality or life years), and/or preference-based measures of health (e.g., quality-adjusted life years [QALYs]).

Importantly, we distinguish between methods that are designed to modify outcomes to account for societal preferences for inequality (e.g., methods that re-weight QALY outcomes) and those that can explicitly measure the impact of a health care policy decision on the distribution of health status or outcomes. Further, given that equitable distribution of health care is typically measured by specific summary measures of inequality or equity,

such as the Gini coefficient, or social welfare functions (SWFs) such as the Atkinson index or the Kolm index, we summarise the measurement metrics used within each of the identified studies in a supplemental appendix[19-22]. We also summarise the reported applications of each of the methods in the identified studies, including a summary of the equity dimensions investigated in each of the studies.

### *B. Traffic light assessment of practical suitability*

We evaluate each of the identified methods within the context of economic evaluation, including their practical suitability for inclusion within economic evaluation studies and HTA frameworks, and different settings (e.g., high- versus low-income countries). We identify three key elements for consideration:

- **Informational and analytical requirements:** What data and analytical requirements and constraints are relevant to the method?
- **Generalisability:** Can the method be applied consistently across heterogeneous applications and populations?
- **Interpretability:** Are the methods and results accessible to stakeholders and do they provide definitive conclusions?

Analytical requirements cover the information/data requirements and practical analytical constraints associated with the methods. With the evolution of modelling methods and the increasing availability of relevant data, the potential complexity of analyses has increased. Whilst analytical complexity may be required to fully realise the outcomes of a particular decision problem, computationally onerous or data intensive methods may not alter conclusions and may result in a lack of transparency and interpretability, deterring widespread adoption. Therefore, it is important that trade-offs between analytical complexity and the requirements of the equity evaluation objectives are considered.

Methods may be considered generalisable if they can be consistently applied and produce comparable evaluations across heterogeneous applications (e.g., different types of intervention) and populations (e.g., different disease areas)[23]. This is particularly important within individual healthcare systems and settings, where the specific objectives and structures of economic analyses can differ, and consequently, where a particular equity evaluation approach may be better suited than another.

Finally, the ease with which the methods and results are accessible and interpretable by a range of stakeholders is important and alludes to the importance of evaluating method complexity and transparency. Conventional cost-effectiveness analysis applies equal weight to the costs and benefits of all individuals and seeks to maximise the total health within a population. One merit of the current economic evaluation framework is the ability to derive definitive conclusions from analyses, such that one intervention, amongst competing interventions, is identified as the optimum intervention, with results typically presented as incremental cost-effectiveness ratios (ICERs) evaluated at appropriate willingness-to-pay (WTP) thresholds[24]. Whilst these metrics are now well established, the introduction of an equity dimension offers the potential for use of measurement metrics that are less familiar and/or more complex in nature. Subsequently, the extent to which equity methods can be readily integrated within current economic evaluation frameworks, provide transparent measurement of changes in outcome inequality, and produce clear conclusions, is assessed. In this respect, preference is given to methods that require no (or little) additional output beyond that of current cost-effectiveness frameworks, alongside methods that are able to explicitly identify an optimum policy amongst all evaluated policies. Additional detail surrounding the assessment of individual components is provided in **Supplemental Appendix C**.

### *C. Equity considerations and typical cost-effectiveness trade-offs*

We attempt to illustrate typical trade-offs that might be evaluated across the spectrum of economic evaluations in health care, for example, the case in a budget constrained system where the loss of alternative health care interventions is traded off against the chosen intervention. Consistent with the published literature on health care inequality and the rhetoric from health care providers and policy makers, we make reference to health care access, health care experience and health outcomes as the key components of health inequalities[25-28]. We subsequently consider whether the equity evaluation methods can accommodate equity considerations arising from the trade-offs described.

Subsequently, we illustrate an application of each of the methods with a worked example evaluating the cost-effectiveness of a hypothetical cancer screening programme in a UK setting. In brief, we compare the addition of universal and targeted cancer screening reminders to a conventional cancer screening program and evaluate outcomes across socioeconomic/deprivation quintiles. Patients are initially invited for screening with the resultant uptake favouring the least deprived. Three scenarios are evaluated:

- Universal reminder: A one-off reminder is sent to all patients that have not yet been screened (increasing uptake by 5%);
- Targeted reminder: Multiple reminders are sent to all patients in the two most deprived socioeconomic quintiles that have not yet been screened (increasing uptake by 15% in the two quintiles targeted);
- Current standard of care (SoC): No screening reminders.

Each strategy directly influences the uptake of screening, which subsequently influences the rate of diagnoses and treatment, and ultimately, total costs and quality adjusted life expectancy (QALE). A complete description of the evaluation methodology is provided in **Supplemental Appendix D**. We aim to demonstrate practical considerations for each of the methods and to highlight the drivers of evaluation conclusions, with such consideration providing further insight into the overall scope of each of the methods. An economic evaluation comparing each of the strategies is undertaken, with preferences for inequality reduction across socioeconomic quintiles captured.

## 3. Results

### *3.1. Search overview*

The search identified 2,410 citations, after excluding duplicates. During the screening of titles and abstracts, a further 2,172 citations were excluded. Upon full-text assessment of the remaining 238 articles, 46 studies met criteria for inclusion. An additional 22 studies were identified through screening of the bibliographies of the most relevant literature reviews that were identified in the search (**Figure 1**). Amongst included studies, methods for evaluating equity in economic evaluations could broadly be grouped into five categories[2]: 1) equity-based weighting (EBW) methods (n=25); 2) distributional cost-effectiveness analysis (DCEA) (n=20); 3) extended cost-effectiveness analysis (ECEA) (n=17); 4) multi-criteria decision analysis (MCDA) (n=6); and 5) mathematical programming (MP) (n=2).

Of the 25 studies describing EBW methods, 17 studies described methods only[29-45], whilst only one was an applied study[46]; the remaining seven studies described simplified or hypothetical case study examples designed to illustrate the use of the underlying method[47-53]. The methodological case studies and the applied study were limited to European (n=6)[46,48,50-53] and Australian (n=2)[47,49] settings; two studies evaluated pharmacological therapies for breast cancer[48,50], three studies looked at multiple diseases and interventions[46,51,52], one looked at optimal versus non-optimal treatment in schizophrenia patients[49], one looked at ICU versus general ward care[47], and the final study evaluated the impact of vaccinating for varicella zoster and herpes zoster[53]. DCEA was used in 20 studies, 18 of which were applied studies or methodological case studies and were conducted in UK (n=8)[54-61], Ethiopian (n=2)[62,63], Tanzanian (n=2)[64,65], South Korean (n=2)[66,67], Dutch (n=1)[68], Malawian (n=1)[69], Brazilian (n=1)[70] and US (n=1)[71] settings; six evaluated cancer or cardiovascular screening interventions[58-61,66,67], five evaluated multiple interventions across multiple disease areas[54-56,69,70], one study evaluated the introduction of a rotavirus vaccination[63], and the remainder evaluated single pharmacological interventions (n=1)[65], general improvements in health care provision (n=2)[62,64] or lifestyle interventions (n=3)[57,68,71].

In total, 15 of the 17 ECEA publications were applied studies, all of which were undertaken in African (n=7)[72-78], Asian (n=6)[79-84], or African and Asian (n=2)[85,86], settings; of these, three studies evaluated vaccination programmes alone (measles [n=1] and rotavirus [n=2])[7973,86], six studies evaluated pharmacological interventions for various disease areas[72,74,76,81,83,84], and one study evaluated both vaccination (cervical cancer)

[2] Some studies described multiple methods and therefore reported totals sum to greater than the number of studies; SLRs were not included in these totals.

and a pharmacological intervention (childhood diarrhoea)[75]. The final five studies focused on public health policy and included the impact of reduced salt intake on cardiovascular disease incidence[77], the impact of a sugar tax on type 2 diabetes outcomes[78], the effect of an increased availability of care workers on general neonatal care outcomes[82], the impact of improved sanitation on childhood diarrhoea outcomes[80], and the influence of improved education on adolescent maternal mortality[85]. Across MCDA publications, three described case studies looking at pharmacological interventions, including an Australian study on coronary heart disease[87], a European study on breast cancer[50] and an Israeli study looking at 18 health care interventions across multiple disease areas[88]. Only one of the two MP studies was an applied study, focusing on HIV treatment in South Africa[89]. An overview of all identified studies can be found in **Supplemental Appendix E**.

### *3.2. Overview of methods*

#### *3.2.1. Equity-based weighting*

EBW involves the use of numerical weights to give greater (or lesser) influence to specific groups of people. In cost-effectiveness/utility analyses, this typically involves weighting utility scores for estimating QALYs and re-evaluating ICERs based on the new weighted utility scores. Alternatively (or in parallel), weighting can be applied to costs or WTP thresholds.

Of the 25 EBW studies, 23 studies proposed conventional EBW methods, 21 of which focused on re-weighting QALYs, with two focusing on re-weighting costs[29,31-47,49-53]. Most prevalent were equity weights based on initial health or disease severity (n=11), propensity for health gain (n=5) and age (n=5). The derivation of weights was described in nine studies, with most describing preference elicitation based on forms of best-worst scaling and discrete choice experimentation[90]. Key data requirements for EBW methods include the underlying equity preference weights and the ability to disaggregate the target of the weighting function (e.g., QALYs) by the relevant equity stratification factor (e.g., socioeconomic status). A summary of the key attributes of each of the equity evaluation methods is presented in **Table 1**.

The remaining two EBW studies proposed less conventional methods. Karnon et al. (2015) described a method aiming to replace the QALY with the 'SAVE' (a non-utility-based measure, equivalent to saving the life of a young person), with a preference elicitation study (using a person trade-off survey approach) undertaken to estimate the number of SAVE's equivalent to relevant outcome events associated with the progression and treatment of early-stage breast cancer[48]. In contrast, Versteegh et al. (2019) used a hypothetical oncology

example that combined probabilistic analysis with different WTP thresholds for different levels of disease severity, to introduce the severity-adjusted probability of cost-effectiveness[30].

### *3.2.2. Extended cost-effectiveness analysis*

As suggested by its title, ECEA represents an extension to cost-effectiveness analysis, by incorporating additional non-health benefits, typically through the evaluation of a policy's ability to provide financial risk protection (FRP). FRP is concerned with the avoidance of financial difficulties associated with individuals being required to partially or entirely fund their own health care and, as such, is commonly evaluated in countries without national single-payer healthcare systems[91]. Equity concerns are captured through the stratification (or subgrouping) of the population based on specific equity criteria, with FRP outcomes subsequently compared across the different strata. It should be noted that ECEA does not always have to be concerned with FRP, with other dimensions encompassing, for example, educational, agricultural, or environmental benefits.

With the exception of one study (De Neve et al. [2018]) that evaluated FRP alongside educational outcomes, all studies focused solely on FRP[35,72-86,92]. In these studies, equity was consistently evaluated across household income quintiles and FRP was evaluated in terms of household expenditure averted, catastrophic health expenditure or impoverishment. Saksena et al. defines catastrophic health expenditure to be when a household's out-of-pocket (OOP) payments are so high relative to its available resources that the household foregoes the consumption of other necessary goods and services[91]. In contrast, impoverishment is defined when OOP payments push households below or further below the poverty line, a country-specific threshold under which even the most basic standard of living is not ensured[91]. The importance of these outcomes relies on the household's ability to 'bounce back' and recover quickly from such an impact (i.e., consideration of whether FRP is afforded over a short or long period of time). The identified studies do not explicitly consider this aspect and typically focus on long-term FRP outcomes.

### *3.2.3. Distributional cost-effectiveness analysis*

Distributional cost-effectiveness analysis (DCEA) measures the change in the distribution of costs and benefits before and after the introduction of a new intervention or policy, in order to identify those that benefit and those that lose out, as a function of displaced programmes. For example, in a screening programme in which both

clinical- and cost-effectiveness is achieved for the average patient, the uptake of the screening programme, and the subsequent health outcomes of patients, might differ significantly by socioeconomic status, with certain groups failing to benefit from such interventions, perpetuating health inequalities. DCEA works by conditioning model input parameters on the relevant equity strata, enabling the distribution of cost and benefit outcomes to be quantified. For a QALY-oriented approach, QALY gains associated with the new programme are added to the QALE of the whole population. Subsequently, the costs of the new programme are converted into foregone QALYs (i.e., the QALYs lost due to the absence of funding for other health care programmes) using a pre-defined monetary valuation for a QALY and are subtracted from the QALE of the whole population. Subsequently, this allows for the identification of the 'winners' and 'losers' amongst the general population, in this case, the socioeconomic groups that (on aggregate) benefit most or least.

A total of 17 studies utilised DCEA as described above (hereupon termed 'conventional DCEA')[34,35,54-68,70,71]. However, a different approach (termed 'aggregate DCEA') was also identified in which aggregate cost-effectiveness outcomes (as opposed to model input data) are disaggregated based on external data and their expected impact across the individual subgroups of a particular equity dimension. Benefit outcomes are disaggregated based on their expected distributional impact across patients with the target disease, whilst cost outcomes are disaggregated based on their expected distributional impact across the wider healthcare system and general population (i.e., estimating the impact of foregone QALYs as in conventional DCEA). Three studies adopted this approach; two of these studies utilised data from the English NHS hospital episode statistics datasets, and the third study utilised data from household surveys based in Malawi to distribute outcomes[54,56,69].

Both DCEA methodologies enable a quantitative assessment of the degree of inequality using metrics such as the Gini index. Using SWFs such as the Atkinson social welfare index, DCEA can also be used to analyse the trade-offs between efficiency, in terms of maximising overall population health, and health equity, in terms of achieving a more equal distribution of health across the chosen equity strata and amongst the general population. The cornerstone of this inequality measure is the concept of Equally Distributed Equivalent (EDE) health, where EDE health is the level of health that, if equally distributed, would provide the same value (social welfare) as the existing unequal distribution, with the difference indicating the change in health-related social welfare. A positive change in EDE therefore represents a scenario in which population health increases and health inequality reduces, or a scenario in which the trade-off between increasing (decreasing) population health by an amount X and increasing (decreasing) health inequality by an amount Y is deemed acceptable; this acceptability is controlled by the inequality aversion parameter. Several studies presented results associated with multiple

different equality measurement metrics (despite consistent analytical objectives), and notably, without justification for their choice, suggesting there is currently no clear consensus on which metrics are most appropriate. The most common measurement metrics used were the Atkinson index (n=8) and the slope index of inequality (n=8) and the most common SWFs were the Atkinson and Kolm social welfare indices (n=10 and n=6, respectively). We regard DCEA as a practical and intuitive approach for estimating the distributional impact of a health care policy on societal welfare and, using the aggregate DCEA approach, avoids the requirement for stratified input data which is rarely available. **Supplemental Appendix F** provides a list of the inequality measurement metrics and SWFs that were described in detail across DCEA studies, alongside additional background information.

#### *3.2.4. Multi-criteria decision analysis*

In contrast to the other methods described herein, cost-effectiveness analysis may only form a component part of MCDA. The premise of MCDA is to evaluate multiple criteria, including those concerned with equity, that are typically heterogeneous in nature. This is implemented by establishing preferences between options (e.g., interventions) by reference to an explicit set of objectives that the decision makers have identified, and for which they have established measurable criteria to assess the extent to which the objectives have been achieved[93,94]. The performance of each option against each criterion is then evaluated, resulting in either a qualitative ranking of options or a quantitative scoring of options through which a decision on the most suitable option can be made. In this context, equity is evaluated and measured through the ranking or scoring of options amongst the criteria that pertain to equity. For example, an equity evaluation criterion might be the uptake of care amongst different groups, with higher scores available for policies promoting equal care uptake. Notably, certain criterion may be given greater weight than others, depending on the overall objectives of the analysis; for example, equity criteria may be given greater weight than those of efficiency.

Six studies described MCDA, with three describing quantitative evaluation through explicitly defined scoring systems, one describing qualitative methods and two a mixture of both[43,50,87,88,92,93]. The most common criterion included in the MCDA frameworks were cost-effectiveness analysis, severity of disease, size of population-level benefit and intervention effectiveness. Only three of the identified studies reported criterion specific to the consideration of equity, including age (with weight given to programmes targeted to younger patients), poverty reduction and socioeconomic status (with weight given to programmes providing health benefits to the most

deprived patient groups), amongst others. Whilst MCDA approaches have been adopted in other areas (most prevalently, the energy, environment and sustainability sectors), there appears to be hesitation to apply them more widely in health care decisions, likely due to the necessity to force direct comparison between fundamentally different components, where the potential subjectivity of decision makers may influence conclusions[95-97].

### *3.2.5. Mathematical programming*

MP approaches use mathematical optimisation techniques with the goal of maximising health gains (or an alternative health care metric) subject to specific constraints[35,89]. Within the context of equity evaluation, specific equity goals are employed as constraints within the cost-effectiveness analysis framework and then mathematical algorithms are used to optimise modifiable aspects (e.g., treatment choice) of the modelled healthcare system. MP is particularly useful in comparing health care policies where there exist a large number of modifiable factors and the most efficient strategy is not immediately obvious (e.g., treatment allocation decisions in complex treatment pathways, as in Baltussen et al.)[93]. However, MP approaches do not explicitly compare equity outcomes, but rather seek to explore the impact of a particular equity constraint on other outcomes. Further, MP relies heavily on the choice of constraints imposed in the analysis. In an equity-oriented example, such constraints could include ensuring a minimum level of service provision for disadvantaged patient groups, or regions, or specifying a maximum level of resource use disparity between patient groups. The choice of constraint and the ability of MP to optimise outcomes are dependent on the availability, suitability, and analytical structure, of modifiable parameters built into the modelling framework, alongside the availability of data relating the relevant constraints, modifiable parameters, and the MP optimisation objective.

Two studies described MP approaches[35,89], with only one describing an application of the method. Cleary et al. described an MP approach to evaluating HIV care strategies in South Africa, focusing on the evaluation of three optimisation strategies: health maximisation, equal treatment, and a third scenario where ‘decent’ minimum social choice rules were specified. The authors suggest the evaluation of further equity constraints in future work and argue that budget constraints should be incorporated more regularly within economic evaluation. This is further emphasised by Epstein et al., who highlight that in practice WTP thresholds are not typically consistent with the existence of an overall fixed budget for health care[98].

### *3.3. Traffic light assessment of practical suitability*

Key practical considerations associated with the use of equity evaluation methods in economic evaluation and HTA frameworks are described in **Figure 2**, alongside a traffic light assessment of each method in the context of each individual consideration. Additional context and justification for each individual assessment is provided in **Supplemental Appendix C**.

