



EQUITY, ECONOMIC EVALUATION, AND DISEASE TRANSMISSION MODELLING

26-27th March 2018

Tom Drake, Graham Medley, Anna Vassall, Gabriela Gomez
Contact: gabriela.gomez@lshtm.ac.uk

This document has been prepared as a pre reading material to the workshop 'Examining the equity of global health interventions using infectious disease transmission models', BMA House (British Medical Association), Tavistock Square, London, 26-27 March 2018.

During this workshop, we will present and expand on concepts, methods, and considerations. This document and the discussions during the workshop aim to inform the Reference Case for Economic Evaluation in Global Health.

Summary

There is significant potential in using disease transmission models and economic evaluation frameworks to consider the *equity* of alternative courses of action in global health. The consideration of who is more or less advantaged, and how best to address these differences when they are unfair, is central to the rationale for the global health sector. Yet, economic evaluation typically assesses policy alternatives in terms of *aggregate* costs and consequences, not including information on who suffers costs and who gains. Further, it may be important to the policy question to consider the distribution of *externalities* in addition to direct costs and consequences. Disease transmission models are increasingly used for economic evaluation and are a suitable tool to simulate the externality effects of infectious disease interventions, accounting for changes in risk to others when an individual benefits from disease treatment or prevention.

In this report, we examine the interface of these three domains: equity, economic evaluation, and disease transmission modelling. First, we present a descriptive review of concepts and methodological approaches and, second, an exploration of key methodological considerations when including equity into economic evaluations using transmission models.

Part 1: Review of equity, economic evaluation, and disease transmission modelling

Any statement about equity includes a value judgement. We describe a range of concepts guiding this judgement including: egalitarianism, the decent minimum, Rawlsian maximin, capability theory, and utilitarianism. We then define four methodological families when including equity in priority setting: i) outcome weighting, ii) additional evaluative criteria, iii) quantification of any trade-offs between efficiency and equity, and iv) inclusion of qualitative equity-related evidence alongside quantitative results. We describe the methods developed in each group and present expand on the approaches with recent applications in low and middle income countries, for example extended cost effectiveness analysis, distributional cost effectiveness analysis, and multi-criteria decision analysis.

Part 2: Key methodological considerations

Building on the methods and concepts described in part 1, we discuss and present a draft checklist of methodological considerations for analysts who wish to incorporate equity in mathematical models used for economic evaluation. These recommendations move sequentially through four key aspects in this space i) defining the policy question, ii) choice of evaluation framework, iii) model structure, and iv) data requirements. First, considering the equity-related decision problems faced in global health, we note that the perspective of the decision maker will be critical to the definition of scope in an equity-informed analysis. However, while some decision problems are explicit in their equity concerns, in other cases there is an interest in equity but no prior specification. Second, we consider the concepts of equity that underpin the analysis and determine the primary metrics for the evaluation. Third, the decision problem, foundational equity concepts, and evaluation metrics determine the selection of an appropriate framing of choice, for example whether the analysis is used to describe equity impact or to explore any potential trade-off between equity and efficiency. We

then explore the structural and data challenges using infectious disease transmission models when applying economic evaluation frameworks that incorporate equity. We outline alternative approaches with differing degrees of integrating heterogeneity and equity into the transmission model structure and discuss the implications for model development, data requirements, and analysis.

This work is supported by the International Decision Support Initiative and is intended to inform future guidance on the Reference Case for economic evaluation in low and middle income countries.

Contents

Summary.....	2
Contents	4
Abbreviations.....	5
Introduction.....	6
Part 1: Review of equity, economic evaluations and disease transmission modelling	7
Equity in health and healthcare	7
Equity considerations in economic evaluation.....	9
Approaches to equity analysis in economic evaluation.....	11
Methods that allow for equity weighting.....	11
Methods that allow for equity to be included as an additional evaluative criteria	12
Methods that quantify trade-offs in equity against efficiency.....	13
Methods that allow the simultaneous qualitative consideration of equity and efficiency ..	14
A cross-sectional literature review of equity in economic evaluations.....	18
Part 2: Key Methodological Considerations	21
Defining the policy question	21
Perspective.....	21
Equity concepts.....	21
Sub-groups of interest.....	21
Choice of evaluation framework.....	22
Outcome of interest	22
Analytical approach.....	22
Structure	24
Heterogeneity dimensions.....	24
Data requirements	29
Interpretation and reporting of results.....	35
Recommendations	36
References	37

Abbreviations

CEA	Cost effectiveness analysis
CBA	Cost benefit analysis
CET	Cost effectiveness thresholds
DALY	Disability adjusted life year
DCEA	Distributional cost effectiveness analysis
DT-EE	Dynamic transmission economic evaluation
ECEA	Extended cost effectiveness analysis
GPS-Health	Guidance on priority setting in global health
HAI	Health achievement index
HTA	Health technology assessment
iDSI	International Decision Support Initiative
LSHTM	London School of Hygiene and Tropical Medicine
LMIC	Low and middle income Country
MAES	Multi-attribute equity state
MCDA	Multi-criteria decision analysis
MP	Mathematical programming
QALY	Quality adjusted life year
RC	Reference Case for Economic Evaluation in Global Health
WHO	World Health Organisation

Introduction

Worldwide, individuals experience systematic differences in their risk of acquiring, developing and transmitting diseases; in health outcomes when they have a disease; in their access to (quality) healthcare; and in the financial burden of healthcare. While the terms *inequality* and *inequity* are sometimes used interchangeably to describe these differences, not all inequalities are inequities. Health inequality is defined as “differences in health status or in the distribution of health determinants between different population groups” (2), whereas health inequity implies a judgement about the fairness or justice of systematic differences in population health and permits the existence of equitable inequalities and inequitable equalities.

In global public health, policy makers in national governments and international donor organisations must make decisions about how best to allocate the resources available to them. Evidence from economic evaluations is increasingly influential in the priority setting process, yet variations in methodological approaches and reporting practices can make evidence synthesis challenging. The Reference Case (RC) for Economic Evaluation in Global Health (3), from the International Decision Support Initiative, is intended to improve the quality of this evidence base going forward. While economic evaluations aim to maximise the health for the resources available, this goal of utilitarian efficiency is not the only criteria for consideration during the decision making process. It is also necessary to consider the distributional effects that may arise from resource allocation decisions on health, healthcare utilisation and healthcare financing. This is reflected in Principle 11 in the RC which recommends that *equity*, or the fairness in the distribution of costs and consequences, should be considered at all stages of an economic evaluation.

Infectious disease remain a priority in global health and mathematical models are increasingly being used to understand and predict the spread of infectious diseases and the impact of global health interventions in terms of both *total* gains and the *distribution* of gains in the population. Such models may be applied within an economic evaluation framework so that estimates of cost-effectiveness include expected externality effects of interventions (4). The combination of transmission models with economic evaluation methods is a potentially powerful approach to estimate the non-linearity of intervention costs and effects over time in infectious disease.

In this document, we start by reviewing the theoretical foundations of equity and the variety of approaches for incorporating them in economic evaluations. We then review applications in the published literature. Finally, we outline methodological challenges to and opportunities for including equity considerations in DT-EEs.

Part 1: Review of equity, economic evaluations and disease transmission modelling

Equity in health and healthcare

Before discussing the approaches for including equity considerations in economic evaluations, we discuss briefly the conceptualisation of fairness in systematic differences observed in health, healthcare utilisation or healthcare financing. While there is no universal consensus as to what can be considered unfair various concepts of what fairness means and frameworks for identifying fair or unfair inequalities have been proposed.

In the seminal paper by Whitehead, inequities are defined as something unjust or unfair and, importantly, something that is avoidable. Examples include health damaging behaviour where the degree of choice of lifestyles is severely restricted or inadequate access to essential health and other public services (5). Braveman and Grushkin argued against the inclusion of the avoidability criterion in the assessment of equity. They suggest that avoidability can be considered implicitly in the concepts of fairness and justice, yet fall short of defining what might be avoidable and the perspective to define avoidability (6). More recently Braveman and others have emphasised the need to define avoidability as “plausibly avoidable, i.e., at least in theory avoidable, based on current scientific knowledge, assuming the existence of political will”. In contrast, the World Health Organisation’s definition of health equity as “the absence of avoidable or remediable differences among groups of people” seems to emphasise avoidability as the principal criterion, implying that all avoidable inequalities can be considered unjust and are therefore inequities (7).

Pereira identifies and critically appraises well-established approaches to assessing whether disparities in both individual and societal choices are unjust (equity foundations), namely: equality, distribution according to entitlement, the ‘decent minimum’, Rawlsian maximin, envy-free allocations, equity as choice or equality of opportunity, and equality in capabilities (Table 1) (8).

Table 1: Summary of principles to define equity.

Guiding Principle	Summary
Equality	The characteristic of interest, such as health outcome, access to healthcare or healthcare investment, are the same for all members of the population.
Distribution according to entitlement	Individuals are entitled to wealth providing it was acquired justly and therefore if they chose to spend more on their health then this remains just.
The ‘decent minimum’	While in general distribution might be according to entitlement, there should be a social safety net that enables access to basic services to individuals who would not otherwise have the means.
Utilitarianism	The highest good is the greatest utility that can be achieved for the greatest number. Here, this could be linked to the concept of Pareto efficiency where

	utilities are distributed in such a way that no one can be made better off without making someone else worse off.
Rawlsian maximin	Maximising benefits to the least well off. Unlike the decent minimum, the maximin principle would continually strive to improve welfare for the least advantaged, independently of the overall distribution of benefits and independently from whether overall inequality is increasing.
Envy-free allocations	Here it is acknowledged that just inequalities may arise from differences in individual preferences. Therefore, an optimal distribution is one in which individuals do not envy the health or healthcare available to others.
Equity as choice	People should be allowed to make individual decisions from equal choice sets.
Equality in capabilities	Capability theory recognises the importance of individual agency (departing from outcome focus principles such as egalitarianism) but notes that in order for individuals to be able to make truly comparable choices they must have equality in basic capabilities. Here, health could be seen either as an outcome dependent on the choices of individuals, or as a component of basic capabilities necessary to make free and fair choices.

