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## **Should we consider including a value for ‘hope’ as an additional benefit within HTA?**

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**Running Title:** Should we consider including a value for ‘hope’ within HTA?

**Keywords:** Cost-effectiveness analysis, health technology assessment (HTA), value of hope, value assessment, risk-seeking preferences in survival

### **Highlights:**

What is already known about the topic?

One of the novel elements of value put forward for consideration within value assessment frameworks is the ‘value of hope’. This would give additional weight to treatments with a skewed distribution of survival benefit.

What does the paper add to existing knowledge?

This paper shows that the evidence for incorporating the ‘value of hope’ based on patients’ stated preferences for uncertain treatment profiles is weak. We propose future research which could strengthen this evidence base and argue for consideration of a broader concept of hope.

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## **Abstract**

Health technology assessment (HTA) typically uses average health-related quality of life (HRQoL) gain as its main measure of benefit used in economic evaluation. However, there have been calls to consider novel aspects of benefit including the 'value of hope', defined as a patients' potential preferences for a wider distribution of treatment benefit with a positive skew, in the hope that they will be one of the lucky ones.

The value of hope may also derive from feeling hopeful as a positive mental state which may be missing from current measures of HRQoL. The value attributed to feeling hopeful could be related to, or additional to, the value derived from possible risk-seeking preferences.

Here we reflect upon the strength of the case for the inclusion of the 'value of hope' taking a critical look at the commonly referenced evidence for including the 'value of hope' as risk-seeking preferences. We also draw attention to other conceptions of hope; as an emotion, a cognitive process or a combination of both and reflect upon the potential of including these broader notions of hope into HTA. The case for the inclusion of the 'value of hope' based on risk-seeking preferences is weak. We suggest research questions that could give further evidence on whether hope is an important missing value from HTA.

## 1. Introduction

The main purpose of Health technology assessment (HTA) is to assess health technologies to support decision-making on which interventions to fund. The question of which benefits to include in these assessments has been widely debated [1].

In 2018 the International Society for Pharmacoeconomics and Outcomes Research's (ISPOR) Special Task Force to define elements of value in healthcare proposed a number of novel elements which could be considered for inclusion in US value frameworks [2]. One of these is the 'value of hope', defined as a patient's potential preference for treatments with a positively skewed outcome distribution, "in the hope that they will be one of the lucky few to benefit" [2]. In other words, patients may express a preference for treatments that give variable and unpredictable levels of benefit where there is some probability of a particularly good outcome compared to treatments with an equivalent but certain expected outcome. This would imply relatively less value would be placed on health benefits arising from interventions where patients faced more certainty around the size of benefit. The context of this ISPOR report is limited to survival benefit, and it is not clear whether this potential preference extends to quality of life benefits. Furthermore, the context was value assessment within the US

If this 'value of hope' is incorporated into HTA it would deviate from the traditional focus on average benefits. This assumes: (i) patients care about the distribution of benefits, not just the average [3]; and (ii) those responsible for health policy should take this into account. Patients may opt for treatments with a high outcome variance because they 'value hope' *ex-ante*. Alternatively, they may opt for lower variance to protect themselves against the unluckiest outcome and/or avoid uncertainty.

Those proposing to include the 'value of hope' into evaluations of (some) healthcare argue that, although individuals may be typically risk averse in most areas of decision making, in situations where they face very poor prospects and have little to lose they are likely to become risk lovers [4-6]. Estimates of this value can be considerable. For example, in a case study looking at a comparison of treatments for advanced lung cancer (second-line nivolumab treatment vs docetaxel), Shafin et al [7] found that incorporating the 'value of hope' (through adjusting the utility function to incorporate risk-seeking

preferences by using a certainty equivalent rather than the expected survival difference) led to 0.04 additional QALY gain for nivolumab.

This conception of hope as risk seeking in survival gains is only one way of interpreting the concept of hope. Hope may mean different things to different patients [8]. In addition to (or instead of) focusing on a possible extension of survival [9], patients may value being able to feel hopeful about their lives such as feeling that they and their families are able to cope with the challenging circumstances they face, that they can focus on the positives, and that their remaining life will be lived at a reasonable quality of life [10]. Hope, conceived this way, may not be linked to the chance of a successful survival outcome or perceiving treatment as possibly curative [10; 11].

