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QALYs and ambulatory status: societal preferences for healthcare decision making

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ABSTRACT

Background: This research aimed to review the theoretical and methodological aspects of the quality-adjusted life year (QALY) which give rise to potential for bias against certain patient populations, including those with problems with walking or an inability to walk (ambulatory disabilities), when health technology assessment decisions rely on QALY gain to show cost-effectiveness. Societal preferences for treating ambulatory versus non-ambulatory patients were also investigated.

Methods: We reviewed published literature to identify information on theoretical underpinnings of the QALY, measurement of utilities for QALY assessment, and empirical evidence of societal preferences for the treatment of ambulatory and non-ambulatory patients.

Results and discussion: Health states which represent mobility impairment and the inability to walk receive low valuation from general public preferences. Non-ambulatory patients, for example those with advanced neuromuscular disease, have lower utilities determined by standardized preference-based measurement (PBM) tools. Any treatment that increases survival but could not restore ambulation would result in lower lifetime QALY gains for non-ambulatory versus ambulatory patients. Treatments could therefore potentially be deemed less cost-effective, or not cost-effective at all for this patient population.

Results and discussion: Empirical research indicates a societal preference for equal treatment of patients regardless of ambulatory status. The main limitation of our review was the non-systematic approach to evidence search and review, however, given the broad scope of content required to meet the aims of the review, we believe that the targeted approach was appropriate. The evidence presented in this article highlights the need for alternatives to strict QALY-based approaches to prevent avoidable health inequities when determining cost-effectiveness of healthcare interventions for non-ambulatory populations against fixed cost-effectiveness thresholds. An alternative metric, the Equal Value of Life Years Gained (evLYG), has been proposed as a supplementary measure for use alongside the QALY for its potential to alleviate bias against disabled patient populations during the assessment of healthcare treatments.

Introduction

The QALY is the most commonly used health outcome measure for cost-effectiveness analysis of new interventions[1], providing a standardized approach to optimize distribution of healthcare resources across all diseases, treatments, and populations. The QALY is calculated by multiplying the health-related quality of life (HRQoL) value for the health state (utility) by the number of years a patient is expected to live in the health state. Utilities can be derived using a number of methods. One of the most commonly used methods preferred by health technology assessment bodies is based on patients completing preference-based measures such as the EQ-5D or HUI, which define the health state they are in. A utility value for this health state is then estimated using the scoring algorithm ("QALY weights" or a "tariff") derived

for the health states that the EQ-5D describes *via* a representative sample of the general population. Depending on the nature of the condition (i.e. cognitively unaware individuals) and/or age of participants it may be necessary to rely on caregivers or other proxy respondents to complete the EQ-5D. Utilities assigned to health states can also be collected directly by asking respondents to provide their preferences for health states using standard gamble or time trade-off methods.

In the US, both methodological and ethical arguments against the use of QALYs have been made for certain populations such as patients with pre-existing, non-reversible disabilities since relying on measuring the valuation of interventions by comparing the cost per QALY gain versus a fixed threshold may limit patient access to treatments for these populations[2,3]. An example of this is the valuation of

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quality of life for people who are unable to walk or have limited ability to walk (ambulatory disability), as is the case for many patients with inherited chronic diseases such as Duchenne muscular dystrophy (DMD). Once a person with DMD has lost the ability to walk and requires a wheelchair, the ambulatory disability is irreversible and therefore the valuation of quality of life for these people is an important aspect to consider when assessing the impact of treatments. The QALY has been criticized on the ground that it gives a lower value to preserving the lives of people with a permanent disability than to preserving the lives of those who are not disabled[4], because the quality of life of those with disability is ranked below that of someone without a disability on the health utility scale[4]. Thus, the QALY gain associated with a treatment for a non-ambulatory patient will always be lower than for a patient who is able to walk, even if the number of life years gained from the intervention is equal. This could lead to variable access to treatment for ambulatory versus non-ambulatory populations when a QALY maximizing approach is applied.

Potentially biased outcomes from QALY-based assessments are not exclusive to conditions affecting ambulation and have also been noted to occur in other conditions, for example among patients who experience visual impairment and blindness following cataract surgery[5,6]. However, for the purposes of this paper we focus specifically on limitations of the QALY framework surrounding ambulatory disability.