With respect to analytical requirements, we observe concerns for EBW and MCDA methods where it is expected that significant further research on preference elicitation for equity weights and the relevant attributes of the MCDA framework would be required. There remains a lack of consensus on the best approaches to elicit such information and, not only would these studies likely have to be large to ensure statistical precision and representativeness, but there is potential for many multiple studies being required if estimates are likely to differ by disease area or intervention, or indeed any relevant population strata. Data requirements for other methods may be more manageable, with the potential to identify data within original sources (e.g., clinical trials), or to utilise existing publications alongside data readily available in large comprehensive national datasets such as the Clinical Research Practice Datalink (CPRD) or the National Health Service (NHS) Hospital Episode Statistics (HES) datasets, as found in the UK[99,100]. However, it is acknowledged that such datasets may not be available, or may not be representative, in poorer countries or in countries without universal healthcare systems.

With regards to generalisability, DCEA provides the most flexible approach with consistent application across disease areas and intervention type, whilst representing equity concerns through the explicit measurement of the extent to which equity is achieved in outcome distribution, something that is relevant to all healthcare systems. In contrast, ECEA utilises an outcome based on FRP which is unlikely to be deemed of significant importance to whole population healthcare systems, that inherently mitigate the impact of adverse health outcomes on household expenditure[101]; as such, certain disease areas or intervention types may observe little to no impact on FRP, making comparisons difficult. Obviously, in settings where out-of-pocket payments for health care are prevalent, FRP becomes a more relevant outcome and the impact on FRP across different disease areas and interventions becomes more variable. EBW, MCDA and MP methods all utilise outcomes based on their underlying economic evaluation framework and therefore, are arguably relevant to most healthcare systems. However, it is likely that these methods require further consideration to account for inputs or criteria that may vary across different disease areas and interventions. For example, it has been demonstrated that the strength of inequality aversion in societal preferences (as required in EBW) is dependent upon disease severity, and

consequently, disease area[102]. Similar considerations are relevant for MCDA criteria elicitation and evaluation, whilst equity constraints applied to MP evaluations may simply not be viable for different disease areas and intervention types. In contrast, despite also requiring estimates of inequality aversion, DCEA is not subject to the same concerns of generalisability, due to a focus on estimating the inequality impacts of individual health care policies on the entire healthcare system, rather than just on the population associated with the individual disease area or intervention. As such, there is no immediately obvious reason to suggest DCEA cannot be applied consistently across disease areas and types of intervention.

Finally, when evaluating interpretability, the only major concerns we identify are the lack of ability of EBW, MCDA and MP methods to explicitly measure changes in the extent to which equitable outcome distribution is achieved, although it is acknowledged that this may not necessarily be a requirement or objective for all healthcare systems or policy makers. These methods rely on pre-specified preferences, criteria or constraints to modify existing outcomes based on preferences for inequality aversion, but do not explicitly measure the extent to which outcome distribution is made more or less equitable by the decision problem. We also highlight two main themes for further consideration: firstly, the use of metrics that are unfamiliar or irrelevant to certain audiences, such as equity measurement metrics and FRP; and secondly, the requirement for additional criteria to be specified relating to the acceptance of equity-efficiency trade-offs (akin to the use of WTP thresholds in cost-effectiveness analysis) before definite conclusions may be obtained[103]. Methods of DCEA, ECEA and MCDA are most susceptible to such concerns.

### *3.4. Equity considerations and typical cost-effectiveness trade-offs*

In **Table 2** we describe examples of some typical trade-offs arising in cost-effectiveness analyses and highlight the evaluation methods that are able to capture the associated equity concerns. Notably, most methods are able to capture a large range of different cost-effectiveness and equity-related trade-offs, with ECEA, on balance, being the least flexible approach, given its inability to capture social preferences for inequality aversion and its focus on FRP outcomes. DCEA and MP are the only methods that explicitly capture trade-offs associated with the measurement of opportunity cost offsets. However, we believe that with adaptation, such considerations could be incorporated within the frameworks of the other methods. Further, neither DCEA nor ECEA are able to capture preferences between extension of life and quality of life, or more generally they are unable to account for preferences between multiple health states or outcome measures.

Cost-effectiveness analyses have the potential to cover (to some extent) multiple different trade-offs. The shaded cells in **Table 2** highlight trade-offs that are not explicitly represented in the studies identified in this review. The transfers typically not represented relate to transfers between those with and without disease, transfers between quality of life and length of life and geographical transfers. Intergenerational transfers are considered to the extent of favouring outcomes for the younger generation (consistent with the 'fair innings' argument) but the explicit impact of the trade-offs are not evaluated. These gaps in the evidence represent opportunities for the methods to be applied to different types of trade-offs to further explore the limitations and suitability of the methods in different contexts.

**Table 3** describes results of a hypothetical example of each method applied to the same decision problem. With no adjustment for equity considerations the base case ICERs associated with Universal and Targeted screening reminders (compared to the current SoC) were ≤£30,000 and £30,000-50,000, respectively; an ICER of >£50,000 was predicted for Targeted versus Universal screening reminders. Detailed results can be found in **Supplement Appendix D**. The EBW method provided additional weighting to QALYs gained by the most deprived quintile of patients, improving cost-effectiveness across all comparisons, but naturally favoured the Targeted strategy the most. Using the ECEA method had no impact on the overall ICERs but additional granularity is provided by reporting ICERs for individual subgroups. In our example, the 'extension' (and equity) component of ECEA considered the expected reduction in the number of patients facing poverty, with both Universal and Targeted strategies reducing poverty compared to SoC.

Under both conventional and aggregate DCEA approaches, the Targeted and Universal strategies were both estimated to reduce overall public health, as the value of foregone QALYs outweighed the population-level health benefits of each strategy. The Universal strategy increased inequality, whilst the Targeted strategy decreased inequality when compared to both the Universal and SoC strategies under the conventional DCEA method, but only when compared to the Universal strategy under the aggregate DCEA method, with such differences attributed to the greater weight given to the distribution of foregone QALYs amongst the most deprived under the aggregate DCEA approach.

Two approaches to MCDA are demonstrated: the value measurement method and the outranking approach, as detailed in Thokala et al. [2012][104]. Strategies were scored based on cost-effectiveness, total QALE gain, provision of equal access, the level of inequality reduction and the level of innovation of the programme, and despite similar scoring and ranking approaches the 'winning' intervention in each scenario differed across the

two approaches. Finally, we note that the MP approach is unable to offer any unique insight into the initial decision problem as there are no optimisable aspects, therefore without modifying the decision problem, outcomes under an MP approach cannot be estimated. A potential useful application of MP beyond the initial decision problem might be the optimisation of a combined Universal/Targeted reminder approach to maximise QALE gains or minimise QALE variation across deprivation quintiles under a fixed screening budget.

## 4. Discussion

To our knowledge this is the first study to review and directly contrast analytical methods for integrating equity value judgements within cost-effectiveness analysis and HTA, in terms of the methods, outcomes, the practical data requirements and the key strengths and weaknesses of each approach. We highlight key practical concerns associated with each of the methods. For example, we identify potential concerns for EBW methods and MCDA with respect to data availability, and EBW methods and MP with respect to an inability to explicitly measure changes in outcome inequality. The only significant concern for ECEA relates to the use of FRP metrics which may not be relevant for all healthcare systems. In contrast, DCEA observed no major concerns but relies on the use of SWFs which may be unfamiliar to some audiences and require societal preference elicitation. Consideration of typical equity-related trade-offs highlighted the flexibility of most methods with respect to their ability to capture such trade-offs. Notable exceptions were trade-offs between quality of life and length of life, for which we find DCEA and ECEA unsuitable, and the assessment of lost opportunity costs, for which we find only DCEA and MP to be suitable. The ability of the evaluation methods to accommodate different concerns is further highlighted through a hypothetical example application, which demonstrates that each method is designed with fundamentally different analytical objectives in mind. The example application imposes the use of each method for the evaluation of the same decision problem and emphasises that, not only are some approaches better suited to particular decision problems than others but also, that significantly different conclusions can be observed depending on the choice of method and the assumptions made.

This review has highlighted that equity evaluation methods can be broadly categorised into those whose objective is to: a) modify aspects of the economic evaluation framework through the introduction of constraints or preference weights; or b) explicitly measure the impact of a health care policy decision on the distribution of health outcomes across relevant equity-relevant strata. Within the context of these broad objectives, EBW methods likely represent the most intuitive and flexible approach for incorporating equity concerns in economic analyses when focused on the first objective. For evaluations seeking to explore the impact of a health care policy decision on the distribution of health care outcomes, DCEA is likely the most suitable choice of method given its focus on outcome distribution measurement, its ease of integration with economic evaluation frameworks and its ability to provide consistent and comparable output across analyses.

For EBW methods that aim to weight costs or health outcomes there is a lack of consensus on weighting preferences and their derivation[105]. For example, consensus exists that there is societal preference for greater

weight to health gains amongst younger people and those with more severe illness but estimates for the size of such weights differ significantly across studies[102,106]. Such differences allude to the difficulties in estimating generalisable social preferences that remain valid across an array of important health care evaluation factors such as the evaluation setting, the disease area and the type of intervention being evaluated, notwithstanding the ever-evolving state of societal opinion. A similar concern is recognised for the use of SWFs in DCEA. SWFs are used to incorporate preferences for inequality aversion and enable conclusions to be made through the evaluation of trade-offs between equity and efficiency, after the distribution of health care outcomes has been quantified through the use of relevant equity measurement metrics. Indeed, the difficulty in derivation and the limited use of measures derived from the views of patients, the public and other stakeholders in social preference elicitation studies may have contributed to the lack of uptake of these methods by decision-makers. With this in mind, we believe that effective future strategies for incorporating societal concern for inequality aversion within economic evaluations might overcome such problems through provision of sensitivity analyses utilising a range of degrees of inequality aversion in decision-maker preferences, starting from the point of no aversion (akin to a typical cost-effectiveness analysis). Such a strategy might only be undertaken for evaluations in which either a very positive or negative impact on inequality is likely. Subsequently, future work might then focus on enabling informed qualitative/deliberative assessment through appropriate communication of equity efficiency trade-offs. Under this type of framework, and without the restriction of a pre-defined inequality 'threshold' for assessment (not dissimilar to a static willingness-to-pay threshold), there remains flexibility to assess the equity-efficiency trade-offs of policies on a case-by-case basis, whilst avoiding onerous undertakings within assessments anticipated to provide little to no equity benefit or harm.

One notable limitation of our study is the lack of direct input from individual stakeholder groups, particularly with respect to their perspectives on the interpretability of equity analysis methods and their results. The perspectives and priorities of each set of stakeholders with respect to costs, health, health inequality, and their trade-offs, is an extremely important aspect requiring further consideration. Our study provides initial steps to considering such aspects, but we would advocate further research involving formal input from different stakeholder groups in order to understand which methods are most relevant to different groups, and how methods might be improved to better cater to a wide range of perspectives. Further, whilst we have endeavoured to provide objective assessment of each of the methods where possible, our assessment framework inherently introduces some subjectivity. However, we view this initial indicative assessment as an important step in the context of promoting further deliberation and discussion before formal adoption of the methods. Finally,

although not necessarily a limitation as such, we also highlight the nature of the hypothetical example application for further consideration. In order to demonstrate the potential impact of the choice of equity evaluation method, the example was necessarily contrived. It is anticipated that such a large range of differences across all methods would not be observed when evaluating real-world applications, due in part to a more consistent equity evaluation approach amongst methods were the specification of constraints, criteria or societal preferences are required, and the greater likelihood of observing larger differences in efficiency and/or equity outcomes between interventions.

Whilst we have attempted to directly contrast each of the methods in the context of pre-defined criteria, the suitability of each of the methods inherently depends upon the objectives of the equity analyses[107]. Indeed, each of the methods has the capacity to offer unique perspectives, therefore, focus should be given to identifying the most appropriate methods for use in the context of the specific equity evaluation objective. Further, in order to fully operationalise these frameworks and enable their full potential, there remains a need to develop consensus over the motivation for equity analyses, with such consensus informed through involvement with all potential stakeholders. Future research on this topic should be a priority, particularly within the context of equity evaluation in HTA, where there remains an unmet need with respect to formal analytical evaluation of equity impacts. In parallel, continued application of the methods beyond their theoretical frameworks, and demonstration of their real-world applicability, should continue to be pursued in order to provide greater opportunity for their evolution and improvement.

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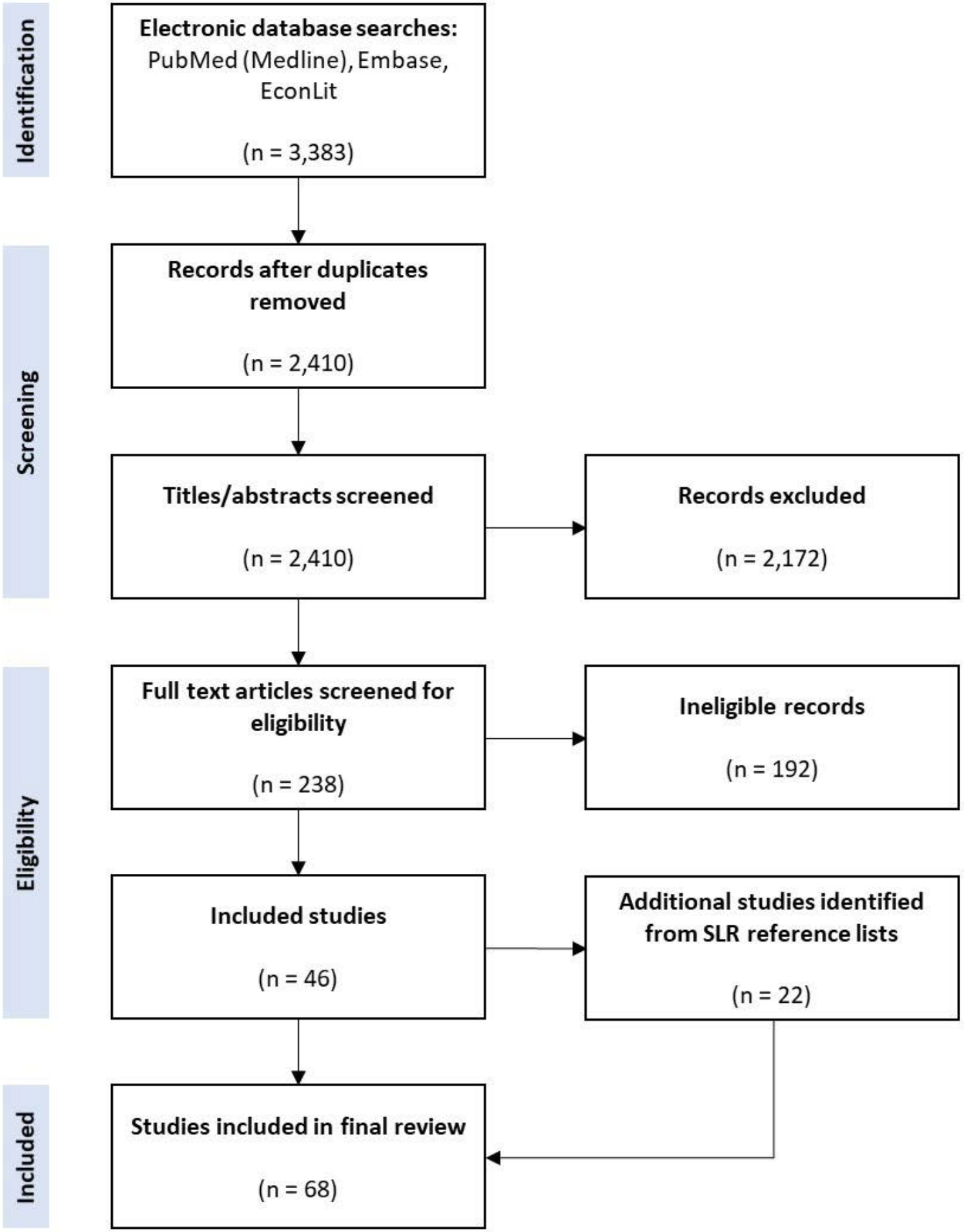
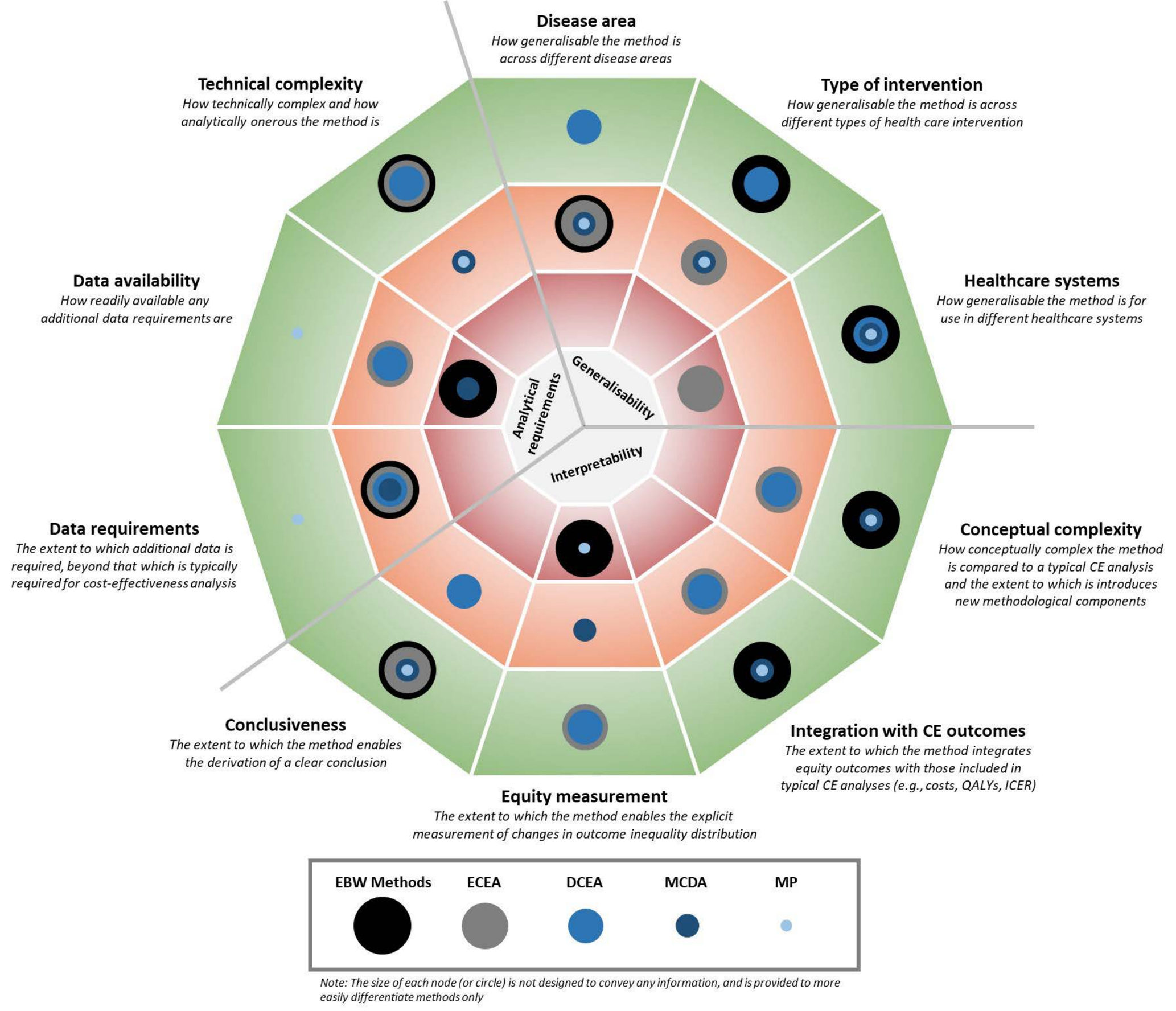