Source: Principles adapted from Pereira (8)

Preferences for competing conceptions of equity are driven in part by ideology (9), underpinning the interpretation of inequalities (which are value-free) to inequities (which include a value judgement). Whether differences in health, access to healthcare or healthcare financing are fair or not may depend on beliefs about the extent to which individuals are themselves responsible for ensuring their own outcomes and access to healthcare. There is a gradient in attitudes towards individual vs collective responsibility, with neoliberal or libertarian ideologies emphasising individual responsibility, for example ‘distribution according to entitlement’ and ‘decent minimum’, and socialist or communitarian ideologies emphasising collective responsibility and a role for government or communities to ensure a more equal health access or outcomes, for example the principles of equality or equality in basic capabilities. Rawlsian maximin perhaps sits more towards the middle, being both focused on improving outcomes for the least advantaged while permitting the better off to maintain or even increase their relative advantage.

In conclusion, Pereira identifies Sen’s framework for conceptualising social value not in terms of material goods and services or even individual utility, but rather as the *capabilities* human beings require to flourish, as the most promising approach, as it focus equity concepts on individual freedom and agency (equality-in-basic-capabilities) (8). Despite efforts by several groups (10,11), capabilities have not been widely taken up as a quantitative outcome metric and health-related outcomes remain dominant in intervention evaluations.

However, health can itself be thought of as a capability rather than utility. That is, individuals do not derive utility directly from good health, but by deriving utility from life, supported by the capability of good health. This could be considered to support the World Health Organisation’s

definition of health equity as “the absence of avoidable or remediable differences among groups of people” (7). Here the goal is not an egalitarian distribution of capabilities required to achieve good health but the equalisation of health itself, wherever possible. In effect, this definition retains only the avoidability criterion from Whitehead’s definition of health equity. Reversing the original argument of Braveman and Gruskin, fairness is subject to the concept of avoidability; if health is a capability then health inequalities that are avoidable are therefore unfair. This view has resonance in the idea of health as a fundamental human right.

At this point, depending on the defining approach to equity considered, a key question then becomes whether it is the distribution of health outcomes, healthcare access or resources (healthcare financing) that should be considered. In a recent report, Braveman and others describe health equity as follows: “health equity means that everyone has a fair and just opportunity to be healthier. This requires removing obstacles to health such as poverty, discrimination, and their consequences, including powerlessness and lack of access to good jobs with fair pay, quality education and housing, safe environments, and health care”. In other words, access to healthcare services is not sufficient, other capabilities should also be supported but, if these are in place, then resulting inequalities in health outcomes or healthcare utilisation (due to individual agency) are not considered inequities. Moreover, more or better health is not the only potential benefit of healthcare or public health investment, for example reduced risk of illness may also reduce the risk of catastrophic out-of-pocket expenditure (12). Culyer takes the view that equality of health itself should be the dominant principle, and that healthcare should be distributed in order to achieve as close to an equal distribution of health as is feasible (13,14). The difference between equality in the distribution of resources and the distribution of outcomes can be considered in terms of “horizontal” and “vertical” equity. According to Culyer, “horizontal equity requires the like treatment of like individuals and vertical equity requires the unlike treatment of unlike individuals” (15). That is, horizontal equity is provision of similar services for people with similar health needs while vertical equity preferentially provides services to less advantaged populations. Both could be seen as fair, yet provide different recommendations on how to act.

Equity considerations in economic evaluation

Healthcare economic evaluation is the assessment of alternative courses of action by comparing their costs and consequences. In standard application of most common economic evaluation frameworks such as cost-effectiveness analysis (CEA) and cost-benefit analysis (CBA), the aim is to maximise benefits given the resources. While the focus is on efficiency, distributional considerations of alternative courses of action should be also addressed in the decision process and so the importance of the conceptualisation of equity lies in determining whether and how to incorporate it into the decision-making and resource allocation processes. In this section, we consider current approaches for the incorporation of equity within economic evaluation.

In examining these approaches, it is useful to consider the theoretical foundations of economic evaluation. As outlined by Brouwer and others, welfarism and extra-welfarism constitute competing epistemological perspectives upon which health economists develop frameworks for

applied economic evaluation (16,17). Welfarism considers the social welfare of a given action to be the sum of the utility gained (or lost) by each individual in the population affected. In this respect, it is an essentially utilitarian framework, seeking the greatest total utility, distribution of gains or losses felt by the population. Extra-welfarism, as the name suggests, seeks to introduce additional characteristics to the welfarist position. These additions have not been codified succinctly or consistently. While acknowledging the various versions of extra-welfarism, the authors go on to suggest that two issues lie at the centre of the differences between the schools of thought: 1) The source and nature of valuation; and 2) The initial distribution of wealth and income and Pareto principle applied to the final state. The implications of these differences in applied economic evaluation are summarised in Table 2.

Because equity relates to both issues (valuation and distribution), it is, for many, an example of an “extra” consideration to a standard welfarist view and is therefore an example of an extra-welfarist issue. With respect to the valuation of outcomes, consideration of equity implies that we value not only individual welfare but also the distribution of welfare in a population.

Table 2: Summary of welfarism and extra-welfarism (from Brouwer 2008)

	Under welfarist economics	Under extra-welfarism
Relevant outcomes	Only individual utility, normally taken to represent preference orderings. Social welfare is a function of individual welfares	May include individual utility as well as extra measures and indicators of well-being. In health policy, common outcomes will include health or health gain and the distribution of health or health gain, but may include other measures like patient satisfaction or caregiver burden. The selection of relevant outcomes is an important element in extra-welfarist evaluation and is context dependent and seems not for economists to decide (rather for decision-makers with authority). Some outcome measures may be based on preference measurement, when this is deemed a useful way to measure characteristics of interest
Valuation of relevant outcomes	As a rule the affected individual	Might be the affected individual, but could also be an expert or a representative sample of the general public or an authoritative decision-maker
Weighting of relevant outcomes	Sometimes permitted in a social welfare function, where the weights normally pertain to the distribution of individual utilities. Unclear whether such weights still classify as utility information	Allowed and often considered important as means of incorporating equity and other considerations. Weights may be based upon a variety of ethical considerations including wealth, need and desert and can relate to the variety of relevant outcomes considered important (e.g. capabilities)
Interpersonal comparability of	Although some theoretical approaches allow it (e.g. in a social welfare function), especially in applied work, normally considered	Explicitly allowed in the relevant outcomes, though normally not in terms of individual utility, but rather in terms of capabilities and characteristics like health,

relevant outcomes	impossible in the relevant evaluative space, i.e. individual utilities	handicap, ability to cope, schooling, ability to exercise discretion
--------------------------	--	--

Approaches to equity analysis in economic evaluation

Recent efforts to improve quality and comparability of economic evaluations across settings led the International Decision Support Initiative to develop a RC for economic evaluation in global health (3). The RC included equity considerations as one of 11 core principles for economic evaluation, noting that:

“There are various methods available for assessing equity implications of an intervention:

- *The method chosen should be appropriate to the decision problem and justifiable to the decision maker*
- *Equity implications should be considered at all stages of the evaluation, including design, analysis and reporting”*

In a 2012 systematic review, Johri and Norheim identify three broad approaches to incorporating equity considerations into economic evaluations: i) Equity weights and social welfare functions, ii) Multi-Criteria Decision Analysis (MCDA), and iii) Mathematical programming (18). Furthermore, a recent review by Cookson and others introduces the concept of the health equity impact plane, drawing attention to two frameworks to incorporate equity considerations into CEA: Distributional Cost-Effectiveness Analysis (DCEA) and Extended Cost Effectiveness Analysis (ECEA) (described further below). Cookson and others also highlight the distinction between equity impact analysis and equity trade-off analysis. Equity trade-off analysis will only be necessary if the equity impact analysis identifies a potential trade-off between efficiency and equity (quadrants II and IV on the equity impact plane).

Building on these reviews, we identified approaches to incorporating equity considerations into economic evaluations through non-systematic database searches supplemented reference screening and categorised frameworks into the following groups:

- a) Methods that allow for equity weighting (multiple cost effectiveness thresholds, HAI, MAES, fairness in CBA)
- b) Methods that allow for equity to be included as an additional evaluative criteria (MCDA, ECEA)
- c) Methods that quantify trade-offs in equity against efficiency (DCEA, MP)
- d) Methods that allow the simultaneous qualitative consideration of equity and efficiency (checklists and embedding frameworks, descriptive analyses)

Below and in Table 3 we review and summarise these approaches by categories.

Methods that allow for equity weighting

A foundational assumption in standard cost-effectiveness or cost-utility analyses is that the value of health gains is identical for all individuals, often described in the refrain “a QALY is a QALY is a QALY”. In 2009 Willoo and others argued that economic evaluation methods were not yet ready for applied equity adjustments to health utility scores (19). However, in the years since, methods for equity weighting have continued to develop and are becoming increasingly popular (20,21). Equity weighting allows the analyst to quantify the relative importance of the relevant equity concepts. Several frameworks for equity weighting of outcomes are described below.

Multiple Cost Effectiveness Thresholds

Differential valuation of health outcomes using separate cost effectiveness thresholds is perhaps the most direct approach to equity adjustment of health outcomes. An example is the decision of the National Institute for Health and Care Excellence (NICE, then National Institute for Health and Clinical Excellence) for England and Wales, to apply a higher cost-effectiveness threshold for end of life care (22), though empirical research into people's acceptance of this differential valuation did not find support and the policy has been criticised by some¹ (23).

Health Achievement Index

Wagstaff's Health Achievement Index (HAI) integrates the average level of health in a population and the inequality in health between the poor and the better-off (24). Ngalesoni and others use HAI to appraise the distribution of outcomes in an economic evaluation of cardiovascular prevention in Tanzania (25). The study is notable as an example of equity economic evaluation in an LMIC.

Multi attribute equity state

Round and Paulden describe a framework for using a multi attribute equity state (MAES) within CEA. Here, different health outcome valuations are incorporated into a single equity state metric. In contrast, to HAI, MAES weighting might reflect empirically measured societal values for differential weighting of outcomes in specific context, such as end-of-life care (21).