The theoretical potential for an imbalanced assessment for people with ambulatory disability when using QALYs is described, as well as methodological factors which may contribute to this potential. We postulate that the value of a treatment for a person who is unable to walk should not be systematically assessed as lower than for a person who is able to walk. The available empirical evidence from public preferences supports this position[7,8]. Finally, the potential alternative approaches to QALY maximization are reviewed which aim to address the shortcomings for treatment assessments for non-ambulatory patients.

Theoretical potential for bias against ambulatory disability

QALYs have been described as denying that the life and health of each citizen is as important as that of any other, using the concept of double jeopardy[9]. The first jeopardy occurs where people with disability have lower ranking quality of life than those without disability, as measured by utilities. The second jeopardy occurs when people with disability then potentially face lower prioritization in QALY-based healthcare allocation[9]. The QALY maximization principle argues that healthcare decision makers should "implement the course of action which results in more QALYs than any alternative"[10]. QALY maximization can inadvertently lead to inequitable assessments among patients[11]; rather than being used to measure outputs of healthcare or as evidence in the choice of rival therapies, QALYs would be used to determine which groups of patients would get priority and often, which would get treated at all[11]. QALY

maximization does not disadvantage people with severe disability if a disability can be reversed by treatment. However, when an underlying ambulatory disability cannot be reversed by treatment, life extension will represent a lower QALY gain, and thus a treatment will be less cost-effective compared with the same treatment for patients without disability. Patients can therefore be considered to experience double jeopardy. This may have concerning implications for treatment access decisions relying on QALY-based cost-effectiveness analyses, where there is comparison of the cost-effectiveness of an intervention against an explicit threshold.

Valuation of ambulatory status and implications for HTA

In HTA for national or local reimbursement based on the assessment of cost-effectiveness, utility estimates are usually based on health state valuation responses from the general public, reflecting the desirability of the given health state to society at large compared with perfect health, as opposed to valuation by the individual patient. Utility scores for non-ambulatory health states assessed using PBMs such as EQ-5D and HUI are lower than those for health states representing some level of ambulatory ability[12,13]. Considering non-ambulatory patients, if the treatment under assessment cannot restore mobility, the potential for QALY gain is severely limited compared with treating ambulatory patients because being unable to walk will exert a ceiling effect on the highest achievable utility estimate for a patient. Lower utility weights occur because the general public values non-ambulatory states much less favorably than being able to walk, but at the same time, this may also be explained by limitations of generic PBMs, namely their ability to accurately assess the impact of mobility impairment on patients' quality of life.

Potential limitations with preference-based measures

The specificity of mobility items of PBMs to distinguish between the inability to walk versus total immobility may contribute to the low scores observed for non-ambulatory compared with ambulatory patients. In the EQ-5D 5 level version the response options regarding the mobility dimension are: I have no problems/slight problems/moderate problems/ severe problems in walking about, with the most severe category being: I am unable to walk about. People who are unable to walk may often still be capable of upper body movement and able to perform self-care tasks such as washing and feeding which would not be the case for those who were totally immobile. Given that the ability to perform self-care can be maintained well beyond losing the ability to walk, it becomes apparent that loss of ambulation does not mean loss of independence for patients. The limited construct coverage (i.e. mobility only defined as walking) and low specificity of available responses prevent other forms and varying degrees of mobility from being fully appraised which in turn gives rise to very low utility values. The use of

a mobility aid such as a wheelchair can provide non-ambulatory patients with the independence to get around, and the opportunity to participate in work and recreational activities, which is not adequately captured within the descriptive system of the EQ-5D. The HUI classification system contains 5 levels of mobility impairment (Table 1). The HUI includes health states which describe the use of mechanical equipment and requirement for help from another person as different levels of mobility impairment. This may help to capture the difference in independence afforded by different levels of impairment. Bray and colleagues have highlighted that the relationship between HRQoL and mobility impairment is complex and have noted concerns with the validity of generic PBMs for assessing ambulatory disability[14]. Bray and colleagues have proposed the development of the MobQoL as an instrument with greater sensitivity to measure the impact of mobility on HRQoL with the intention to develop this into a PBM for use in generating utilities for health states associated with mobility impairment in the future[15].

