2020-2023 Value Assessment Framework

Response to Public Comments

January 31, 2020

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1. Introduction

ICER thanks the 60 organizations who provided input during an open call for suggested revisions and the 41 organizations who gave feedback on the draft proposals released in August 2019. We deeply appreciated the time, thought, and effort that went into each of these submissions, and apologize for not being able to respond in-depth to all of the comments we received. Readers of this document are encouraged to view it as a complement to the justifications provided in the draft revisions proposed in August 2019, as well as the rationale provided in the 2020-2023 Value Assessment Framework itself. This, in particular, applies to suggestions and criticisms that we have not addressed in this document.

2. Comparative Clinical Effectiveness

Real-World Evidence

Some commenters were concerned that RCTs did not sufficiently reflect the net health benefit of an intervention and therefore wanted ICER to increase the amount of real-world evidence (RWE) used in its reports to provide additional data or relevant contextual information. Others wanted reassurance that only high-quality validated RWE would be used. Still others believed a value assessment was not possible without RWE.

ICER has always incorporated RWE in its reports and has a commitment to further explore how "real-world" evidence can contribute to a more comprehensive and accurate view of the risks, benefits, and costs associated with any intervention. ICER will also apply best practices in real-world data analysis as described in guidelines from ISPOR and other authoritative methods bodies. Further our commitment to the use of RWE extends not only from using available published sources, but includes the possibility of working with life science companies, patient groups, or data aggregator companies to develop and analyze new sources of real-world evidence in a way that will meet the evidentiary standards relevant to the questions being addressed.

In short, ICER has a flexible and ecumenical approach to sources of evidence and, while stressing the importance of the rigor of clinical trial data in any assessment, the value framework and ICER's methods incorporate multiple sources and types of evidence, seeking the evidence that is most helpful in understanding the long-term net health benefits for patients of different care options.

German Rating System

Although there is enthusiasm for a standard international approach to rating evidence, commenters were concerned that ICER's proposal to cross-reference evidence ratings with the German system would complicate, rather than clarify, interpretation of ICER's report findings. Commenters noted that judgements of benefit are somewhat subjective and may vary across cultures and health care systems.

ICER's proposal to provide complementary evidence ratings using the German categories of "added benefit" was motivated by the belief that a secondary rating system could provide decision makers with different ways to consider the strength of evidence behind new interventions. We intended for the crosswalk to spur further dialogue and calibration of evidence assessments across important pharmaceutical markets. Nevertheless, stakeholder feedback suggested that this approach carried the inherent risk of confusing decision makers. Therefore, after careful consideration of these

comments, ICER will not seek to translate its judgments of evidence into the rating system for added clinical benefit used in Germany.

Heterogeneity and Subgroups

Commenters said that ICER should highlight patient heterogeneity and subgroup effects when discussing the clinical benefits and harms of treatments; they also noted that ICER's evidence ratings should account for subgroup differences.

ICER's reports highlight and will continue to highlight subgroup effects as part of our presentation of the clinical evidence. In order to broaden the discussion of heterogeneity and subgroups in our Evidence Reports, all reports will now include a sub-section called "Heterogeneity and Subgroups", either to present the primary discussion of subgroup effects, or to highlight the other sections of the evidence review that discuss subgroup effects. Depending on the nature of the evidence, the health technology under consideration, and the magnitude of the subgroup effects, subgroup differences may on occasion carry through to different evidence ratings for different subgroups. In addition, when there are substantial knowable subgroup effects, subgroup economic analyses have been and will continue to be undertaken, pending data availability, when ICER believes that the health technologies are likely to be approved or have been used extensively within these subgroups of interest.

3. Incremental Cost Effectiveness

Perspective

Commenters said that ICER should include both the health care and societal perspective analyses as co-base cases in all reports.