Fairness in CBA

Samson and others adapt the cost-benefit framework, whereby health outcomes are converted to monetary value, using an equity adjusted rate of equivalent income. Unlike some other economic evaluation frameworks, the use of CBA as a basis of equity analysis allows the inclusion of non-health outcomes.

Methods that allow for equity to be included as an additional evaluative criteria

In contrast to equity weighting, where different valuations on health are incorporated into a single measure, other frameworks include equity, or equity-related measures, as an additional criteria that is separate from the quantification of expected health gains.

Multi Criteria Decision Analysis

Baltussen and others argue that the plurality of evaluative frameworks to inform priority setting highlights the need for an approach to quantitatively compare alternative courses of action using multiple criteria. Multi Criteria Decision Analysis (MCDA) allows analysts to combine costs, effects, equity and other considerations through a systematic quantitative weighting of the value of each criterion by decision makers. While MCDA has more commonly been applied in high income countries it has also been applied in some low and middle income countries (30).

¹ The criticism centres on the argument that QALYs at the end of life are not inherently more valuable and permitting expenditure on interventions which are therefore less cost-effective has an opportunity cost, preventing the provision of more beneficial services.

Extended Cost Effectiveness Analysis

As part of the Disease Control Priorities project, Verguet and others have proposed Extended Cost Effectiveness Analysis (ECEA), a framework for incorporating financial protection impact as well as health outcomes in economic evaluation (31). ECEA presents the expected impacts of an intervention on financial protection, for example averted catastrophic out-of-pocket health expenditure or averted cases of poverty, in addition to and alongside health outcomes. This is particularly relevant in LMICs where the cost of healthcare can require the sale of assets and property among poor populations, threatening livelihoods (32). Unlike MCDA or equity-weighting approaches, outcomes in ECEA are not aggregated into a single result.

Methods that quantify trade-offs in equity against efficiency

Distributional cost-effectiveness analysis

Asaria and others describe a framework for Distributional Cost-Effectiveness Analysis (DCEA). This framework has two stages: 1) modelling of the changes to baseline health distribution due to the intervention and adjust them for social value judgements of fairness; and 2) quantification of changes in total population health if all unfair differences in are removed and evaluation of trade-offs between improving population health and reducing unfair health inequality. DCEA also emphasises the importance of the distribution of opportunity costs in the population, since alternative spending to an intervention of interest could also be expected to affect the distribution of health outcomes (33,34).

Mathematical Programming

The Mathematical Programming approach (or constrained optimisation) typically frames a decision problem in terms of a desirable outcome to be maximised (the objective function) and a set of one or more constraints limiting maximisation. In this framework, various equity conditions may be included as a constraint to the maximisation of health. For example, Cleary and others examine HIV treatment in South Africa and constrain the objective function by both cost and various social welfare considerations including equal treatment, a decent minimum and health maximisation (35). It is also possible to include equity in the objective function alongside health maximisation as Verguet does in an analysis of HIV prevention also in South Africa (36). In both approaches, any trade-off between health maximisation and equity constraints or maximisation can be presented as scenario analysis.

A drawback of a Mathematical Programming approach is that the decision problem is typically more locally constrained than CEA. The use of a cost effectiveness threshold in CEA reflects (in theory) the opportunity cost of alternative marginal investment in the health sector and therefore widespread and quality application of CEA supports efficient health sector planning. In contrast, Mathematical Programming considers the opportunity cost of direct alternatives available to the model.

Methods that allow the simultaneous qualitative consideration of equity and efficiency

Checklists and embedding frameworks

In addition to the frameworks for quantitatively incorporating equity considerations into economic evaluation described above, several supporting checklists have been proposed. Culyer and Bombard (50) offer a framework to guide and appraise health technology assessments. As part of a WHO initiative on health equity, Norheim and others propose to embed the consideration of cost-effectiveness analysis evidence in a framework they call Guidance for Priority Setting in Healthcare or GPS-Health. The framework aims to be a comprehensive checklist to support decision makers in the consideration of equity issues potentially missing from cost-effectiveness evidence (37). Daniels and others emphasise a transparent deliberative process for decision makers to consider Health Technology Assessment (HTA) evidence, they call "Accountability for Reasonableness (A4R) (38,39).

Descriptive analysis and qualitative comparison

It is relevant to mention methods for descriptive analysis of health-related equity that do not attempt to compare costs and consequences and are therefore not economic evaluation methods but can help inform the decision making process. On the simplest level, economic evaluation may be applied to two alternative courses of action where one is considered more equitable than another (depending on the conceptions of equity outlined in the previous section). The costs and consequences of each course of action are assessed and if the superior option in terms of equity is also more efficient (cost-effective) then this choice dominates. If the superior choice in terms of equity is less efficient then a qualitative judgement must be made as to whether the difference in efficiency outweighs the difference in equity.

Further analysis may support a quantitative understanding of intervention equity and therefore compliment the quantitative analysis of cost-effectiveness. Benefit incidence analysis evaluates the distribution of health impacts in a population while financing incidence analysis and resource allocation comparisons respectively appraise from which population groups funds are raised and to whom they are distributed (40–42). Such analysis is potentially complementary to economic evaluation, though as Cookson and others point out, unlike economic evaluation these analyses tend to consider average rather than marginal effects (43), with some exceptions (44).

Table 3: Summary of equity frameworks relevant for healthcare economic evaluation.

Thematic Approach	Framework	Brief Description	Interaction with Transmission Models	Outcome Metric	Selected References
<i>Equity weights and social welfare functions</i>	Multi-attribute equity state	Quantitative inclusion of equity into health outcome measurement through equity weighting on multiple dimensions.	The application of differential weights to transmission model outcomes is straight forward and analogous to the weighting of outcomes from other health economic models.	Health Utility	Round and Paulden (21)
	Health Achievement Index (HAI)	Combines the distribution of health with the mean for an aggregate measure of efficiency and equality for a given inequality aversion parameter.	As above	Health Utility	Wagstaff (24)
	Multiple cost-effectiveness thresholds	Using different thresholds for different populations is equivalent to applying weights to health utility scores, both are an adjustment to the value of health for different populations.	As above	Health Utility	(22,23,45)
	Cost-based equity weight	Weights costs rather than outcome measures.	As above	Any	Ong et al. (46)
	CBA with social welfare function – equivalent income	Defines welfare loss in terms of “equivalent income” i.e. richer individuals may have a lower equivalent income than poor individuals if they are in poor health. Different preferences in health are allowed. Aggregation of net benefit factors in distribution of equivalent income through a social welfare function. However, valuation of	There is the potential to use <i>individual</i> WTP with individual based models for this framework. However, there would be a complication with individual-based transmission models due to the externality effects. That is, an individual may value not only their own gains but also gains for others.	Monetary Equivalent	Samson et al (47)

		health remains dependent on income, raising ethical objections.			
<i>Additional Criteria</i>	Extended Cost Effectiveness Analysis (ECEA)	Inclusion of an assessment of financial protection outcomes in addition to health outcomes.	In addition to straightforward post-simulation accounting of health effects, costs and financial protection, it would be possible to link healthcare seeking decisions to ability-to-pay, therefore assessing impact of financial protection on indirect health effects.	Health Utility and Financial Protection	Verguet and others (31,48,49)
	Multi Criteria Decision Analysis (MCDA)	MCDA sees costs and effects as only two out many potential criteria that would inform a policy decision. The framework seeks to quantify and weigh all relevant criteria to inform a decision.	MCDA would simply embed any transmission modelling analysis and allow quantitative consideration of factors not included in the model.	Health Utility or disease specific measures in addition to non-health outcomes	Baltussen and others (26–30)
	Cost-Consequence Analysis (CCA)	CCA allows the reporting of non-quantified costs or consequences in addition to quantified results in a tabular balance-sheet format.	As above	As above	(50)
<i>Equity-Efficiency Trade-off focused Analyses</i>	Mathematical programming	Mathematical programming is a term referring to the use of mathematical models to address health economic questions (constrained optimisation) but does not include disease transmission modelling.	Algorithmic resource allocation using constrained optimisation rather than CEA decision rules	Health utility, disease-specific measures or goal-oriented optimisation	Examples: Stinnett and others (51); Cleary and others (35)
	Distributional Cost Effectiveness Analysis (DCEA)	Quantitative assessment of equity impact and potential trade-offs between efficiency and equity through fairness-adjusted health estimation.	Unlike some equity economic evaluation equity frameworks, DCEA emphasizes the simultaneous assessment of multiple dimensions of equity. Integrating several dimensions of heterogeneity into a	Health Utility	Asaria, Cookson and others (33,34)

			dynamic transmission model may be challenging.		
<i>Embedding Frameworks and Descriptive Analysis</i>	Resource allocation comparison Financing incidence analysis Benefit incidence analysis	Descriptive analysis of the population distribution of resources, health gains and /or financial burden of an intervention.	These approaches do not attempt quantitative integration with economic evaluation and therefore can be applied in the same way to dynamic transmission economic evaluations.	-	Various (40–42,52–54)
	Guidance on Priority setting in Healthcare (GPS-Health)	A checklist of equity criteria that are relevant to health care priority setting and may be considered in addition to cost-effectiveness analysis.	As above	-	Norheim et al (37)
	Checklist	As above	As above	-	Culyer and Bombard (55)
	Accountability for Reasonableness (A4R)	Embed HTA in a “fair, deliberative process”.	As above	-	Daniels et al (38,39)

A cross-sectional literature review of equity in economic evaluations

It is widely acknowledged that equity is an important consideration in health policy, and discussions of whether, and how, to include it in healthcare economic evaluation can be traced back to the origins of the disciplines. However, equity does not commonly feature in such analyses. A review of HTA agency practices between 2006 and 2011 found that consideration of health equity was not standard practice (56). Furthermore, Johri and Norheim identified only 51 economic evaluations that included equity from a search of the Pub Med and EMBASE databases between 1996 and 2008 (18).