Extreme mobility impairment is associated with a larger utility decrement compared to the same level of impairment across other domains of the EQ-5D (Table 2). Loss of ambulation therefore has a significant impact on utility score.

For example considering EQ-5D-5L and an adapted UK value set[13], a patient who was unable to walk but was otherwise in perfect health would not be able to achieve a utility estimate higher than 0.336 due to the high undesirability placed by the general population ex ante on the health state defined by immobility/inability to walk. This ceiling effect on utility estimates is particularly relevant in progressive diseases with high unmet need, where mobility cannot be restored, but prevention of deterioration and worsening of symptoms are important aims of treatment[16].

The utility decrements associated with moving from ambulatory to non-ambulatory health states may not truly represent the status of people with slowly progressive disease ("experienced utility"), in whom the transition from ambulatory to non-ambulatory is often subtle. In addition,

Table 1. Mobility levels in the Health Utilities Index.

Level	Health state description
1	Able to walk, bend, lift, jump, and run normally for age.
2	Walks, bends, lifts, jumps, or runs with some limitations but does not require help.
3	Requires mechanical equipment (such as canes, crutches, braces, or wheelchair) to walk or get around independently
4	Requires the help of another person to walk or get around and requires mechanical equipment as well.
5	Unable to control or use arms and legs.

Table 2. Utility decrements associated with extreme impairment across EQ-5D-5L domains.

Domain	Health state description	Utility decrement
Mobility	I am unable to walk about	−0.664
Self-care	I am unable to wash or dress myself	−0.564
Usual activities	I am unable to do my usual activities	−0.444
Anxiety/ depression	I am extremely anxious or depressed	−0.586

Utility decrements were calculated using the adapted value set for UK based on mapping to the EQ-5D-3L[13].

mobility assistance (e.g. wheelchair provision) can offer independence and a good quality of life to people who are non-ambulatory[17]. These considerations may not be reflected upon or captured by general public valuations of the EQ-5D health states and may also contribute to the low utilities associated with the non-ambulatory health state.

Example of potential QALY discrimination

Two conditions which have a major impact on ambulatory ability and for which utilities have been documented are DMD and Spinal Muscular Atrophy (SMA). Low utilities have been reported for non-ambulatory patients with DMD and SMA compared with ambulatory patients, when scored using EQ-5D and HUI[18,19]. The considerably lower utility values associated with non-ambulatory versus ambulatory patients could lead to poorer outcomes in QALY calculations which in turn, will result in treatments being deemed less cost-effective and of lower value for non-ambulatory versus ambulatory patients, even if treatment costs and treatment benefits were the same. Within the context of cost-utility analysis, assuming that the cost of an intervention would be the same for both ambulatory and non-ambulatory populations, the lower QALY gain for non-ambulatory patients would result in the cost per QALY being considerably higher for those patients compared with the ambulatory population. The treatment would therefore be considered less cost-effective for the non-ambulatory population versus the ambulatory population giving rise to the non-ambulatory population potentially facing restricted access to treatment. HTA bodies such as the National Institute for Health and Care Excellence (NICE) in the UK are aware of the potentially discriminatory nature of conducting subgroup analyses based on health states for whether patients can walk or not so it is unlikely that restrictions would be applied based on ambulatory health state. However, the low QALY gain associated with maintaining people over remaining lifetime in a non-ambulatory health state means that the QALY gain will be lower for interventions in chronic conditions causing ambulatory disability than in others where patients are able to walk. This will affect all evaluations where the assessment of cost-effectiveness is considered against an explicit standard cost per QALY threshold range such as NICE in the UK and the NCPE in Ireland. A systematic literature review of cost-effectiveness thresholds and their rationale noted that 17 countries have an explicit or implicit threshold and that most thresholds identified fall within the 1–3 times GDP per capita ratio recommended by the World Health Organisation[20].

Health state valuation by the general population versus patients

Evidence suggests that the general public's perception of living with a disability is worse than the lived experience of people with disabilities. This was highlighted in a report from the National Council on Disability (NCD) in the United States[2], citing a UK study in which 24% of over 1,000 members of the general public valued wheelchair requirement for

the rest of their life as being worse than death[21]. The low valuation of the non-ambulatory state is reflected in the lower utilities observed for people in non-ambulatory versus ambulatory states.