Given the current discussions around value assessment frameworks [2; 3; 5; 6; 12] and the potential impact of incorporating this novel aspect of value (including a reduced incentive to identify subgroups of patients with highest clinical benefit because the uncertainty itself would have value were outcomes to have a positive skew) it is timely to reflect upon the strength of the case for the inclusion of the value of hope within a measure of social value used to guide reimbursement policy. The aim here is to take a critical look at the commonly referenced evidence for including the 'value of hope' as risk-seeking preferences and reflect upon the potential of including hope as a mental state into HTA. We place these possible sources of value for hope into a broader context and consider future research questions.

## **2. Evidence for including the value of hope based on risk-seeking preferences**

Two empirical studies are referenced to support the claim for consideration of the value of hope as an additional source of value in HTA within the ISPOR task force [2]. These studies [4; 13] present patients with hypothetical scenarios for their own treatment involving poor baseline survival prognosis and offer two choices which have the same expected outcome with one option presented as a gamble.

Lakdawalla et al [13] elicited preferences from breast cancer patients (n=150) finding that 77% preferred the hopeful gamble. Additional questions asking about willingness to pay for the chosen option found that

on average respondents were willing to pay \$54,362 for the 'hopeful therapy'. The authors conclude that, *"most cancer patients may prefer a therapy with the possibility of a large survival gain, even if the therapy's average or median survival is similar to that of alternative therapies."*

A replication study [4] was conducted online with three groups: (1) patients with advanced stage lung cancer (n=84); (2) patients with advanced stage melanoma (n=81); and (3) oncologists (n=94). The authors found that over 60% of patients preferred the therapy with uncertain survival duration and, on average, were willing to give up one year of survival to gain the possibility of longer survival. The physicians, however, reported a preference to prescribe the therapy with a certain survival duration.

These two studies suggest a fairly strong preference for right skewed survival outcomes however, their framing of the choice scenarios in , and the challenges of interpreting choices based on gambles means these results should be treated with caution.

The studies rely upon respondents accurately interpreting and calculating complex probabilities (for example, in Lakdawalla et al [13] respondents are required to calculate the expected survival duration when 50% of patients live 13 months or less, 40% live more than 13 months but less than 48 months, and 10% than live 48 months or more). However, deficiencies in people's interpretation of probabilities are well documented [14]. Tversky and Kahneman [15] for example, show that people tend to overweight low probabilities, and this finding has been supported in the context of 'decisions from description' [16]. The low probability of the unlikely successful outcome may be subjectively interpreted as greater than stated, or the probability neglected altogether given that this is an outcome which is likely to produce strong emotions [17; 18], making estimates of the expected value from gambles as perceived by the individual problematic – and hence preferences towards skewed distributions challenging to measure.

There is an additional problem in how the probabilities are set out within the Shafrin et al [4] and Lakdawalla et al [13] studies in that expected survival cannot be adequately calculated because lower and upper bounds are not fully specified within the uncertain option presented (for example, in the above example the best possible outcome is stated as 48 months or more). Whilst respondents may have

accurately interpreted the preamble that specified equivalent average life expectancy between the two options there is no way of knowing what respondents were thinking when expressing their preferences.

Other research has identified lower levels of preference for risk seeking in survival gains. Doctor et al [19] found that 53% of a sample of the public stated a preference for sacrificing mean survival to gain a chance at a good outcome. Using a discrete choice experiment, Hauber et al [20] found that patients diagnosed with NSCLC expressed a preference for increasing best case survival (of the 85<sup>th</sup> percentile) relative to expected survival (of the 50<sup>th</sup> percentile). However, a clearer presentation of the survival options presented in a similar DCE by Reed et al [21] with respondents with a history of cancer found that although respondents preferred options with a 5% and 10% chance of long-term survival when holding constant expected survival, at a 20% chance of survival preferences were reversed.

This body of research should be interpreted with care. Firstly, studies find that some patients prefer treatment risk others do not; whilst standard methods for estimating the value of health states accommodate heterogeneity in terms of relative value across attributes of quality of life the direction of improvement in that respect is reasonably taken as consistent across people (i.e. less pain is better than more pain).

