

## Exploring the Implications of the “Value of Hope”

May 20, 2019

### RESEARCH QUESTION

How does accounting for patients’ attitudes towards risks in treatment outcomes affect value?

### KEY TAKEAWAYS

- Value of hope has been suggested as one of the elements to augment conventional cost-effectiveness analysis
- Value of hope revolves around the risk that a particular treatment may or may not work that well for a given patient, and patients are not risk-neutral regarding the possible outcomes of treatment
- Incorporating risk preferences may meaningfully impact cost-effectiveness estimates under certain circumstances, but it remains unclear when incorporating value of hope will affect the rank-order of treatments in terms of value
- Future research is needed to generate data on risk attitudes in different diseases and to evaluate and improve methods for incorporating risk preferences

### QUANTIFYING VALUE

New health technologies can bring improvements in efficacy, safety, convenience, or adherence – and sometimes all of the above. The introduction of new medical innovations can also significantly affect health care costs. In a world of rising overall health care spending and constrained resources, as is currently the case in the United States, this often requires difficult decisions about where to invest in new technologies. To make the decisions that ultimately best serve patients, it is important to consider the value of new technologies compared to one another and to established standards of care.

Estimating the value of health technologies – in other words, examining costs relative to benefits for a specified population – is not a new practice. Arguably, the most established approach is cost-effectiveness analysis (CEA). In CEA, two or more treatments are compared to the standard of care in terms of incremental changes in costs relative to incremental changes in health benefits, generally measured in terms of quality-adjusted life years (QALYs).

Typically, CEA is based on the expected health care costs and health impacts, but there are increasingly calls for augmented approaches to value assessment that take into account the patient perspective and greater societal benefits of health. For example, the ISPOR Special Task Force on Value Assessment Frameworks recently recommended that CEA studies incorporate “novel” components of value, such as the value of hope.<sup>i</sup>

### VALUE OF HOPE

A novel element of value, the value of hope arises from the risk that a particular treatment may or may not work that well for a given patient. Value of hope aims to better reflect value to patients by incorporating patient’s attitudes toward risk in treatment decisions.<sup>ii</sup> Specifically, the value of hope emerges from analyzing patient risk preferences when treatments with equivalent expected health benefits differ in their overall benefit distributions. This is especially true when a benefit distribution has a “long right tail” (indicating longer-term survival for a small number of patients).

Late-stage treatments in oncology provide a salient example. Imagine a newly-approved therapy that has similar expected overall survival benefits when compared to standard of care. The majority of patients on this new therapy experience lower overall survival, but a small share of treated patients experience long-term, durable survival benefits. In this case, patients may actually prefer the “gamble” of using the new treatment because the possibility of long-term survival is preferable to the “sure bet” of standard of care. In this case, where both treatments would be considered to have equivalent health benefit in conventional CEA, consideration of value of hope may impact the assessment of relative value.

The concept of value of hope is relatively new, however, and the potential impact of its use in value assessment remains to be tested. In this exploratory analysis, we aimed to shed light on the question: how does the level of risk tolerance affect the measure of value?

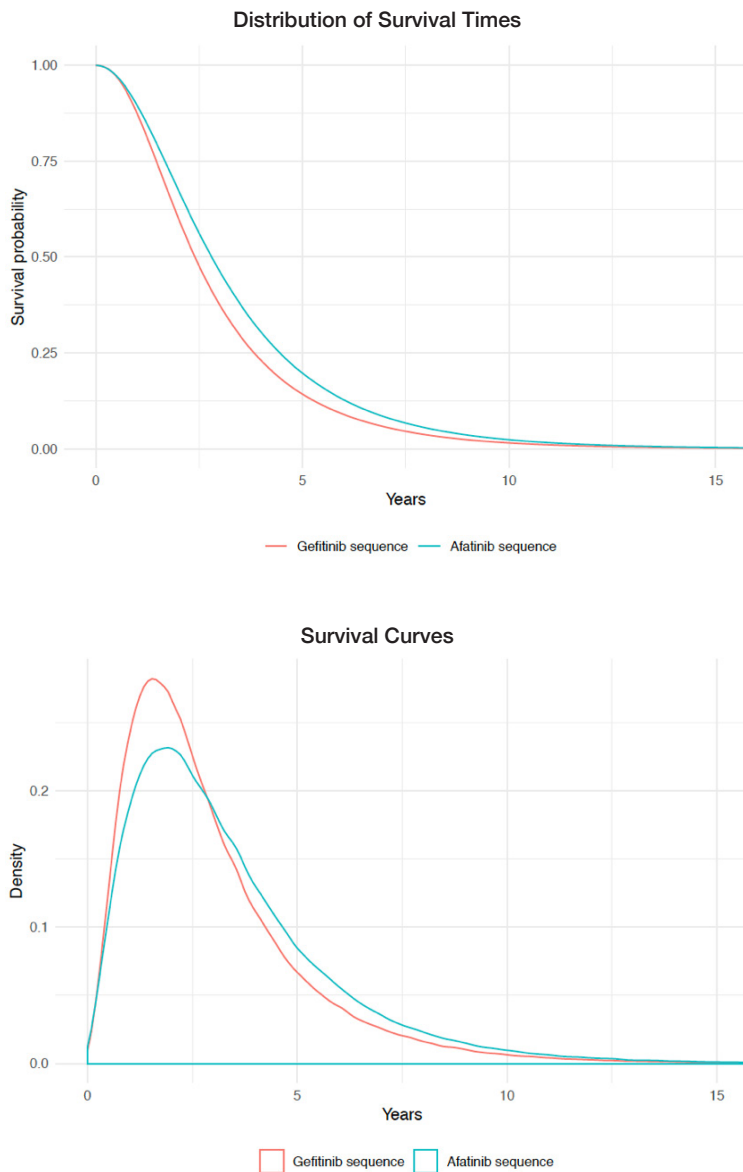
### ILLUSTRATION USING THE IVI-NSCLC MODEL

