



Adapted Value Assessment Methods for High-Impact “Single and Short-Term Therapies” (SSTs)

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Introduction

This paper presents adaptations to the ICER value assessment framework methods when the topic under review is a high-impact single or short-term therapy (SST). The adapted methods described below will be implemented beginning with ICER reviews launching in January 2020. As will be noted, several new methods described below will be applied in the review of all topics going forward and therefore dovetail with the overall update to the ICER value framework that will be presented in December. In the future, updates to methods for high-impact SSTs will be performed simultaneously with the updates to the overall value assessment framework.

These adapted methods arise following a full-year process during which ICER has sought input from multiple sources. We conducted a systematic review of methods considered for “cures” or “potential cures;” sought input from CADTH, NICE, and other international health technology assessment (HTA) bodies; and performed interviews with leading methods experts and stakeholders, including patient advocacy groups, payers, plan sponsors, and life science companies. From this work ICER developed a separate [technical brief](#) that serves as background to the adapted methods presented here.

An initial draft of proposed methods adaptations was posted on August 6, 2019 and subject to public comment. ICER also hosted a full-day in-person deliberation with a select group of stakeholders on September 17, 2019. The video of this full-day meeting is available [here](#).

ICER acknowledges the important insights gained from public comment and from discussions with patient groups, drug manufacturers, payer organizations, health economists, and international HTA collaborators. Assessing the value of SSTs often presents important challenges, including distinctive types of uncertainty at the time of launch that raise the risk of high unrecoverable costs; questions regarding additional dimensions of value for patients or the health system; time divergence between costs and benefits; and concerns about affordability and fair sharing of any savings created by preventing the downstream costs of expensive chronic treatment. For all stakeholders, it is critical that the methods that guide assessment and recommendations for fair value-based pricing of SSTs are ready for these challenges and are well adapted to guide and support the innovation of new therapies that are affordable to individual patients and to the health system.

Final Methods Adaptations

1. Determining those treatments for which adapted assessment methods will be used

1.1 High-impact “single and short-term therapies” (SSTs).

ICER will use an adapted assessment approach for high-impact SSTs, defined as: *“therapies that are delivered through a single intervention or a short-term course (less than one year) of treatment that offer a significant potential for substantial and sustained health benefits extending throughout patients’ lifetimes.”*

SSTs include two subcategories:

- *Potential cures* that can eradicate a disease or condition; and
- *High-impact therapies* that can produce sustained major health gains or halt the progression of significant illnesses.

1.2 All forms of interventions, including non-drug interventions, may be considered high impact SSTs.

1.3 Determination of qualification for consideration as a high-impact SST.

ICER will include in its initial draft scoping document a statement on whether a therapy is judged to meet the above definition. Following formal public comment and discussions with stakeholders, ICER will make a final decision on whether the therapy meets these criteria and will be assessed using an adapted approach.

1.3.1 When a treatment is deemed to qualify as both SST and for an ultra-rare disease (URD), all elements of both methods adaptations will be pursued. However, we will only create optimistic and conservative scenarios (discussed below in Section 2.2) for the health care system perspective base case.

1.3.2 When an SST topic is reassessed, a judgment will be made on whether the treatment should still be considered as an SST based on available evidence.

Discussion

There have been various attempts to define the term “cure,” with divergent views on what constitutes a cure and on how long it is necessary to wait before declaring a treatment is a cure. For HTA purposes, it is most important to decide which characteristics of a new treatment would raise distinctive evaluation challenges such that alternative assessment methods should be considered. We believe it will be useful to consider alternative methods not just for potential cures,

but also for certain disease-modifying treatments that produce a high-impact health gain from short-term treatment, as many of the issues related to greater uncertainty and the disconnect between cost and longer-term benefits will apply. In general, therapies that offer substantial and sustained health benefits will be those that treat diseases or conditions that are near-term life threatening or severely debilitating, or those that would cause a life-long significant disability if left untreated.

This focus on single or short-term treatments also implies that we do not believe that treatments taken on a chronic basis, even if they may be true cures that eradicate disease, warrant consideration of special assessment methods. We believe that current assessment methods are adequate for these kinds of treatment and that it is the combination of short-term treatment with the potential for substantial long-term gain that generates the key challenges meriting consideration of alternative assessment approaches.