To assess the extent to which equity is considered in economic evaluations, we make use of an existing resource: Pitt and others undertook a comprehensive search of multiple databases and grey literature sources to identify 2844 economic evaluations published between January 2012 and May 2014 (57). We searched titles and abstracts of studies in this dataset for the key words; equity, inequity, inequality, distributional, fairness or justice. The criteria for inclusion were i) that the study is an applied economic evaluation and ii) includes quantitative consideration of equity for any sub-population grouping. The evaluation framework, outcome measure and outcome model type were extracted for each study.

The search returned 33 results from 2844 records. Of these, eight met the inclusion criteria (Table 4), approximately 1 in 355 studies. Most studies used a cost-effectiveness or cost-utility analysis framework or similar (n=7) with a descriptive analysis of equity considerations, with one study using a constrained optimisation or mathematical programming approach (36). One study applied cost-benefit analysis alongside CEA (58). Two studies used DALYs as the outcome measure (59,60) and one uses QALYs (61) with the remaining using versions of 'natural' outcome units for the relevant context. Only one study used a dynamic Markov simulation to estimate health outcomes (61) and there were no studies that included dynamic simulation of disease transmission.

Consideration of equity in applied economic evaluations is thus rare and mainly descriptive. When equity is considered, simple disaggregation of results and scenario analysis of alternative more or less equitable courses of action is the most common approach. Methodological approaches to quantitatively assess equity impact and equity trade-offs were not found to be applied in these studies.

Table 4: Economic evaluation that include analysis of health equity (2012-14)

Year	First Author	Title	Framework	Outcome	Outcome model	Equity Approach	Journal	Source
2014	Blakely T	Cost-effectiveness and equity impacts of three HPV vaccination programmes for school-aged girls in New Zealand	CEA/CUA	QALYs	Dynamic compartmental (Markov) without dynamic transmission	Descriptive analysis and qualitative comparison	Vaccine	(61)
2012	Hounton S	Applying the Net-Benefit Framework for Analysing and Presenting Cost-Effectiveness Analysis of a Maternal and Newborn Health Intervention	CEA & CBA	Institutional delivery & monetary equivalent	Empirical & OLS regression	Descriptive analysis and qualitative comparison. Including regression analysis of determinants of cost-effectiveness	PLOS ONE	(58)
2012	Waters D	Optimizing community case management strategies to achieve equitable reduction of childhood pneumonia mortality: an application of Equitable Impact Sensitive Tool (EQUIST) in five low- and middle-income countries	CEA/EQUIST	Lives Saved	Static deterministic	Descriptive analysis and qualitative comparison	Journal of Global Health	(62)
2012	Rheingans R	Distributional impact of rotavirus vaccination in 25 GAVI countries: Estimating disparities in benefits and cost-effectiveness	CEA/CUA	DALYs	Static deterministic	Descriptive analysis and qualitative comparison	Vaccine	(59)

2012	Cobiac L	Cost-effectiveness of extending the coverage of water supply fluoridation for the prevention of dental caries in Australia.	CEA/CUA	DALYs	Static deterministic	Descriptive analysis and qualitative comparison*	Community Dentistry and Oral Epidemiology	(60)
2013	Baker J	Ethnic differences in the cost-effectiveness of targeted and mass screening for high cardiovascular risk in the UK: cross-sectional study	CEA	High-risk person detected	Static deterministic	Descriptive analysis and qualitative comparison **	Heart	(63)
2013	Verguet S	Efficient and equitable HIV prevention: a case study of male circumcision in South Africa.	Constrained optimisation	-	Static deterministic	Equity-Efficiency Trade-Off Analysis Comparison of efficient and egalitarian optimisation constraints	Cost Effectiveness and Resource Allocation	(36)
2012	Carrera A	The comparative cost-effectiveness of an equity-focused approach to child survival, health, and nutrition: a modelling approach.	CEA-like (outcome per expenditure)	Under 5 mortality	Static deterministic	Descriptive analysis and qualitative comparison	Lancet	(64)

* Cobiac and others argue *for* the intervention in smaller communities despite conducting a regular CEA and finding that the marginal extra rollout is not cost effective. ** Baker and others make a qualitative inference about equity impact but do not model this.

Part 2: Key Methodological Considerations

In this section, we discuss the key methodological considerations when including equity in economic evaluations using transmission models. For each consideration, we state the problem, and define the methodological steps needed to be taken by the analyst.

Defining the policy question

The purpose of economic evaluation is to support decision making, so at the beginning of any analysis, it is important to define the policy question. When doing so, analysts will need to consider the equity concept of interest and the perspective of the decision maker.

Perspective

In global health, there are global payers in addition to domestic payers. In the same way that different payers will have different cost-effectiveness decision rules, in equity-informed economic evaluations, one can expect different perspectives in the value judgement needed to define the equity question. Currently, there are various methods and processes to support decision makers and analysts who support them in including equity-relevant considerations in the decision-making process. Decision makers could be interested in including equity (quantitatively or qualitatively) as an additional evaluative criteria (26,31,37,55), quantify trade-offs between equity and efficiency (34,51), or weighting cost-effectiveness results on equity measures (21,22,24,47). We do not elaborate on these various methods and processes in this report. We have reviewed them in the previous equity review that will be made available before the workshop. During the workshop, we will aim to discuss whether more extensive guidance is needed. However, central to the methodological steps to perform an equity-informative economic evaluation and developed further will be the type of equity that concerns decision makers.

Equity concepts

The difference between inequalities (heterogeneity between population groups) and inequities is a value judgement about whether the observed inequality is fair or just. There are a range of philosophical frameworks that underpin the inequities (summarised in Table 1). A choice between these equity-defining principles will frame the analysis in terms of choices in metrics, evaluative frameworks, model structure, and analysis plan.

Sub-groups of interest

The conceptual principles informing the characterisation of equity in economic analysis might not always be explicitly defined (9). Policy makers may be concerned with prioritisation of gains within a pre-specified vulnerable population group or achieving more equal distribution of benefits, without prior specification of a population group of interest. For example, Verguet *et al.* consider the trade-off between efficiency (maximising HIV infections averted) and equity (geographical equity in access to services) of alternative programmes for male circumcision as

HIV prevention among men in South Africa (2). In this case, we approach the policy question aiming to evaluate equity from the perspective of access to care for men, specifically. Alternatively, the decision maker may have no pre-specified equity goal but nevertheless be keen to consider the impact of a particular course of action on the distribution of benefits as well as total gains (65).

Choice of evaluation framework

After defining the equity problem broadly, the analyst will need to choose an evaluation framework for analysis. In making this choice, considerations should be given to the outcome of interest and the analytical approach.

Outcome of interest

Decision-makers may be interested in equity considerations in health, access to healthcare, healthcare financing, financial protection, well-being including non-health factors, or capabilities. A choice to focus on health financing or access rather than health itself, for example, would fall out of a concept of equity, such as equality in capabilities, that places the onus on the provision on access or means to ensure access to healthcare to individuals, but does not accept policy responsibility for ensuring their health outcomes.

Analytical approach

In economic evaluation, the choice of outcome also defines the choice of economic evaluation analytical approach to assess efficiency. For example, expressing outcomes in monetary terms implies a cost-benefit analysis (CBA) while disease-specific measures imply cost-effectiveness analysis (CEA).

The selection of analytical approaches for equity considerations in economic evaluations will also be informed by the choice of primary metric of interest, among others. There are several analytical approaches in economic evaluation that have clear ideological foundations with respect to equity. Unlike CEA or cost utility analysis (CUA), CBA converts all costs and consequences to monetary units and presents results in terms of the aggregated Net Benefit (benefits minus costs), by valuing health using an individual's willingness-to-pay (WTP) for expected health gains. The notion that it is *individual* decisions that reflect rational self-interest that should be used to value health implicitly accepts inequalities in ability-to-pay and therefore aligns with a "distribution according to entitlement" ideology of health-related equity (see previous report). That is, what matters is the value an *individual* places on health given the resources at their disposal. While a population average WTP is often used, as Robinson and Hammitt note, in terms of the CBA normative framework for valuing health this over-weights the preferences of poorer individuals and under-weights the preferences of the wealthy (66). The incorporation of a social welfare function² into CBA allows the analysis to shift the framework from a "distribution according to entitlement" ideology to a more pro-poor or egalitarian approach by differentially weighting gains according to the sub-groups within which they accrue.

² A function to value social states as more or less desirable.

Box1: Increasing vaccine coverage

What is the problem? To illustrate the impact of inclusion of transmission effects on alternatives tested and conclusions

What do we know already? Investments to increase coverage across a population will be faced with a differential uptake across subpopulations. Additional targeted resources to increase coverage in those harder-to-reach is potentially not cost-effective when judged on mean effects. But if those harder-to-reach are poorer or rural populations, then this prioritisation could be considered equitable. Example: Distributional cost-effectiveness analysis in low-and middle-income countries: illustrative example of rotavirus vaccination in Ethiopia (39).

What will this illustration add? The added value of transmission modelling as a frame for the analysis will be two-fold:

- 1) Provides the opportunity to test additional equity-relevant policy options, for example: additional targeted resources to increase coverage in the remainder of the population (easy-to-reach group). The change in analysis frame allows us to examine direct and indirect impacts so that targeting easy-to-reach groups may result in both a reduction of inequities and a cost-effective alternative.
- 2) Presents challenges in acceptability of recommendations and the communication of results as it may not be acceptable for policy makers to be seen as prioritising population groups already at an advantage, even though this course of action could be considered more cost effective and produce equitable outcomes.

What would be the relevant message for the following stakeholders?

- 1) national and regional governments/payers: challenges of interpreting results for within country decisions when equity concerns are being explicitly stated.
- 2) global donors/development partners: help frame equity and political considerations at country level that might influence countries priority setting in applications for funding.
- 3) researchers in LMICS and HICs: key methods considerations on how to frame the equity question and the results that could be discussed using this example.
- 4) iDSI : illustration of the added value of transmission models when applying the reference case to economic evaluations.

Again, it may be important to be transparent and explicit about shifts in foundational equity concepts as equity economic evaluation is increasingly applied.