The general public's perception regarding the "goodness" or "badness" of living with chronic ill health may not accurately reflect living with ill health from the patient's perspective[22]. In a study by McPherson et al., EQ-5D scores were recorded from patients with rheumatoid arthritis, multiple sclerosis, or stroke ($n = 1,036$) and compared to general population-based ratings ($n = 1,360$). Population derived ratings of health status were systematically lower than the self-valuation and the differences in these ratings increased as the health state worsened, providing further evidence that population-derived EQ-5D valuation estimates may be an inaccurate representation of patients' experience with disabling and chronic conditions[23].

Ubel and colleagues outlined three potential causes of the discrepant patient versus public perceptions of quality of life: a failure to get patients and the general public to compare the same health states; a failure to get them to use the same 'measuring stick'; and real differences of opinion about the severity of various illnesses or disabilities. The authors concluded that decisions about whose values to measure for the purposes of economic analyses, and how to measure discrepancies, should take these potential contributing factors into account[24].

Differences between general public- and patient-based health state valuation indicate that the general public and patients view health from different perspectives. When assessing the desirability of hypothetical health states, members of the general public tend to imagine the transition from their own health state to the hypothetical health state, rather than considering the health state from the point of view of the patient affected. Thus, when ambulatory disability, occurring gradually over time, is presented in the form of a hypothetical health state, the focus on personal transition means that processes of adaptation to one's illness and its integration into one's life context is not accounted for, resulting in misconception of what it might be like to live with disability[24]. Consequently, health state valuations for ambulatory disability which are derived from public preferences may differ with valuations by patients living with ambulatory disabilities[21,23,25].

Another important consideration is the perception of "full health". A member of the general population may perceive full health as being free from any illness or disability, whereas a person with ambulatory disability may have an alternative perception of full health which may encompass improved functioning and independence. This consideration exemplifies the "failure to use the same measuring stick" described by Ubel[24].

Societal preferences for treating people with ambulatory disability

Empirical evidence of a societal preference for equal treatment regardless of ambulatory status would support the case for considering alternatives to QALY maximization.

A study of 289 prospective jurors from the US reported a preference to help patients with more severe over less severe disabilities, which did not differ when the treatment offered was preventive or curative[26]. A separate study assessed the US general public's preference for allocating life-saving treatment to people with or without pre-existing paraplegia who experienced a life-threatening illness. Participants ($n = 251$) placed equal importance on saving the lives of people with pre-existing paraplegia and those who could be returned to perfect health because they did not have pre-existing paraplegia[8]. Therefore, members of the general public were not found to prioritize providing treatment to people who can benefit more versus those who can gain more moderately from a treatment in QALY terms. More recently, McKie and Richardson demonstrated that the societal value of an intervention is not proportional to the size of the health improvement and that there is substantial support for the equal treatment of people with disabilities and chronic illness[7]. Collectively, this evidence shows a societal preference which supports treating patients equally, regardless of the patients' ambulatory status prior to receiving treatment.

There is also evidence that societal preferences are complex and may reflect a range of principles. While the principle of reducing inequalities in people's lifetime experience of health was favored by a sample of the UK general public in one study, other ethical principles were also regarded as important; giving priority to those in immediate pain or suffering, or facing an immediate threat to life (the "rule of rescue" principle), and the health maximization principle[27]. Additionally, studies have documented a general public preference for treating people who would gain the most from treatment in terms of length or quality of life[28–30]. In one particular study, a French general population sample ($n = 958$) was reported to value the impact of drugs on the duration of life, and in particular large gains in life expectancy, much more than quality of life[30]. This observation, where the general public prioritized large gains in life expectancy over quality of life aligns with the "fair innings" argument, in which everyone is entitled to some "normal" span of health, usually expressed as 70 life years[31]. Applying the "fair innings" argument within the context of mobility impairment would argue that children with mobility impairment should be given priority over adult patients for treatment to enable them to fulfil their entitlement to a "fair innings" and thus engage in a personally meaningful life.

There is substantial evidence of a public preference for equal treatment of patients regardless of ambulatory status prior to treatment. Therefore, a case for consideration of societal preference factors to QALY maximization during HTA of treatments for patients affected by pre-existing, non-reversible ambulatory disability may be argued.