From a procedural standpoint, when beginning the scoping process for a new drug, ICER will review available information in the literature and from stakeholders regarding the nature of the treatment to make a preliminary judgment whether it should be considered as a high-impact SST. ICER will seek consultation during the scoping process with manufacturers, the patient community, clinical experts, and others on the anticipated impact of the treatment. Following formal public comment on the draft scope, ICER will make a final decision on whether the treatment meets the criteria for high-impact SSTs and will be evaluated using the adapted assessment methods described below. When an SST topic is reassessed, a judgment will be made on whether the treatment should still be considered as an SST based on available evidence.

2. Assessing and Describing Uncertainty

2.1 Cure proportion modeling.

ICER will make cure proportion modeling its standard reference case for high-impact SSTs whenever relevant, but to address uncertainty we will also provide survival analysis based on other modeling approaches when feasible.

Discussion

As discussed in the [technical brief](#), the use of cure proportion models may help to better fit survival data in certain cases, and may be especially relevant for SSTs, where a proportion of patients may be expected to be cured or benefit from a complete halt in the progression of a serious illness. For SSTs, traditional parametric curves may not adequately fit the available survival data due to the heterogeneity of the population (with some patients cured and others not). We will model SSTs that show evidence of plateaus in survival data with newer techniques such as flexible parametric and other cure proportion analyses, using model fit statistics to determine the best fit to the available data. Where data are not mature enough to determine if the survival curve actually shows a sustained plateau, scenario analyses using various survival analytic techniques will help to characterize the range of potential results that may plausibly fit the available data to date. In such cases, the presentation of results from several types of survival models can be used to develop a range around estimated long-term survival until more data become available.

2.2 Optimistic and conservative benefit scenarios.

In addition to the base case and associated sensitivity analyses, ICER will develop two specific scenario analyses to reflect an optimistic and a conservative assumption regarding the benefit of SSTs under review. Input for best approaches to modeling the optimistic and conservative scenarios will be sought beginning with the scoping phase and will be included as part of the model analysis plan. These scenario analyses will be presented in conjunction with the base case for consideration by the independent appraisal committees.

As discussed in the [technical brief](#), HTA assessments that involve cost-effectiveness often present decision-making bodies with multiple different sensitivity and scenario analyses. Sensitivity analyses are frequently run to demonstrate the impact of varying one or more inputs into the model, such as an assumption about the quality of life related to a particular health state. The distinction between sensitivity analyses and scenario analyses is not always clear, but in many cases the term scenario analysis is used to imply a more substantial shift from the base case approach, such as using a different overall perspective (e.g. societal vs. health system), a different age cohort, or a different time horizon.

For high-impact SSTs, there may be many dimensions of uncertainty that are relevant for decision-makers. Most often, the one modeling assumption that will have the largest impact on the judgment of long-term value for money will be the duration of benefit. Short-term results must be

cast forward in time, often for decades, and if an SST seems to provide a cure or a transformational improvement in the short-term, it is likely that the most consequential modeling decision will be how to estimate the duration of that benefit over the long-term. However, in other cases, there are other types of uncertainty around benefit that may be more important to investigate. Some examples of types of uncertainty that might be explored in these scenarios include:

- Duration of benefit (varying time in a “cured” health state for an average population before effect wanes)
- Magnitude/quality of benefit (varying how much the cure might improve clinical outcomes)
- Proportion that achieve a specific benefit (varying the percent of patients who are in the “cure” proportion)
- Different types of survival models (fitting different survival curves to data and using model fit to determine conservative and optimistic scenarios)
- Relative treatment benefit under alternative assumptions (e.g., proportional hazards vs. alternate functions for hazards)

The base case economic model must represent the best judgment for a single estimate of the benefit. However, decision-makers should explore alternative assumptions, and feedback from stakeholders during the public comment phase has confirmed the relevance of an “optimistic” and a “conservative” scenario analysis. These scenarios will not test every assumption or input in the models, such as the utilities used in the model, which will still be tested via sensitivity analyses, but will focus on aspects of the clinical benefit from treatment. Rather than frame these scenarios comprehensively as being optimistic or conservative on all assumptions, we believe that focusing on the clinical benefit alone will highlight the impact of this key assumption without enmeshing it in the labyrinth of other assumptions within the model.

Developing these alternative scenarios will still require judgments to be made. These scenarios will be evidence based and not arbitrary. An optimistic scenario will not always mean that the SST must be assumed to be a perfect cure for all patients for the rest of their lives. Similarly, a conservative scenario will not always assume that the benefit from an SST evaporates the day after the end of the time horizon captured in the pivotal clinical trials. ICER will develop its approach to the optimistic and conservative scenarios through discussion with patient groups, clinical experts, manufacturers, and other stakeholders. The outline of these scenarios will be shared with stakeholders and will be open to comment.