Second, ECEA includes impact on financial protection, or the avoidance of catastrophic expenditure due to out-of-pocket payments, alongside costs and health effects. The concept of catastrophic expenditure requires a threshold to be applied to determine which out-of-pocket payments should be considered catastrophic. In equity terms, this threshold approach recalls a “decent minimum” equity standard, whereby there is collective responsibility to ensure certain minimum standards are applicable to all or a Rawlsian focus on improving outcomes for the least advantaged without consideration of the overall distribution of benefits.

Finally, Cookson *et al.* separate equity economic evaluations into two distinct groups i) equity impact analysis and ii) analysis of potential equity-efficiency trade-offs (67). Equity impact analysis is descriptive and provides information on the distribution of costs and consequences while trade-off analysis considers the extent to which aggregate health gains are reduced, if at

all, by interventions intended to improve equity in some way compared to those simply seeking to maximise total (i.e. average) health. In both equity impact analysis and equity trade-off analysis, judgements about the fairness of results are, to some extent, exogenous to the analysis. As descriptive analysis, equity economic evaluation frameworks employed for equity impact analysis may employ various approaches to quantitatively or qualitatively appraise the distribution of costs and consequences. The interpretation of these results may be left to the reader or included in the discussion of the results in the paper but the value-judgement is unlikely to be contained in the analysis.

In equity trade-off analyses, like DCEA (34), alternative scenarios that are compared and the analysis focus on the trade-offs between maximising efficiency or equity. Are we willing to accept a loss in total health gains for a pro-poor screening programme that improves outcomes for those in the lowest income group? A more extreme question (which we believe will not be uncommon as this approach develops) is to what extent are we willing to accept negative health gains in a subpopulation even if the total (i.e. average) health gains are positive. In some cases, the value-judgement of the trade-off may be left to the reader, however, value-judgements, sometimes implicit, may have shaped the characterisation of the “equity” scenario in a comparison of equity-efficiency trade-offs. For example, this may take the form of assuming greater equality of outcomes is desired between a marginalised group and the rest of the population. To what extent do we value improving outcomes among this disadvantaged group compared with simply improving health in the population as a whole? Again, this will be framed in general terms by the equity perspective guiding the analysis.

Structure

Heterogeneity dimensions

Transmission models sit within the standard economic evaluation frameworks in broadly the same way as non-transmission models. That is all produce average estimates of costs and effects for an intervention for a defined population over a defined time period, and the economic evaluation framework uses the model outputs to generate summary measures of efficiency. A key methodological challenge, when considering the integration of equity considerations into the economic evaluation frame, is the decision around whether to (and how to) incorporate equity-related dimensions of heterogeneity (equity heterogeneity) into the evaluation, in addition to risk-related dimensions (risk heterogeneity) already part of the transmission model structure. This poses a range of questions relating to model structure and data requirements.

To illustrate the potential implications of equity analysis for model structure and data, let us consider the role of financial protection on individual behaviour such as treatment seeking. In this case, a programme to reduce user fees may both reduce catastrophic expenditures and, because of this, increase uptake and timeliness of treatment, further reducing transmission, particularly among those at risk of impoverishment through ill health, who in turn are at an increased risk of infection. The heterogeneity that drives the distribution of each of the aspects of the impact on user fees, uptake, risk and infection may be different.

In transmission modelling, the principal reason for inclusion of heterogeneity is to capture variation in risk of infection (and/or disease), without value judgement – our risk dimension. For example, behavioural risk factors, such as occupation, sexual activity and migration, or contextual risk factors such as ecological suitability for disease vectors, density of urban living spaces or access to quality healthcare. Equity analysis adds a further consideration to the structural decisions of a transmission model, in that the equity heterogeneity should also be linked to the definition of subgroups by characteristics where differences in outcomes will be considered unjust, such as differences in access to care between groupings by ethnicity or differences in health outcomes by socio-economic status.

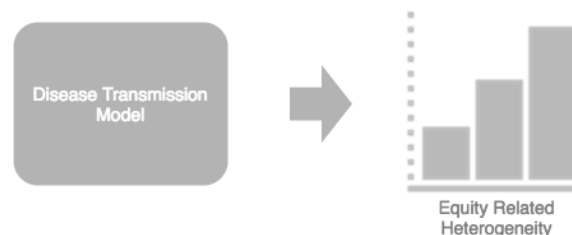
Certain dimensions of heterogeneity are commonly found in both equity analysis and transmission modelling, for example, age and gender. More generally, a key concern when deciding the population groups to distinguish in the model is to assess whether equity and risk dimensions are correlated or not. In some cases, data available for analysis of heterogeneities may occur at a level of population aggregation rather than at individual level. For example, geography, usually in terms of administrative boundaries such as provinces districts or villages, is a natural way to define population sub-groups and can be used to consider heterogeneity in some characteristics. Care should be taken as aggregation may in some cases mask heterogeneity observable at higher resolution.

After the relevant heterogeneity (equity and risk) dimensions are defined, an important structural consideration will be the extent to which equity heterogeneity is integrated into the transmission model structure or treated separately. To unpack these structural challenges, we consider a number of general approaches from simplest to most complex, below.

Cases distributed through equity dimension(s) post-simulation

Let us consider a transmission model that is homogenous with respect to the equity dimension(s) of interest. This transmission model is still useful with respect to an economic evaluation in that it estimates the indirect effects of reduced transmission; however assumptions must be made about the distribution of all effects (direct and indirect) with respect to equity related heterogeneity.

Figure 1: Simple post-simulation inclusion of equity-related heterogeneity



For example, if a pre-existing transmission model of influenza vaccination estimates a 60% decline in cases for the whole population, while in contrast, an impact calculation considering the direct protective effect of those who receive the vaccine might estimate a 40% reduction.

Any equity analysis that previously may have used the “static” impact calculation may instead use the transmission model outputs and improve on this average estimate. That is, the added benefit in using a transmission model is a more precise estimate of total average impact rather than changes in distribution of those impacts.

This approach will work if the dimensions of risk and equity heterogeneity are completely independent. Influenza risk is not related to geography, so that if a policy-maker wishes to consider the consequence of a national vaccination programme on regional inequity, then the distribution of benefit between regions can be done after the national analysis of the impact of vaccination. Although it is probably quite rare for heterogeneity and equity dimensions to be completely independent, in reality, this approach might be useful given its relative ease. In particular, the data requirements for this approach are relatively light.

Cases distributed through equity dimension(s) with parallel unlinked models

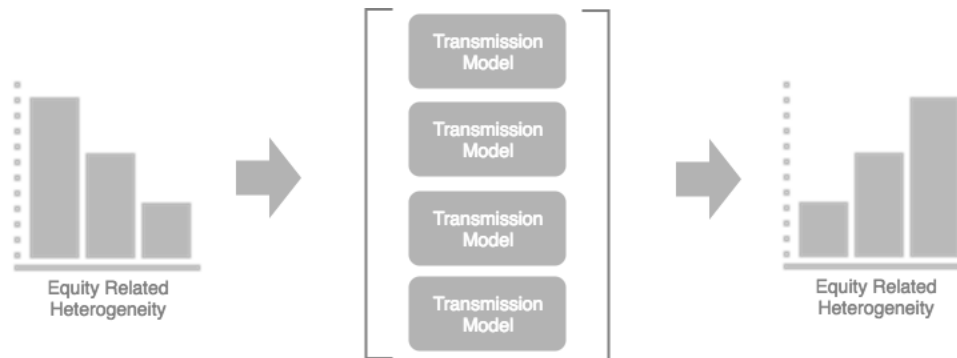
The next approach to dynamic transmission equity analysis considered is to group the population by equity strata prior to the simulation of disease transmission. Here, the transmission model is run in parallel for each equity group. Groups are assigned a prior risk of infection and simulations may be run with or without interventions, i.e. distributing interventions unevenly across the equity strata could be a policy option.

The added advantage of a series of parallel models compared to post-simulation assumptions about the distribution of cases by equity related sub-groups is that there are non-linearities in how different levels of disease transmission might respond to interventions. This approach therefore includes the differing effects of reduced transmission in different population sub-groups, resulting in a different post-simulation distribution of disease burden.

To continue the influenza example, mortality is related to pre-existing conditions, such as chronic obstructive pulmonary disease, which are not uniformly distributed geographically. A policy-maker might wish to include regional specific outcomes by running the transmission dynamic model for each region separately. Such an approach might demonstrate that differential targeting of different regions reduces the inequity in mortality risk between regions.

As with the previous approach, considering multiple separate populations could be a pragmatic approach to equity analysis as existing transmission models may be used. The separate models can be parameterised differently, if say the age-related contact structure differs between equity sub-groups, so there are additional data requirements to determine if this is necessary. However, it may be less common to explore policy questions where it may be accurate to consider each equity sub-group as entirely separate, with no transmission of infection between sub-groups.

Figure 2: Equity-related heterogeneity is propagated through parallel transmission models



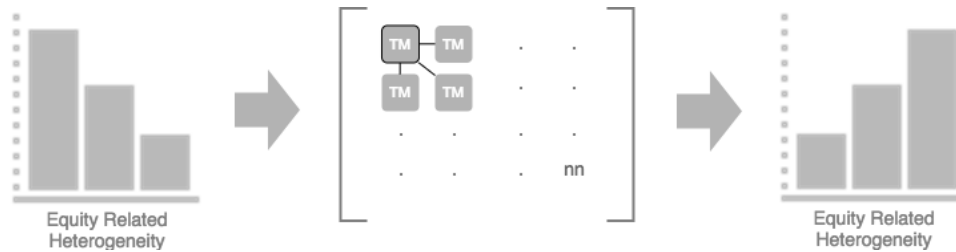
Cases distributed through equity dimension(s) integrated into model – independent risk and equity heterogeneities

In many cases, it will be important to consider transmission between equity-defined sub-groups in order to capture accurately the distributional outcomes of interventions. In order to relax the assumption of independent sub-groups we need to introduce a contact matrix which specifies the degree of transmission that occurs within sub-groups and between them. That is, an infectious individual in sub-group A infects other individuals in sub-group A at a certain rate and infects individuals in sub-group B at a different rate. Note that the transmission models in each of the previous approaches will likely already include a contact matrix for the risk heterogeneity dimension(s), so that the requirement here is for an additional contact structure. The approach has the benefit of more accurately capturing the indirect impacts of interventions targeted at different equity-defined sub-groups. It may be justifiable to provide services selectively to disadvantaged groups, not only because of equity principle but because the wider population also benefits substantially through reduced risk.