Identification
Screening
Eligibility
Included
Electronic database searches: PubMed (Medline), Embase, EconLit
(n = 3,383)
Records after duplicates removed
(n = 2,410)
Titles/abstracts screened
(n = 2,410)
Records excluded
(n = 2,172)
Full text articles screened for eligibility
(n = 238)
Ineligible records
(n = 192)
Included studies
(n = 46)
Additional studies identified from SLR reference lists
(n = 22)
Studies included in final review
(n = 68)




*Note: The size of each node (or circle) is not designed to convey any information, and is provided to more easily differentiate methods only*

**Table 1:** Overview of key equity evaluation method attributes

| | Equity-based weighting | Extended cost-effectiveness analysis (ECEA) | Distributional cost-effectiveness analysis (DCEA) | | Multi-criteria decision analysis (MCDA) | Mathematical programming (MP) |
|---|---|---|---|---|---|---|
| | | | Conventional DCEA | Aggregate DCEA | | |
| **Scope** | | | | | | |
| **Approach aim** | To evaluate the impact of societal preference for inequality aversion on CE outcomes | To evaluate and measure the distributional impact of health care policies on poverty and personal financial outcomes | To evaluate and measure the distributional impact of health care policies on CE outcomes | | To combine and evaluate multiple disparate criteria in a decision-making framework | To provide optimal solutions to economic allocation decisions subject to relevant constraints |
| **Ability to capture multiple equity dimensions?** | ✓ | ✓ | ✓ | | ✓ | ✓ |
| **Approach to equity incorporation (direct or indirect)[1]** | Direct: Incorporates equity weights within evaluation | Indirect: Reports/ measures changes in outcome inequality distribution | Indirect: Reports/ measures changes in outcome inequality distribution | | Indirect: Equity component stands apart from CE component until combined through weighted scoring/ranking | Direct: Incorporates equity constraints within evaluation |
| **Possible to explicitly measure the extent to which health care outcomes are distributed equitably?** | × | ✓ | ✓ | | ×[2] | × |
| **Methods** | | | | | | |
| **Core equity mechanism** | Weighting of outcomes/costs | Derivation of distributional CE/FRP outcomes | Derivation of distributional CE/equity impact and use of SWFs | | Evaluation and weighting of outcomes across multiple criteria to rank/score strategies | Equity constraints in an optimisation analysis |
| **Requires modification to underlying CE model?** | ✓ if focus of weighting is not readily disaggregated (× otherwise) | ✓ | ✓ | × | × | ✓ |
| **Impact on benefit (e.g., QALYs) and costs** | Re-weighted based on pre-defined preferences for inequality aversion | Distribution of cost and QALY outcomes | Distribution of cost and QALY outcomes assessed across relevant groups | | Unchanged | Potentially modified in line with the optimisation approach |

| | | | | | | |
|---|---|---|---|---|---|---|
| | amongst different groups[3] | assessed across relevant groups | | | | |
| **Uses aggregate CE outcomes data only?** | ✓ | × | × | ✓ | ✓ | × |
| **Outcomes** | | | | | | |
| **Equity evaluation outcome** | ICER | ICER and measurement of FRP or equivalent | ICER, specific inequality measure (e.g., slope index of inequality) & SWF | | Score or rank (alongside results of individual evaluation criteria) | ICER or the specific optimisation target |
| **Overview of criteria used to elicit policy reimbursement conclusions** | WTP threshold | WTP threshold | WTP & inequality aversion parameter | | Highest ranking/ scoring policy | WTP threshold or the specific optimisation target |
| **Data** | | | | | | |
| **Data requirements beyond those of typical cost-effectiveness analyses** | • Equity preference weights;<br>• Stratification of relevant outcomes (i.e., the target of the weighting function) by the relevant equity stratification factor. | • Out-of-pocket payment outcomes stratified by relevant equity stratification factor;<br>• Poverty or 'catastrophic' spending threshold. | • Baseline population health (e.g., QALE) stratified by relevant equity stratification factor;<br>• Estimates of relevant CE model inputs stratified by relevant equity stratification factor;<br>• Knowledge on distribution of opportunity costs.<br>• Preferences for inequality aversion. | • Baseline population health (e.g., QALE) stratified by relevant equity stratification factor;<br>• Stratification of relevant outcomes by the relevant equity stratification factor;<br>• Health care utilisation for specific indication and for whole population stratified by relevant equity stratification factor;<br>• Preferences for inequality aversion. | • Consensus on MCDA criteria;<br>• Consensus on scoring/ranking strategy for each MCDA criteria;<br>• Preference weights (if certain criteria are to be valued above others). | • MP optimisation objective;<br>• Relevant equity constraints;<br>• Data to relate the relevant constraints, modifiable parameters, and the MP optimisation objective. |
| **Strengths and weaknesses** | | | | | | |
| **Key method strengths** | Analytically and conceptually simple | Provides additional granularity and information on aspects beyond cost-effectiveness | Possible to explicitly measure the extent to which health care outcomes are distributed equitably | | Able to evaluate multiple disparate components (including those outside of the CE framework) | Ability to incorporate budget constraints and cost-offset impacts |

| | | | | | |
|---|---|---|---|---|---|
| **Key method weaknesses** | Potentially requires significant further research on inequality preference elicitation | FRP outcomes likely not relevant to some health care systems | Significant amount of additional data required | Requires consensus over both the overarching MCDA framework criteria, and its scoring/ranking rules | Potentially requires significant adaptation to underlying CE model |
| | Decision problems for which there is a need to incorporate equity concerns within the existing ICER-oriented CE framework and for which outcomes in different groups of people are valued differently (and such value is known) | Decision problems in which additional non-health benefits are important (typically those associated with FRP) | Decision problems for which an explicit measurement of the extent to which inequality/inequity of health outcomes increases or decreases | Decision problems in which multiple components beyond CE are of significant importance to the decision panel | Decision problems in which there exist modifiable and influential constraining factors that influence outcomes and where the optimal solution or decision is not immediately obvious |

CE: cost-effectiveness; DCEA: distributional cost-effectiveness analysis; ECEA: extended cost-effectiveness analysis; ICER: incremental cost-effectiveness ratio; FRP: financial risk protection; MCDA: multi-criteria decision analysis; MP: mathematical programming; QALE: quality-adjusted life expectancy; QALY: quality-adjusted life year; SWF: social welfare function; WTP: willingness-to-pay.

**Notes**

[1]Direct approaches incorporate fairness considerations into the economic analysis by, for example, imposing weights or constraints which directly impact the subsequent cost-effectiveness calculations and outcomes. Indirect approaches, however, make no attempt to modify the economic analysis calculations. Instead, they report fairness considerations alongside the economic analysis, allowing for discrete comparisons within the final fairness informed economic evaluation.

[2]Not typically included in such analyses but it would be possible to measure the distributional equity impact if this was included as its own independent criterion within the MCDA framework – but this would likely then necessitate some form of DCEA.

[3]Does not require both QALYs and costs to be adjusted

**Table 1:** Examples of typical equity-related trade-offs that might be evaluated in cost-effectiveness analyses across the spectrum of economic evaluation in health care

| Types of transfer | Example trade-offs | | Illustrative application | Example intervention or comparison | Equity concern | Is the equity evaluation method able to capture the equity concern described?[1] | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | EBW Methods | ECEA | DCEA | MCDA | MP |
| Transfers between the types of patients that will receive care | Increased inequality in health outcomes | Increased population health | Intervention that extends life but with an unequal distribution of benefit | Targeted cancer screening versus no cancer screening | Preferences for equality of outcomes | ✓ | ✓ | ✓ | ✓ | ✓ |
| Intertemporal transfers | Short- to medium-term costs to change behaviours | Longer term health care benefits | Public health intervention | Promotion of specific behaviours or habits that can improve physical, mental, and emotional health (e.g., food labels) | Accounting for potential opportunity costs associated with spending on alternative programmes in the short-term | × | × | ✓ | × | ✓ |
| Transfers between the types of patients that will receive care | Small life expectancy benefit to many (possibly all) | Large life expectancy benefit to few | High cost, high efficacy treatment versus low cost, low efficacy treatment | HIV treatment regimes in budget constrained health care systems | Preferences for equality of care provision | ✓ | ✓ | ✓ | ✓ | ✓ |
| Intergenerational transfers | Current generations changing behaviours and bearing costs in terms of lower growth | Future generations benefit in terms of improvements in environment and health | Societal policies | Environmental policies | Intergenerational equity (e.g., the 'fair innings' argument[18]) | ✓ | ✓ | ✓ | ✓ | ✓ |
| Transfers between those with and without disease | Health gain to small number of people who will contract cancer | Health lost to those that do not have cancer and that undergo unnecessary investigations | Test thresholds for diagnostic testing | Changes in the referral thresholds for further testing of patients | Preferences for health gains or resource distribution based on initial health status | ✓ | ✓ | ✓ | ✓ | ✓ |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Transfers between quality of life and length of life | Life extending treatments | Increases in quality of life alone | Treatment extending life or improving quality of life | Stroke prevention versus rehabilitation | Preferences between quality of life and length of life | ✓ | × | × | ✓ | ✓ |
| Geographical transfers | An increase in the opportunity of those currently untreated to access and receive treatment | Probability that rural patients (with less access) gain but urban patients (with better access) lose out with respect to health | Access to care | Relocation of hospital services from urban to rural locations | Preferences for equality of care access | ✓ | ✓ | ✓ | ✓ | ✓ |

DCEA: distributional cost-effectiveness analysis; EBW: equity-based weighting; ECEA: extended cost-effectiveness analysis; HIV: human immunodeficiency virus; MCDA: multi-criteria decision analysis; MP: mathematical programming.

**Notes**

Shaded cells contain examples of trade-offs that are not explicitly represented in the studies identified in this review; intergenerational transfers are considered to the extent of favouring outcomes for the younger generation (consistent with the 'fair innings' argument) but the explicit impact of the trade-offs are not evaluated.

[1]These results attempt to highlight which equity evaluation methods may be used to capture aspects of the particular equity concern, but we do not attempt to rank methods, nor delineate between the relative strengths and weaknesses of the equity evaluation attributes, as described previously. We evaluate each of the methods within the context of their core methodology, acknowledging that with adaptation some of the methods may be able to account for additional equity concerns, although the potential for such adaptation is not described here.

**Table 1:** Results of an illustrative application of each of the equity evaluation methods

| Evaluation method | ICER (£/QALY) | | | Inequality impact[1] | | | Dominant intervention (direct comparison)[2] | | |
|---|---|---|---|---|---|---|---|---|---|
| | U v SoC | T v SoC | T v U | U v SoC | T v SoC | T v U | U v SoC | T v SoC | T v U |
| Standard cost-effectiveness analysis | ≤£30,000 | £30,000-50,000 | >£50,000 | NA | NA | NA | U | SoC | U |
| EBW (QALYs) | NC | ≤£30,000 | £30,000-50,000 | Unclear | Unclear | Unclear | NC | T | NC |
| ECEA | All subgroups: ≤£30,000 | All subgroups: £30,000-50,000 | All subgroups: ≤£30,000 or £30,000-50,000[3] | Reduces poverty | Reduces poverty | Dependent on deprivation status[4] | Unclear | Unclear | Unclear |
| DCEA (conventional) | NC | NC | NC | Reduces PH / increases inequality | Reduces PH / reduces inequality | Reduces PH / reduces inequality | SoC | T | T |
| DCEA (aggregate) | NC | NC | NC | Reduces PH / increases inequality | Reduces PH / increases inequality | Reduces PH / reduces inequality | SoC | NC | T |
| MCDA (value measurement approach) | NC | NC | NC | None | Unclear, but targeted strategy focused to most deprived | Unclear, but targeted strategy focused to most deprived | NC | T | NC |
| MCDA (outranking approach) | NC | NC | NC | None | Unclear, but targeted strategy focused to most deprived | Unclear, but targeted strategy focused to most deprived | NC | T | T |

DCEA: distributional cost-effectiveness analysis; EBW: equity-based weighting; ECEA: extended cost-effectiveness analysis; MCDA: multi-criteria decision analysis; MP: mathematical programming; NC: no change; OO: optimisation objective; PH: population health; QALY: quality-adjusted life year; SoC: standard of care; T: Targeted strategy; U: Universal strategy

**Notes**

Shaded cells represent selection conclusions that are different to those of the 'standard cost-effectiveness analysis' scenario.

NC represents no change relative to the 'standard cost-effectiveness analysis' scenario.

[1]The equity impact is evaluated within the context of the specific example application and the individual method approaches; those with an 'Unclear' equity impact are described in this way as the method does not explicitly describe equity impact outcomes.

[2]Dominance criteria are based on the approaches described for each individual method; for the standard cost-effectiveness analysis, a WTP threshold of £30,000 is assumed; those described as 'Unclear' are described in this way as the method does not define explicit criteria for the preference of one intervention over another.
[3]ICERs in the ≤£30,000 range represented negative incremental costs and negative incremental QALYs and so would NOT be deemed cost-effective.
[4]Comparisons for the Q1-3 (least deprived) groups favour the Universal strategy and comparisons for the Q4-5 (most deprived) groups favour the Targeted strategy (when results are aggregated the Universal strategy is preferred); a similar relationship with poverty reduction is observed.

**Supplemental Appendix A**

In brief, searches have been informed by previous literature reviews and published literature review filters. Economic analysis search terms (e.g. PubMed: #1-17) were informed by a review of economic evaluation filters; the National Health Service Economic Evaluation Database search filter was chosen as it offered a sensitivity of 0.999 and was more than twice as precise as the two filters that were more sensitive (sensitivities of 1.000) [1]. Specific cost-effectiveness search terms were subsequently combined with the pre-defined search filter (e.g. PubMed: #18-19). Outcome search terms (e.g. PubMed: #20-23) were informed by a review of candidate publications that were identified as potential targets of the review [2-6].

**Proposed PubMed search strategy**

**Table.** PubMed search strategy

| # | Search terms | Number of records |
|---|---|---|
| **Study design** | | |
| 1 | (economics[mh:noexp]) | 27,285 |
| 2 | ("costs and cost analysis"[mh]) | 242,129 |
| 3 | (economics, dental[mh:noexp]) | 1,915 |
| 4 | (economics, hospital[mh]) | 24,922 |
| 5 | (economics, medical[mh:noexp]) | 9,117 |
| 6 | (economics, nursing[mh:noexp]) | 4,002 |
| 7 | (economics, pharmaceutical[mh:noexp]) | 2,969 |
| 8 | (economic*[Title/Abstract] OR cost[Title/Abstract] OR costs[Title/Abstract] OR costly[Title/Abstract] OR costing[Title/Abstract] OR price[Title/Abstract] OR prices[Title/Abstract] OR pricing[Title/Abstract] OR pharmacoeconomic*[Title/Abstract]) | 857,536 |
| 9 | (expenditure*[Title/Abstract] NOT energy[Title/Abstract]) | 31,483 |
| 10 | (value[Title/Abstract] AND money[Title/Abstract]) | 3,217 |
| 11 | (budget*[Title/Abstract]) | 30,763 |
| 12 | #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 | 1,000,732 |
| 13 | ((energy[Title/Abstract] OR oxygen[Title/Abstract]) AND cost[Title/Abstract]) | 30,059 |
| 14 | (metabolic[Title/Abstract] AND cost[Title/Abstract]) | 8,559 |
| 15 | ((energy[Title/Abstract] OR oxygen[Title/Abstract]) AND expenditure[Title/Abstract]) | 27,777 |
| 16 | #13 OR #14 OR #15 | 61,651 |
| 17 | #12 NOT #16 | 963,928 |
| 18 | (cost-util*[Title/Abstract] OR cost util*[Title/Abstract] cost-benefit*[Title/Abstract] OR cost benefit*[Title/Abstract] OR cost-effect*[Title/Abstract] OR cost effect*[Title/Abstract] OR cost-min*[Title/Abstract] OR cost min*[Title/Abstract] OR cost-consequence*[Title/Abstract] OR cost consequence*[Title/Abstract] OR economic | 168,714 |

| | | |
|---|---|---|
| | evaluation*[Title/Abstract] OR economic assessment*[Title/Abstract] OR economic analys*[Title/Abstract] OR health technolog*[Title/Abstract]) | |
| 19 | #17 AND #18 | 156,691 |
| **Outcomes** | | |
| 20 | (equit*[Title/Abstract] OR inequit*[Title/Abstract] OR inequalit*[Title/Abstract] OR disparit*[Title/Abstract] OR equalit*[Title/Abstract]) | 140,201 |
| 21 | (health[Title/Abstract] OR healthcare[Title/Abstract]) | 2,169,366 |
| 22 | (method[Title/Abstract] OR methods[Title/Abstract] OR methodolog*[Title/Abstract] OR approach*[Title/Abstract) | 7,905,813 |
| 23 | #20 AND #21 AND #22 | 43,153 |
| **Language** | | |
| 24 | English[Language] | 27,340,288 |
| **Combine** | | |
| 25 | #19 AND #23 AND #24 | 1,296 |