The process of selecting optimistic and conservative scenarios will begin with the scoping phase. In our interviews with stakeholders during the scoping period, we will specifically query the inputs and assumptions that would go into an optimistic and conservative scenario for the treatment(s) being assessed. Based on available data and clinical expert input, we will develop an approach to the optimistic and conservative scenarios. This approach will be described in a Model Analysis Plan, which will include descriptions of the inputs and assumptions to be used in each scenario. This Model Analysis Plan (and preliminary model presentation) will be subject to comment from

stakeholders, and will be revised as needed. Methods and results for the optimistic and conservative scenarios will be included in our draft reports, which are again subject to a public comment period. Following any necessary revisions based on feedback on the draft report, results for these scenarios will be presented in our final report.

The development of these alternative scenarios will not in any way diminish ICER's usual approach to exploring uncertainty through univariate and multivariate sensitivity analyses. Nor will these scenarios displace the broader discussion of uncertainty that occurs as part of deliberation by the independent appraisal committees. It is envisioned that results from the optimistic and conservative benefit scenarios will be reported alongside the base case findings in key ICER documents intended to help inform decision-making.

2.3 Threshold analyses for durability of effect.

When the SST price is known or can be estimated, assessments of SSTs will also include a scenario with a threshold analysis determining the duration of beneficial effect (e.g. cure) for those patients receiving short-term benefit that would be needed to achieve standard cost-effectiveness thresholds (e.g., \$150,000/QALY).

Discussion

For judgments of value when the price of the SST is known, decision-makers may find it helpful to know the specific number of years that the benefits of a drug would need to be sustained in order to reach certain cost-effectiveness benchmarks. Knowing the results of this kind of threshold analysis may help decision-makers judge whether it is reasonable to assume that the duration of benefit is likely to continue for that span of time or not. This threshold analysis may also help inform the time horizon for outcomes-based contracts should payers and manufacturers wish to use a cost-effectiveness threshold as a target for establishing fair value.

2.4 A new economic review section on “Uncertainty and Controversies.”

ICER will add a new section in the “Long-Term Cost-Effectiveness” section of ICER reports which will discuss “Uncertainty and Controversies” related to the economic evaluation. This new section will be added to all ICER reports, not just those for high-impact SSTs.

Discussion

The current content of ICER reports includes commentary on factors related to uncertainty, including lack of information on natural history, limitations of the data on patient outcomes, and difficulties translating existing data into measures of quality of life. However, we feel it will be helpful to consolidate and expand discussion of these issues in a designated section of the report. This section will also include specific areas of disagreement and controversy regarding the model structure and inputs. This section will therefore be used to expand discussion of alternative model structures or inputs suggested by manufacturers or other stakeholders.

3. Additional Elements of Value

3.1 Additional elements of value.

For all ICER reviews (not only those for high-impact SSTs), we will add three additional domains of “potential other benefits or disadvantages” for voting by independent appraisal committees:

(1) A potential advantage for therapies that offer a new treatment choice with a different balance or timing of risks and benefits that may be valued by patients with different risk preferences;

(2) a potential advantage for therapies that, if successful, offer the potential to increase access to future treatment that may be approved over patients’ lifetime; and

(3) a potential disadvantage for therapies that, if not successful, could reduce or even preclude the potential effectiveness of future treatments.

Discussion

Our review of additional elements of value that are not traditionally included in cost-effectiveness analyses identified some that could be viewed as especially relevant for SSTs: the value of hope (often confused with the value for patients of treatments that have not demonstrated a chance for any benefit), insurance value, scientific spillover effects, and real option value. However, as described in the technical brief, there are important conceptual counterarguments for the inclusion of these additional elements of value as a quantitative element in value assessment. For several of the considered additional elements, we believe that there are significant risks of double counting within the QALY or within existing “other benefits” or “contextual considerations” that ICER already includes as part of its value framework.

A second counterargument against inclusion of additional elements of value is that they are all unidirectional: they all “add” value to treatments, and none have negative scores that would help balance out added value within an opportunity cost framework for determining the cost-effectiveness threshold. As discussed in the technical brief, many health economists believe that should any of these additional elements of value be incorporated quantitatively in determinations of cost-effectiveness, the operative cost-effectiveness threshold used for value-based pricing would need to be lowered, but by how much it is impossible to determine.

