June 10, 2019

Steven D. Pearson, MD, MSc, FRCP
President, Institute for Clinical and Economic Review
Two Liberty Square, Ninth Floor
Boston, MA 02109

RE: ICER Seeks Public Input for 2020 Value Assessment Framework

Dear Dr. Pearson:

The Innovation and Value Initiative (IVI) appreciates the opportunity to offer comments on the Institute for Clinical and Economic Review's (ICER) value assessment framework.

IVI is a non-profit research organization whose mission is to advance the science and improve the practice of value assessment in healthcare by adapting a more collaborative, open and tailored approach to examining value, exploring new methods and building models that can support flexible decision making.

Prior to offering specific comments on ICER's value assessment methods and procedures, we believe it's important to recognize some degree of misalignment between ICER's approach and the unique characteristics of the U.S. healthcare marketplace that ICER's assessments are intended to influence.

The U.S. health system is highly decentralized and composed of many different stakeholders facing difficult, and often overlapping, decisions. Furthermore, decision-makers within each group are highly diverse, and all of these decisions are made in different contexts, under unique constraints and conditions. Consistent across decision-makers is the goal of identifying options that provide the most value under their own unique conditions. Approaching value assessment with a focus on one "best" answer – in this case, using the conventional cost-effectiveness and budget impact analysis conducted from a generalized health system perspective under ICER's existing value framework – ignores the reality that different stakeholders have different criteria to assess value. Value assessment should be approached from the frame of those individual decision contexts, using multiple models and methods that can support such flexibility and multi-dimensional analysis.

A further challenge exists regarding the need for a long-term view when quantifying the value of a medical technology and the frequent short-term budget-driven perspective of decision making. We agree that the long-term value of a therapy is the most important consideration, and this is certainly true for patients, their families, and society at large. In a system where health plans make coverage decisions based on short-term budget impacts, however, there is little incentive for insurers and others to prioritize investments in therapies with higher short-term costs but

greater long-term value. This issue is acknowledged and discussed in the existing ICER value framework. We are concerned, however, that merely listing long-term value alongside short-term budget impact leaves the decision-maker with the easy option to ignore long-term value. The potential disincentives to invest in treatments with long-term societal benefits are a pressing issue that confronts our society as whole, but through the reports and policy analyses produced by ICER, there is an opportunity to educate audiences on the issue and generate discussion about potential solutions.

To deliver credible and relevant information about value to U.S. healthcare decision-makers, value assessment must:

- Provide flexible models that can be fit to diverse contexts and updated as evidence evolves;
- Be totally transparent to all stakeholders;
- Explicitly acknowledge and address uncertainty;
- Incorporate non-clinical attributes and outcomes in value estimates; and
- Actively take a patient-centered focus throughout all stages of the research to assess the value of medical technology.

The following comments expand upon these issues.

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Embrace Transparency by Moving Value Assessments to Open-Source Environment

As discussed above, vastly different stakeholders make healthcare decisions in equally diverse contexts, based on their own unique preferences and constraints. All of these decisions are informed by some level of value assessment, but every decision stands to benefit from rigorous, credible, and relevant information on value that applies to their specific decision, to the greatest extent possible.[1]

Given the lack of consensus about the appropriate framework, modeling approaches, and relevant evidence among different stakeholders (i.e. patients, insurers, and providers), it is important to move all value assessment into a transparent, open-source environment.[1-3] While ICER has taken important initial steps in this regard, including providing manufacturers with limited access to cost-effectiveness models during the review period, further commitment to full transparency and open access is needed. We strongly recommend that ICER provide complete *public* access to models, underlying data, and other materials. By taking this step, ICER would make important progress toward allaying stakeholder concerns and engaging in a constructive discussion about methods.

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Expand evaluation of uncertainty in estimates of value beyond parameter uncertainty and acknowledge structural uncertainty

While ICER's value assessment framework accounts for sensitivity and scenario analysis, we are concerned by the tendency to understate the degree of uncertainty in analyses/estimates and the potential impacts on decision making.