Secondly, the value of possible survival extension should be considered alongside the negative consequences of encouraging hope which is subsequently dashed. Giving additional weight to treatments with a wider distribution of expected benefit because they are in line with a patient's *ex ante* preferences may lead to different priorities than if benefit was valued *ex-post*. Do patients (and their families) who experience hope because they hold to the belief that they will be lucky experience more misery and distress than would otherwise have been the case if they had adapted to a more certain future? The experience of false or unrealistic hope, both for patients and their families, is also relevant. Feelings of regret and hopelessness that may become apparent at the end of life for unlucky patients should also be considered.

Indeed, the anticipation of potential regret may be a driving force behind patient choice in the above studies [22; 23]. If the anticipated regret over 'what might have been' is made in reference to the best



possible outcome this could result in a preference for the risky option. If anticipated regret is behind respondent choices this has different policy implications than a preference for risk seeking as the value of the treatment survival profile arises due to the difference between choice sets rather than inherent value of the high-risk option. The normative significance of anticipated regret versus actual regret or disappointment is not clear.

Thirdly, the 'value of hope' potentially overlaps with 'option value' of medical innovations in the future (the value arising from keeping people alive long enough to see future novel therapies) which has been presented as a potential additional value to be included within HTA by several analyses [24-27]. Patients (and decision makers) may re-interpret the treatment benefit profile from the risky option so that the best survival outcome is perceived as including the chance of a cure being developed during that period – and this consideration may be focused only on the long survival outcome rather than a perception of probability of new cures during all survival durations. Any extension of life expectancy would then be perceived as having both a direct value plus the possibility of an indirect benefit due to an as yet non-existent cure.

If some notion of perceived option value of future innovation drives preferences for treatment profiles with a high survival option (even where they have low probability) then this may not reflect a risk-seeking preference. The 'option value' of treatments could be estimated separately and patient preferences toward distributions of survival benefit identified using scenarios that exclude the potential for 'option value' from possible outcomes (through, for example, instructions within surveys which rule out that possibility). However, there is no consensus that option value of future innovation should be included in HTA, nor on how to identify those interventions which could be considered to be on the brink of major innovations. Indeed, dealing with related and unrelated future costs and benefits (and their associated uncertainty) in HTA remains a vexing issue [28].

Fourthly, the evidence for individual preference for variability in treatment outcomes should be interpreted alongside other evidence of preferences towards distribution of health gain. There is an extensive literature exploring preferences towards distributions of health gain which generally finds inequality aversion within public preferences (e.g. [29-34]). However, this work explores preferences over health distributions at the societal level (where people adopt the role of decision maker) rather than private preferences over the distribution of potential benefit for individual patients themselves. It may be possible to simultaneously value dispersed benefit from the patient perspective and care about equity at the decision-maker level and (all else equal) for decision makers to give additional weight to treatments with a less unequal distribution.

The evidence for the 'value of hope' as risk-seeking preference is limited, suggesting a need for better evidence. However, the value of hope as a directly experienced emotional state or as a cognitive mechanism which indirectly contributes towards positive emotional states should also be considered. This is explored in the following section.

### **3. Various conceptions of hope**

Hope has been variously conceived as an emotion [35], a cognitive process [36] or a state with "both affective and cognitive qualities" [37]. Snyder developed a theory of hope as an individual's pathways and strategies to meet valuable and uncertain goals along with the motivation and agency and emotional feedback to enable them to use those pathways. Or more poetically described as "a personal rainbow of the mind" that "lifts our spirits and makes us think of what is possible" ([38] p269). This theory of hope shares components with optimism, self-esteem and self-efficacy but remains a distinct construct.

Similarly, other theorists also extend hope to be not just about an expectation for a positive outcome in the future but about a lived experience in the present, something which gives meaning to our lives.

Callina describes hope as something which "enhances our agency, helping us to achieve our goals and cope with obstacles and challenges. It orientates us positively toward the possibilities inherent in the future and also gives us meaning and zest in our experiences in the present" ([39] p20). Despite the

disagreement within conceptions of hope, and ambiguity around the dependency of hope on internal versus external factors [40], 'hope' as commonly conceived is about more than risk seeking preferences.