Alternative approaches to QALY maximization

Equal Value of Life Years Gained (evLYG) has been proposed as an alternative method that may address QALY equity concerns[32,33] and has been presented in recent ICER

assessments alongside the QALY as a supplementary measure[34–36]. The evLYG evenly measures any gains in length of life across recipients irrespective of pre-existing disabilities and regardless of a treatment's ability to improve patients' quality of life. The evLYG is not as flexible as the QALY in capturing benefits to quality of life during any additional gains in survival but seeks to reflect one view of how social values should be translated into cost-effectiveness analyses[37]. It is for this reason, Pearson highlights that "ICER is determined to present cost-effectiveness analysis results in all reports moving forward based both on the QALY and the evLYG"[33]. Recent ICER assessments have presented the results of cost-effectiveness analysis in terms of both QALYs and evLYG, however the evLYG metric has not yet been used by ICER in its base case assessment for decision making[35,36]. The evLYG metric represents a step in the right direction to address potential healthcare access inequities for people with ambulatory disabilities. Further research is required to ascertain the usefulness of evLYG as one component of the base case economic analysis of healthcare treatments to inform decision making, particularly regarding patients with ambulatory disabilities.

Multi-criteria decision analysis (MCDA) involves calculating weighted scores to estimate the potential value of each decision option based on a set of criteria[38]. The use of MCDA as a potential decision-making framework for HTA has been investigated by NICE in the United Kingdom, concluding that there were a number of general practical issues that might arise from using an MCDA approach in the HTA process[38]. Subsequently, Marsh and colleagues highlighted the use of additive models, a lack of connection between criteria scales and weights, and problems associated with the inclusion of economic criteria as key challenges in using MCDA for HTA. The authors concluded that "more attention needs to be paid to MCDA good practice guidelines by researchers, journal editors, and decision makers and further methodologic developments are required if MCDA is to achieve its potential to support HTA"[39].

Lakdawalla and Phelps have proposed methods which take account of diminishing returns to health using a novel method called the Generalized Risk-Adjusted Cost-Effectiveness (GRACE) approach[40]. The authors note, among other things, that applying the GRACE methodology results in the valuation of improved HRQoL for disabled people as being greater than for similar people without disability.

Discussion

This review presented evidence supporting the need for consideration of alternatives to QALY maximization in healthcare decision-making for treating populations with different levels of ambulatory ability. The review focused on the potential discriminatory effect of QALY maximization on access to treatments for diseases which irreversibly affect ambulation. When assessing the value of treatments for the patient whose condition had not yet progressed to a point where they had lost ambulation, they would be able to achieve a much higher QALY gain than a patient whose condition has progressed to a non-ambulatory stage. In effect, QALY maximization would place greater value on the life of a patient who could walk than a patient who could not. The impact of lower QALY values for inherited chronic conditions affecting mobility will depend on HTA bodies' decision-making criteria. Those with a fixed cost per QALY threshold against which interventions are assessed have the potential to deprioritize the treatment of conditions with lifetime irreversible ambulatory disability. Societal preference literature supports the need to consider alternative approaches to value assessment which would allow equitable access to these treatments for patients regardless of their ambulatory status.

The main limitation of this research is the targeted nature of the literature review which was undertaken. While a systematic review methodology would have provided more rigorous selection criteria for articles to be included or excluded, we believe that the methodology used for this research was appropriate given the broad range of topics considered and the extensive literature available both supporting and criticising the use of QALYs for priority setting in health care and its potential impact on patients with pre-existing disabilities.

Conclusions

There has been growing hesitancy and resistance against the use of QALYs, particularly within the context of people with disabilities[41,42]. QALY gains for treatments in people who are non-ambulatory are likely to be lower than for those with the same underlying condition who are able to walk, which will lead to treatment of non-ambulatory chronic conditions being considered less cost-effective during HTA. Empirical evidence from the general public does not support the prioritization of interventions for those who are able to walk compared with those who are non-ambulatory. Collectively, the findings of this review highlight the need to consider alternatives to QALY maximization to prevent avoidable health inequities when assessing the value of treatments for people with pre-existing, non-reversible ambulatory disabilities.

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