ICER's value framework continues to use the health care system perspective for the base case, as the most relevant for decision-making by insurers, provider groups, and policymakers in the United States. However, ICER acknowledges that there are cases in which the societal perspective may produce substantially different incremental cost-effectiveness ratios than the analysis using the health care sector perspective.

ICER's value framework will now promote the societal perspective analysis to be a co-base case along with the health care perspective when the societal costs of care are large relative to the direct health care costs and the impact of treatment on these costs is substantial (i.e., there are substantial differences in the cost effectiveness findings between the two perspectives). This will be applied for all reviews when the impact of care outside the health system is substantial in proportion to health effects, not just those of treatments for ultra-rare disease. In cases where ICER calculates incremental cost-effectiveness from the health care system perspective as its base case, we will continue to perform a societal perspective analysis in a scenario including work productivity and other indirect impacts when available.

Patient Populations

Commenters said that ICER should account for patient heterogeneity by including subgroup analyses in its models and accounting for differences in patient characteristics and preferences.

ICER's Evidence Reports will now include a sub-section on "Heterogeneity and Subgroups" in order to broaden discussion of heterogeneity and subgroups within the patient population. Our Reference Case calls for the inclusion of different patient subgroups when analyzing the cost-effectiveness of health technologies, to the extent possible. ICER's economic evaluations will include analysis of patient subgroups when robust data and relevant inputs from clinical trials and/or real-world evidence are available to do so. Such subgroup analyses have been and will continue to be undertaken when ICER believes that health technologies are likely to be approved or have been used extensively within these subgroups of interest, and as mentioned earlier, pending data availability.

In addition, this sub-section will discuss treatments' potential impact on socioeconomic inequality when relevant, and may include a scenario analysis discussing potential impacts on inequality when the appropriate data are available. We have sought to explore different ways that we might capture this social value in our reviews. While we cannot directly apply published inequality indices given lack of data in the US context, we will explore the possibility of using modified versions as scenario analyses in reviews where this is especially relevant.

Outcomes (Measures of Health Gains)

Several commenters said that ICER should no longer use the quality-adjusted life year (QALY) as a metric in its analyses. Other commenters suggested that ICER use alternatives to the QALY, such as the quality- and risk-adjusted life years (QRALY) or disability-adjusted life years (DALY).

ICER's assessments report several complementary outcome measures, including quality-adjusted life-years (QALYs), equal value life years gained (evLYG), life-years, and a condition-specific outcome achieved (e.g., treatment response, event avoided). ICER includes the QALY as the academic and policy standard for measuring how well a medical treatment improves and lengthens patients' lives, making treatments that alleviate serious illness look especially valuable. Because the QALY records the degree to which a treatment improves patients' lives, treatments for people with serious disability or illness have the greatest opportunity to demonstrate more QALYs gained and justify a higher price. Other measures, such as disability-adjusted life-years (DALY) or quality- and risk-adjusted life years (QRALY), are more recent than the QALY and have not been commonly used in the US setting.

Cost-Effectiveness Thresholds

Commenters said that ICER should adopt variable WTP thresholds based on factors such as societal preferences, or disease characteristics such as patient age, unmet need or lack of alternative treatments.

ICER's reports will provide a set of results using standardized cost-effectiveness thresholds from $50,000-$200,000 per QALY and per evLYG. ICER will provide cost-per-QALY results at $50,000, $100,000, $150,000 and $200,000 per QALY and per evLYG for all assessments, including those for treatments of ultra-rare disorders. The range for health benefit-based price benchmarks remains $100,000-$150,000 per QALY and evLYG, reflecting commonly cited cost-effectiveness thresholds between $100,000 and $150,000 per QALY gained. However, ICER's Evidence Reports will present a broader range of results symmetrically around this range, from $50,000-$200,000 per QALY/evLYG.