A third concern with these additional elements of value is that the methods for measuring them consistently across different types of treatments are not mature and the only consensus among health economists seems to be that further research is needed before it can be determined how to measure them.

We have considered these concerns and have decided to propose no quantitative integration of additional elements of value into the value assessment framework for the assessment of SSTs. However, interviews with patient groups and other stakeholders leads us to propose three additions to our list of potential other benefits and disadvantages that are important components of ICER's value framework. The first captures the basic idea of what others have called the "value of hope," but that we have chosen to call the value of having the *choice* among treatments with a different balance and timing of risks and benefits. This dimension of value can be appreciated if considering treatment options for patients facing a life-threatening condition. Best current treatment might offer a 2% chance for a five-year survival. A new treatment, however, might offer a different clinical profile: a higher chance of serious short-term side effects and death, but a 10%-15% chance of five-year survival. The total average QALYs gained for the two treatments might be the same, but for some patients there would be a special advantage in having the choice of accepting a higher short-term risk in order to have a greater chance at long-term survival. We propose to seek patient input on this potential other benefit during the review process for SSTs and have this issue debated during the public meeting and put to a vote of the appraisal committee in order to have its salience recognized by policymakers.

We also propose to include a new potential benefit or disadvantage related to the option of receiving future treatments. The potential advantage is related to what has previously been described as option value: the ability to benefit from future treatments that the patient would not otherwise have been able to receive. The potential disadvantage is that some SSTs might, by their mechanism of action or triggering of immune responses, lead to a decreased chance at effective treatment by a future generation of therapies in the pipeline. This concern has already been raised with some treatments for hemophilia and childhood blindness. We feel it is important to consider this potential benefit or disadvantage as part of a broader judgment of long-term value for money within the ICER value framework.

4. Time Divergence Between Costs and Benefits

4.1 Discounting.

ICER will make no change to its reference case 3% discounting to be applied to both health outcomes and costs.

Discussion

The use of a 3% discount rate as standard for both costs and outcomes has been standard practice for most cost-effectiveness analyses in the United States, as recommended by the 2nd Panel on Cost-Effectiveness.¹ This rate is based on estimates of the real consumption rate of interest and data on real economic growth, which are thought to reflect the social rate of time preference. The technical brief discusses in detail some of the arguments ongoing in HTA groups around the world over the basis for discount rates and whether there should be any deviation from a standard for certain kinds of treatments, such as SSTs. While some have criticized the use of the 3% discount rate (or of discounting *per se*), we have made the judgment that there is no persuasive evidence for the use of another rate at this time. We also see no convincing rationale for using a different discount rate or scheme for SSTs as opposed to non-SSTs, or for using differential discount rates for costs and outcomes. The use of a single, uniform discount rate for all assessments will allow for consistent comparisons across different or prior evaluations. We also do not propose presenting sensitivity analyses that vary the discount rate, as we do not believe this would provide additional information that is useful to decision-makers in this context. ICER encourages continued research into the appropriate discount rate to use for health economic evaluations, as well as periodic updates of the appropriate discount rate, as necessary.

5. Sharing of Health System Savings

5.1 Hypothetical shared savings scenarios.

To stimulate further consideration of how the cost offsets generated by new treatments should be incorporated in calculations of the value and value-based price for a new treatment, ICER will develop two new hypothetical economic analysis scenarios that evaluate cost-effectiveness outcomes with a different approach to the cost offsets from a new treatment. Threshold analyses for treatment price will be presented but will not be suggested as normative guides to pricing. These two hypothetical scenarios will be generated for all high-impact SSTs under review, as well as other (non-SST) treatments with relevant and substantial potential cost-offsets. In most cases this will be situations in which potential cost offsets are greater than \$1 million over a lifetime:

1. A 50/50 shared savings model in which 50% of the lifetime health system cost offsets from a new treatment are “assigned” to the health system instead of being assigned entirely to the new treatment; and
2. A cost-offset cap model in which the health system cost offsets generated by a new treatment are capped at \$150,000 per year but are otherwise assigned entirely to the new treatment.

Discussion

Several factors lead us to believe that shared savings scenarios will provide useful information to stimulate a broader societal discussion on the use of cost-effectiveness to guide value-based pricing for SSTs and other new health care interventions. As discussed in ICER’s accompanying technical brief, high-impact SSTs have the potential to lead to very large cost offsets by preventing the need for expensive, chronic treatments. This is a benefit for both patients and the health system, but this traditional approach, when used to calculate cost-effectiveness findings, can suggest value-based prices at extreme levels – for example, more than \$80 million for a cure for one severe form of hemophilia.