To continue the influenza example, it might become clear that it is no longer possible to assume that geographical regions of interest can be considered as epidemiologically separate – for example, if there is significant daily commuter traffic between regions. In this case, vaccination in one region will influence the transmission in another region.

Adding additional dimensions to transmission dynamic models adds significant complexity, particularly with respect to defining and estimating contact matrices. For example, to incorporate a single equity dimension such as household income with n strata will require n^2 additional parameters (or assumptions). Note that the implicit assumption in this framework is that the equity and heterogeneity dimensions remain independent – individuals can be infected from other heterogeneity groups or risk strata such that infection from other strata does not depend on their heterogeneity group.

Figure 3: Equity-related heterogeneity is integrated into transmission model



Cases distributed through equity dimension(s) integrated into model – correlated risk and equity heterogeneities

Each of the previous approaches makes the assumption of no interaction between the two dimensions of heterogeneity (risk and equity). A model considering a correlation between risk and equity dimensions will allow separate contact rates for all of the heterogeneity compartments. To continue the influenza example, this approach allows the model to have specific contact rates for individuals by both risk and equity heterogeneity groups, reflecting that the daily commuting between regions is, say, age-specific.

It will be important to consider whether this complexity will be required to answer the policy questions of interest. While the model structure should represent realistic mechanisms and interactions, unnecessary complexity should be avoided. Parameterisation and validation of a model becomes more complex if models have to include multiple dimensions of risk heterogeneity (e.g. age, gender and sexual behaviour) and equity heterogeneity (e.g. household income, ethnicity and region). This complexity is likely to be the greatest barrier to combining equity economic evaluation frameworks designed to compare multiple dimensions of heterogeneity, such as Distributional Cost Effectiveness Analysis (DCEA), with transmission dynamic models.

The majority of transmission models have been based on compartmental models, in which the population is divided up into groups based on their risk of infection, risk of disease and infection status. The model framework (typically differential equations) then determines the flow of individuals between compartments. However, if equity dimensions and differential uptake (perhaps on a different dimension) are included, then this approach becomes increasingly unwieldy. If the size of compartments become small (<30 individuals), then stochastic effects can become important. This creates a push towards individual-based, stochastic models (68).

Technically, the issues of solving, parameterising, and validating such models is far from an exact science, although there has been considerable recent progress (69,70). As the models become more complex, the number of possible model structures increases. This has led to increasing

formation of model comparison exercises and consortia to try and understand and account for structural uncertainty in decision-making (71–76).

Box 2: Differential placement of Xpert MTB/RIF

What is the problem? To illustrate the impact of heterogeneity definitions on recommendations

What do we know already? The placement of Xpert MTB/RIF (a new point-of-care diagnostic tool of tuberculosis) at lower levels of health system is expected to improve access to diagnostics in difficult-to-access settings (equity) at higher costs. Exploring the epidemiological impact of universal access to rapid tuberculosis diagnosis using agent-based simulation. Conference: 2017 Winter Simulation Conference (WSC) (40).

What will this illustration add? We propose to explore two scenarios based on different assumptions of correlation between risk and equity distributions: 1) no correlation: high and low TB risk groups distributed homogeneously across urban and rural settings; and 2) Correlation: the distribution of TB risk is correlated to the setting (urban populations are also at higher risk). This illustration will help understand how the inclusion of a correlation between distributions of risk and equity dimensions change the nature and size of efficiency/equity trade-offs in economic evaluations.

What would be the relevant message for the following stakeholders?

- 1) national and regional governments/payers: this example will help illustrate the uncertainty related to data availability when presenting the trade-off between CE and equity considerations
- 2) global donors/development partners: as above
- 3) researchers in LMICS and HICs: there are key methods and data needs considerations on how to approach an equity-efficiency trade off analysis as well as the development of communication tools to inform effectively decisions will be discussed.
- 4) iDSI : we will aim to use this example to illustrate the data considerations when applying the reference case to economic evaluations

Data requirements

The choice of which (risk or equity) heterogeneity dimensions to include in a model depend on the societal view of the importance of potential differences, logical consistency of the model structure in relation to known epidemiology, and the data available to parameterise them. However, it is impossible for models to have complete accuracy, and many of the risk heterogeneity groupings included are surrogates for highly correlated variables. For example, including age as a heterogeneity in models of childhood viral infections actually stands for school attendance, and adults working in schools are not specifically included. Further, the risk and equity dimensions are likely to be linked through combinations of causality, correlation, and confounding. For example, if household income is related to number of children, then income status is related to age, which is related to schooling and infection risk. Such complexity is very common, which is why we suggest that, depending on the policy question, the first three model structure approaches are less likely to be sufficient.

As the model and equity analysis become more complex, the data required to support the analysis can become very great (see text box 3). The standard data needs for a transmission model are:

1. Direct estimates of some parameters (e.g. demographic estimates of population size)
2. Training data used to fit the model, including incidence or prevalence of infection/disease in the same dimensions as the model (i.e. including all the heterogeneity and equity groups at least as marginal distributions)
3. Validation data used to check the model performs as expected and includes data different from the training data

All parameters used in the model must be specified using appropriate sources or fitted, and it is critical for complex models that the uncertainty in parameter values is carried forward through all subsequent stages of analysis, which usually implies a Bayesian approach.

As we introduce heterogeneity into a homogenous model, data will then be required to describe this structure. To divide a homogeneous population into sub-groups we need to know the population in each group and whether any of the model parameters differ between groups. These are the minimum data requirements for Approach 2. For Approach 3 and above we must also obtain data on (or make assumptions about) the extent to which each group is connected with the other groups. In addition, it will be important to consider the extent to which there are

Box 3: Contact data requirements

Let $\beta(i, j)$ be the contact rate between groups i and j in the risk dimensions, and $\varphi(a, b)$ be the contact rate between groups a and b in the equity dimensions. Suppose there are n risk groups and m equity groups.

Then in the first approach only $\beta(i, j)$ is defined, which has n^2 elements.

In the second approach, it is possible to define $\beta(i, j)$ for each equity group, $\beta(i, j, a)$ but $\varphi(a, b)$ is undefined. The extended contact matrix has $m.n^2$ elements.

In the third approach $\beta(i, j, a)$ and $\varphi(a, b)$ are both defined and the risk of infection for an individual in risk dimension i and equity dimension a is given as:

$$\lambda(i, a) \propto \sum_j \beta(i, j, a) + \sum_b \varphi(a, b)$$

The maximum number of elements (i.e. parameters) for this structure is $m.n^2 + m^2$.

In the fourth, and most complicated approach, the rates of infection between individuals are defined jointly by their risk and equity heterogeneity:

$$\lambda(i, a) \propto \sum_j \sum_b \rho(i, j, a, b)$$

where $\rho(i, j, a, b)$ is the contact rate between an individual in risk group i and equity group a with an individual in risk group j and equity group b . The maximum number of separate parameters is $n^2 m^2$.

To give numerical reality, if we have 5 heterogeneity groups and 3 equity strata, then the maximum number of parameters for each of the four approaches is 25, 75, 84 and 225 respectively.

correlations between parameter changes between groups. For example, baseline immunity may

be correlated with baseline risk of infection and these may or may not be correlated with equity-related heterogeneity of interest.

In summary, the data considerations (to be obtained or fitted) when defining changes to model heterogeneity are:

1. Data to describe the distribution of population in each sub-group – equity and risk heterogeneity
2. Changes in model parameter values between groups, for example assuming access to treatment changes by sub-group.
3. Data to parameterise correlations between heterogeneity dimensions
4. Data to characterise between-group connectivity

We summarise these model typologies in Table 5 and consider differences in terms of improvements to quantifying equity impacts and with respect to the key domains that determine transmission dynamics.

Table 5: Summary of methodological approaches to using disease transmission models to assess equity in economic evaluations

Analytic approach	Summary	Equity-related data requirements
Transmission model with post-simulation distribution of cases across equity sub-groups	<p>The <i>distribution</i> of risk after modelling the impact of an intervention is assumed to be the same as before. The total impact, including impact due to reduced transmission, is estimated by the model but the <i>proportional</i> reduction in risk and disease burden is assumed to be equal in all sub-groups.</p> <p>This approach is limited in that transmission dynamics of equity related sub-groups are not modelled. The approach does include some estimate of the total impact on transmission but with respect to distributional changes is similar to the application of static models.</p>	The pre-intervention distribution of infection or disease between equity sub-groups
Unlinked parallel transmission models for each equity-related sub-group	<p>As above, this approach still requires minimal adaptation of the transmission model but includes the ability to estimate nonlinearities between how equity sub-groups may respond to interventions. However, important limitations remain.</p> <p>Each equity-related sub-group is treated as a separated population and nonlinearities in the relationship between interventions and their effect on transmission are simulated. Unlike the above example, this means that the post-simulation distribution of disease burden across equity sub-groups may differ from prior information on the distribution of risk.</p> <p>This approach implicitly assumes a mixing pattern where <i>within</i> equity sub-group mixing is homogeneous and <i>between</i> equity – sub-group mixing is zero. The major limitation of this approach is that this might be an epidemiologically unacceptable assumption.</p>	The distribution of infection or disease between equity sub-groups (applied as an input to the model rather than to the output as above). Any sub-group specific transmission model parameterisation. For example, reduced access to treatment or greater likelihood of infection from an infectious contact, among low-income groups.
Equity related heterogeneity is integrated into the transmission model but not structurally linked with risk related heterogeneity	<p>As above, each equity sub-group is assigned a transmission sub-model with group specific prior information on risk. However, in this case a contact matrix is defined which specifies contact probabilities between different equity sub-groups. Structurally this is more realistic than the previous “island populations” approach but obtaining data on the contact between equity groups can be a challenge.</p> <p>It may be important to include between group contacts if modelling strategies for targeting the intervention to one or more equity sub-groups. For example,</p>	As above plus a contact matrix to allow (unequal) transmission between equity sub-groups.

	targeting equity groups with high disease risk may also reduce transmission among groups not receiving the intervention.	
Equity related heterogeneity is integrated into the transmission model and structurally linked with risk related heterogeneity	In this, most comprehensive, approach, contact heterogeneities are fully integrated and quantified.	As above with a comprehensive contact matrix relating all risk and equity sub-groups to each other

In this section, we highlighted that while heterogeneity in certain characteristics such as age or sex is commonly found in disease transmission models, many characteristics that may be relevant to equity analysis are not. We go on to outline a spectrum of approaches that are available when using disease transmission models to estimate healthcare costs and effects across sub-populations of interest and highlight the substantial data needs of integrating heterogeneity into the transmission model. There is a balance between model and analytical simplicity, parsimony, and practicality against precision of results. Where this balance lies is likely to depend on the specifics of the policy question.