This range is meant to accommodate the needs of decision-makers in the US to think about their own desired interpretation of cost-effectiveness thresholds while considering uncertainty, other

benefits or disadvantages, and contextual considerations. We appreciate the idea that decision-makers in the US and international settings may give special weighting to other benefits and contextual considerations that could lead to coverage and funding decisions at higher thresholds for some conditions such as ultra-rare diseases than may be applied to decisions about other treatments. However, we feel it important on an equity basis to maintain a consistent range of cost-effectiveness thresholds, while acknowledging that policymakers may choose alternative thresholds.

Health Benefit Price Benchmarks

Commenters said that ICER should modify its health-benefit price benchmarks to use different thresholds or ranges.

ICER will continue to report price benchmarks that would achieve cost-effectiveness thresholds of $100,000 and $150,000 per QALY and per evLYG in its reports. However, we will now call these "Health-Benefit Price Benchmarks," rather than value-based price benchmarks. Note that this change is meant to underscore that we are looking at the added health benefit of new treatments. ICER's health benefit price benchmarks suggest a price range, net of any discounts and rebates, that aligns fairly with a treatment's added benefits for patients over their lifetime. Prices at or below these thresholds help ensure that the health benefits gained by patients using new treatments are not outweighed by health losses due to long-term cost pressures that lead individuals to abandon care or lose health insurance.

ICER believes that there is a confluence of results between research exploring opportunity cost thresholds and willingness to pay thresholds in the US setting, although for conceptual reasons, ICER favors a view of thresholds based in an opportunity cost paradigm. While there is a case for multiple thresholds based on willingness-to-pay which may differ by payer type, there is also a widely accepted ethical goal in the US to have a common standard of care available for all patients, albeit with acknowledged differences in access due to network constraints, out-of-pocket payment, and other benefit design features. That the US does not yet achieve the goal of a common standard of care available for all patients does not imply, in our view, that ICER should abstain from framing a range of cost effectiveness that should apply broadly across many, if not all, health insurance systems in the US.

Despite the lack of an explicit overall budget for health care in the US, the current environment of the US health care system is one in which policy-makers sense that the opportunity cost for current spending is already substantial, and that real harm is being done as health care costs continue to rise. We believe that anecdotal evidence and testimony from these policymakers further supports ICER's decision to apply an opportunity cost approach to a threshold range, the goal being to ensure that the prices paid for health gains from effective new treatments are aligned with the magnitude

of those health gains, such that greater health is not lost through the effects of rising health costs at the system and societal level.

Therefore, ICER continues to use the cost-effectiveness range of $100,000 to $150,000 to support health benefit price benchmark recommendations. ICER recognizes that single cost-effectiveness thresholds should not be used as a blunt decision rule, and that decision-makers may want to consider different thresholds given their own view of their opportunity costs and their interpretation of a treatment's potential other benefits and contextual considerations. For more information regarding ICER's rationale for the cost-effectiveness threshold range used for the health benefit price benchmarks, please see Appendix D of ICER's Value Assessment Framework.

4. Potential Other Benefits or Disadvantages and Contextual Considerations

Several organizations commented on the additional category representing treatments that offer a special advantage to patients by virtue of a notably different balance or timing of benefits and risks. The majority of these comments pertained to whether this category encompasses the concept of "value of hope," and noted alternative definitions of the concept.

ICER appreciates the discussion surrounding this potential other benefit. We continue to believe that the concept of "value of hope" is poorly named to convey the advantages that some treatments may offer if they have a distinctly different timing or balance of risks and benefits compared to other available treatments. As mentioned in our proposals document, the classic example of this concept is a treatment for cancer that may have, overall, the same total QALYs gained as existing options, but which has a higher risk of short-term death and a higher chance of longer-term survival. For risk-taking patients this treatment option, although its QALYs are identical to other options, offers a special advantage. We note that this definition encompasses the concept raised by some commenters – the ability to live a longer and/or healthier life and to enjoy the attendant experiences. We note that choice is an important element in this concept, whether it be for the first available treatment that is compared to standard of care, or a new treatment that provides a different set of advantages or disadvantages related to the timing of benefits and risks than existing options.

