



The professional society for health economics and outcomes research

Improving healthcare decisions

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Dear ICER:

ISPOR – the professional society for health economics and outcomes research (HEOR) - is pleased to respond on behalf of its membership to your consultation entitled “2023 Value Assessment Framework - Proposed Changes.”

ISPOR is a scientific and educational society with many of its members engaged in evaluating health technologies, including pharmaceuticals, medical devices, and other interventions. We have a large membership living and working in 110 countries globally, across a range of disciplines, including health economics, epidemiology, public health, pharmaceutical administration, psychology, statistics, medicine, and more, from a variety of stakeholder perspectives, such as the life sciences industry, academia, research organizations, payers, patient groups, government, and health technology assessment bodies. The research and educational offerings presented at our conferences and in our journals are relevant to many of the issues and questions raised in this request for information.

The response to this consultation was led by the Policy Outlook Committee of our most senior advisory body, the Health Science Policy Council. To engage our membership, we consulted with interested members of Institutional Council (ie, industry and consulting), the 2023 ISPOR Health Technology Assessment Roundtable – North America, and our Real-World Evidence, Health Equity in Research, Rare Disease, and Patient Centered Special Interest Groups, as well as soliciting our general membership for comments. The attached document provides both summary and line-by-line responses based on their comments. We hope they prove useful.

ISPOR would be happy to answer any questions about our response, and to participate in any follow-up consultations on the relevant program items mentioned within the report.

Sincerely,

Robert Abbott
CEO & Executive Director
ISPOR

“ICER 2023 Value Assessment Framework - Proposed Changes”

General comments

We applaud ICER on its efforts to regularly update its value assessment framework based on emergent scientific and societal considerations as well as stakeholder input. The proposed changes address several areas in which there have been recent developments that merit explicit treatment in the framework. Unfortunately, the public comment period was too brief to allow for us to solicit and curate a robust set of comments from ISPOR members, so we provide some brief comments below which we hope will be helpful.

Comments by section

2.1 Clinical Trial Diversity

We agree that it is helpful to encourage and measure clinical trial diversity, as well as to pay closer attention to the US subgroup of global trials. The “representation score” approach per se seems novel and potentially fit-for-purpose though it will take some time to test and ascertain its utility. It should be recognized that as a “nudge” for sponsors to ensure diversity in trial populations, albeit not the only voice in this area, it may take some time for it to take effect given that many trials that will support drug approvals in the near future are already complete or nearly so.

2.2 Subpopulation Analyses

We also encourage attention to subpopulation analysis, both for the designated demographic groups and for other subpopulations viewed as relevant to the specific treatment, as long as there is due attention to statistical and other evidence considerations. We find it interesting that you choose not to estimate cost-effectiveness by subgroup when such differences are found, however. Certainly, any such differences should not drive pricing that discriminates across subgroups. However, heterogeneity of treatment effect is most often driven by baseline risk differences¹, and marginalized and other vulnerable patient groups often have higher baseline risk. Thus, finding that treatment is more cost-effective in such groups could allow for more proactive approaches with them for treatment awareness and access. We understand reluctance to accept a situation in which evidence suggests a disadvantaged group may get less treatment benefit. However, a nuanced and flexible approach can be adopted if equity is viewed as important.

3. Long term cost effectiveness

3.1. Perspective in Economic Models

Productivity costs for both patient and carer are legitimate and important aspects of a societal perspective in cost-effectiveness analysis (CEA), and we support their inclusion in ICER’s calculations. The recent work of Jiao and Basu² provides a useful approach to calculating productivity costs for patients when health related quality of life (HRQoL) data are available but productivity data per se are not, and a lower value for lost leisure consumption time seems justified. Further thought may be needed regarding estimation/modelling of long-term productivity costs given the many factors and incentives involved.

3.2 Dynamic Pricing

¹ Kent, D.M., J. Nelson, I.J. Dahabreh, P.M. Rothwell, D.G. Altman, and R.A. Hayward. 2016. Risk and treatment effects heterogeneity: re-analysis of individual participant data from 32 large clinical trials. *International Journal of Epidemiology* 45(6): 2075-2088.

² Jiao B, Basu A. Associating Health-Related Quality-of-Life Score with Time Uses to Inform Productivity Measures in Cost-Effectiveness Analysis. *PharmacoEconomics*. 2023 Mar 6:1-3.

We appreciate that ICER recognizes that conventional CEA, when used to justify a launch price, has generally ignored the fact that patented medicines eventually go off patent and the compound is usually subject to generic or biosimilar competition. We would argue that our field and ICER should make a concerted effort to model this more accurately. Plausible transitions to generic/biosimilar competition could be modeled. Arguably, modeling could consider how value and price might be affected during the patent protection period were follow-on compound to enter and compete. At this point that should be a cited limitation of the proposed updated framework.

ICER's plan to only do "dynamic pricing" for only the Medicare-eligible population is too narrow. Assuming that manufacturer would receive the IRA "ceiling price" seems unrealistic given the power of CMS in the negotiation. A plausible range should be used.

More generally, our field and ICER needs to begin to explore the impact of considering the value generated for the entire population over entire product life cycle. A recent themed section (March 2023) in *Value in Health* illustrates this perspective and provides numerical examples and estimates.

3.3. Additional Elements of Value

We appreciate the recognition that ICER has given to the work of the ISPOR Special Task Force (STF) on US Value Frameworks that led to the ISPOR Value Flower and the STF recommendation that, for purposes of health technology assessment and formulary inclusion, we need to move beyond conventional CEA to consider other elements of value related to uncertainty and to broader societal impacts.