Using the IVI-NSCLC model, we illustrate the potential impact of including value of hope in a CEA. The IVI-NSCLC model, part of IVI’s Open-Source Value Project (OSVP), is an open-source simulation model designed to assess the costs, benefits, and risks of sequences of treatment for EGFR+ non-small cell lung cancer (NSCLC). The IVI-NSCLC model includes an experimental module for calculating the value of hope.<sup>1</sup>

<sup>1</sup>For full details or to access the IVI-NSCLC model, visit <https://www.thevalueinitiative.org/ivi-nsclc-value-model/>.

We first simulated expected costs and outcomes for two possible treatment sequences. In Sequence 1 (used as the comparator), first-line treatment was gefitinib, whereas first-line treatment in Sequence 2 was afatinib. Second and post-second line treatments were identical.<sup>2</sup> In this example, the afatinib sequence was associated with a greater survival than the gefitinib sequence, as illustrated in Figure 1. In addition, Sequence 2 is characterized by a wider distribution of survival times – in other words, it has a longer “right tail.” Corresponding QALYs and total healthcare costs (both discounted at 3%) for these two treatment sequences are presented in Table 1.

**FIGURE 1. Survival Distributions for the Two Alternative Treatment Strategies**



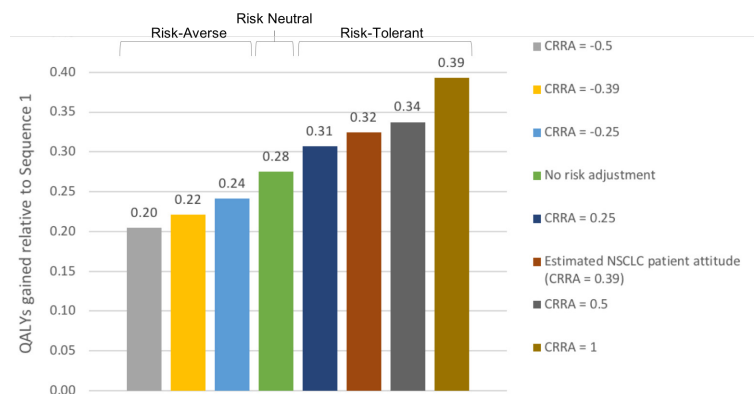
**TABLE 1. Expected Outcomes for the Two Alternative Treatment Strategies**

	Sequence 1 (gefitinib)	Sequence 2 (afatinib)
Life years (undiscounted)	2.98	3.40
QALYs (discounted)	1.92	2.20
Costs (discounted)	\$424,844	\$452,451

To compare the health benefits of Sequence 1 and 2 without factoring in patient risk preferences, we would simply subtract the expected QALYs per patient for Sequence 1 from the expected QALYs with Sequence 2 to determine the incremental QALY gain with Sequence 2. In our example, this tells us that, for the average and risk-neutral patient, we could expect an estimated 0.28 additional QALYs using Sequence 2 than we would with Sequence 1 (Figure 2).

To add the value of hope to the QALYs in this example, we start by estimating the certainty equivalent, or the QALYs a patient would need to obtain to be indifferent between Sequence 1 and 2, given their attitude toward risk. This risk attitude is represented by the constant relative risk aversion parameter (CRRA). For someone who is entirely neutral toward risk, the CRRA value would be zero. A CRRA less than zero reflects aversion to risk, whereas values greater than zero reflect a “risk-seeking” attitude – in this case, a preference for “gambling” on a low probability but high payoff outcome. The farther from zero these values are, the greater the degree of the risk-averse or risk-seeking attitude. To examine the impact of risk attitudes on value, we varied the level of CRRA and calculated the certainty equivalent (in QALYs) and resulting incremental cost-effectiveness ratio (ICER) at each CRRA level.