**Proposed Embase search strategy**

**Table.** Embase search strategy

| # | Search terms | Number of records |
|---|---|---|
| **Study design** | | |
| 1 | health-economics.sh. | 33,339 |
| 2 | exp economic-evaluation/ | 314,841 |
| 3 | exp health-care-cost/ | 299,173 |
| 4 | exp pharmacoeconomics/ | 206,733 |
| 5 | (econom$ OR cost OR costs OR costly OR costing OR price OR prices OR pricing OR pharmacoeconomic$).ti,ab. | 1,126,840 |
| 6 | (expenditure$ not energy).ti,ab. | 42,345 |
| 7 | (value adj2 money).ti,ab. | 2,535 |
| 8 | budget$.ti,ab. | 40,299 |
| 9 | #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 | 1,497,004 |
| 10 | (metabolic adj cost).ti,ab. | 1,590 |
| 11 | ((energy OR oxygen) adj cost).ti,ab. | 4,481 |
| 12 | ((energy OR oxygen) adj expenditure).ti,ab. | 32,921 |
| 13 | #10 OR #11 OR #12 | 37,864 |
| 14 | #9 NOT #13 | 1,489,223 |
| 15 | (cost-util$ OR cost util$ OR cost-benefit$ OR cost benefit$ OR cost-effect$ OR cost effect$ OR cost-min$ OR cost min$ OR cost-consequence$ OR cost consequence$ OR economic evaluation$ OR economic assessment$ OR economic analys$ OR health technolog$).ti,ab. | 234,126 |
| 16 | #14 AND #15 | 229,174 |
| **Outcomes** | | |
| 17 | (equit$ OR inequit$ OR inequalit$ OR disparit$ OR equalit$).ti,ab. | 162,505 |
| 18 | (health OR healthcare).ti,ab. | 2,729,031 |
| 19 | (method OR methods OR methodolog$).ti,ab. | 9,970,498 |

| | | |
|---|---|---|
| 20 | #17 AND #18 AND #19 | 43,131 |
| **Language** | | |
| 21 | English.lg. | 30,726,170 |
| **Combine** | | |
| 22 | #16 AND #20 AND #21 | 1,407 |

**Proposed EconLit search strategy**

**Table.** EconLit search strategy

| # | Search terms | Number of records |
|---|---|---|
| **Outcomes** | | |
| 1 | AB (equit* OR inequit* OR inequalit* OR disparit* OR equalit*) | 66,601 |
| 2 | TI (equit* OR inequit* OR inequalit* OR disparit* OR equalit*) | 30,687 |
| 3 | AB health OR TI health OR AB healthcare OR TI healthcare | 53,703 |
| 4 | AB (method OR methods OR methodolog*) OR TI (method OR methods OR methodolog*) | 137,706 |
| 5 | (#1 OR #2) AND #3 AND #4 | 726 |
| **Language** | | |
| 6 | LA English | 1,653,473 |
| **Combine** | | |
| 7 | #5 AND #6 | 680 |

**References**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**Supplemental Appendix B**

**Table.** Overview of previous SLRs evaluating equity concepts in cost-effectiveness analyses

| **Study** | **Sassi et al. (2001) [1]** | **Johri et al. (2012) [2]** | **Dukhanin et al. (2018) [3]** | **Lal et al. (2018) [4]** | **Carlson et al. (2020) [5]** | **Avancena et al. (2021) [6]** |
|---|---|---|---|---|---|---|
| **Objective** | The aims of this project were threefold:<br>1. To review the methodological solutions proposed for addressing equity concerns through economic evaluation and to determine whether these are consistent with the theoretical foundations of economic evaluation, | To systematically review published studies describing formal methods to consider equity in the context of cost-effectiveness analysis (CEA). | To identify existing methodological solutions that would be suitable for adaptation to integrating social justice concerns into economic evaluation, and to characterize and analyse the challenges traditionally faced by those solutions in their previous implementations. | To assess current approaches to inclusion of equity in economic analysis of public health interventions and to recommend best approaches and future directions. | To identify proposed alternatives to the conventional QALY metric, assess them for feasibility, and illustrate how their use might affect model outcomes and resource allocation decisions | To catalogue and describe peer-reviewed applications of equity-informative CEAs to date, and to explore what conditions and interventions these methods have been used for and in what settings, alongside the shift in outcome favourability after the introduction of an equity dimension. |

| | | | | | | |
|---|---|---|---|---|---|---|
| | whether they are practically viable, and whether their adoption would be sufficient to confer normative strength to the results of economic analyses<br>2. To assess whether and how the potential distributional effects of resource allocation decisions have been taken into consideration in existing economic evaluations<br>To examine the cost-effectiveness and the | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| | distributional implications of selected healthcare policies currently in use in the UK, with the aim of identifying possible equity–efficiency trade-offs and determining how these have been dealt with in the absence of appropriate analyses | | | | | |
| **Databases** | • Medline | • PubMed | • PubMed<br>• Embase<br>• PsychINFO<br>• EconLit<br>• Philosopher's Index<br>• Scopus | • Medline Complete<br>• Health Economics Evaluations Database<br>• EconLit | • PubMed<br>• EconLit<br>• Web of Science<br>• Embase/MEDLINE | • MEDLINE |
| **Inclusion criteria** | • Articles concerned with health interventions directly | • Article describes or elaborates on a formal proposal to | • Publications needed either to contain actual economic | • Studies that assessed public health interventions using | • Studies that discussed an alternative or | • Studies that are applied CEAs that explore the costs and |

| | | | | | | |
|---|---|---|---|---|---|---|
| | aimed at improving the health of individuals or populations<br>• Evidence of consideration of costs and outcomes of two or more alternatives<br>• Article describes original research<br>• Costs explicitly evaluated<br>• Effectiveness measured quantitatively<br>• Cost-effectiveness or cost-benefit analysis<br>• Cost-consequence analysis | integrate equity with CEA<br>• Primary purpose of article was to advance quantitative methods enabling equity concerns to be considered explicitly with cost-effectiveness results for health interventions<br>• Review papers were retained only if judged to have made a novel contribution<br>• No language restrictions were applied | evaluation (e.g., cost-effectiveness analysis, cost-utility analysis, cost-benefit analysis) or consider the application of theory for economic analysis<br>• Publications were also required to capture fairness considerations that (a) involve intended beneficiaries' cross-dimensional subjective personal life experience and (b) can be manifested at the | economic evaluation techniques that compare alternative courses of action in terms of both costs (resource use) and consequences (outcomes, effects)<br>• **Study stratified data or outcomes by socioeconomic position group/s**<br>• Studies aimed at whole population, whole community, or were targeted at specific individuals and groups of people within a country, | adjustment to the conventional QALY | health benefits of two or more alternatives<br>• Studies that explicitly mention equity as a consideration or decision-making principle<br>• Studies that apply an equity-informative CEA method to analyse or incorporate at least one equity criterion |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | level of subpopulations<br>• Inclusion eligibility was dependent on the provision of a methodological solution or characterization of an associated challenge. To be included, solutions must have been used for, or must have been described as suitable for, integrating fairness considerations that share key | community or organisation | | |

| | | | | | | |
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| | | | characteristics (a) and (b) above | | | |
| **Exclusion criteria** | • Studies where the abstract was not available were excluded | • Monographs, reports, and conference abstracts<br>• Papers that were not about CEA, not about equity, or failed to offer specific, formal methodological proposals.<br>• Articles whose primary purpose was:<br>  ○ to assess the fit of public values with the standard CEA model or; | • Publications that were unrelated to medicine, healthcare, or public health<br>• Publications were not eligible if they addressed fairness considerations that were exclusively objective in nature (such as age or income quintiles) or limited to the individual level.<br>• Publications that pertained only to procedural justice | • Studies that were not public health interventions or policies<br>• **<u>Studies that examined groups that were not SEP-based</u>**<br>• Studies that analysed a low-income country as one population<br>• Non-English language studies | • None reported | • Tutorial or methods papers, systematic or narrative reviews, and non-peer-reviewed publications indexed in Medline<br>• Studies featuring MCDAs |

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| | | ○ to elicit empirical values for equity preferences were also judged not to satisfy the relevancy criterion | • Publications whose discussions of fairness were derived solely from public deliberation | | | |
| **Dates over which searches were conducted** | • The following specific years: 1987, 1992, 1995, 1996, 1997 | • Database inception to 6th March 2011 | • 1st January 1995 to 26th November 2015 | • Database inception to date of search (although date of search not reported) | • Not reported | • Database inception to 13th August 2019 |
| **Outcomes** | • Study characteristics<br>• Intervention type<br>• Analysis type<br>• Outcome measure | • Study identification (authors; journal; date of publication; type of study, study location, funding sources); | • Verbatim passages pertaining either to methodological solutions or to associated challenges | • Study characteristics<br>• Study objectives<br>• Interventions<br>• Measures of socioeconomic position | • Type of alternative method<br>• Strengths and weaknesses of method<br>• Data availability | • Article details (title, authors, date of publication)<br>• Country/geography |

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| | • Patient subgroup used in equity dimension<br>• Distributional effects methodology | • Study design and methods (perspective, design, outcomes, interventions considered, respondent sample for empirical studies); and<br>• Equity concepts | • Descriptive themes in the extracted data | • SEP specific modelling inputs<br>• Use of health equity impact plane<br>• Health inequality measures<br>• Equity weights<br>• Financial impacts<br>• Analysis of opportunity costs | • Calculation burden<br>• Overall implementation feasibility | • Setting (national, subnational, healthcare/clinical)<br>• Study population<br>• Disease area<br>• Intervention type<br>• Prevention stage (primary, secondary, or tertiary).<br>• Perspective of the analysis<br>• Interventions/ scenarios and comparators<br>• Measure of health benefit<br>• Method of cost and benefit estimation |

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| | | | | | | • Currency and costing year<br>• Sources of data for transition probabilities, costs, and utilities<br>• Equity or distributional criterion incorporated<br>• Type of equity-informative CEA<br>• Base-case cost-effectiveness finding and equity analysis result |
| **Search terms reported** | Yes – although unclear which strategy used in final review (example | Yes | Yes | Yes – search terms cited but not described | Yes | Yes |

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| | below is an example of their 'gold standard' search) | | | specifically for each database | | |
| **Search terms** | 1. 'Costs and cost analysis'/<br>2. Economics.sh.<br>3. 1 and 2<br>4. 'animal'/<br>5. 'human'/<br>6. 4 not (4 and 5)<br>7. 3 not 6<br>8. Journal article.pt.<br>9. (English or French or Italian or Spanish).la.<br>1. 7 and 8 and 9 | 2. "Cost-Benefit Analysis"[Majr] OR "Quality-Adjusted Life Years"[Mesh] OR "DALY"[tw])<br>3. "Social Justice"[Mesh] OR "Social Values"[Mesh] OR "Resource Allocation"[Mesh] OR "Health Care Rationing"[Mesh] OR "Equity" [tw] OR "Health | Extensive search term list provided in direct copy of Dukhanin et al supplemental appendix (see below file).<br>  <br>Dukhanin 2016. Search Terms..docx | ("cost-effectiveness" OR "cost-utility" OR "cost-benefit" OR "cost-consequence" OR "economic evaluation" OR "economic analysis") AND (socioeconomic* OR "social class" OR "social hierarchy" OR "social inequality" OR depriv* OR disadvantage* OR income OR educational OR occupation OR residence) | "QALYs" and "methodology" and "alternatives" | **Equity search terms:** ((((((((((equit*[Title/Abstract]) OR inequitable[Title/Abstract]) OR "distributional issues"[Title/Abstract]) OR distributi*[Title/Abstract]) OR inequality[Title/Abstract]) OR "unequal distribution"[Title/Abstract]) OR unequal[Title/Abstract])))) |

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| | | Priorities/economics ”[Mesh] OR “Health Priorities/ethics”[Mesh]<br>4. 1 & 2 | | NOT “low income countr*” | | **CEA search terms:** ((((((((((((((((("cost-utility analysis"[Title/Abstract]) OR "cost-effectiveness analysis"[Title/Abstract]) OR "cost-value analysis"[Title/Abstract]) OR cost-utility[Title/Abstract]) OR cost-effectiveness[Title/Abstract]) OR cost-value[Title/Abstract]) OR "economic evaluation"[Title/Abstract]) OR CEA[Title/Abstract]) OR "incremental cost- |

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| | | | | | | effectiveness ratio"[Title/Abstract]) OR ICER[Title/Abstract]) OR incremental cost-effectiveness ratio[Title/Abstract]) OR CUA[Title/Abstract]) OR "resource allocation"[Title/Abstract]) OR resource allocat*[Title/Abstract])))<br><br>**CEA MEsH terms:**<br>((((((("Technology Assessment, Biomedical"[Mesh]) OR "Cost-Benefit Analysis"[Mesh]) OR "Cost Allocation"[Mesh]) |

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| | | | | | | OR "Costs and Cost Analysis"[Mesh])))))) AND (English[lang]) |
| **Number of initial 'hits'** | 4,951 | 683 | 2,388 | 426 | 3,248 | 8,910 |
| **Number of studies included in review** | 424 | 51 | 26 | 29 | 28 | 54 |
| **Key literature review limitations** | • Broad review objectives<br>• Outdated<br>• Focused to one database only<br>• Statement describing results as poor: "The overall picture illustrated above is | • Limited search strategy<br>• Focused to one database only<br>• Outdated<br>• Minimal discussion on merits of approaches in different applications | • Restrictive inclusion criteria<br>• The review may not have uncovered the full set of challenges hampering the use of identified solutions for the integration of social justice | • Limited search strategy<br>• Focused on SEP-based analyses only<br>• Minimal discussion on merits of approaches in different applications | • No limitations reported specifically for the literature review aspect | • Searched only one database<br>• Only 1 author conducted several steps in the qualitative assessment<br>• Exclusion of other methods of |

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| | very disappointing, and certainly the worst that could have been expected before starting this literature review.” | • Comparison through qualitative summary and discussion only | concerns; moreover, the identified challenges might not represent a complete real-world spectrum<br>• Only English publications considered<br>• Only healthcare and public health areas considered | • Comparison through qualitative summary and discussion only | | examining equity effects in CEAs (eg, MCDA)<br>• The CHEERS checklist does not evaluate the quality of CEAs and only how they are reported |

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**Supplemental Appendix C**

**Table 1:** Traffic light assessment guide

| Component | | Overview | Description of assessment criteria | | |
|---|---|---|---|---|---|
| | | | **Green** *No concerns* | **Orange** *Potential minor concerns* | **Red** *Potential major concerns* |
| **Informational and analytical requirements** | **Data requirements** | The extent to which additional data is required, beyond that which is typically required for cost-effectiveness analysis | No additional data requirements beyond those of a typical CE analysis | Some additional data requirements beyond those of a typical CE analysis | Extensive additional data requirements beyond those of a typical CE analysis |
| | **Data availability** | How readily available any additional data requirements are | Data is readily available from sources used in the current CE analysis framework | Data will require sourcing but is likely available from published sources or from relevant healthcare bodies (or equivalent) | Data is not likely to be available currently, with further research studies required |
| | **Technical complexity** | How technically complex and how analytically onerous the method is | Requires little additional technical understanding beyond that required for typical CE analysis | Some additional technical knowledge required | Extensive additional technical knowledge required |
| **Generalisability** | **Disease area** | How generalisable the method is across different disease areas | Method is applied consistently across disease areas with no differences in method-specific input data | Method is applied consistently across disease areas but with differences in method-specific input data | Method cannot be applied to all disease areas (for any reason) |
| | **Type of intervention** | How generalisable the method is across different types of health care intervention | Method is applied consistently across intervention types with no differences in method-specific input data | Method is applied consistently across intervention types but with differences in method-specific input data | Method cannot be applied to all intervention types (for any reason) |
| | **Healthcare system** | How generalisable the method is for use in different healthcare systems | Method outcomes are likely to be applicable to all healthcare systems | - | Method outcomes are unlikely to be applicable to all healthcare systems |
| **Interpretability** | **Conceptual complexity** | How conceptually complex the method is compared to a typical CE analysis and the extent to which is introduces | The method is no more conceptually complex than typical CE analysis and does not introduce unfamiliar methodological components | The method is no more conceptually complex than typical CE analysis but does introduce potentially new methodological components | The method is conceptually complex and introduces significant methodological complexity |

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| | | new methodological components | | | |
| | **Integration with CE outcomes** | The extent to which the method integrates equity outcomes with those included in typical CE analyses (e.g., costs, QALYs, ICER) | The method is used to modify typical CE outcomes (e.g., the ICER) and no additional output is presented | Additional output is presented alongside (or in combination with) typical CE outcomes | Method does not integrate with typical CE outcomes |
| | **Equity measurement** | The extent to which the method enables the explicit measurement of changes in outcome inequality distribution | The method inherently measures changes in outcome inequality distribution | The method can provide a measure of change in outcome inequality distribution but only under specific circumstances that are unique to the particular method | The method cannot measure changes in outcome inequality distribution |
| | **Conclusiveness** | The extent to which the method enables the derivation of a clear conclusion | The method is able to explicitly identify a favoured policy amongst all policies | The method is able to explicitly identify a favoured policy amongst all policies for individual outcomes but does not provide an assessment of policy preference amongst multiple outcomes | The method is unable to identify a favoured policy amongst all policies |
| CE: cost-effectiveness; ICER: incremental cost-effectiveness ratio. | | | | | |

**Table 2:** Traffic light assessment results - additional context and justification for assessment result

| Component | | Context/justification for assessment result | | | | |
|---|---|---|---|---|---|---|
| | | **EBW** | **ECEA** | **DCEA** | **MCDA** | **MP** |
| **Informational and analytical requirements** | **Data requirements** | Preferences for inequality aversion | FRP data | Input stratification; preferences for SWF evaluation | MCDA approach, components and preferences | |
| | **Data availability** | Preferences for inequality aversion | FRP data | Input stratification; preferences for SWF evaluation | MCDA approach, components and preferences | |
| | **Technical complexity** | | | | Dependent on structure and size of MCDA approach | Model adaptation; optimisation analysis |
| **Generalisability** | **Disease area** | Different preferences for inequality aversion | Some diseases observe no impact on FRP | | Different MCDA components or preferences | Different constraints and/or objectives |
| | **Type of intervention** | | Some interventions observe no impact on FRP | | Difference MCDA components and preferences | Difference constraints and/or objectives |
| | **Healthcare system** | | FRP likely not relevant to all healthcare systems | | | |
| **Interpretability** | **Conceptual complexity** | | Introduces potentially new methodological components (e.g., FRP) | Introduces potentially new methodological components (e.g., equity measurement metrics and SWFs) | | |
| | **Integration with CE outcomes** | | FRP outcomes not integrated with CE outcomes | Movement away from the ICER | | |
| | **Equity measurement** | Cannot measure changes in outcomes inequality | | | Measurement possible if included as its own component | Measurement in the context of the objective only |
| | **Conclusiveness** | | Additional criteria required to combine CE and FRP outcomes | | | |

CE: cost-effectiveness; DCEA: distributional cost-effectiveness analysis; ECEA: extended cost-effectiveness; FRP: financial risk protection; ICER: incremental cost-effectiveness; MCDA: multi-criteria decision analysis; MP: mathematical programming; SWF: social welfare function

**Supplemental Appendix D**

**Opening note:** Readers should be aware that the example presented herein is purely hypothetical, and whilst some input data and assumptions are based on published estimates, a large proportion of inputs and assumptions are contrived in order to demonstrate particular applications. As such, results should be considered within the context of their hypothetical nature.

