Coyle *Health Economics Review* (2024) 14:90
https://doi.org/10.1186/s13561-024-00556-w

Health Economics Review

COMMENT Open Access

Considerations when applying equity weights within economic evaluation when making drug reimbursement decisions

Doug Coyle[1,2*]

Abstract

When decision-makers use economic evaluation to facilitate making decisions about reimbursing whether to reimburse pharmaceuticals within a publicly funded health care system, they may consider whether to prioritise specific patient populations or diseases: e.g., cancer or rare disease. This can be achieved through applying equity weights to outcomes such as QALYs. Decision makers, however, must choose whether equity weights are applied to solely the treatment of a specific disease or to treatments of the patient with the specific disease. Without such clarification, confusion may arise which can hinder the work of those who must make reimbursement recommendations and decisions. This study examines the repercussions of implementation of equity weights. For illustration, two hypothetical case studies relating to a rare disease are considered. The first case study demonstrates that applying equity weights only to the treatment of the rare disease of interest can lead to a patient with that rare disease accruing less benefits at a higher cost to the payer. The second case study demonstrates that if equity weights are applied to the patients who have a specific rare disease, then funding of a treatment for a common disease may be restricted only to those patients for whom treatment is more costly and less effective. As discussions continue with respect to applying equity weights within economic evaluation, it is important that the repercussions outlined are recognised.

Keywords Decision-making, Equity, Cost effectiveness, Pharmaceuticals

Introduction

Given the scarcity of health care resources, decision makers are increasingly aware that to justify funding for new technologies such as drugs, it is necessary to demonstrate that they provide value for money in comparison with other potential interventions. Economic evaluations are designed to assist decision makers in making optimal choices with respect to the allocation of scarce health care resources. However, a limitation in the appropriate adoption of economic evaluation is the lack of explicit statements from health care funders with respect to the underlying objective of the health care system. Typically, economic evaluation is conducted under the assumption that a decision maker wishes to maximise the health of the population covered under the system. When a budget for health care is considered restrained, the cost effectiveness threshold should reflect the potential loss in the health when resources are reallocated away from one treatment to another. This is referred to as the supply side threshold. By restricting the funding of treatments

*Correspondence:
Doug Coyle
dcoyle@uottawa.ca
[1]School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, 600 Peter Morand Cres, Ottawa, ON K1G 5Z3, Canada
[2]Health Economics Research Group, Department of Health Sciences, Brunel University, London, Uxbridge, UK

to only those patients for whom treatment is cost effective. the level of health across the covered population will increase, relative to the previous state where no new treatments were reimbursed.

Over time as a health care system becomes more efficient at producing health benefit, the supply side threshold should be expected to fall. Any increase in the real value of resources available for health care, however, can lead to an increase in the supply side threshold.

In assessing the supply side threshold, it is necessary to consider the relevant decision maker's equity position. Whilst, previously, economic evaluations were considered without the adoption of explicit equity positions, more recent guidance adopts an explicit equity statement; e.g. that a gain of one QALY is of equal value regardless of who is the beneficiary [1].

The validity of an assumption assuming a QALY is of equal value regardless of the beneficiary has been increasingly a topic of debate. There has been broad discussions about the role of a health care system to reduce inequities in health and to ameliorate financial losses from ill-heath [2]. In many jurisdictions, decision makers are considering whether reimbursement criteria decisions should prioritise specific patient populations or diseases: e.g. end of life care, cancer and rare disease [3–8]. Such discussions, however, do not appear to relate to health inequalities per se but rather are often framed around similar contexts such as fairness, caring externalities, social value and positive externalities [9–12].

The adoptions of higher threshold can be seen to be a simple approximation to applying equity weighting of outcomes such as QALYs, as equity weights can simply involve weighting the existing threshold value [9, 13–16]. However, simply applying the weight to the current threshold will ignore the impact of weights on the supply side threshold.

Equity weighting of QALYs requires changing the objective of the health care system to the maximization of weighted QALYs through the application of weights to QALY gains based on "equity-relevant" characteristics [15]. These weights should be reflective of societal values; ideally obtained from relevant stakeholders such as the members of the general public or appropriately appointed policymakers.