Interpretation and reporting of results

Consideration should be given to the presentation of results depending on the equity question with emphasis to facilitating the relaying of information and not pre-empting the decision to be made. We could envisage a descriptive presentation of distribution of benefits across both equity and risk dimensions or should we be interested in a trade-off analysis, it might be important to illustrate the magnitude of these trade-offs using scenario analyses. Further research might be needed to develop aggregate value scores as an integrated representation of the risk-efficiency-equity interaction.

Recommendations

We summarise the analytical process of including equity in transmission based economic evaluations as a set of steps. In line with the IDSI Reference Case guidance, we discussed the methodological considerations at the different steps suggested. These are tools to guide the analysts own decision making, rather than a prescriptive set of specifications. These guidance steps are a first draft and will be reviewed by participants of the workshop.

Table 6: Consideration checklist for analysts considering equity-informed economic evaluation using a disease transmission model

Domain	Considerations
Policy question	Perspective of decision maker Equity principle of interest Sub-groups of interest
Evaluation framework	Outcome of interest Analytical approach
Model structure	Heterogeneity dimensions Level of integration of risk and equity dimensions
Data needs	Description of distributions across equity and risk heterogeneity Parameterisation of correlations between heterogeneity dimensions Characterisation of between-group connectivity
Interpretation and reporting of results	Description of distribution of (direct and indirect) effects and costs Visualisation of trade-offs between equity, risk, and efficiency Aggregate value score

For example, a decision problem relating to providing healthcare insurance for people living below the poverty line has a clear pre-specified group of interest and an equity goal to provide a *decent minimum* standard of care and maximise benefits for the least advantaged (Rawlsian). In turn this suggests that key metrics will include health gains and financial protection, the key dimension of heterogeneity will be socio-economic status and the most appropriate framework could be ECEA. The model design and data requirements will depend on the specifics of the study question, whether developed transmission models exist, whether data are available as well as the time and resources available.

References

1. Verguet S, Riumallo-Herl C, Gomez GB, Menzies NA, Houben RMGJ, Sumner T, et al. Catastrophic costs potentially averted by tuberculosis control in India and South Africa: a modelling study. *Lancet Glob Health*. 2017 Nov 1;5(11):e1123–32.
2. WHO | Glossary of terms used [Internet]. WHO. [cited 2017 Jun 28]. Available from: <http://www.who.int/hia/about/glos/en/index1.html>
3. Wilkinson T, Sculpher MJ, Claxton K, Revill P, Briggs A, Cairns JA, et al. The International Decision Support Initiative Reference Case for Economic Evaluation: An Aid to Thought. *Value Health*. 2016 Dec 1;19(8):921–8.
4. Drake TL, Devine A, Yeung S, Day NPJ, White LJ, Lubell Y. Dynamic Transmission Economic Evaluation of Infectious Disease Interventions in Low- and Middle-Income Countries: A Systematic Literature Review. *Health Econ*. 2016 Feb;25(Suppl Suppl 1):124–39.
5. Whitehead M. The Concepts and Principles of Equity and Health. *Int J Health Serv*. 1992 Jul 1;22(3):429–45.
6. Braveman P, Gruskin S. Defining equity in health. *J Epidemiol Community Health*. 2003 Apr 1;57(4):254–8.
7. WHO | Equity [Internet]. WHO. [cited 2017 Jul 21]. Available from: <http://www.who.int/healthsystems/topics/equity/en/>
8. Pereira J. What does Equity in Health Mean? *J Soc Policy*. 1993 Jan;22(1):19–48.
9. McIntyre D, Mooney G, editors. *The Economics of Health Equity*. 1 edition. Cambridge: Cambridge University Press; 2007. 296 p.
10. Lorgelly PK, Lawson KD, Fenwick EAL, Briggs AH. Outcome Measurement in Economic Evaluations of Public Health Interventions: a Role for the Capability Approach? *Int J Environ Res Public Health*. 2010 May;7(5):2274–89.
11. Greco G, Lorgelly P, Yamabhai I. Outcomes in Economic Evaluations of Public Health Interventions in Low- and Middle-Income Countries: Health, Capabilities and Subjective Wellbeing. *Health Econ*. 2016 Feb 1;25:83–94.
12. Xu K, Evans D, Kawabata K, Zeramdini R, Klavus J, Murray C. Household catastrophic health expenditure: a multicountry analysis. *The Lancet*. 2003 Jul 12;362(9378):111–7.
13. Culyer AJ, Wagstaff A. Equity and equality in health and health care. *J Health Econ*. 1993 Dec 1;12(4):431–57.
14. Culyer AJ, van Doorslaer E, Wagstaff A. Access, utilisation and equity: A further comment. *J Health Econ*. 1992 Aug 1;11(2):207–10.
15. Culyer AJ. Equity - some theory and its policy implications. *J Med Ethics*. 2001 Aug 1;27(4):275–83.
16. Brouwer WB, Koopmanschap MA. On the economic foundations of CEA. Ladies and gentlemen, take your positions! *J Health Econ*. 2000 Jul;19(4):439–59.
17. Brouwer WBF, Culyer AJ, van Exel NJA, Rutten FFH. Welfarism vs. extra-welfarism. *J Health Econ*. 2008 Mar 1;27(2):325–38.
18. Johri M, Norheim OF. CAN COST-EFFECTIVENESS ANALYSIS INTEGRATE CONCERNS FOR EQUITY? SYSTEMATIC REVIEW. *Int J Technol Assess Health Care*. 2012 Apr;28(2):125–32.
19. Wailoo A, Tsuchiya A, McCabe C. Weighting Must Wait. *PharmacoEconomics*. 2009 Dec 1;27(12):983–9.

20. Gu Y, Lancsar E, Ghijben P, Butler JR, Donaldson C. Attributes and weights in health care priority setting: A systematic review of what counts and to what extent. *Soc Sci Med*. 2015 Dec 1;146:41–52.
21. Round J, Paulden M. Incorporating equity in economic evaluations: a multi-attribute equity state approach. *Eur J Health Econ*. 2017 Jun 1;1–10.
22. Appraising life-extending, end of life treatments. National Institute for Health and Clinical Excellence; 2009.
23. Cookson R. Can the NICE “End-of-Life Premium” Be Given a Coherent Ethical Justification? *J Health Polit Policy Law*. 2013 Dec 1;38(6):1129–48.
24. Wagstaff A. Inequality aversion, health inequalities and health achievement. *J Health Econ*. 2002 Jul 1;21(4):627–41.
25. Ngalesoni FN, Ruhago GM, Mori AT, Robberstad B, Norheim OF. Equity impact analysis of medical approaches to cardiovascular diseases prevention in Tanzania. *Soc Sci Med*. 2016 Dec 1;170:208–17.
26. Baltussen R, Niessen L. Priority setting of health interventions: the need for multi-criteria decision analysis. *Cost Eff Resour Alloc*. 2006 Aug 21;4:14.
27. Baltussen R, Youngkong S, Paolucci F, Niessen L. Multi-criteria decision analysis to prioritize health interventions: Capitalizing on first experiences. *Health Policy*. 2010 Aug 1;96(3):262–4.
28. Thokala P, Devlin N, Marsh K, Baltussen R, Boysen M, Kalo Z, et al. Multiple Criteria Decision Analysis for Health Care Decision Making—An Introduction: Report 1 of the ISPOR MCDA Emerging Good Practices Task Force. *Value Health*. 2016 Jan 1;19(1):1–13.
29. Marsh K, Ilzerman M, Thokala P, Baltussen R, Boysen M, Kaló Z, et al. Multiple Criteria Decision Analysis for Health Care Decision Making—Emerging Good Practices: Report 2 of the ISPOR MCDA Emerging Good Practices Task Force. *Value Health*. 2016 Mar 1;19(2):125–37.
30. Jehu-Appiah C, Baltussen R, Acquah C, Aikins M, d’Almeida SA, Bosu WK, et al. Balancing equity and efficiency in health priorities in Ghana: the use of multicriteria decision analysis. *Value Health J Int Soc Pharmacoeconomics Outcomes Res*. 2008 Dec;11(7):1081–7.
31. Verguet S, Kim JJ, Jamison DT. Extended Cost-Effectiveness Analysis for Health Policy Assessment: A Tutorial. *Pharmacoeconomics*. 2016 Sep;34(9):913–23.
32. Kruk ME, Goldmann E, Galea S. Borrowing And Selling To Pay For Health Care In Low-And Middle-Income Countries. *Health Aff (Millwood)*. 2009 Jul 1;28(4):1056–66.
33. Asaria M, Griffin S, Cookson R, Whyte S, Tappenden P. Distributional Cost-Effectiveness Analysis of Health Care Programmes – A Methodological Case Study of the UK Bowel Cancer Screening Programme. *Health Econ*. 2015 Jun 1;24(6):742–54.
34. Asaria M, Griffin S, Cookson R. Distributional Cost-Effectiveness Analysis. *Med Decis Making*. 2016 Jan;36(1):8–19.
35. Cleary S, Mooney G, McIntyre D. Equity and efficiency in HIV-treatment in South Africa: the contribution of mathematical programming to priority setting. *Health Econ*. 2010 Oct 1;19(10):1166–80.
36. Verguet S. Efficient and equitable HIV prevention: A case study of male circumcision in South Africa. *Cost Eff Resour Alloc*. 2013;11:1.
37. Norheim OF, Baltussen R, Johri M, Chisholm D, Nord E, Brock D, et al. Guidance on priority setting in health care (GPS-Health): the inclusion of equity criteria not captured by cost-effectiveness analysis. *Cost Eff Resour Alloc*. 2014;12:18.