Both parameter and structural uncertainty are important to consider when evaluating the value of a medical technology. Methods for examining the impacts of uncertainty are available for parameter uncertainty – probabilistic sensitivity analysis, for example – but the impacts of structural uncertainty are more challenging to measure. This does not mean that they should be ignored, however. In previous research, IVI examined the impact of structural assumptions using the IVI-RA value model,[a] in which 384 different model structures are possible,[4] to assess the impact of structural assumptions on CEA outcomes. For a set of 32 sets of structural assumption, created based on the possible combinations of four factors[b], the authors generated incremental cost-effectiveness ratios for sequential treatment with biologic disease-modifying anti-rheumatic drugs (DMARDs), relative to conventional DMARDs. The results (see *Figure 1*) illustrate the potential impacts of structural uncertainty on cost-effectiveness results, and therefore for decision-making – indeed, if a threshold of $150,000 per QALY gained is adopted for decision-making, basic structural assumptions could determine whether the intervention is considered cost-effective.[5]

We recognize that it is impossible to model, or even discuss, all of the possible modeling structures and assumption sets that are possible for a given analysis, but acknowledgement and some exploration of the issue is needed in assessments conducted by ICER. ICER's current approach does include a discussion of uncertainty in the evidence, which is an important first step.

The impacts of both parameter and structural uncertainty should be explicitly and thoroughly addressed in ICER reports. We recommend that all reports include a section with detailed assessment and discussion of the impacts of uncertainty on modeling, including structural uncertainty and the potential impacts of assumptions made.

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[a] The IVI-RA model is an open-source individual patient simulation model for simulating outcomes and estimating value of sequences of biopharmaceutical therapies in moderate to severe rheumatoid arthritis. The IVI-RA model is part of IVI's Open-Source Value Project. For more information or to access the model, visit https://www.thevalueinitiative.org/ivi-ra-value-model/.
[b] Four structural factors were varied:
- Impact of treatment on HAQ: 1) Treatment->ACR->HAQ; 2) Treatment->ACR->EULAR->HAQ; 3) Treatment->HAQ
- Pathways for treatment switching: 1) ACR->switch; 2) ACR->DAS28->switch; 3) ACR->EULAR->switch; 4) DAS28->switch
- Progression of HAQ in the absence of efficacious treatment: 1) constant rate of progression; 2) non-linear development with latent class growth model
- Utility: 1) Mixture model by Hernandez-Alava et al (2013); 2) Wailoo et al (2006)

For more information on these structural factors, see: Incerti D, Jansen J. A Description of the IVI-RA Model v1.0. 2017. https://innovationvalueinitiative.github.io/IVI-RA/model-description/model-description.pdf.

Figure 1: Sensitivity of IVI-RA model cost-effectiveness findings to 32 competing structural assumptions

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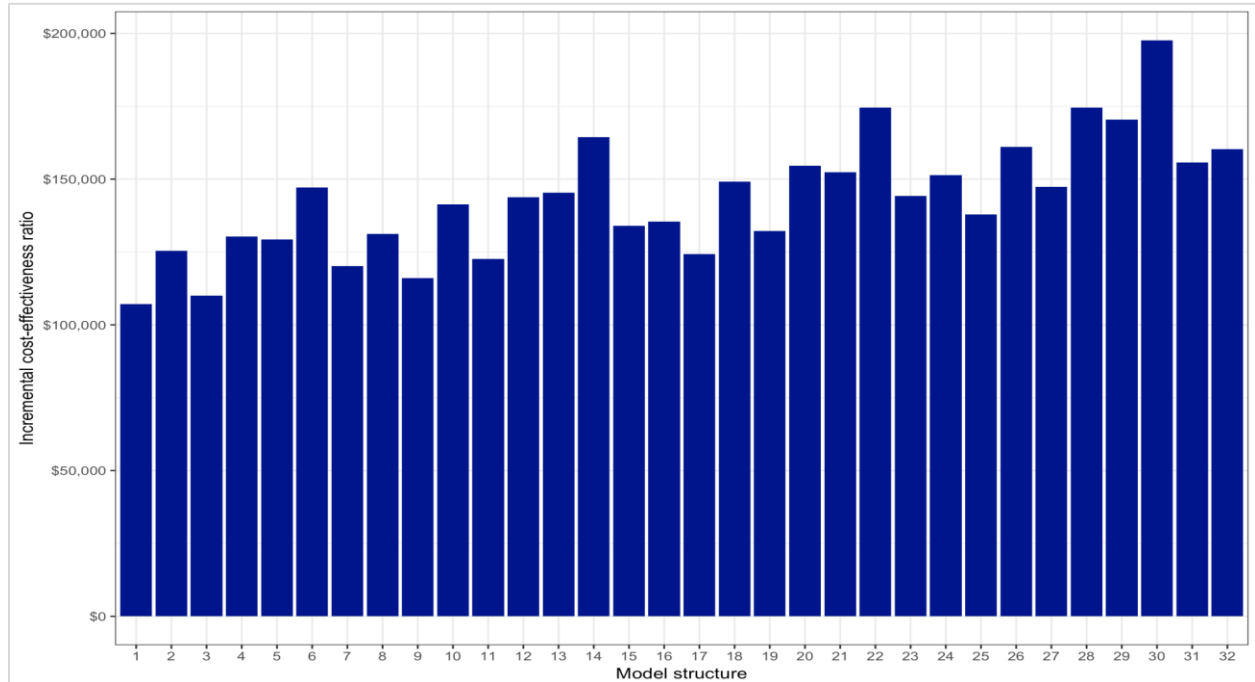
Improve Incorporation of Non-Clinical Attributes