Examples of both implicit and explicit weighting exist. For example, in England and Wales, NICE (National Institute for Health and Care Excellence) has introduced the concept of disease severity decision modifier [17]. This allows QALY weightings to be applied based on disease severity characterised by the shortfall in health for individuals currently living with the disease. QALY weights of 1.2 or 1.7 can be applied [17]. A weight of 1.2 is applied if the absolute QALY shortfall (i.e. the loss in QALY due to the condition under consideration when compared to the general population) is between 12 and 18 or the proportion of QALYs lost compared to the general population is between 85 and 95%. A weight of 1.7 is applied if the absolute QALY shortfall is greater than 18 or the proportional QALY shortfall is greater than 95%. Similarly, NICE has introduced a decision modifier relating to highly specialised technologies (typically treatments for rare diseases). Under these arrangements, The QALY threshold for drugs for very rare diseases is increased from £20,000 and £30,000 to £100,000 and, in addition, QALY weights of between 1 and 3 can be applied dependent on the size of any QALY gains. The combination of the higher threshold and QALY weights implies equity weights of between 3.33 (100,000/33,000 * 1) and 15 (100,000/20,000 * 3). Of note, the NICE approach implicitly ignores the impact of applying equity weights on the supply-side threshold. Less explicit are the approaches to funding cancer and rare diseases in Canada, both nationwide and specific to the Province of Ontario. For cancer, a weight twice the weight for non-cancer treatments implicitly appears to be considered appropriate [18, 19]; whilst for rare disease, no threshold appears to be considered thus implying an infinite weight [20]. A recent review of decision-making frameworks for orphan medicinal products identify a number of European countries which had introduced considerations analogous to the imposition of equity weighting [21]. Orphan diseases are diseases which affects a small percentage of the general population– however, there is no consensus over what constitutes a small percentage. In all of the examples cited above, the equity weights were neither empirically estimated nor reflective of societal values. Similarly, in all of the examples, the implications of applying equity weights on the supply side threshold were not considered.

Some jurisdictions have gone further in considering reimbursement decisions differently based on patient characteristics by developing different processes for making reimbursement decisions for treatments for specific conditions e.g. cancer and rare disease [3–5]. Adoption of differential processes for drug reimbursement has gone hand in hand with higher thresholds being adopted for treatments considered under these processes when compared to treatments considered under a more general process [5, 18].

Discussions around whether equity weights should be applied based on the presence or absence of specific conditions frequently ignore a critical factor; is the equity weight to be applied solely to the treatment of a specific disease or to all treatments of a patient with this specific disease. In highly thoughtful articles discussing the implications of applying preferential funding based on specific criteria; the difference between these choices are often ignored and in some cases the authors appear to switch

back and forth between referencing the disease and the patients with the disease [22, 23].

The objective of this study is to highlight the importance of this distinction by examining the potential impact of implementation of equity weights when applied to solely the treatment of the disease as compared to the application of weights to all treatments of the patient with the disease. This will highlight the potential implications of this choice.

Methods

Assume that similar to many publicly funded health care systems, a health care decision maker wishes to achieve technical efficiency within a constrained budget. The decision maker's objective will be to maximise the possible improvement in an outcome from the resources available to them. If the outcome of interest is the overall health of the population, which can be represented by QALYs, then in making reimbursement decisions it would be appropriate for the decision maker to adopt a "supply-side" estimate of the cost-effectiveness threshold, with the threshold representing the current marginal cost of generating one QALY [24].

If a decision maker wishes to place equity weights on a QALY under certain scenarios, then the repercussion will be that more technologies which are subject to such equity weights will be funded. Consequently, certain technologies that are currently funded will need to be displaced. As the objective is now to maximise equity weighted QALYs, the number of weighted QALYs generated by the system will increase but the number of unweighted QALYs will fall leading to a reduction in the overall health of the population.

The application of equity weights require the re-estimation of the supply side threshold. Imposing equity weights to treatments which meet the criteria can lead to such treatment being funded despite exceeding the previous cost -effectiveness threshold than currently adopted. This will necessarily lead to a reduction in the supply side cost effectiveness threshold for those treatments not meeting this criterion: i.e., treatments which previously were cost effective without equity weights may no longer be so if they do not meet the new reduced threshold. The greater the number of treatment scenarios for which higher weights are applied then the lower the supply side threshold for all treatments. Thus, if the weights are applied to patients with a specific disease rather than treatment of that disease per se, the supply side threshold will necessarily be lower than if they were applied solely to the disease.

This paper will present two case studies relating to the choice between applying equity weights based on the disease treated or the patients with the disease. In both case studies, for illustrative purposes, the consequences of applying higher equity weights relating to rare disease are explored. Rare diseases are adopted as an example of a potential criteria for equity weights; but the conclusions from this study will apply to other criteria. It is, though, relevant to recognise that there is little empirical support of societal preferences for applying equity weights in the context of rare diseases; however, given that specific jurisdictions have enacted such weights, even though implicitly, consideration of the impact of their application in this context appears appropriate.