5. Potential Budget Impact Analysis

Methods

Commenters said that ICER should report per-patient budget impact results and should use historical data from analogous conditions/treatments to predict uptake of new treatments in its potential budget impact analyses.

ICER will present the results of its potential budget impact analyses as a cumulative per-patient potential budget impact for each year over a five-year time horizon, with results being presented graphically for each intervention assessed. ICER would also like to note once again that our potential budget impact analysis does not attempt to estimate the uptake of a new intervention. Rather than try to estimate real-world uptake, the analysis presents information on a national level that allows stakeholders to ascertain the potential budget impact of a new service given a range of prices. The goal of ICER's potential budget impact analysis is to estimate the net cost per patient treated with new interventions so that decision-makers can use their own assumptions about uptake and pricing to determine their own estimate of potential budget impact. We also seek to produce calculations that will help policy makers identify situations in which the potential uptake of a new treatment, at various pricing levels, might exceed a budget impact threshold that signifies that the budget impact in the near term (over five years) would contribute to overall health care cost growth at a higher rate than growth in the national economy (plus 1%).

6. Procedures

Patient Engagement

Commenters suggested several revisions to ICER's proposals regarding patient engagement. These included the creation of disease-specific advisory workgroups, a standing patient advisory committee, and earlier stakeholder notifications. In addition, comments were generally supportive of ICER proposals to create a standalone report section on "Patient Perspectives" that will include a subsection on "Impact on Caregivers" and formal post-meeting debriefs with engaged patient groups.

ICER thanks commenters for their feedback on our approaches to patient engagement and, in reflection of these comments and ongoing conversations with other patient groups, has incorporated many of these suggestions into an expanded Patient Engagement Program, described in Section 6.3 of the 2020-2023 Value Assessment Framework. With regards to the advisory role played by patient organizations, ICER has adopted somewhat similar approach to early outreach to patient groups from major disease areas (i.e., rheumatoid arthritis, psoriasis, multiple sclerosis, etc.) under which we will hold annual discussions with major patient groups to gather their perspectives on new developments that may need to be considered in an updated assessment. ICER will also provide earlier notification and guidance to patient groups outside of these specific stakeholders, generally when it has greater than 50% certainty that it may pursue a review of a specific technology. We believe this approach will balance the importance of early outreach to patient organizations, as noted by commenters, with the possibility that a new development will lead ICER to select another topic for review. These early conversations will provide an opportunity for patient groups to familiarize themselves with ICER's processes, and identify sources of RWE and/or opportunities to generate new RWE describing patient preferences and perspectives.

In addition, ICER looks forward to its continued work with the patient community to improve its approach to patient outreach and engagement (i.e., improved engagement guides, educational webinars, etc.), details of which will be released as they are available in the coming year.

Review Updates

Commenters were broadly supportive of ICER's efforts to determine whether its reports require updates to reflect new evidence that may emerge soon after interventions enter clinical practice. Several commenters requested additional information about the types of evidence ICER will consider in these updates, including how RWE will be incorporated; the process for report updates; and how stakeholders will be engaged.

We have elaborated on our process to report updates in Section 6.2 of the 2020-2023 Value Assessment Framework and provided additional information about the ICER's approach to including RWE in the sections describing comparative clinical effectiveness analyses and cost-effectiveness modeling. Section 6.2 describes two broad approaches, a "12-Month Report Check-Up" and a pilot effort to partner with external organization(s) to generate new RWE and incorporate it into its analyses for select drugs approved under accelerated pathways. These sections also provide context as to what ICER would consider to be new evidence that could impact the findings of its initial report (i.e., evidence that could lead to a different evidence rating, or that would lead to a substantial shift in the incremental cost-effectiveness results as determined by reviewing the results of one-way sensitivity analyses). ICER looks forward to continued engagement with stakeholders during the first of these projects so that we may continue to refine our approach to incorporating important new evidence in our assessments.