Extensive public comment and discussion on this point has revealed that many stakeholders disagree that valuation of SSTs that incorporate sizeable cost offsets represents a problem. Other stakeholders do favor exploration of new methods to stimulate further societal discussion on how to use cost-offsets in calculating value-based prices.

We initially explored an option for sharing the savings generated by cost offsets by linking the time frame for cost-offsets to the intended 12-year period of exclusivity established by the US Congress for new biologics. While this option has some conceptual justification, we benefited from public comment pointing out that some SSTs would have cost offsets many years after the initial 12-year period (e.g. a preventive cure for Alzheimer’s Disease that must be administered to healthy middle-

aged adults). We also found in empirical tests that this problem with the “length of exclusivity” approach could not be fixed by taking a yearly average of cost offsets and assigning 12 years to the treatment because this approach was not technically possible in cure proportion models.

We have therefore opted to introduce two other hypothetical approaches that address cost offsets in different ways. The first is an arbitrary 50/50 split of cost-offsets in which half is “assigned” to the treatment as part of its valuation, whereas half is assigned to the health system. Public comment and other discussions have suggested some principles by which the share of savings could be determined, including the degree to which federal investments underpinned the research leading to the treatment, the relative overall cost of development, and the relative size of the future patient population (i.e. whether treatment will eradicate a disease entirely, eradicate all current disease but treat newly incident cases, etc.). We are opting to develop a single 50/50 shared savings scenario to foster continued discussion on these points.

A related concern about extremely large cost offsets and the impact they have on cost-effectiveness results is that in some cases a new treatment may prevent the need for treatments that are, themselves, so expensive as to be highly cost-ineffective.² Pricing a new treatment that reduces or removes the need for such services by applying all cost-offsets to the price of the new treatment has the risk of reinforcing a pattern of spending that fails to maximize health within a health system. Health economists have therefore previously explored the idea of “re-pricing” the health services that are eliminated by a new treatment in a way that brings them into alignment with the overall cost-effectiveness threshold used to guide pricing.³

We sought to explore this option and found that re-pricing individual services so that they, as a group, would meet a particular cost-effectiveness threshold, was not technically feasible. Instead, we will seek the same general goal by developing a scenario that caps all health system cost offsets at \$150,000 per year. The figure of \$150,000 is being selected because it is at the top of the ICER range for value-based pricing for an additional QALY. Even though many treatments will not produce a full QALY in a single year, we feel that providing a cost-offset of \$150,000 in a single year represents a reasonably liberal approach to experimenting with the idea of applying cost offset caps to the massive cost offsets that may occur for high impact SST valuations.

Capping cost offsets is another way to share the savings that some SSTs (and other treatments) produce in the health system. We believe presenting this approach alongside the 50/50 shared savings approach will be beneficial because it will convey that there is certainly no consensus on whether – much less how – high valuations of some SSTs should be managed through changes to the methods of cost-effectiveness. We will work with all stakeholders to ensure that the preliminary, hypothetical nature of these scenarios is not mistaken as a normative statement about value-based pricing for SSTs. We will also add caveats to these scenarios noting that they may not be applicable in situations where there are outcomes-based contracts or other risk-sharing arrangements in place.

Conclusion

We undertook our exploration of potential adaptations to our assessment methods for SSTs with an open mind and a desire to ensure that we evolve our methods to keep pace with that of innovation in treatments and the needs of decision-makers. We look forward to learning from the experience we will gain from the implementation of these new methods, and will stand ready to make mid-course corrections should we feel at any time that they are having unintended consequences that outweigh their benefits. For these insights, and for our future thinking on evolution of these methods, we will continue to welcome the input of patients, clinicians, and all other stakeholders in how ICER reports contribute to a health care system defined by fair prices, fair access, and future innovation.

References

1. Neumann PJ SG, Russell LB, Siegel JE, Ganiats TG, editors. *Cost-effectiveness in health and medicine*. New York: Oxford University Press; 2016.
2. Drummond M, Towse A. Is rate of return pricing a useful approach when value-based pricing is not appropriate? *The European Journal of Health Economics*. 2019.
3. Claxton K. OFT, VBP: QED? *Health economics*. 2007;16(6):545-558.