Undertaking a therapy regimen with a chance – even a very small chance - of extended survival may enable people to experience hope as conceived in these broader senses. But hope could arise from many other means: religion, strong social support, or positive mental health. Hope is much more than a preference for positively skewed outcome distributions. The concept could capture patients' feelings of hopefulness and ability to enjoy each remaining day, to cope with their condition and treatment and to feel optimistic about how their family will cope after their death.

Most standard multi-attribute utility instruments (MAUIs) such as EQ-5D, HUI3 and SF-6D do not directly capture feelings of 'hope' – at least not beyond correlation with self-reports of anxiety and depression. One exception is the AQoL-8D which includes an item on 'despair' which can be thought of as the absence of hope [41]. Hope may be an important missing value from some utility estimates.

In a recent literature review on quality of life of patients (with a range of health problems), social care users and carers, hope was identified as important across all groups [16]. Feeling hopeful (or hopeless, framed as having nothing to look forward to) was perceived as sufficiently important and generic to be included in a new health and wellbeing measure (EQ-HWB see: <http://euroqol.org>). Feelings of hope have been found to be related to other positive states of mind for chronic patients, such as ability to cope, feelings of control, better relationships, protection against anxiety [42] and stress [36] and sense of self [43; 44].

Feeling hopeful as a mental state could be captured within MAUIs whereas preferences towards distribution cannot. Using a more descriptive term for the latter, such as the 'value of risk-seeking preferences towards survival' may help clarify this distinction. Indeed, the Institute for Clinical and Economic Review 2020-2023 Value Assessment Framework for 2020 [45] noted that the 'value of hope' was poorly named, preferring to frame this benefit in terms of the value of alternative treatments that offer a distinctive "balance or timing of risks and benefits" although this framing could capture other

distributional preferences. Without a change in terminology there is a risk of misinterpretation when referring to the 'value of hope' within value assessment frameworks.

#### **4. Conclusions**

We have good reason to think that hope and the associated ability to cope with difficult circumstances is important and potentially underrepresented in standard MAUIs. The case for including the 'value of hope' within HTA [2; 5] has focused on patient risk-seeking preferences, however, an exploration of a fuller conceptualisation of hope is warranted.

There are several questions which could be explored in future research including replication of past empirical work. Future research could also explore whether preferences for a wider skewed distribution of benefit remain when patients are offered the opportunity to gain new information which would reduce the uncertainty they face.

The quality of studies could also be enhanced through larger sample sizes, research conducted outside the US, and confirmation that the uncertain profiles are well understood. Complementary qualitative studies could explore the motivation behind preferences and the extent to which they may be motivated by a re-interpretation of probabilities (i.e. respondents think 'I'll be the lucky one'), or by some concept of 'option value', or concern with anticipated regret, or because respondents think having hope will give them a better quality of life. The personal perspective of patients with limited life expectancy may not generalise to other patient groups or beyond survival benefit to quality of life. The role of hope within non-terminal conditions has been argued to be conceptually different from terminal patients [46], hence exploring the role of hope both as a preference for skewed quality of life benefit distribution is also interesting.

It is also important to have better understanding of the positive states captured by the notion of 'maintaining hope' (e.g. feeling like life is worth living, dealing well with a disease etc.), and the negative states arising from unrealised expectations and the extent to which these states are captured in existing MAUIs.

If the lived experience of hope could be captured through utility measures, then 'hope' will no longer be a missing source of value. A measure that can capture the value of non-health attributes, such as hope, would also be able to capture the lived experience of patients and loved ones throughout treatment and when the treatment outcome is realised. Whether patient preferences towards the distribution of outcomes at the start of treatment should be included above and beyond the lived experience of all patients remains unclear. The justification for the inclusion of individual preferences towards risk and outcome distributions, which may be identified through revealed or stated preferences (self-referencing rather than framed as a 'citizen'), within a collective, pooled resource allocation system remains unclear. Healthcare decision makers are likely to require a stronger theoretical justification and considerably more empirical evidence before recommending including any additional value to an outcome distribution with a positive skew. Ultimately, what is included within a measure of benefit for HTA is a normative judgement and the legitimate role of decision makers [47]. It is possible that the US decision making context (with multiple payers and greater reliance upon welfarist evaluations in which individual willingness to pay is the source of value), may make some elements of value more relevant in the US than elsewhere.

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