To this end, we welcome the proposal to include productivity effects, as we comment in section 3.1 above. We also welcomed the inclusion of an interpretation of the "value of hope" in the 2020 ICER Methods Guide. We note and welcome the proposals to use absolute and proportional shortfall measures to help provide a qualitative estimate of disease severity. This is a helpful step towards potentially including a quantitative severity adjustment. We recognize concerns over any potential double counting of benefits or lack of consideration of opportunity cost. We would argue, however, that generalized risk-adjusted CEA (GRACE) calculations could also be considered. Our field has made significant progress in the last five years in moving this "augmented CEA", as it was called by the STF, forward. In particular, the work of Darius Lakdawalla and Chuck Phelps on GRACE^{3,4,5,6} has advanced to the point that it can be estimated, using a number of assumptions, at the very least in a way that can provide an alternative scenario analysis for qualitative consideration in ICER assessments.

One important implication of the GRACE framework is that there would be, in effect, a variable cost-effectiveness threshold that depends on the severity of the underlying condition (or disability level) of the patient. For some conditions, the cost-effectiveness (CE) threshold could be below the \$100K threshold that

³ Lakdawalla DN, Phelps CE "Health Technology Assessment with Risk-Aversion in Health," Journal of Health Economics, July, 2020, 102346.

⁴ Lakdawalla. DN and Phelps, CE. "Health Technology Assessment with Diminishing Returns to Health: The Generalized Risk- Adjusted Cost-Effectiveness (GRACE) Approach, Value in Health 2021; 24(2): 1244-249

⁵ Lakdawalla DN, Phelps CE "A Guide to Extending and Implementing Generalized Risk-Adjusted Cost-Effectiveness. (GRACE)", European Journal of Health Economics, Sept 8, 2021.

<https://doi.org/10.1007/s10198-021-01367-0>.

⁶ Lakdawalla DN, CE Phelps. "The Generalized Risk-Adjusted Cost-Effectiveness (GRACE) Model for Measuring the Value of Gains in Health: An Exact Formulation," Journal of Benefit-Cost Analysis, 2023 14(1):1-24.

ICER uses, and for others, particularly rare conditions, it could be much higher. As we noted above, there is still work to be done to deal with concerns about double-counting, but these issues are being addressed in a way that means we can move forward, at least in a qualitative sense. In addition, the (incremental) value of health risk protection—ie, the peace of mind that a health plan member can get from knowing that something can be done about a condition were they to get it—can provide substantial value that is not reflected in conventional CEA and should be given consideration by ICER.

3.4 Health Benefit Price Benchmarks

We agree that ICER should use a range of alternative cost-effectiveness thresholds to illustrate the potential range of prices that ICER's assessment of clinical value would support. US has heterogeneous plans with very different opportunity costs, and it makes sense, at a minimum, to keep the use of \$100K and \$150K. We note, however, that the paper quoted that concludes with an estimate of an opportunity cost of \$104K is intended to be an estimate of the marginal health impact on those on low incomes having to drop or reduce insurance coverage in response to premium increases. It is not obvious to us how this estimate can be used to support use of a \$50K threshold. We note also the use of a much higher figure than \$150K by the Congressional Budget Office (CBO) when reviewing the potential impact of drug price negotiations as proposed in the Elijah E. Cummings Lower Drug Costs Now Act.⁷ It seems to us that a number of alternative additional thresholds above and below the current ICER illustrative figures of \$150K and \$100K could be relevant and should be considered.

On shared savings analysis we agree it is useful to continue. Arguably the conceptually correct approach is to price the comparator at a price at which it is cost-effective, although we recognize that this may reduce the incentive for companies to develop drugs that will save health systems money. The proposed alternatives (1b i. and ii.) on page 14 therefore make sense.

We would also argue that neither the HEOR field nor ICER have adequately addressed the issue of how the CE threshold from a societal perspective would differ from that for the healthcare perspective. Until this is addressed, it will be difficult for users of ICER's analyses to factor this into their decision making.

3.5 Other changes

We encourage the use of real-world evidence (RWE) in all its various facets in ICER reviews – external control arms for comparisons, baseline costs and risks, other modelling parameters, generalizability to real-world populations and subpopulations, etc.

4. Voting

Just one minor comment, given the short time frame. In point 2, when you consider “average” Likert scores, we suggest you consider both mean and median scores (you may already be doing so), given that strategic voting can skew mean scores. In general, we support ICER's pragmatic approach to voting approaches and its willingness to evaluate how well particular arrangements have worked. We realise this is difficult. However, we would appreciate a longer input period to give more considered feedback.

A.2

We agree that there is merit to having clear mechanisms for integrating health equity considerations into topic selection.

⁷ Congressional Budget Office, 2021. : <https://www.cbo.gov/system/files/2021-02/56905-Drug-Price-Negotiations.pdf>

A.3 Stakeholder engagement

Getting patients onboard is essential, so this process is pivotal. Yet doing this through an online form may not be adequate. A qualitative approach like semi-structured interviews or focus groups should also be considered to engage with patients, caregivers, the general public, and possibly from industry as well. Also consider the framework for patient engagement proposed by Mullins et al.⁸

We would like to acknowledge ISPOR members Lou Garrison and Adrian Towse for their assistance in assembling these comments, as well as ISPOR staff Richard Willke and Kelly Lenahan.

⁸ Mullins CD, Abdulhalim AM, Lavalley DC. Continuous Patient Engagement in Comparative Effectiveness Research. *JAMA*. 2012;307(15):1587–1588. doi:10.1001/jama.2012.442