38. Daniels N, Porteny T, Urritia J. Expanded HTA: Enhancing Fairness and Legitimacy. *Int J Health Policy Manag.* 2016 Jan 1;5(1):1–3.
39. Daniels N, Sabin JE. *Setting Limits Fairly: Can we learn to share medical resources?* Oxford, New York: Oxford University Press; 2002. 208 p.
40. Wiseman V, Asante A, Price J, Hayen A, Irava W, Martins J, et al. Ten best resources for conducting financing and benefit incidence analysis in resource-poor settings. *Health Policy Plan.* 2015 Oct 1;30(8):1053–8.
41. Anselmi L, Lagarde M, Hanson K. Equity in the allocation of public sector financial resources in low- and middle-income countries: a systematic literature review. *Health Policy Plan.* 2015 May 1;30(4):528–45.
42. Asante A, Price J, Hayen A, Jan S, Wiseman V. Equity in Health Care Financing in Low- and Middle-Income Countries: A Systematic Review of Evidence from Studies Using Benefit and Financing Incidence Analyses. *PLOS ONE.* 2016 Apr 11;11(4):e0152866.
43. Cookson R, Mirelman AJ, Griffin S, Asaria M, Dawkins B, Norheim OF, et al. Using Cost-Effectiveness Analysis to Address Health Equity Concerns. *Value Health.* 2017 Feb 1;20(2):206–12.
44. Kruse I, Pradhan M, Sparrow R. Marginal benefit incidence of public health spending: evidence from Indonesian sub-national data. *J Health Econ.* 2012 Jan;31(1):147–57.
45. Baker R, Bateman I, Donaldson C, Jones-Lee M, Lancsar E, Loomes G, et al. Weighting and valuing quality-adjusted life-years using stated preference methods: preliminary results from the Social Value of a QALY Project. *Health Technol Assess Winch Engl.* 2010 May;14(27):1–162.
46. Ong KS, Kelaher M, Anderson I, Carter R. 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.* 2009;8:34.
47. Samson A-L, Schokkaert E, Thébaut C, Dormont B, Fleurbaey M, Luchini S, et al. Fairness in cost-benefit analysis: A methodology for health technology assessment. *Health Econ.* 2017 Jun 16;
48. Verguet S, Laxminarayan R, Jamison DT. Universal Public Finance of Tuberculosis Treatment in India: An Extended Cost-Effectiveness Analysis. *Health Econ.* 2015 Mar 1;24(3):318–32.
49. Verguet S, Murphy S, Anderson B, Johansson KA, Glass R, Rheingans R. Public finance of rotavirus vaccination in India and Ethiopia: An extended cost-effectiveness analysis. *Vaccine.* 2013 Oct 1;31(42):4902–10.
50. Mauskopf JA, Paul JE, Grant DM, Stergachis A. The role of cost-consequence analysis in healthcare decision-making. *PharmacoEconomics.* 1998 Mar;13(3):277–88.
51. Stinnett AA, Paltiel AD. Mathematical programming for the efficient allocation of health care resources. *J Health Econ.* 1996 Oct 1;15(5):641–53.
52. McIntyre D, Ataguba JE. How to do (or not to do) ... a benefit incidence analysis. *Health Policy Plan.* 2011 Mar 1;26(2):174–82.
53. Wagstaff A. Benefit-incidence analysis: are government health expenditures more pro-rich than we think? *Health Econ.* 2012 Apr 1;21(4):351–66.
54. Analyzing Health Equity Using Household Survey Data [Internet]. World Bank. [cited 2017 Jun 19]. Available from: <http://www.worldbank.org/en/topic/health/publication/analyzing-health-equity-using-household-survey-data>

55. Culyer AJ, Bombard Y. An Equity Framework for Health Technology Assessments. *Med Decis Making*. 2012 May 1;32(3):428–41.
56. Panteli D, Kreis J, Busse R. CONSIDERING EQUITY IN HEALTH TECHNOLOGY ASSESSMENT: AN EXPLORATORY ANALYSIS OF AGENCY PRACTICES. *Int J Technol Assess Health Care*. 2015 Jan;31(5):314–23.
57. Pitt C, Goodman C, Hanson K. Economic Evaluation in Global Perspective: A Bibliometric Analysis of the Recent Literature. *Health Econ*. 2016 Feb 1;25:9–28.
58. Hounton S, Newlands D. Applying the Net-Benefit Framework for Analyzing and Presenting Cost-Effectiveness Analysis of a Maternal and Newborn Health Intervention. *PLOS ONE*. 2012 Jul 19;7(7):e40995.
59. Rheingans R, Atherly D, Anderson J. Distributional impact of rotavirus vaccination in 25 GAVI countries: Estimating disparities in benefits and cost-effectiveness. *Vaccine*. 2012 Apr 27;30:A15–23.
60. Cobiac LJ, Vos T. Cost-effectiveness of extending the coverage of water supply fluoridation for the prevention of dental caries in Australia. *Community Dent Oral Epidemiol*. 2012 Aug 1;40(4):369–76.
61. Blakely T, Kvizhinadze G, Karvonen T, Pearson AL, Smith M, Wilson N. Cost-effectiveness and equity impacts of three HPV vaccination programmes for school-aged girls in New Zealand. *Vaccine*. 2014 May 7;32(22):2645–56.
62. Waters D, Theodoratou E, Campbell H, Rudan I, Chopra M. Optimizing community case management strategies to achieve equitable reduction of childhood pneumonia mortality: An application of Equitable Impact Sensitive Tool (EQUIST) in five low- and middle-income countries. *J Glob Health [Internet]*. 2012 Dec;2(2). Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3529311/>
63. Baker J, Mitchell R, Lawson K, Pell J. Ethnic differences in the cost-effectiveness of targeted and mass screening for high cardiovascular risk in the UK: cross-sectional study. *Heart*. 2013 Dec 1;99(23):1766–71.
64. Carrera C, Azrack A, Begkoyian G, Pfaffmann J, Ribaira E, O’Connell T, et al. The comparative cost-effectiveness of an equity-focused approach to child survival, health, and nutrition: a modelling approach. *The Lancet*. 2012 Oct 13;380(9850):1341–51.
65. Hallett TB, Alsallaq RA, Baeten JM, Weiss H, Celum C, Gray R, et al. Will circumcision provide even more protection from HIV to women and men? New estimates of the population impact of circumcision interventions. *Sex Transm Infect*. 2011 Mar;87(2):88–93.
66. Boston 677 Huntington Avenue, Ma 02115 +1495-1000. Phase 2: Prepare Methods Papers and Case Studies [Internet]. Guidelines for Benefit-Cost Analysis. 2017 [cited 2018 Feb 8]. Available from: <https://sites.sph.harvard.edu/bcguidelines/methods-and-cases/>
67. Cookson R, Mirelman AJ, Griffin S, Asaria M, Dawkins B, Norheim OF, et al. Using Cost-Effectiveness Analysis to Address Health Equity Concerns. *Value Health*. 2017 Feb;20(2):206–12.
68. Chen MI, Ghani AC, Edmunds WJ. A metapopulation modelling framework for gonorrhoea and other sexually transmitted infections in heterosexual populations. *J R Soc Interface*. 2009 Sep 6;6(38):775–91.
69. Klein DJ, Eckhoff PA, Bershteyn A. Targeting HIV services to male migrant workers in southern Africa would not reverse generalized HIV epidemics in their home communities: a mathematical modeling analysis. *Int Health*. 2015 Mar;7(2):107–13.
70. Andrianakis I, Vernon I, McCreesh N, McKinley TJ, Oakley JE, Nsubuga RN, et al. History matching of a complex epidemiological model of human immunodeficiency virus

transmission by using variance emulation. *J R Stat Soc Ser C Appl Stat.* 2017 Aug 1;66(4):717–40.

71. Penny MA, Verity R, Bever CA, Sauboin C, Galaktionova K, Flasche S, et al. Public health impact and cost-effectiveness of the RTS,S/AS01 malaria vaccine: a systematic comparison of predictions from four mathematical models. *Lancet Lond Engl.* 2016 Jan 23;387(10016):367–75.

72. Brady OJ, Slater HC, Pemberton-Ross P, Wenger E, Maude RJ, Ghani AC, et al. Role of mass drug administration in elimination of *Plasmodium falciparum* malaria: a consensus modelling study. *Lancet Glob Health.* 2017 May 26;5(7):e680–7.

73. Eaton JW, Menzies NA, Stover J, Cambiano V, Chindelevitch L, Cori A, et al. Health benefits, costs, and cost-effectiveness of earlier eligibility for adult antiretroviral therapy and expanded treatment coverage: a combined analysis of 12 mathematical models. *Lancet Glob Health.* 2014 Jan;2(1):e23-34.

74. Menzies NA, Gomez GB, Bozzani F, Chatterjee S, Foster N, Baena IG, et al. Cost-effectiveness and resource implications of aggressive action on tuberculosis in China, India, and South Africa: a combined analysis of nine models. *Lancet Glob Health.* 2016 Nov;4(11):e816–26.

75. Houben RMGJ, Menzies NA, Sumner T, Huynh GH, Arinaminpathy N, Goldhaber-Fiebert JD, et al. Feasibility of achieving the 2025 WHO global tuberculosis targets in South Africa, China, and India: a combined analysis of 11 mathematical models. *Lancet Glob Health.* 2016 Nov;4(11):e806–15.

76. Keebler D, Revill P, Braithwaite S, Phillips A, Blaser N, Borquez A, et al. Cost-effectiveness of different strategies to monitor adults on antiretroviral treatment: a combined analysis of three mathematical models. *Lancet Glob Health.* 2014 Jan;2(1):e35–43.