In Scenario A, it is assumed that there is a patient cohort with both a rare and common disease. Two new drug treatments have become available; one treatment is for treating the rare disease and the other is for treating the common disease co-morbidity.

In Scenario B, it is assumed that there is a new treatment for a common disease. It is further assumed that the drug treatment of this common disease will lead to differential costs and benefits in those with and without a rare disease co-morbidity. Differences may arise due to less capacity to benefit from treatment with those with a rare disease. Thus, analysis will focus on a stratified analysis assessing cost effectiveness within the two groups of patients: those with a rare disease co-morbidity and those without a rare disease co-morbidity [25].

In both scenarios, the impact of applying an equity weight of 2 to either the treatment of a rare disease or to patients with a rare disease is examined. In both scenarios, by definition, the equity weight for all other diseases (non-rare i.e., common) will be 1. Thus, the imposition of equity weights suggests that the benefits gained from treatment of a rare disease or the treatment of patients with a rare disease are of twice the societal value of the same health benefits from treating a common disease.

As detailed above, the imposition of equity weights must lead to the supply side threshold of a weighted QALY being lower than the current threshold. For illustration, it is assumed that without weighting the threshold was $50,000 per QALY. It is assumed that when equity weights are applied to the treatment of rare disease, the supply side threshold was estimated and leads to a threshold of $47,500 per weighted QALY.

If the equity weight of 2 is to be applied to treating patients with rare diseases not to treatment of the rare disease per se, then equity weights will apply to a greater number of treatments than above. It is assumed, for illustration, that the threshold will now be $45,000 per weighted QALY.

Results

Scenario A

Table 1 presents the results of a hypothetical scenario assessing the cost effectiveness of two drug treatments for a patient with a rare disease: one, relating to the rare

Table 1 Results of cost utility analyses under scenario A

	New Drug	Standard of Care	Increment
a. Treatment of a Patient's Rare Disease			
QALYs	4.45	4.2	0.25
Weighted QALYs	8.9	8.4	0.5
Costs	$42,000	$19,000	$23,000
Incremental cost per QALY gained			$92,000
Incremental cost per weighted QALY gained			$46,000
b. Treatment of a Patient's Co-morbidity			
QALYs	4.5	4.2	0.3
Weighted QALYs	4.5	4.2	0.3
Costs	$33.550	$19,000	$14,550
Incremental cost per QALY gained			$48,500
Incremental cost per weighted QALY gained			$48,500

disease and the other relating to a common co-morbidity. Without either treatment the expected QALYs and costs for this patient cohort would be 4.2 and $19,000, respectively.

Treating the patient's rare disease would lead to incremental unweighted QALYs of 0.25 (4.45 versus 4.2) with incremental costs of $23,000 ($42,000 versus $19,000). This leads to an incremental cost per unweighted QALY gained of $92,000. Treating the patient's common disease would lead to incremental unweighted QALYs of 0.3 (4.5 versus 4.2) with incremental costs of $14,550 ($33,550 versus $19,000). This generates an incremental cost per QALY gained of $48,500. If no equity weighting were applied relating to rare disease, then treatment of the co-morbidity would be considered cost effective, but treatment of the rare disease would not.

If an equity weight of 2 was applied to the treatment of rare disease, then the treatment of the patient's rare disease would now be considered cost effective as it would meet the revised threshold of $47,500 per weighted QALY. However, with equity weighting applied only to the treatment of rare disease, the incremental cost per weighted QALY for treating the common disease would be greater than the revised threshold and the treatment would not be funded.

This is the inevitable repercussion of imposing equity weights; treatments which previously would be cost effective but are not subject to higher weighting may no longer be cost effective and treatments which were previously not cost effective but are subject to higher equity weighting may now be cost effective. In this example, however, a less obvious potential implication of equity weighting occurs. Note that treating the patient's common disease generates more incremental QALYs (0.3 versus 0.25) at a lower incremental cost ($14,550 versus $23,000) than treating their rare disease. Thus, the imposition of equity weighting would lead to lower health benefits at a higher cost for the treatment of the SAME patient. The patient who is eligible for the equity weighting will lose out by its imposition.

If equity weights are applied to a condition (e.g., rare disease), this example demonstrates a potential area of concern for decision makers:

> *Applying equity weights can lead to patients that have both a rare disease and a common condition accruing less health benefits at a higher cost to the payer.*

This occurred because the incremental benefits obtained from treating their common disease are greater and the incremental costs are lower BUT the incremental cost per weighted QALY gained for treating the common disease no longer meets the reduced supply side threshold; yet treating the rare disease meets the revised threshold.