## Hypothetical applied example: Methodology overview

We illustrate an application of each of the equity evaluation methods with a hypothetical worked example, evaluating the cost-effectiveness of a hypothetical cancer screening programme in a UK setting. We compare the addition of universal and targeted cancer screening reminders to a conventional one-time cancer screening program and evaluate outcomes across socioeconomic/deprivation quintiles. **Figure 1** provides an overview of the screening process.

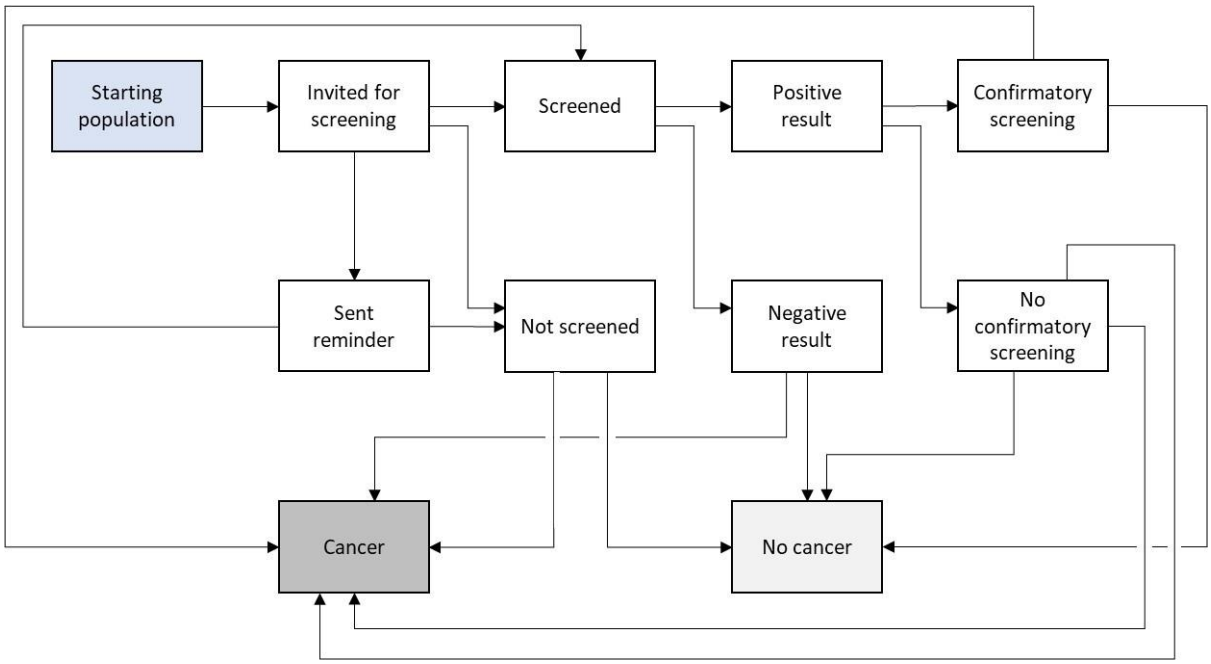


**Figure 1:** Cancer screening flow diagram

All patients are initially invited for cancer screening and those that accept the screening offer are assumed to undertake a low-cost blood test. Subsequently, and upon a positive test result, patients are invited to a more complex and costly confirmatory screening test. Sensitivity and specificity of the initial blood tests are assumed

to be 99% and 95%, respectively. We assume that the confirmatory test has a sensitivity and specificity of 100%. The initial blood test is assumed to cost £3 per-person, and the confirmatory test is assumed to cost £600 per-person.

Screening uptake is stratified by deprivation quintile. Under the two screening reminder scenarios, it is assumed that universal screening reminders increase the uptake of initial screening by 5% and that targeted screening reminders increase the uptake of initial screening by 15%, irrespective of deprivation quintile. The screening reminders are assumed to have no affect on the uptake of confirmatory screening. An overview of cancer prevalence and screening uptake estimates is provided in **Table 1**. The universal screening reminder is assumed to consist of a one-off reminder in the form of a letter, whilst the targeted reminder is assumed to consist of multiple letter- and telephone-based reminders. The universal and targeted reminders are assumed to cost a total of £2 and £8 per-person, respectively.

Subsequently, cancer patients that are identified by the screening programme are assumed to be diagnosed at an earlier cancer stage than those diagnosed away from the screening programme (i.e., those that either were not screened or those that returned a false negative result). We assume that the lifetime cost of cancer patients identified by the screening programme is lower than that of those identified away from the screening programme as we assume that treatment of earlier stage cancer is less expensive. All cost data used in the analysis is summarised in **Table 2**. Similarly, we also assume that cancer patients identified by the screening programme observe a greater quality-adjusted life expectancy (QALE). Estimates of QALE for each group are summarised in **Table 3** and are stratified by deprivation quintile. As a simplifying assumption, we assume no differentiation in costs by deprivation status.

We focus on the evaluation of equity within the context of socioeconomic/deprivation status, with the broad goal of incorporating concerns for the achievement of equitable outcomes across this equity dimension. We assume a cohort size of 10,000,000 people and evaluate two scenarios against the current standard of care (SoC) (i.e., no universal or targeted screening reminders):

- Universal reminder: A one-off reminder is sent to all patients that have not yet been screened
- Targeted reminder: Multiple reminders are sent to all patients in the two most deprived socioeconomic quintiles (Q4 and Q5) that have not yet been screened

**Table 1:** Overview of prevalence and screening uptake estimates

| Deprivation quintile | Proportion of population (%) | Cancer prevalence (%) | Initial blood test screening uptake – current SoC (%) | Confirmatory screening uptake (%) |
|---|---|---|---|---|
| Q1 (least deprived) | 14.29% | 0.05% | 69.07% | 85.64% |
| Q2 | 22.45% | 0.05% | 65.36% | 83.59% |
| Q3 | 26.53% | 0.05% | 61.08% | 79.62% |
| Q4 | 20.41% | 0.05% | 55.20% | 78.10% |
| Q5 (most deprived) | 16.33% | 0.05% | 45.00% | 76.25% |
| Q: quintile; SoC: standard of care | | | | |

**Table 2:** Overview of costs applied in the analysis

| Cost item | Cost (£) |
|---|---|
| **Screening (per-person)** | |
| Initial blood test screening | £3 |
| Subsequent confirmatory screening | £600 |
| Universal reminder | £2 |
| Targeted reminder | £8 |
| **Lifetime cancer care costs (per-patient)** | |
| Cancer detected through screening programme | £20,000 |
| Cancer detected away from screening programme | £30,000 |

**Table 3:** Overview of QALE estimates

| Deprivation quintile | Health distribution (average QALE) | | |
|---|---|---|---|
| | Cancer (identified through screening) | Cancer (not identified through screening) | No cancer |
| Q1 (least deprived) | 71.55 | 66.23 | 73.67 |
| Q2 | 69.73 | 64.55 | 71.80 |
| Q3 | 67.85 | 62.81 | 69.86 |
| Q4 | 66.32 | 61.40 | 68.29 |
| Q5 (most deprived) | 60.87 | 56.35 | 62.68 |
| Q: quintile; QALE: quality-adjusted life expectancy | | | |

**Hypothetical applied example: Equity-based weighting (EBW) method**

**Overview of equity application:** With an EBW method the objective is to incorporate societies preferences for equitable distribution by re-weighting outcomes, giving greater weight to outcomes observed in subgroups for which society feels are underserved.

**Description of example approach:** We opt to adopt a QALY weighting approach where QALY outcomes of the analysis are re-weighted for societies preferences for resource allocation. We first aggregate outcomes by deprivation quintile and then apply the weights to the QALY outcomes. We assume equal weighting for all deprivation quintiles (i.e., weighting of 1.00), except for the most deprived quintile (Q5) for which we apply a weighting of 1.52 (informed by Lal et al. [2018]), inherently increasing the value of QALYs gained in this patient subgroup [1].

**Hypothetical applied example: Extended cost-effectiveness analysis (ECEA)**

**Overview of equity application:** ECEA is an expansion of cost-effectiveness analysis, which compares the relative costs and gains in health outcomes of interventions. ECEA also includes non-health benefits such as financial risk protection and distributional consequences like equity in the economic evaluation of health policies. This enables health policy makers to take into account multiple criteria and make trade-offs among competing demands.

**Description of example approach:** We first stratify results by deprivation quintile in order to assess the impact within the individual subgroups and provide assessors with an indication as to the impact of the screening programmes amongst our pre-defined equity dimension (deprivation status). Next, we attempt to estimate the impact of each of the screening programmes on poverty. To do this, we first estimate the annual disposable income of people in each deprivation quintile and the annual disposable income lost as a result of a cancer diagnosis. We then assume that income is normally distributed and estimate the corresponding proportion of people in each deprivation quintile that lie below the UK poverty line, which we assume to be represented by a weekly income of £268 after housing costs for a working-age couple [2]. **Table 4** provides an overview of the income data used in the example.

**Table 4:** Overview of income data used in the ECEA example

| Deprivation quintile | Annual disposable income (£) | Annual income loss (cancer identified through screening) | Annual income loss (cancer not identified through screening) |
|---|---|---|---|
| Q1 (least deprived) | £75,000 | £2,000 | £5,000 |
| Q2 | £40,000 | £2,000 | £5,000 |
| Q3 | £30,000 | £2,000 | £5,000 |
| Q4 | £20,000 | £2,000 | £5,000 |
| Q5 (most deprived) | £10,000 | £2,000 | £5,000 |

Q: quintile.

**Notes:** To estimate the proportion of people in each deprivation quintile that lie below the UK poverty line we convert the annual disposable income and the annual income loss to a weekly equivalent, and assuming a standard deviation of 20% of the mean weekly disposable income (before cancer income losses), use the normal distribution to approximate the proportion of patients in each deprivation quintile with a weekly income less than £268.

**Hypothetical applied example: Conventional DCEA**

**Overview of equity application:** Conventional DCEA attempts to account for the opportunity costs associated with the introduction of a new policy or intervention by valuing such costs in terms of foregone QALYs. These foregone QALYs are subsequently included in the distribution of health gains and used to estimate the change in health distribution over any relevant equity strata. DCEA also attempts to analyse the trade-offs between improving population health and improving health equality.

**Description of example approach:** We use the study by Asaria et al. (2016) as a guide for this example [3]. As described in the publication, the main steps in the modelling stage are:

1. Estimating the baseline health distribution;
2. Modelling changes to this baseline distribution due to the health interventions being compared, allowing for the distribution of opportunity costs from additional resource use;
3. Adjusting the resulting modelled health distributions for alternative social value judgments about fair and unfair sources of health variation.

For steps 1 and 2 in the modelling stage, the baseline health distribution (i.e., per-person QALE estimates) and changes to this distribution are estimated based on the average health distribution data observed in **Table 3**, accounting for the total number of cancer patients identified through each of the screening strategies. We assume our SoC scenario represents the baseline QALE. We model each of the screening strategies as in the

standard cost-effectiveness analysis approach. To account for opportunity costs from displaced activities, we take the incremental expenditure of the universal and targeted scenarios (compared to SoC) and convert these costs to foregone QALYs using a value of £20,000/QALY. We then assume that these foregone QALYs are distributed equally (proportionally) across deprivation quintiles, and we subtract these from the total population QALYs estimated under each of the screening reminder strategies. For step 3, we take a simplistic approach and make a social value judgement that assumes all differences in QALE across deprivation quintiles can be considered 'unfair'. Therefore, we make no adjustments in line with this modelling step.

Subsequently, we use the estimated distributions to quantify the change in total population health and analyse trade-offs between improving population health and reducing unfair health inequality. To analyse trade-offs, we calculate the equally distributed equivalent (EDE) level of health for the Atkinson index using the following equation:

$$\boldsymbol{h_{ede}} = [\frac{\mathbf{1}}{\boldsymbol{n}}\sum_{\boldsymbol{i=1}}^{\boldsymbol{n}} \boldsymbol{h_i}^{(\mathbf{1}-\boldsymbol{\varepsilon})}]^{(\frac{\mathbf{1}}{\mathbf{1}-\boldsymbol{\varepsilon}})}$$

Where $\boldsymbol{h_i}$ is the QALE of each person in the cohort, ε is the inequality aversion parameter and n is the total number of persons in the evaluation. We utilise an inequality aversion parameter of 10.95 [4].

EDE is the common level of health in a hypothetical equal distribution of health that has the same level of social welfare as the actual unequal distribution of health, with the difference indicating the change in health-related social welfare. Comparing the incremental QALYs to the incremental EDE provides the QALY valuation of any change in inequality. For example, if an intervention increases population health by 100,000 QALYs and increases EDE by 101,000 QALYs, the reduction in health inequality attributed to the intervention is valued at 1,000 QALYs.

**Hypothetical applied example: Aggregate DCEA**

**Overview of equity application:** In a similar approach to conventional DCEA, aggregate DCEA attempts to account for the opportunity costs associated with the introduction of a new policy or intervention by valuing such costs in terms of foregone QALYs. These foregone QALYs are subsequently included in the distribution of health gains and used to estimate the change in health distribution over any relevant equity strata. DCEA also attempts to analyse the trade-offs between improving population health and improving health equality. The main

difference between DCEA methodologies, is that aggregate DCEA is designed to be used with aggregated cost-effectiveness outcomes and estimates the distribution of foregone QALYs using external data.

**Description of example approach:** We use the study by Love-Koh et al. (2019) as a guide for this example [5]. The methodology generally mirrors that of conventional DCEA with two exceptions. The first exception relates to the distribution of outcomes across deprivation quintiles, which under an aggregate DCEA approach would be estimated from a single set of aggregated cost-effectiveness outcomes, disaggregated based on observed resource use in the disease area of interest. Since we already have the disaggregated outcomes and there is no need to estimate these, we do not undertake this step. The second exception relates to the distribution of foregone QALYs. In the conventional DCEA example we assumed that foregone QALYs were equally (proportionally) distributed across deprivation quintiles. In this aggregate DCEA example we assume that foregone QALYs are distributed based on the estimated distribution of total medical resource use across deprivation quintiles, as estimated by Love-Koh et al. (2020) [6]. This distribution is presented in **Table 5**.

**Table 5:** Health opportunity cost distribution

| Deprivation quintile | Health opportunity cost distribution | | |
|---|---|---|---|
| | Males | Females | Total (used) |
| Q1 | 0.08 | 0.06 | 0.14 |
| Q2 | 0.09 | 0.07 | 0.16 |
| Q3 | 0.12 | 0.10 | 0.22 |
| Q4 | 0.12 | 0.10 | 0.22 |
| Q5 | 0.14 | 0.12 | 0.26 |
| Q1 | 0.08 | 0.06 | 0.14 |

## Hypothetical applied example: MCDA

**Overview of equity application:** MCDA aims to provide a framework from which to evaluate multiple criteria that are typically heterogeneous in nature. Criteria associated with the achievement of healthcare equity may be specified, and given the nature of MCDA, significant flexibility with regards to the evaluation or inclusion of equity concerns is possible.

**Description of example approach:** We use the study by Thokala et al. (2012) as a guide for this example [7]. We demonstrate the use of two MCDA approaches, namely the value measurement method and the outranking

approach. Both methods are described in detail in the guiding publication. We first specify the criteria through which each screening programme is to be assessed, and in our example, we include cost-effectiveness, total QALE gain, provision of equal access, the level of inequality reduction and the level of innovation of each programme. An overview of the criteria, their explicit scoring algorithms and the weights applied to each criterion are summarised in **Table 6**. Two of the criteria may be considered as criteria related to the consideration of equity, namely the provision of equal access and the inequality reduction criteria.

For the value measurement method, the score for each criterion is multiplied by the respective weight and tallied for each screening programme. The screening programme with the highest score is the 'winner'. For the outranking approach, we are concerned with dominance and aim to evaluate when a strategy outranks the other strategy. We compare scores across each criterion as in the value measurement method but consider only those in which a score difference (after weighting) of 2 or more (our indifference threshold) exists. For each criterion for which this is the case we derive the concordance index. For our universal strategy, the concordance index is defined as the ratio of the sum of weights in the criteria for which the universal screening reminder is at least as good as the targeted screening reminder, to the sum of weights in all criteria (and vice versa for the targeted screening reminder). Subsequently, the screening programme with the highest concordance index is the 'winner'.

It is worth noting here that we only discuss the 'preferred' strategy and we do not consider, for example, that in order to be reimbursed (or indeed be considered further at all), a specific minimum score threshold could be set.

**Table 6:** Overview of MCDA criteria

| **MCDA evaluation criteria** | **Scoring algorithm for each criterion** | **Weight applied to each evaluation criterion** |
|---|---|---|
| Cost-effectiveness | Score of 3 for ICER <£20,000; score of 2 for ICER between £20,000 and £30,000; score of 1 for ICER between £30,000 and £50,000; 0 otherwise. Additional 1 point for most cost-effective strategy. | 2 |
| Total QALE gain | Score of 3 to interventions that provide a QALE gain greater than 1 (per patient); additional score of 1 to the strategy which provides the greatest QALE gain. | 2 |
| Provision of equal access | Score of 2 for interventions that provide approximately equal opportunity across patient groups (qualitative assessment); 0 otherwise. | 1 |

| | | |
|---|---|---|
| Inequality reduction | Score of 2 for pro-poor QALE gains (i.e., QALE gains favour the poor), score of 1 if QALE gains approximately equally distributed (qualitative assessment); score of 0 otherwise. | 3 |
| Innovation | Score of 2 if intervention or programme can be considered novel or innovative; score of 0 otherwise. | 1 |
| ICER: incremental cost-effectiveness ratio; MCDA: multi-criteria decision analysis; QALE: quality-adjusted life expectancy | | |

**Hypothetical applied example: MP**

**Note:** we note that the MP approach is unable to offer any unique insight into the initial decision problem as there are no optimisable aspects, therefore without modifying the decision problem outcomes under an MP approach cannot be estimated. Therefore, we do not present results of an MP analysis in the main manuscript body. However, below we attempt to illustrate a potentially useful application of MP beyond the initial decision problem.