Regardless of the underlying cost-effectiveness model or perspective ICER chooses, we urge efforts to improve the incorporation of factors that are not generally captured in conventional cost-effectiveness analysis but may be important when evaluating the value of medical technology.

Since the last ICER value framework update, ICER has begun taking steps to better communicate the "potential other benefits and contextual considerations" that may impact the value of therapies and, ultimately, coverage decisions. IVI commends ICER for these efforts.

ICER's current approach to these factors is insufficient, however. In the current approach, these non-clinical factors are briefly described in ICER reports and voted on by the reviewing Council prior to release of the final report. These factors are not reflected in the substantive results that are the focus of readers, however, and are only accounted for in value judgements through Council votes when treatments' incremental cost-effectiveness results fall between $50,000 and $175,000 per QALY in "base case" analysis.

Non-clinical outcomes are currently excluded from ICER analyses because of a lack of commonly accepted practices for measuring and accounting for these elements, and also due to lack of or uncertainty in the evidence needed to parameterize them. While we agree that value

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assessment should reflect the most accurate and reliable evidence possible, the exclusion of these important non-clinical dimensions is itself an assumption that affects results – essentially, the structural assumption that the impact of these factors on costs or benefits is zero. While attempting to incorporate these dimensions introduces uncertainty, so does their exclusion.

IVI recommends that ICER expand modeling efforts and analyses to incorporate additional non-clinical factors, even where methods are developing or imperfect, and where evidence is currently lacking. These analyses need not be presented as primary results, but they should serve to both illustrate their potential impact on value and highlight areas where improved methods and evidence are needed.

Where these parameters are quantifiable, it is particularly important that ICER endeavor to explicitly incorporate these attributes into analyses. For example, lost wages due to absenteeism or additional costs for treatment-related lodging and transportation should be considered. Patient preferences for treatment attributes such as mode and frequency of administration should also be explicitly addressed. In addition, capturing heterogeneity in preferences may be of interest.

To support this expansion to include non-clinical factors, ICER should seek partners in the patient and research communities. For example, a small-scale study with patients could be used to generate preliminary data on the impacts of changes in clinical measures or side effects on caregivers, which could then be linked to individual therapies' relative effects to compare caregiver impact across therapies. Such a study could be conducted in partnership with an existing patient group or research institution.

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Again, we appreciate your willingness to invite comments on ICER's current value assessment framework and hope we have offered substantive recommendations that enhance your organization's methods and models.

Sincerely,

[signature: Jennifer L. Bright]

Jennifer Bright, MPA
Executive Director

References

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2. Jansen JP, Incerti D, Linthicum MT. An Open-Source Consensus-Based Approach To Value Assessment. *Health Affairs Blog.* 2017. https://www.healthaffairs.org/do/10.1377/hblog20171212.640960/full/.
3. Hay JW. Now Is the Time for Transparency in Value-Based Healthcare Decision Modeling. *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research.* 2019;22(5):564-569.
4. Incerti D, Jansen J. A Description of the IVI-RA Model v1.0. 2017. https://innovationvalueinitiative.github.io/IVI-RA/model-description/model-description.pdf.
5. Incerti D, Curtis J, Lorenzi M, Jansen J. Exploring Structural Uncertainty With An Open-Source Cost-Effectiveness Model For Rheumatoid Arthritis. *Value in Health.* 2017;20(9):A751.