A further potential concern can arise if, however, the equity weighting is applied to all treatments for patients with a rare disease. The revised threshold would now be $45,000 per weighted QALY and, therefore, the treatment of the patient's rare disease would now not be considered cost effective as it would not meet this threshold. Expanding the criteria for applying equity weights would now lead to the treatment of the comorbid disease being considered cost effective as it would be subject to the lower revised threshold.

If equity weights are applied to all treatments for patients who meet a particular condition (e.g., have a rare disease), this example demonstrates a potential area of concern for decision makers:

> *Expanding the criteria for equity weighting for patients with a rare disease to the treatments for all the patients' underlying conditions, can lead to the treatment of a patient's rare disease not being cost effective; when it would be cost effective if the imposition of the equity weight was limited to treatment of the disease, per se.*

This occurs because the treatment of the rare disease meets the threshold for cost effectiveness if equity weights are applied to the treatment of rare disease but fails to meet the reduced threshold if the same equity weights are applied to all treatments of patients with rare disease.

Scenario B

Table 2 illustrates another potential implication of imposing equity weights on patients with the disease of interest. It is assumed that a new drug has become available for a common disease. Patients can be stratified into two strata: those with a specific comorbid rare disease and those without. The rare disease may be a risk factor with respect to developing the common disease. Without this new treatment, patients with the rare disease comorbidity will have reduced life expectancy leading to differential expected costs ($15000 versus $27,000) and expected QALYs (9.2 versus 1.25) when compared to those without the rare disease comorbidity.

Treating the common condition with the new treatment in patients with a rare disease comorbidity would lead to incremental unweighted QALYs of 0.25 (1.5 versus 1.25) with incremental costs of $20,000 ($35,000 versus $15,000) (Table 2a). This leads to an incremental cost per QALY gained of $80,000. This would not be considered cost effective if there were no equity weighting. However, applying an equity weight of 2, leads to an incremental cost per weighted QALY of $40,000 ($20,000/0.5). Thus, given the revised threshold of $45,000 per weighted QALY, the treatment would now be considered cost effective.

Treating the same common condition with the new treatment in patients without the rare disease comorbidity would lead to incremental weighted QALYs of 0.3 (9.5 versus 9.2) with incremental costs of $13,800 ($40,800 versus $27,000). This generates an incremental cost per QALY gained of $46,000, not meeting the revised threshold for funding of $45,000 per weighted QALY.

Thus, treating the disease in patients without the rare disease comorbidity generates more incremental QALYs (0.3 versus 0.25) at a lower incremental cost ($13,800 versus $20,000) than treating the same disease in patients with the rare disease comorbidity. Without the imposition of equity weights, only the treatment of patients without the rare disease comorbidity would have been considered cost effective. With equity weighting, however, only treating patients with the rare disease comorbidity would be reimbursed.

Thus, if equity weights are applied to patients with a particular disease (not just to treating the disease), Table 2 demonstrates potential inequities:

> *Applying equity weighting can lead to the funding of a specific treatment for a disease being restricted only to those for whom treatment is more costly and less effective.*

This occurs, similar to Scenario A, when the benefits from treating the same condition in the patient without rare disease are greater and the lifetime costs of treatment are lower; BUT treating the patient without rare disease does not meet the reduced threshold; yet treating the patient with the rare disease comorbidity meets the new higher threshold.

Discussion

The above illustrates three potential areas of concerns with respect to imposing equity weights within economic evaluation. The study uses illustrative rather than real examples to highlight the potential unexpected consequences of imposing equity weights within economic evaluation. The reliance on illustrative examples may be seen to be a weakness but they are designed to highlight the further equity concerns that arise if equity weights are applied either to the patient or the disease. The illustrative examples may be criticized for being potentially

Table 2 Results of cost utility analyses under scenario B

	New Drug	Standard of Care	Increment
a. Treatment of Patients with a Rare Disease			
QALYs	1.50	1.25	0.25
Weighted QALYs	3.00	2.50	0.50
Costs	$35,000	$15,000	$20,000
Incremental cost per QALY gained			$80,000
Incremental cost per weighted QALY gained			$40,000
b. Treatment of a Patients without the Rare Disease			
QALYs	9.50	9.30	0.20
Weighted QALYs	9.50	9.30	0.20
Costs	$40,800	$27,000	$13,800
Incremental cost per QALY gained			$46,000
Incremental cost per weighted QALY gained			$46,000

unlikely, but this does not invalidate the concerns which arise.