**Overview of equity application:** Typical cost-effectiveness analyses are undertaken with the aim of directly comparing two (or more) policies or interventions in a particular setting. MP is typically concerned with optimising outcomes based on a given set of constraints and objectives, and therefore requires modification to the underlying assessment framework, potentially making comparisons with the underlying 'standard' cost-effectiveness analysis difficult. Equity constraints may be introduced so that the effectiveness of policies can be assessed in scenarios in which a particular equity goal is important, but it is important to note that MP does not offer measurement of equitable distribution, nor does it provide a more granular understanding of equity issues without first imposing additional constraints on the analysis.

**Description of example approach:** Two optimisation analyses are undertaken. Under each scenario, the proportion receiving each type of screening reminder (universal or targeted) in each deprivation quintile was allowed to vary freely. The first scenario (Scenario A) is constrained by a maximum screening budget with the goal of maximising QALE gains; the second scenario (Scenario B) utilises the same budget constraint but with the goal of reducing the total QALE variation across deprivation quintiles. **Table 7** provides an overview of the optimisation objectives and constraints used in each scenario.

The Solver application in Excel was used to generate results for each scenario. The Evolutionary solver method was used. Settings used for the Solver application are provided in **Table 8**.

**Table 7:** MP optimisation objectives and constraints

| | Scenario A | Scenario B |
|---|---|---|
| **Optimisation target** | Total QALYs (maximisation) | Variation of total QALYs across deprivation quintiles (minimisation) |
| **Total screening budget (£)** | **Constraint:** Not greater than the average total of the Universal and Targeted screening costs as observed in the standard cost-effectiveness analysis | |
| **Proportion of patients receiving screening reminders** | **Constraint:** The proportion must be greater than or equal to 0 and smaller than or equal to 1; a single patient cannot receive multiple sets of reminders | |
| QALY: quality-adjusted life year | | |

**Table 8:** MP Solver settings

| Solver setting | Value |
|---|---|
| **Solver method** | Evolutionary |
| **Constraint precision** | 0.0000001 |
| **Convergence** | 0.000001 |
| **Mutation rate** | 0.075 |
| **Population Size** | 1,000 |
| **Random Seed** | 0 |
| **Maximum Time without improvement** | 60 |
| **Notes:** All other settings remain as Excel default. | |

**Hypothetical applied example: Detailed results**

More detailed results of the analyses are provided in **Table 9**.

**Table 9:** Results of an illustrative application of each of the equity evaluation methods

| Equity evaluation method | Approach overview | Outcome | Evaluation conclusion | Reason for evaluation conclusion | Key conclusion drivers |
|---|---|---|---|---|---|
| Standard cost-effectiveness analysis | Universal screening reminders and targeted screening reminders compared to current SoC; No equity evaluation component | **U v SoC (ICER):** £24,616<br>**T v SoC (ICER):** £31,724<br>**T v U (ICER):** £3,036,798 | Universal strategy cost-effective versus SoC at WTP threshold of £30,000/QALY<br><br>Targeted strategy not cost-effective versus SoC at WTP threshold of £30,000/QALY<br><br>Targeted strategy not cost-effective versus Universal strategy at WTP threshold of £30,000/QALY | Conclusion is dependent on the ICER being above or below the WTP threshold | - |
| EBW (QALYs) | QALY outcomes for patients in the most deprived quintile are given additional weighting | **U v SoC (ICER):** £22,951<br>**T v SoC (ICER):** £26,065<br>**T v U (ICER):** £48,710 | Both Universal and Targeted strategies are cost-effective versus SoC at WTP threshold of £30,000/QALY<br><br>Targeted strategy not cost-effective versus Universal strategy at WTP threshold of £30,000/QALY | Adjusted ICERs are below the WTP threshold | Chosen QALY weights |

<table>
<tr>
<td>ECEA</td>
<td>Cost-effectiveness outcomes are stratified by age group: ages 50-54; ages 55-59; ages 60-64; ages 65-69. Further, using UK-specific income data and poverty definitions, the impact of the intervention on the proportion of patients living in poverty is assessed for each age group.</td>
<td>
ICER
<table>
<tr><th></th><th>U v SoC</th><th>T v SoC</th><th>T v U</th></tr>
<tr><td>Q1</td><td>£24,125</td><td>NA</td><td>£24,125</td></tr>
<tr><td>Q2</td><td>£24,425</td><td>NA</td><td>£24,425</td></tr>
<tr><td>Q3</td><td>£24,986</td><td>NA</td><td>£24,986</td></tr>
<tr><td>Q4</td><td>£24,620</td><td>£31,639</td><td>£31,639</td></tr>
<tr><td>Q5</td><td>£24,808</td><td>£31,843</td><td>£31,843</td></tr>
<tr><td>Average</td><td>£24,616</td><td>£31,724</td><td>£3,036,798</td></tr>
</table>
Reduction in the proportion of cancer patients facing poverty (%)
<table>
<tr><th></th><th>U v SoC</th><th>T v SoC</th><th>T v U</th></tr>
<tr><td>Q1</td><td>0.00%</td><td>0.00%</td><td>0.00%</td></tr>
<tr><td>Q2</td><td>0.01%</td><td>0.00%</td><td>-0.01%</td></tr>
<tr><td>Q3</td><td>0.09%</td><td>0.00%</td><td>-0.09%</td></tr>
<tr><td>Q4</td><td>0.97%</td><td>2.87%</td><td>1.89%</td></tr>
<tr><td>Q5</td><td>0.17%</td><td>0.58%</td><td>0.40%</td></tr>
<tr><td>Average</td><td>0.25%</td><td>0.68%</td><td>0.43%</td></tr>
</table>
</td>
<td>Universal strategy cost-effective versus SoC at WTP threshold of £30,000/QALY<br><br>Targeted strategy not cost-effective versus SoC at WTP threshold of £30,000/QALY<br><br>Targeted strategy not cost-effective versus Universal strategy at WTP threshold of £30,000/QALY<br><br>Targeted strategy offers greater poverty reduction than universal strategy and SoC</td>
<td>Conclusion is dependent on the ICER being above or below the WTP threshold (although, alternative subgroup decisions might be made based on disaggregated analyses); the reduction in poverty of each strategy may also change conclusions but such criteria are not specified here</td>
<td>Effectiveness estimates by subgroup (deprivation quintile)<br><br>Poverty reduction: Poverty line; Income estimates; Cancer-related income loss estimates</td>
</tr>
<tr>
<td>DCEA (Conventional)</td>
<td>Cost-effectiveness analyses are stratified by deprivation quintile. The opportunity costs associated with a new intervention are evaluated and the resulting change in the distribution of health amongst the population is measured using relevant inequality measurement metrics.</td>
<td>
U v SoC<br>
ICER: £24,616<br>
Incremental population QALYs: -230 (after opportunity costs accounted for)<br>
ΔEDE: -288<br><br>
T v SoC<br>
ICER: £31,724<br>
Incremental population QALYs: -586 (after opportunity costs accounted for)<br>
ΔEDE: 32<br><br>
T v U<br>
ICER: £3,036,798
</td>
<td>Universal strategy cost-effective versus SoC at WTP threshold of £30,000/QALY but reduces population health and increases health inequality<br><br>Targeted strategy not cost-effective versus SoC at WTP threshold of £30,000/QALY and reduces population health but reduces health inequality</td>
<td>ICERs remain unchanged as they are not modified to account for opportunity cost.<br><br>As new interventions with an ICER greater than the cost per QALY of forgone alternatives (assumed to be £20,000) would be expected to reduce the total health of the population, we observe reduced incremental population QALYs for both screening strategies.</td>
<td>Value of foregone QALYs; baseline and changes in QALE distribution; Distribution of foregone QALYs (although not assessed here); inequality aversion parameter</td>
</tr>
</table>

| | | | | | |
|---|---|---|---|---|---|
| | | **Incremental population QALYs**: -356 (after opportunity costs accounted for)<br>Δ**EDE**: 320 | Targeted strategy <u>not cost-effective</u> versus Universal strategy at WTP threshold of £30,000/QALY and <u>reduces population health</u> but <u>reduces health inequality</u> | EDE is the common level of health in a hypothetical equal distribution of health that has the same level of social welfare as the actual unequal distribution of health, with the difference indicating the change in health-related social welfare. | |
| DCEA (Aggregate) | Aggregated cost-effectiveness results are disaggregated across deprivation quintiles based on external resource use data (although in our example this is not necessary as we have the disaggregated output). The opportunity costs associated with a new intervention are evaluated and the resulting change in the distribution of health amongst the population is measured using relevant inequality measurement metrics. Opportunity costs are distributed based on external resource use data. | **U v SoC**<br>**ICER:** £24,616<br>**Incremental population QALYs**: -230 (after opportunity costs accounted for)<br>Δ**EDE**: -520<br><br>**T v SoC**<br>**ICER:** £31,724<br>**Incremental population QALYs**: -586 (after opportunity costs accounted for)<br>Δ**EDE**: -268<br><br>**T v U**<br>**ICER:** £3,036,798<br>**Incremental population QALYs**: -356 (after opportunity costs accounted for)<br>Δ**EDE**: 252 | Universal strategy <u>cost-effective</u> versus SoC at WTP threshold of £30,000/QALY but <u>reduces population health</u> and <u>increases health inequality</u><br><br>Targeted strategy <u>not cost-effective</u> versus SoC at WTP threshold of £30,000/QALY but <u>reduces population health</u> and <u>increases health inequality</u><br><br>Targeted strategy <u>not cost-effective</u> versus Universal strategy at WTP threshold of £30,000/QALY and <u>reduces population health</u> but <u>reduces health inequality</u> | | Value of foregone QALYs; baseline and changes in QALE distribution; Distribution of foregone QALYs; inequality aversion parameter |
| MCDA | Evaluation criteria are based on cost-effectiveness, total QALE gain, provision of equal access, the level of inequality reduction and the level of innovation of the program; for each criterion and screening | **Value measurement method:** The universal strategy scores 11 and the targeted strategy scores 9<br><br>**Outranking approach:** The universal strategy has a concordance index of 0.22 and the | Value measurement method: <u>Universal strategy preferred</u> with score of 11 (compared to 9)<br><br>Outranking approach: <u>Targeted strategy preferred</u> | The value measurement method sums the weighted scores for each criterion and compares the total, with the higher value representing the preferred strategy. | Underlying MCDA approach; Choice of evaluation criteria; Scoring system; Weights applied to each criterion; |

| | | | | | |
|---|---|---|---|---|---|
| | strategy, a score is estimated, with total scores subsequently weighted by the relative importance of each criterion. Two MCDA approaches are undertaken (the value measurement method and the outranking approach)[105]. | targeted strategy has a concordance index of 0.33 | with a concordance index of 0.33 (compared to 0.22) | The outranking approach compares only those criteria in which a significant positive difference is observed (defined by a user-defined indifference threshold) and then divides each score through by the sum of the weights to create an index, with the higher value representing the preferred strategy.<br><br>We only discuss the 'preferred' strategy and we do not consider, for example, that in order to be reimbursed (or indeed be considered further at all), a specific minimum score threshold could be set. | Indifference threshold (outranking approach only) |
| MP | Two optimisation analyses are undertaken. Under each scenario, the proportion receiving each type of screening reminder (universal or targeted) in each deprivation quintile was allowed to vary freely.<br><br>The first scenario (Scenario A) is constrained by a maximum screening budget with the goal of maximising QALE gains and the second scenario (Scenario B) utilises the same | **Scenario A v SoC**<br>**ICER:** £25,678<br>**Incremental QALYs:** 0.22<br>**Q1-Q5 QALY range:** 11.57<br><br>**Scenario B v SoC**<br>**ICER:** £31,134<br>**Incremental QALYs:** 0.18<br>**Q1-Q5 QALY range:** 10.94 | Unclear as strict conclusion criteria not specified; further, in order to accommodate an MP approach, the analysis moves away from a strict policy versus policy comparison and focuses on further optimising policies or exploration of policy impacts under specific constraints | Scenario A provides either universal or targeted screening reminders to all, with targeted screening focused to the least deprived where a greater initial screening uptake will go further due to the increased subsequent likelihood of uptake of the confirmatory screening. This results in a lower ICER and greater QALY gain, but also a wider gap in terms of total QALY between the most and least deprived. | Optimisation objectives; Evaluation constraints |

| | | | | | |
|---|---|---|---|---|---|
| | budget constraint but with the goal of reducing the total QALE variation across deprivation quintiles. | | | Scenario B provides either universal or targeted screening reminders to all patients in the Q4 and Q5 subgroups (and to a proportion in the Q3 subgroup) but no reminders to patients in the Q1 and Q2 subgroups. This results in a lower gap in terms of total QALY between the most and least deprived, but a greater ICER and lower total QALY gain (compared to Scenario A). | |
| DCEA: distributional cost-effectiveness analysis; EBW: equity-based weighting; ECEA: extended cost-effectiveness analysis; EDE: equally distributed equivalent; ICER: incremental cost-effectiveness ratio; MCDA: multi-criteria decision analysis; MP: mathematical programming; Q: quintile; QALE: quality-adjusted life expectancy; QALY: quality-adjusted life year; SoC: standard of care; T: targeted; U: universal; WTP: willingness-to-pay. | | | | | |

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**Supplemental Appendix E**

**Table.** Overview of studies

| Method Type | Author & Publication Year | Title | Journal | Study type* | Country of application | Disease Area | Comparison** | Equity stratification factors^ | Inequality measurement/valuation^^ |
|---|---|---|---|---|---|---|---|---|---|
| DCEA (aggregate) | Arnold, et al. (2020) | Distributional impact of the Malawian Essential Health Package | Health Policy Plann | Applied | Malawi | Multiple disease areas / broad healthcare | **Pharmacological, vaccination & general healthcare**: Multiple (73) interventions | Household wealth; Urban/rural status | **Inequality measurement:** Atkinson index<br><br>**SWF:** Atkinson EDE |
| DCEA (aggregate) | Love-Koh, et al. (2019) | Aggregate Distributional Cost-Effectiveness Analysis of Health Technologies | Value Health | Applied | UK | Multiple disease areas / broad healthcare | **Pharmacological:** Multiple (27) interventions | Socioeconomic status | **Inequality measurement:** Slope index of inequality; Relative index of inequality; Atkinson index; Kolm index<br><br>**SWF:** Atkinson EDE; Kolm EDE |
| DCEA (aggregate) | Griffin, et al. (2019) | Evaluation of Intervention Impact on Health Inequality for Resource Allocation | Med Decis Making | Methodological Case Study | UK | Multiple disease areas / broad healthcare | **Pharmacological, education, lifestyle, and general healthcare**: Multiple (134) interventions | Socioeconomic status | **Inequality measurement:** Slope index of inequality; Relative index of inequality; Atkinson index; Kolm index<br><br>**SWF:** Atkinson EDE; Kolm EDE |
| DCEA (conventional) | Love-Koh, et al. (2020a) | Equity and economic evaluation of system-level health interventions: A case study of Brazil's Family Health Program | Health Policy Plann | Applied | Brazil | Multiple disease areas / broad healthcare | **General healthcare:** Programme Saude da Familia (PSF) (a community-level primary care system intervention); No PSF | Region | **Inequality measurement**: Slope index of inequality; relative index of inequality<br><br>**SWF:** Atkinson EDE; Kolm EDE |
| DCEA (conventional) | Allen, et al. (2015) | Potential of trans fats policies to reduce socioeconomic inequalities in mortality from coronary heart disease in England: cost effectiveness modelling study | BMJ | Applied | England | Coronary heart disease | **Policy:** Total ban on trans fatty acids in processed foods; Improved labelling of trans fatty acids; Bans on trans fatty acids in restaurants and takeaways; Current SoC | Socioeconomic status | **Inequality measurement:** Slope index of inequality<br><br>**SWF:** None reported |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| DCEA (conventional) | Olsen, et al. (2021) | Reducing regional health inequality: a sub-national distributional cost-effectiveness analysis of community-based treatment of childhood pneumonia in Ethiopia | Int J Equity Health | Applied | Ethiopia | Pneumonia (children) | **General healthcare:** Community-based treatment; No treatment | Region | **Inequality measurement:** Gini coefficient<br><br>**SWF:** None reported |
| DCEA (conventional) | Oosterhoff, et al. (2020) | Lifetime cost-effectiveness and equity impacts of the Healthy Primary School of the Future initiative | BMC Public Health | Applied | Holland | Weight-based chronic disease (children) | **Lifestyle:** Healthy Primary School of the Future Programme; Physical Activity School Programme; SoC | Socioeconomic status | NR |
| DCEA (conventional) | Lee, et al. (2018) | Strategic distributional cost-effectiveness analysis for improving national cancer screening uptake in cervical cancer: A focus on regional inequality in South Korea | Cancer Res Treat | Applied | South Korea | Cervical cancer | **Screening:** Current strategy (screening biennially); current strategy plus postal recommendation for those in high-risk areas; Universal screening with postal screening recommendation; Universal screening with strong postal screening recommendation | Health inequality | **Inequality measurement:** Atkinson index<br><br>**SWF:** Atkinson ICER |
| DCEA (conventional) | Lee, et al. (2016) | Cost effectiveness of colorectal cancer screening interventions with their effects on health disparity being considered | Cancer Res Treat | Applied | South Korea | Colorectal cancer | **Screening:** Annual FOBT; Annual FOBT with basic reminders for provinces with higher mortalities than the national average; Annual FOBT with basic/enhanced reminders for all provinces (universal reminder 1 and 2); No screening | Health inequality | **Inequality measurement:** Atkinson index<br><br>**SWF:** Atkinson ICER |
| DCEA (conventional) | Ngalesoni, et al. (2016) | Equity impact analysis of medical approaches to cardiovascular diseases prevention in Tanzania | Soc Sci Med | Applied | Tanzania | Cardiovascular disease | **Pharmacological:** No medical prevention; WHO approach (patients with a moderate or high CVD risk treated); Differentiated risk threshold by age approach (different risk thresholds were applied to different age groups such that treatment is provided to a proportion of the population); ESC approach (assumed a scenario in which Tanzania is willing to pay more than one GDP per capita for a unit of health gain such that it would become “very cost-effective” to treat all individuals with a 10- | CVD risk group | **Inequality measurement:** Gini coefficient<br><br>**SWF:** Achievement index |