**FIGURE 2. Incremental QALY Gains with Sequence 2 Relative to Sequence 1 at Varying CRRA Levels**



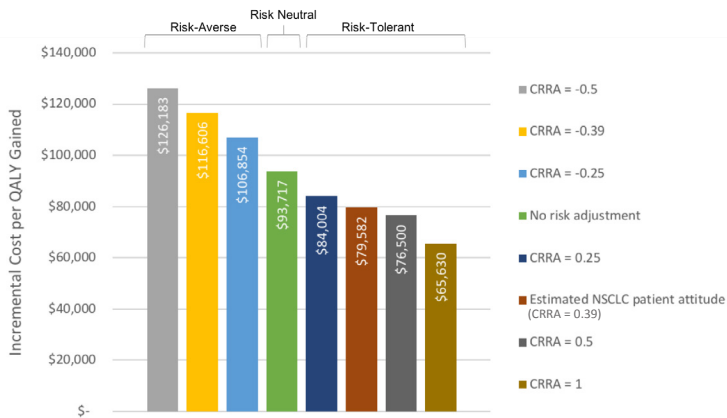
Patients with NSCLC may not actually be risk-neutral, however – a recent study estimates that CRRA for NSCLC patients is closer to 0.39.<sup>iii</sup> In this example, a CRRA of 0.39 would correspond to 0.32 incremental “QALY equivalents” with Sequence 2 (relative to Sequence 1), or approximately 2 quality-adjusted weeks of life more than when risk preferences are not included. At higher CRRA levels, this incremental benefit continues to increase. The converse also holds true – at CRRA levels below zero (indicating aversion to risk), incremental QALY gains are less than standard risk-neutral estimates.

These changes in relative benefit consequently affect estimates of value. Without incorporating risk preferences, the incremental cost-effectiveness ratio (ICER) for Sequence 2 compared to Sequence 1 is just over \$93,000. If patients are risk-averse,

<sup>2</sup>Second line: osimertinib if T790M positive, platinum-based doublet chemotherapy (PBDC) if T790M negative. Post-second line: PBDC and atezolizumab regardless of T790M status.

however, the incremental cost per QALY may be higher – if CRRA is -0.5, for example, the ICER increases to more than \$120,000 in this example analysis. On the other hand, greater risk tolerance among patients may suggest lower costs per QALY gained. Using the above-mentioned estimate of 0.39 for the CRRA, the ICER is reduced to about \$80,000.

**FIGURE 3. Incremental Cost Effectiveness Ratio for Sequence 2 Relative to Sequence 1 at Varying Levels of CRRA**



## IMPLICATIONS FOR VALUE ASSESSMENT

Value of hope is a relatively new concept in the field of health economics, but may capture important considerations left out of conventional approaches to CEA. While our analysis should be seen as illustrative and not definitive, it does highlight the potential impact that incorporating risk preferences can have on estimates of value.

To effectively incorporate the value of hope, however, a number of key elements are needed. First, patients and providers cannot anticipate long-term tradeoffs without information on the full distribution of health outcomes over time. In order to move quickly toward regulatory approval, though, many clinical trials may not provide information in the “right tail,” and statistical extrapolation may be needed. However, this is also required for conventional CEA. Second, better mechanisms for measuring risk attitudes are needed. This includes both empirical estimates for populations of patients in various disease areas and straightforward approaches to estimate risk preference in the case of specific patients. Furthermore, because risk attitudes are likely to vary across subgroups within patient populations, heterogeneity in risk attitudes is an important consideration.

## CONCLUSION

When navigating diagnosis and treatment, patients often face significant risks, whether from the potential health impacts of disease, the consequences of treatment decisions, or impacts on the stability and quality of their lives. Despite the value of hope being a relatively new concept, the consideration of patients’ risk preferences is an important component of moving toward more patient-centered value assessment methods. To rigorously incorporate patient attitudes toward risk into value assessment, however, further research is needed – both to generate data on outcomes and risk attitudes and to evaluate and improve methods for incorporating risk preferences.

## ABOUT THE INNOVATION AND VALUE INITIATIVE

IVI is a nonprofit organization committed to advancing the science and improving the practice of value assessment in healthcare through collaboration among thought leaders in academia, patient organizations, payers, life science firms, providers, delivery systems and other organizations.

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<sup>1</sup> Lakdawalla DN, Doshi JA, Garrison LP, Phelps CE, Basu A, Danzon PM. Defining Elements of Value in Health Care—A Health Economics Approach: An ISPOR Special Task Force Report [3]. *Value Health*. 2018;21(2):131-139.

<sup>2</sup> Lakdawalla DN, Romley JA, Sanchez Y, Maclean JR, Penrod JR, Philipson T. How Cancer Patients Value Hope And The Implications For Cost-Effectiveness Assessments Of High-Cost Cancer Therapies. *Health Aff (Millwood)*. 2012;31(4):676-682.

<sup>3</sup> Shafrin J, Schwartz TT, Okoro T, Romley JA. Patient Versus Physician Valuation of Durable Survival Gains: Implications for Value Framework Assessments. *Value Health*. 2017;20(2):217-223.