These unexpected consequences of imposing equity weights have not previously been clearly identified in the literature. Authors such as Paulden and colleagues have highlighted that the unthinking application of equity weights can ignore who benefits and losses from their imposition [26]. Authors have commented on how equity weights can be applied based on various characteristics; age (old versus young), income (poor versus wealthy), and type of disease (rare disease versus common disease) [16]. Of note, the first two categories are clearly dichotomous but the latter category is not in that a patient can clearly have both a rare and common disease. This paper highlights the problem when equity weights are applied to the latter form of characteristic.

Applying equity weights must lead, *ceterus paribus*, to a reduction in the supply side threshold for cost effectiveness – the threshold for a weighted QALY must be lower than the threshold for an unweighted QALY. In papers discussing the role of equity weighting, this has not always been consistently recognised [16]. The approach by which weights are applied can lead to different treatments for the same patient can be subject to different weights, leading to patients for whom equity weights may apply losing out by their imposition. For example, with respect to patients with rare disease, the equity weights which are applied may not be sufficient for the treatments of their rare disease to be considered cost effective but can result in the treatments of their common conditions no longer meeting the reduced threshold for cost effectiveness.

The above analysis and discussion are rooted in the belief that an appropriate supply side threshold would be the optimal threshold to adopt in determining which technologies to reimburse for which patients [27]. However, there are a number of challenges involved in accurately estimating such thresholds particularly in relation to the quality of data available to derive the threshold and the appropriateness of the econometric techniques adopted [28]. Hence, any supply side threshold will have a degree of uncertainty around its estimation. Thus, any attempts to further modify a threshold to allow for the adoption of equity weighting will bring further challenges and heighten the already considerable uncertainty around the appropriate threshold.

Scenario A highlights an extreme consequence of applying equity weights; illustrating how the decision on whether to apply equity weights to only the treatment of a specific condition of interest or more generally to the treatment of patients with the specific condition. If equity weights were applied to the treatment of the specific condition, in this case a rare disease, certain patients, whose treatment meet the equity criteria, will now accrue less health benefits at a greater cost because the treatment for a rare disease now funded but the more beneficial treatment for their common disease comorbidity will no longer be funded. Thus, by applying equity weights, patients with the disease of interest can generate fewer health benefits than if equity weights were not imposed. Given that imposing equity weights will necessarily mean less health benefits for those within the population who do not meet the equity criteria, theoretically, their imposition could lead to every member of the population losing health benefits.

Scenario A also illustrates a further potential consequence of expanding the criteria for which equity weights are applicable. If the criteria are expanded to all treatments for patients who meet a specific criterion (e.g., patients with a rare disease), rather than specifically treatments relating to this criterion (e.g., treatment of the rare disease), this will require a greater reduction in the threshold for cost effectiveness for both patients with and without a rare diseases. Thus, by expanding the criteria to which equity weights are funded, the treatment of rare disease, the specific area of concern, may no longer be cost effective.

The application of equity weights can lead to different weights being applied to patients with the same condition [26]. This is illustrated by Scenario B. Applying equity weights to patients with a specific attribute, can lead to a willingness to give preference to one group of patients with a disease (those with this attribute) over another group of patients with the same disease (those without this attribute) when the health benefits to be gained from treatment are similar. This may be of concern to decision makers with regards to horizontal equity. A greater concern may be the situation illustrated in Scenario B when preference is given to patients who both will benefit less and will cost more to treat.

The purpose of this article is to highlight what may be the unintended consequences of the imposition of such weights. The consequences are the logical repercussions of imposing equity weights but the implications for decision makers have not been adequately highlighted. The article does not take the position that weights should not be applied when determining which technologies should be reimbursed. There may be well scenarios whereby society is willing to accept a potential reduction in the health of the population for a more acceptable distribution of health. This is the inevitable repercussion of applying equity weights to outcomes gained as society is no longer concerned with health maximization. If equity weights are to be applied, however, the methods by which they are determined should be based explicitly within a theoretical paradigm relating to the role of economic evaluation in decision making. Weights may be determined based on direct evidence of societal preferences

or by decision makers empowered to act in the interests of society. Based on the above, decision makers must be clear to what cases such weights apply – either specific to an individual patient or a disease. This article suggests that regardless of which of these are chosen, further equity related concerns will arise.

Acknowledgements
I am grateful to Drs. Mike Paulden, Petros Pechlivanoglou and Lauren Cipriano for their helpful comments, and to the reviewers for taking the time to provide such thoughtful comments.

Author contributions
DC wrote the manuscript and came up with the concept.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Analysis is not based on patient data, so no ethics approval was required.

Consent for publication
Analysis is not based on patient data, so additional consent for publication was required.

Competing interests
The authors declare no competing interests.

Financial support
No financial support for this study was provided,

Received: 13 December 2023 / Accepted: 10 September 2024
Published online: 13 November 2024

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