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|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | year CVD risk equal to or above 5%) | | |
| DCEA (conventional) | Kypridemos, et al. (2018) | Future cost-effectiveness and equity of the NHS Health Check cardiovascular disease prevention programme: Microsimulation modelling using data from Liverpool, UK | PLoS Med | Applied | UK | Cardiovascular disease | **Screening & lifestyle:** Current implementation of NHS Health Check (A); NHS Health Check `targeted' toward the most deprived areas (B); `Optimal' NHS Health Check coverage, uptake, treatment and lifestyle change; A combined with structural population-wide interventions targeting unhealthy diet and smoking; B combined with structural population-wide interventions targeting unhealthy diet and smoking; No NHS Health Check | Socioeconomic status | **Inequality measurement:** Absolute equity slope index; Relative equity slope index<br><br>**SWF:** None reported |
| DCEA (conventional) | Love-Koh, et al. (2020b) | How health inequalities accumulate and combine to affect treatment value: A distributional cost-effectiveness analysis of smoking cessation interventions | Soc Sci Med | Methodological Case Study | England | Diseases associated with smoking | **Pharmacological & lifestyle:** Multiple (21) interventions | Socioeconomic status | **Inequality measurement:** Slope index of inequality; relative index of inequality<br><br>**SWF:** Atkinson EDE; Kolm EDE |
| DCEA (conventional) | Dawkins, et al. (2018) | Distributional Cost-Effectiveness Analysis in Low- and Middle-Income Countries: Illustrative Example of Rotavirus Vaccination in Ethiopia | Health Policy Plann | Methodological Case Study | Ethiopia | Rotavirus | **Vaccination:** No vaccination; Standard vaccination; Hypothetical 'pro-poor' vaccination programme | Wealth | **Inequality measurement:** Atkinson index<br><br>**SWF:** Atkinson EDE |
| DCEA (conventional) | Robberstad, et al. (2011) | Incorporating concerns for equal lifetime health in evaluations of public health programs | Soc Sci Med | Methodological Case Study | Tanzania | Hypertension (adults) and pneumococcal diseases (children) | **Pharmacological & vaccination:** Hydrochlorothiazide (hypertension); Vaccination (children) | Health inequality | **Inequality measurement:** Gini coefficient<br><br>**SWF:** Achievement index |
| DCEA (conventional) | Asaria, et al. (2015) | Distributional cost-effectiveness analysis of health care programmes - A methodological case study of the UK bowel cancer screening programme | Health Econ | Methodological Case Study | UK | Bowel cancer | **Screening:** Universal reminder; Targeted reminder; Standard screening; No screening | Socioeconomic status; Gender; Ethnicity | **Inequality measurement:** Relative gap index; Relative index of inequality; Atkinson index; Gini index; Absolute inequality indices; Absolute gap index; Slope index of inequality; Kolm index |

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|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | **SWF:** Atkinson EDE; Kolm EDE |
| DCEA (conventional) | Asaria, et al. (2016) | Distributional Cost-Effectiveness Analysis: A Tutorial | Med Decis Making | Methodological Case Study | UK | Bowel cancer | **Screening:** Universal reminder; Targeted reminder; Standard screening; No screening | Socioeconomic status; Gender; Ethnicity | **Inequality measurement:** Relative gap index; Relative index of inequality; Atkinson index; Gini index; Absolute gap index; Slope index of inequality; Kolm index<br><br>**SWF:** Atkinson social welfare index; Kolm social welfare index |
| DCEA (conventional) | Collins, et al. (2020) | Universal or targeted cardiovascular screening? Modelling study using a sector-specific distributional cost effectiveness analysis | Prev Med | Methodological Case Study | UK | Cardiovascular disease | **Screening:** No screening; 'Current' basic universal screening; Enhanced universal screening with 'increased' population-wide delivery; 'Universal plus targeted' with top-up delivery to the most deprived fifth | Socioeconomic status | **Inequality measurement:** Slope index of inequality<br><br>**SWF:** None reported |
| DCEA (conventional) | Pitt, et al. (2020) | Public Health Interventions with Harms and Benefits: A Graphical Framework for Evaluating Tradeoffs | Med Decis Making | Methodological Case Study | USA | Obesity | **Policy:** Meat price increase of 5%; Meat price increase of 10%; Meat price increase of 25%; Meat price increase of 50% | Ethnicity; Gender | **Inequality measurement:** Gini coefficient<br><br>**SWF:** None reported |
| DCEA (conventional) | Cookson, et al. (2009) | Explicit Incorporation of Equity Considerations into Economic Evaluation of Public Health Interventions | Health Econ Policy L | Methodology | - | - | - | NR | NR |
| DCEA (conventional) | Cookson, et al. (2017) | Using Cost-Effectiveness Analysis to Address Health Equity Concerns | Value Health | Methodology | - | - | - | NR | NR |
| EBW (costs) | Ong, et al. (2009) | A cost-based equity weight for use in the economic evaluation of primary health care interventions: case study of the Australian Indigenous population | Int J Equity Health | Methodological Case Study | Australia | Primary healthcare | **Hypothetical non-specific example** | Race | NA |
| EBW (costs) | Daems, et al. (2013) | Equity in pharmaceutical pricing and reimbursement: | Value Health Regional | Methodology | - | - | - | Regional GDP | NA |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Crossing the income divide in Asia Pacific | | | | | | | |
| EBW (other) | Karnon, et al. (2015) | Cost-Value Analysis and the SAVE: A Work in Progress, But an Option for Localised Decision Making? | Pharmacoeconomics | Methodological Case Study | England | Breast cancer | **Pharmacological:** Tamoxifen; Letrozole | Disease severity | NA |
| EBW (QALYs) | Lindemark, et al. (2017) | Costs and expected gain in lifetime health from intensive care versus general ward care of 30,712 individual patients: a distribution-weighted cost-effectiveness analysis | Crit Care | Applied | Norway | Multiple disease areas / broad healthcare | **General healthcare:** ICU care; General ward care | Disease severity | NA |
| EBW (QALYs) | Carr, et al. (2006) | What is the value of treating schizophrenia? | Aust NZ J Psychiat | Methodological Case Study | Australia | Schizophrenia; Depression; Anxiety | **General healthcare:** Optimal' treatment; 'Non-optimal' treatment | Disease severity; QALE gain | NA |
| EBW (QALYs) | Baeten, et al. (2010) | Incorporating equity-efficiency interactions in cost-effectiveness analysis - Three approaches applied to breast cancer control | Value Health | Methodological Case Study | Europe | Breast cancer | **Screening & pharmacological:** Intervention; No intervention | Age; Stage of diagnosis | NA |
| EBW (QALYs) | Bleichrodt, et al. (2005) | A Nonparametric Elicitation of the Equity-Efficiency Trade-Off in Cost-Utility Analysis | J Health Econ | Methodological Case Study | Holland | Multiple disease areas / broad healthcare | **Pharmacological & surgical:** Multiple (12) interventions | QALE without intervention | NA |
| EBW (QALYs) | Stolk, et al. (2004) | Reconciliation of Economic Concerns and Health Policy | Pharmacoeconomics | Methodological Case Study | Holland | Multiple disease areas / broad healthcare | **Pharmacological, surgical & vaccination:** Multiple (10) interventions | QALE without disease; Disease-related QALY loss | NA |
| EBW (QALYs) | Luyten, et al. (2021) | Integrating Alternative Social Value Judgments Into Cost-Effectiveness Analysis of Vaccines: An Application to Varicella-Zoster Virus Vaccination | Value Health | Methodological Case Study | UK | Varicella zoster and herpes zoster (children) | **Vaccination:** Vaccination; No vaccination | Disease type; Age; Vaccination status | NA |

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|---|---|---|---|---|---|---|---|---|---|
| EBW (QALYs) | Versteegh, et al. (2019) | Severity-Adjusted Probability of Being Cost Effective | Pharmacoeconomics | Methodology | Holland | Broad oncology | **Hypothetical non-specific example** | Disease severity | NA |
| EBW (QALYs) | Haaland, et al. (2019) | A flexible formula for incorporating distributive concerns into cost-effectiveness analyses: Priority weights | PLoS ONE | Methodology | - | - | - | NR | NA |
| EBW (QALYs) | Bleichrodt, et al. (1997) | Health Utility Indices and Equity Considerations | J Health Econ | Methodology | - | - | - | NR | NA |
| EBW (QALYs) | Bleichrodt, et al. (2004) | Equity Weights in the Allocation of Health Care: The Rank-Dependent QALY Model | J Health Econ | Methodology | - | - | - | QALE without intervention | NA |
| EBW (QALYs) | Cookson, et al. (2009) | Explicit Incorporation of Equity Considerations into Economic Evaluation of Public Health Interventions | Health Econ Policy L | Methodology | - | - | - | NR | NA |
| EBW (QALYs) | Cookson, et al. (2017) | Using Cost-Effectiveness Analysis to Address Health Equity Concerns | Value Health | Methodology | - | - | - | NR | NA |
| EBW (QALYs) | Dolan, et al. (1998) | The measurement of individual utility and social welfare | J Health Econ | Methodology | - | - | - | Pre-treatment health status; Post-treatment health status | NA |
| EBW (QALYs) | Gafni, et al. (1991) | Equity Considerations in Utility-Based Measures of Health Outcomes in Economic Appraisals: An Adjustment Algorithm | J Health Econ | Methodology | - | - | - | NR | NA |
| EBW (QALYs) | Nord, et al. (1999a) | Incorporating societal concerns for fairness in numerical valuations of health programmes | Health Econ | Methodology | - | - | - | Severity of illness; Limitations in potential for health | NA |

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|---|---|---|---|---|---|---|---|---|---|
| EBW (QALYs) | Nord, et al. (1999b) | Towards cost-value analysis in health care? | Health Care Anal | Methodology | - | - | - | Severity of illness; Limitations in potential for health | NA |
| EBW (QALYs) | Nord, et al. (2005) | Concerns for the worse off: fair innings versus severity | Soc Sci Med | Methodology | - | - | - | Overall QALE; Disease severity | NA |
| EBW (QALYs) | Rodriguez, et al. (2000) | The social value of health programmes: Is age a relevant factor | Health Econ | Methodology | - | - | - | Age | NA |
| EBW (QALYs) | Round, et al. (2018) | Incorporating Equity in Economic Evaluations: A Multi-attribute Equity State Approach | Eur J Health Econ | Methodology | - | - | **Hypothetical non-specific example** | Age; Disease severity | NA |
| EBW (QALYs) | Sussex, et al. (2013) | Operationalizing Value-Based Pricing of Medicines | Pharmacoeconomics | Methodology | - | - | - | NR | NA |
| EBW (QALYs) | Tsuchiya, et al. (1999) | Age-related preferences and age weighting health benefits | Soc Sci Med | Methodology | - | - | - | Age | NA |
| EBW (QALYs) | Ubel, et al. (2000) | Improving value measurement in cost-effectiveness analysis | Med Care | Methodology | - | - | - | Severity of illness; Limitations in potential for health | NA |
| ECEA | Levin, et al. (2015) | An extended cost-effectiveness analysis of publicly financed HPV vaccination to prevent cervical cancer in China | Vaccine | Applied | China | Cervical cancer (children) | **Screening & vaccination:** Vaccination plus screening; Screening | Wealth | NA |
| ECEA | Pecenka, et al. (2015) | Health gains and financial risk protection: an extended cost-effectiveness analysis of treatment and prevention of diarrhoea in Ethiopia | BMJ Open | Applied | Ethiopia | Diarrhoea (children) | **Pharmacological, general healthcare & vaccination:** Publicly financed diarrhoeal treatment alone; Publicly financed diarrhoeal treatment and rotavirus vaccination | Wealth quintiles | NA |

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| ECEA | Driessen, et al. (2015) | Comparing the health and social protection effects of measles vaccination strategies in Ethiopia: An extended cost-effectiveness analysis | Soc Sci Med | Applied | Ethiopia | Measles | **Vaccination:** Routine immunisation; Routine immunisation with financial incentives; Mass campaigns (known as supplemental immunisation activities) | Income | NA |
| ECEA | Johansson, et al. (2017) | Health Gains and Financial Protection Provided by the Ethiopian Mental Health Strategy: An Extended Cost-Effectiveness Analysis | Health Policy Plann | Applied | Ethiopia | Mental health | **Pharmacological & general healthcare:** Increased coverage of interventions; Current coverage | Income | NA |
| ECEA | Johansson, et al. (2015) | Health gains and financial protection from pneumococcal vaccination and pneumonia treatment in Ethiopia: results from an extended cost-effectiveness analysis | PLoS ONE | Applied | Ethiopia | Pneumococcal disease and pneumonia (children) | **Vaccination & general healthcare:** Increased vaccination coverage (pneumococcal disease) and increased case management (pneumonia); Current SoC | Income groups | **Inequality measurement:** Gini coefficient<br><br>**SWF:** None reported |
| ECEA | Nandi, et al. (2017) | Reduced burden of childhood diarrheal diseases through increased access to water and sanitation in India: a modeling analysis | Soc Sci Med | Applied | India | Childhood diarrheal diseases | **Sanitation:** Coverage rates of piped water and improved sanitation are separately increased across all Indian households randomly to a 95% level; Coverage rates of piped water and improved sanitation are increased to at least 95% level separately within each state | Wealth quintiles | NA |
| ECEA | Megiddo, et al. (2016) | Health and economic benefits of public financing of epilepsy treatment in India: an agent-based simulation model | Epilepsia | Applied | India | Epilepsy | **Pharmacological & surgery:** First-line anti-epilepsy drugs (AEDs); first- and second-line AEDs; first- and second-line AEDs and surgery | Income quintiles | NA |
| ECEA | Nandi, et al. (2016) | Health and economic benefits of scaling up a home-based neonatal care package in rural India: a modelling analysis | Health Policy Plann | Applied | India | Neonatal diseases | **General healthcare:** Delivery of Home-based Neonatal Care (HBNC) through the current accredited social health activists (ASHA) network; Increasing the number of ASHAs such that 90% of the rural population in each state receives neonatal care through | Wealth quintiles | NA |

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| | | | | | | | existing channels or the new HBNC package | | |
| ECEA | Raykar, et al. (2016) | An extended cost-effectiveness analysis of schizophrenia treatment in India under universal public finance | Cost Eff Resour Alloc | Applied | India | Schizophrenia | **Pharmacological & general healthcare:** Enhanced public financing of schizophrenia treatment; Current SoC | Income quintiles | NA |
| ECEA | Verguet, et al. (2015) | Universal public finance of tuberculosis treatment in India: an extended cost-effectiveness analysis | Health Econ | Applied | India | Tuberculosis | **General healthcare:** Universal public financing of tuberculosis treatment; No universal financing | Income quintiles | NA |
| ECEA | Verguet, et al. (2013) | Public finance of rotavirus vaccination in India and Ethiopia: An extended cost-effectiveness analysis | Vaccine | Applied | India & Ethiopia | Rotavirus (children) | **Vaccination:** Publicly financed vaccination coverage; Vaccination with no public funding | Income | NA |
| ECEA | Verguet, et al. (2016) | Maternal-related deaths and impoverishment among adolescent girls in India and Niger: findings from a modelling study | BMJ Open | Applied | India and Niger | Adolescent maternal mortality | **Education:** One-year increase in the education level of young girls; Current SoC | Income quintiles | **Inequality measurement:** Gini coefficient<br><br>**SWF:** None reported |
| ECEA | De Neve, et al. (2018) | Health, financial, and education gains of investing in preventive chemotherapy for schistosomiasis, soil-transmitted helminthiases, and lymphatic filariasis in Madagascar: a modeling study | PLoS Negl Trop Dis | Applied | Madagascar | Schistosomiasis, soil-transmitted helminthiases, and lymphatic filariasis (children) | **Pharmacological:** Praziquantel (schistosomiasis); Albendazole (ascariasis); Albendazole (hookworm disease); Albendazole (trichiasis); Albendazole (lymphatic filariasis) | Intervention; Disease type | NA |
| ECEA | Watkins, et al. (2016) | Cardiovascular disease and impoverishment averted due to a salt reduction policy in South Africa: an extended cost-effectiveness analysis | Health Policy Plan | Applied | South Africa | Cardiovascular disease | **Lifestyle:** Lowering daily salt intake to 5g; No change in salt intake | Income quintiles | NA |
| ECEA | Saxena, et al. (2019) | The distributional impact of taxing sugar-sweetened beverages: findings from an extended cost-effectiveness analysis in South Africa | BMJ Glob Health | Applied | South Africa | Type 2 diabetes | **Policy:** 10% sugar tax; No sugar tax | Socioeconomic status | NA |

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| ECEA | Cookson, et al. (2017) | Using Cost-Effectiveness Analysis to Address Health Equity Concerns | Value Health | Methodology | - | - | - | NR | NA |
| ECEA | Phelps, et al. (2018) | Approaches to Aggregation and Decision Making-A Health Economics Approach: An ISPOR Special Task Force Report [5] | Value Health | Methodology | - | - | - | NR | NA |
| MCDA (qualitative) | Banham, et al. (2011) | An equity-Effectiveness framework linking health programs and healthy life expectancy | Aust J Prim Health | Methodological Case Study | Australia | Coronary heart disease | **Pharmacological & lifestyle:** Clinical review, optimised pharmacotherapy, and lifestyle modification; No intervention | Socioeconomic status | NA |
| MCDA (quantitative & qualitative) | Phelps, et al. (2018) | Approaches to Aggregation and Decision Making-A Health Economics Approach: An ISPOR Special Task Force Report [5] | Value Health | Methodology | - | - | - | NR | NA |
| MCDA (quantitative & qualitative) | Sussex, et al. (2013) | Operationalizing Value-Based Pricing of Medicines | Pharmacoeconomics | Methodology | - | - | - | NR | NA |
| MCDA (quantitative & qualitative) | Baltussen, et al. (2006) | Priority setting of health interventions: the need for multi-criteria decision analysis | Cost Eff Resour Alloc | Methodology | NR | Multiple disease areas / broad healthcare | **Pharmacological & general healthcare:** ART (HIV); Treatment (childhood pneumonia); Inpatient care (Schizophrenia); Plastering (simple fractures) | NR | NA |
| MCDA (quantitative) | Baeten, et al. (2010) | Incorporating equity-efficiency interactions in cost-effectiveness analysis - Three approaches applied to breast cancer control | Value Health | Methodological Case Study | Europe | Breast cancer | **Screening & pharmacological:** Intervention; No intervention | Age; Stage of diagnosis; Number of beneficiaries; Individual health benefit; Poverty reduction; Cost-effectiveness | NA |
| MCDA (quantitative) | Golan, et al. (2012) | Which health technologies should be funded? A prioritization framework | Isr J Health Policy | Methodological Case Study | Israel | Multiple disease areas / broad healthcare | **Pharmacological, devices and dental care:** Multiple (18) interventions | The extent to which, if the technology were | NA |

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| | | based explicitly on value for money | | | | | | not to be funded, patients would be denied treatment due to a lack of alternative treatments or difficulties accessing them; and the existence of other important equity-related social or ethical benefits, such as the technology being targeted at specific populations with prima facie special claims (e.g. children or minorities) or serving to reduce health gaps (inequalities), etc. | |
| MP | Cleary, et al. (2010) | Equity and efficiency in HIV-treatment in South Africa: the contribution of mathematical programming to priority setting | Health Econ | Application | South Africa | HIV | **Pharmacological:** No ART; First-line ART; First- and second-line ART | Treatment inequality (i.e., opportunity for treatment) | NA |
| MP | Cookson, et al. (2017) | Using Cost-Effectiveness Analysis to Address Health Equity Concerns | Value Health | Methodology | - | - | - | NR | NA |
| SLR | Avanceña, et al. (2021) | Examining Equity Effects of Health Interventions in Cost-Effectiveness Analysis: A Systematic Review | Value Health | SLR | - | - | - | - | - |
| SLR | Carlson, et al. (2020) | Alternative Approaches to Quality-Adjusted Life-Year Estimation Within Standard Cost-Effectiveness Models: Literature Review, | Value Health | SLR | - | - | - | - | - |

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| | | Feasibility Assessment, and Impact Evaluation | | | | | | | |
| SLR | Dukhanin, et al. (2018) | Integrating social justice concerns into economic evaluation for healthcare and public health: A systematic review | Soc Sci Med | SLR | - | - | - | - | - |
| SLR | Johri, et al. (2012) | Can cost-effectiveness analysis integrate concerns for equity? Systematic review | Int J Technol Assess | SLR | - | - | - | - | - |
| SLR | Lal, et al. (2018) | Inclusion of equity in economic analyses of public health policies: systematic review and future directions | Aust NZ J Publ Heal | SLR | - | - | - | - | - |

ART: anti-retroviral therapy; CVD: cardiovascular disease; DCEA: distributional cost-effectiveness analysis; EBW: equity-based weighting; ECEA: extended cost-effectiveness analysis; EDE: equally distributed equivalent; FOBT: faecal occult blood test; HIV: human immunodeficiency virus; ICER: incremental cost-effectiveness ratio; ICU: intensive care unit; MCDA: multi-criteria decision analysis; MP: mathematical programming; NA: not applicable; NHS: national health service; NR: not reported; QALE: quality-adjusted life expectancy; SLR: systematic literature review; SoC: standard of care; SWF: social welfare function; WHO: World Health Organisation

**Notes**

General: Where studies appear in the table more than once it is because they describe more than one methodology.

*'Applied' studies focus on a dedicated application of the equity evaluation method to a particular decision problem; 'Methodological case studies' focus predominantly on describing methodology but provide either an applied case study example or a hypothetical non-specific worked example; 'Methodology' studies describe only the underlying methodology of the equity evaluation method and do not provide any form of worked example.

**'Lifestyle' interventions include those aimed at modifying a person's behaviour or lifestyle; 'General healthcare' interventions include those were no description of the specific intervention was provided, and those aimed at improving healthcare in the widest context (which may therefore encompass all aspects of healthcare provision).

^Equity stratification factors are described if relevant and if the study describes an application, case study or hypothetical example

^^Equity measurement metrics and social welfare functions are evaluated only for DCEA and ECEA studies

**Supplemental Appendix F**

## Overview

This supplemental appendix provides a brief overview of each of the inequality measurement metrics and social welfare functions (SWFs) utilised in studies identified in the review. We do not attempt to summarise the relative strengths and weaknesses of each approach as this has been studied previously [1-4]. Rather, we focus on providing their formulaic representation in the context of health inequality, focusing on health as measured by the QALY.

## Inequality measurement metrics

### Gini coefficient

Original publication: Gini (1936) [5]

Like most inequality and inequity measurement metrics, the Gini coefficient has a background in economics, specifically in wealth distribution measurement, and is strongly associated with the Lorenz curve. In a wealth-based context, the Lorenz curve graphically represents the distribution of wealth within a population, with the x-axis representing the cumulative proportion of individuals ranked from least wealthy to most wealthy, and the y-axis representing the cumulative share of wealth. Substituting health in place of wealth gives us the Lorenz curve as observed in **Figure 1**, where the x-axis now represents the cumulative proportion of individuals ranked from least healthy to most healthy, and the y-axis represents the cumulative share of health.

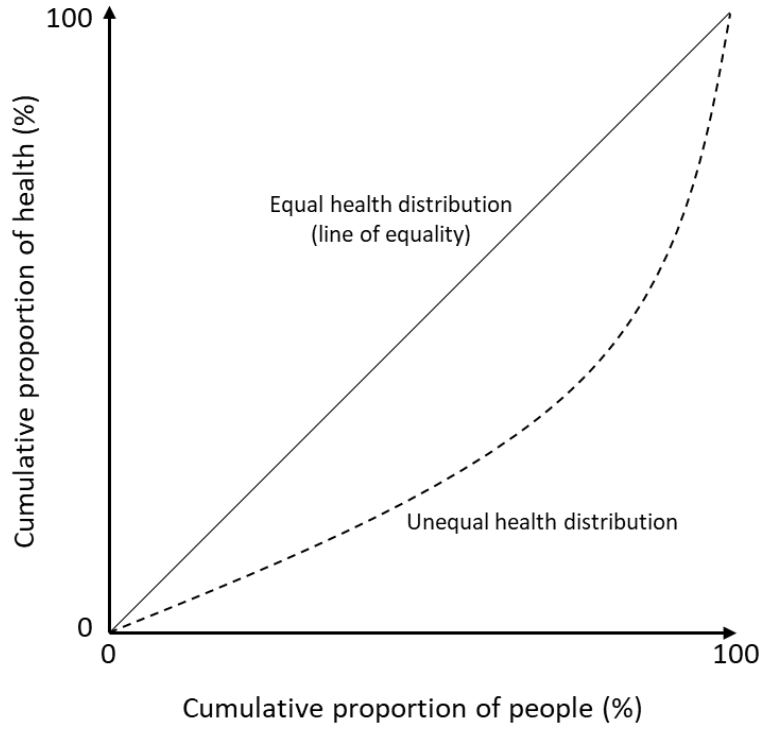


**Figure 1:** Health-based Lorenz curve

Under this framework, a diagonal line represents equal health among individuals, whilst the larger the deviation from the diagonal, the larger the degree of inequality. The Gini index or coefficient is calculated based on this curve, where the magnitude of the index can range from 0 (where the curve coincides with the diagonal) to 1 (where all the health of the population is concentrated in a single person). The Gini index is calculated using the following formula:

$$G = \frac{\sum_{i=1}^{n-1} |p_i - q_i|}{\sum_{i=1}^{n-1} p_i}$$

Where $p_i$ and $q_i$ represent the proportion of individuals (or groups) by health level and the cumulative total proportion of health of these individuals (or groups), respectively.

**Atkinson Index**

Original publication: Atkinson (1970) [6]

The Atkinson index was developed as a relative measure of income inequality and is useful in determining which end of the distribution contributes most to the observed inequality. Of particular significance is the use of

an inequality aversion parameter ε which gives greater weight to changes in a given portion of the income distribution. The Atkinson index can be used as a measure of health-based inequality by replacing measures of income with measures of health. The Atkinson index defined in the contest of quality-adjusted life expectancy (QALE) can be constructed as:

$$A_\varepsilon = 1 - \left[\frac{1}{N}\sum_{i=1}^{N}\left(\frac{Q_i}{\bar{Q}}\right)^{1-\varepsilon}\right]^{\frac{1}{1-\varepsilon}}$$

Where N is the total population size, $Q_i$ is the QALE estimate of the $i$th individual, $\bar{Q}$ is the mean QALE of the population and $\varepsilon$ is the level of inequality aversion ($\varepsilon \geq 0$).

As $\varepsilon$ increases, the Atkinson index becomes more sensitive to changes at the lower end of the health distribution. Conversely, as $\varepsilon$ decreases, the Atkinson index becomes less sensitive to changes in the lower end of the distribution. The Atkinson index is never highly sensitive to changes at the upper end of the distribution, as ε is strictly non-negative. In the UK, published evidence suggests that, at current levels of QALE, the general public are willing to weight health gains to the poorest fifth of people in society six to seven times as highly as health gains to the richest fifth, resulting in an ε parameter value of 10.95 [7]. The theoretical range of Atkinson values is between 0 and 1, with 0 representing a state of equal distribution.

A special case of the Atkinson index where $\varepsilon = 1$ is represented by the following equation:

$$A_\varepsilon = 1 - \left[\sum_{i=1}^{N}\frac{Q_i}{\bar{Q}}\right]^{\frac{1}{N}}$$

**Kolm Index**

Original publication: Kolm (1976) [8]

In a similar fashion to the Atkinson index, the Kolm index was developed as a measure of income inequality, but with a focus on measuring absolute inequality as opposed to relative inequality. It similarly uses an equality aversion parameter α to give greater weight to changes in a given portion of the income distribution. The Kolm index is represented by the following equation:

$$K_\alpha = \left(\frac{1}{\alpha}\right)\log\left(\frac{1}{N}\sum_{i=1}^{N} e^{\alpha(\bar{Q}-Q_i)}\right)$$

Where N is the total population size, $Q_i$ is the QALE estimate of the $i$th individual, $\bar{Q}$ is the mean QALE of the population and α is the level of inequality aversion ($\alpha > 0$).

Much like the Atkinson index, as α increases, the Kolm index becomes more sensitive to changes at the lower end of the health distribution. Conversely, as α decreases, the Kolm index becomes less sensitive to changes in the lower end of the distribution. The Kolm index is never highly sensitive to changes at the upper end of the distribution, as α is strictly non-negative. In the UK, published evidence suggests that, at current levels of QALE, the general public are willing to weight health gains to the poorest fifth of people in society six to seven times as highly as health gains to the richest fifth, resulting in an α parameter value of 0.15 [7].

**Slope Index of Inequality and Relative Index of Inequality**

Both the slope and relative indices of inequality are simple regression-based indices. They rely on a regression relating health outcomes with the relative position of groups across a relevant distribution, for example, the relative position of social groups on the socioeconomic distribution [9]. An example of such a regression is presented in **Figure 2**. The slope index of inequality (SII) corresponds to the slope of the regression line, representing an absolute measure of inequality, whilst the relative index of inequality (RII) is obtained by extrapolating the regression line towards the extreme groups on the x-axis (i.e., 0 and 1 in **Figure 2**) and calculating the ratio of the value at the bottom of the hierarchy (e.g., the intercept) to the value at the top of the hierarchy (e.g., the intercept plus the slope), and represents a relative measure of inequality.

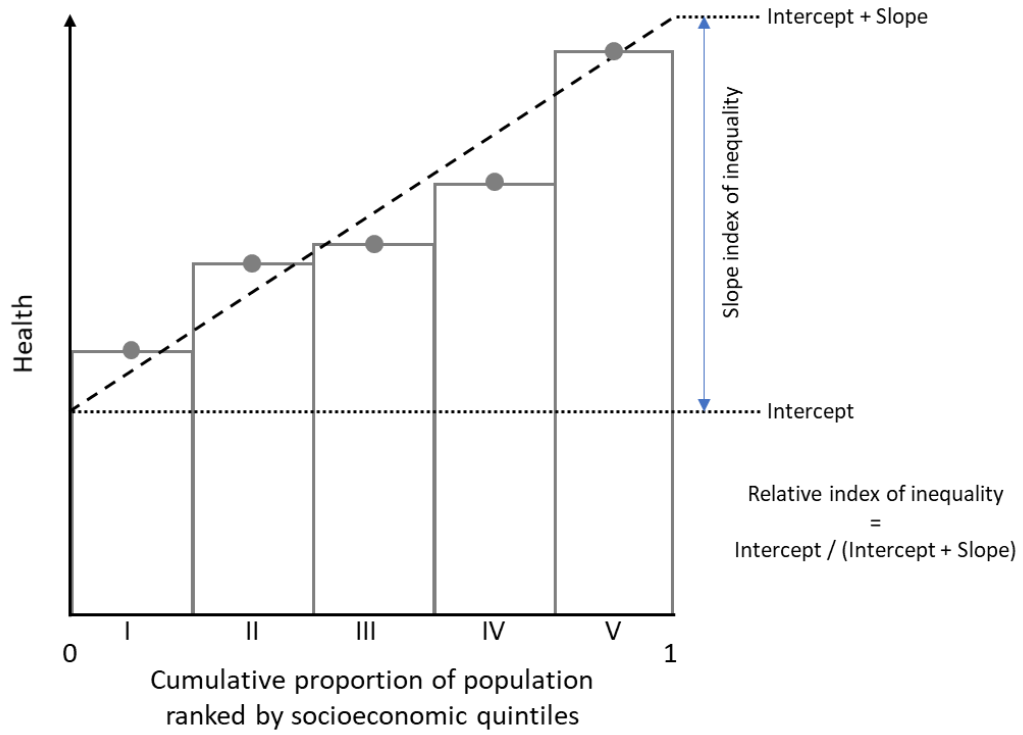


**Figure 2:** Hypothetical example of the difference in health across socioeconomic quintiles and the associated slope and relative indices of inequality (informed by examples from Khang et al. [2019] and Renard et al. [2019]) [9-10]

**Absolute Gap Index and Relative Gap Index**

The absolute and relative gap indices are simple measures of differences in inequality between the two most extreme groups observed in a distribution. As illustrated in **Figure 3**, the gap index is simply calculated as the difference in health between the two most extreme socioeconomic quintiles, whilst the relative gap index is calculated as the ratio of health outcomes between the two most extreme socioeconomic quintiles.

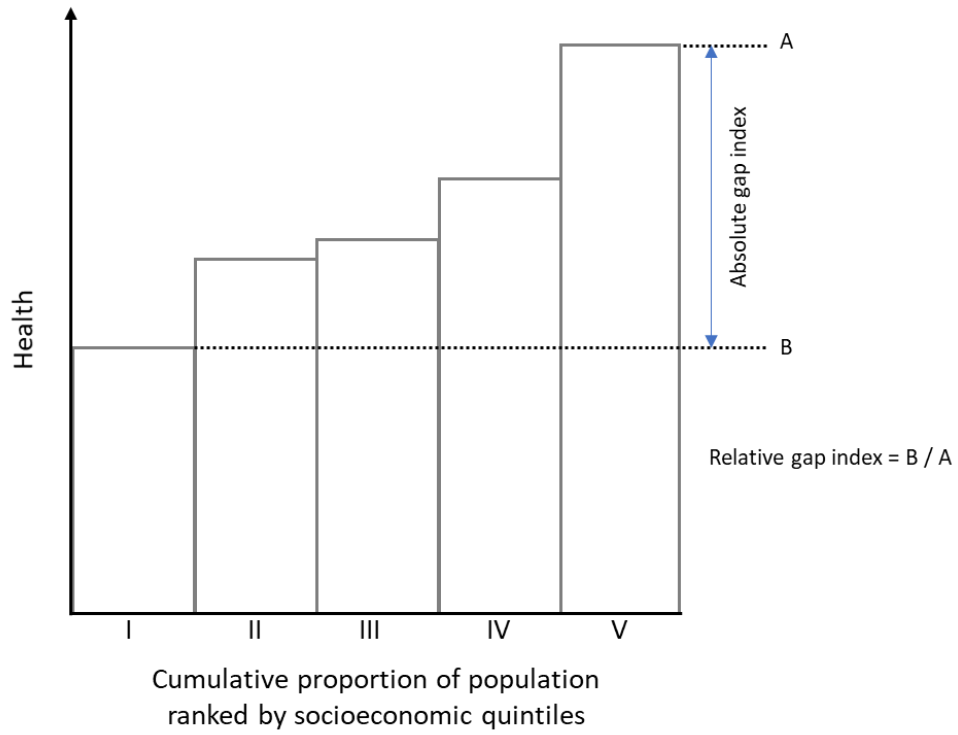


**Figure 3:** Hypothetical example of the difference in health across socioeconomic quintiles and the associated absolute and relative gap indices

**Social Welfare Functions**

SWFs can be used to analyse the trade-offs between efficiency, in terms of maximising overall population health, and health equity, in terms of achieving a more equal distribution of health across the chosen equity strata and amongst the general population. The cornerstone of this inequality measure is the concept of Equally Distributed Equivalent (EDE) health, that is a common level of health in a hypothetical equal distribution of health that has the same level of social welfare as the actual unequal distribution of health, with the difference indicating the change in health-related social welfare. A positive change in EDE therefore represents a scenario in which population health increases and health inequality reduces, or a scenario in which the trade-off between increasing (decreasing) population health by an amount X and increasing (decreasing) health inequality by an amount Y is deemed acceptable; this acceptability is controlled by the inequality aversion parameter.

When subtracted from 1 and multiplied by the mean level of health, the Atkinson and Kolm indices can be used to summarize the value of a distribution of health in terms of the equally distributed equivalent (EDE) level of health [11]. In a QALY-based example, the EDE is the level of population health (expressed in QALYs) that, if

provided uniformly to everyone in a population, would yield the same amount of social welfare to the distribution of health being evaluated. An intervention estimated to reduce health inequality will have an EDE health impact more positive than its net population health impact. Conversely, an intervention that increases health inequality would have an EDE more negative than their net population health impact, with the difference showing the loss of social welfare in terms of QALYs.

Combining the Atkinson and Kolm indices with the mean level of health in the distribution to obtain the EDE level of health gives the following equations [12]:

$$EDE_{A,\varepsilon} = (1 - A_{\varepsilon})\bar{Q}$$

$$EDE_{K,\alpha} = \bar{Q} - K_{\alpha}$$

When $\varepsilon = 0$, marginal increases in health produce the same level of social welfare whether they go to a less healthy or healthier individual. In this case, the EDE level of health is equal to mean health in the population, and the Atkinson index is zero. Similarly, when $\alpha = 0$, the EDE level of health is equal to mean health in the population, and the Kolm index is zero.

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