

June 30, 2023

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

Dear Dr. Pearson,

We write representing patients, older adults and people with disabilities nationwide living with diverse conditions and diseases, as well as their families, caregivers, and providers. We are pleased to provide feedback on the Institute for Clinical and Economic Review's (ICER) proposed changes for its 2024 Value Assessment Framework.

Primarily, we reiterate our past comments and urge ICER to put patients and people with disabilities at the center of its assessments. While we share your interest in lowering health care spending and addressing affordability, ICER's use of value assessments methods that discriminate and fail to accurately capture outcomes that matter to patients only emboldens payers to use utilization management tools restricting patient access, thereby limiting the ability of patients and their providers to make decisions about the best treatment path for them. This puts the most vulnerable at an increased risk of worse health outcomes and increased out-of-pocket costs associated with their care and potential adverse events. ICER's value assessments do not promote affordability for patients, but instead give payers justification to create barriers to coverage of treatments that benefit their own bottom line. Yet, when patients and people with disabilities are treated first with the right treatment for their individual condition, they are more likely to adhere to treatment, become healthier, and holistically save the health care system money.

We would urge ICER to use a lens centered on patients and people with disabilities as it updates its value framework. In in that spirit, we provide the following comments:

ICER continues to rely on metrics that devalue patients and what they care about.

In its proposed changes, ICER maintains its reliance on the discriminatory Quality-Adjusted Life Year (QALY) and the similarly flawed equal value of life-years gained (evLYG). We would like to strongly reiterate our criticism of the QALY and reinforce that the evLYG is not sufficient to address its methodological shortcomings.

As we have stated consistently, QALYs discriminate against patients and people with disabilities by placing a lower value on their lives and insufficiently accounting for outcomes that they value. The National Council on Disability (NCD), an independent federal agency, concluded in a

2019 report that QALYs place a lower value on treatments which extend the lives of people with chronic illnesses and disabilities, and that the use of the QALY violates the Americans with Disabilities Act (ADA). NCD therefore recommended that policymakers and insurers reject QALYs, indicating that the use of the QALY would be contrary to United States disability policy and civil rights laws.¹

Due to its discriminatory implications, QALYs and similar summary metrics of cost-effectiveness have been precluded from use in our public insurance programs. Medicare is prohibited by law from using a QALY-based threshold to determine coverage,² and in 1992, the George H.W. Bush administration determined state use of a QALY based system to determine Medicaid coverage would potentially violate the ADA.³

In its framework, ICER is seeking to provide payers and policymakers with an alternative to the QALY in the form of the evLYG, saying, “*we will emphasize that policymakers who prefer or who may be mandated to consider only measures of health gain other than the quality-adjusted life year (QALY) can find results at every threshold based solely on the equal value of life-years gained (evLYG).*” Yet, ICER recognized that the QALY is a problematic measure of health gain without addressing many of its failings. The evLYG is not a better substitute for the QALY and in fact has many of the same underlying shortcomings of the QALY, as it is built on the same faulty inputs.

The evLYG still fails to account for the full nuance in patient conditions when translating condition-specific measures into utility weights. Oftentimes, dimensions of data are lost when translating condition specific patient-reported outcome measures (PROs) into utility weights, and more frequently, ICER relies on generic PROs, like the EuroQoL instrument (EQ-5D). It is important that the dimensions used by instruments such as the EQ-5D bear some relationship to the QOL of patients, as emphasized by the U.S. Food and Drug Administration (FDA) in their guidance to industry on the use of the patient reported outcome (PRO).⁴ As such, the FDA notes that “*PRO instrument item generation is incomplete without a range of patients with the condition of interest to represent appropriate variations in severity and in population characteristics such as age or sex.*” The EQ-5D, translated into QALY utility weights, does not meet this standard as it relies upon weightings constructed by populations unfamiliar with the conditions being evaluated and therefore does not have the legitimacy obtained by consulting with patients. Criticism of this disconnect is widespread and growing.^{5,6} The EQ-5D often

¹ National Council on Disability, *Quality-adjusted Life Years and the Devaluation of Life with Disability*, 2019. https://ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf

² 111th Congress of the United States of America. (2010). H.R. 3590 The Patient Protection and Affordable Care Act. *Section 1182*. Washington, DC.

³ “Oregon Health Plan Is Unfair to the Disabled.” The New York Times, September 1, 1992. <https://www.nytimes.com/1992/09/01/opinion/1-oregon-health-plan-is-unfair-to-the-disabled-659492.html>.

⁴ US Food and Drug Administration *Guidance for Industry: Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims*. 2009. [2020-07-15].

⁵ Cubi-Molla P, Shah K, Burström K. Experience-Based Values: A Framework for Classifying Different Types of Experience in Health Valuation Research. *Patient*. 2018 Jun;11(3):253–270.

⁶ Helgesson G, Ernstsson O, Åström M, Burström K. Whom should we ask? A systematic literature review of the arguments regarding the most accurate source of information for valuation of health states. *Qual Life Res*. 2020 Jul;29(6):1465–1482

underestimates both the baseline burden of these diseases in patient populations, as well as the impact of treatments, compared to the more accurate disease-specific measures that were developed with those diseases in mind.⁷ Studies have shown that the content of the EQ-5D is often poorly aligned with patient perceptions in diseases such as asthma⁸, mental health⁹ and cancer,¹⁰ and whole population groups such as older adults.¹¹

ICER's attempt to shift focus to the evLYG in the wake of criticism of the QALY is concerning, as the evLYG does not solve many of the baseline issues that exist with the QALY. We encourage ICER to join the academic work ongoing by many other institutions to develop new alternative metrics that explicitly aim to exclude biases inherent to the QALY and better represent the needs, preferences, and outcomes of patients and people with disabilities.

ICER voices a desire to advance health equity but does not take simple actions to do so within its new framework.

We acknowledge the need for improvements in clinical trial diversity but were disappointed to see ICER's commentary imply that it can do nothing to address the limitation of diversity in trials in ICER's own modeling. There are reputable methodologies in economic modeling that have emerged in recent years to incorporate or address the problems of health inequalities – specifically, intervention-induced inequalities.^{12,13,14} ICER implies that these are not fit for this purpose and instead suggests that they should not be seen as a way of avoiding solving health inequality through policy. While we agree that changes must be made to ensure the clinical trial enterprise is prioritizing diversity, if ICER is continuing to conduct assessments without such diversity, ICER bears a responsibility to take every measure within its power to ensure its assessments are representative.

ICER has, in the past, acknowledged systematic health inequalities in the American healthcare system and committed to being part of the solution. ICER – and the payer community involved in its work – believes itself to be an arbiter of value, which directly affects current and future investment decisions in health care. This in turn impacts how – and to whom – healthcare is delivered and, ultimately, who benefits and who loses — the latter a detrimental loss to patients and communities already at a disadvantage. As a result, ICER does bear a moral responsibility to

⁷ Payakachat N, Ali MM, Tilford JM. Can the EQ-5D detect meaningful change? A systematic review. *Pharmacoeconomics*;2015;33:1137–1154.

⁸ Whalley D, Globe G, Crawford R. et al. Is the EQ-5D fit for purpose in asthma? Acceptability and content validity from the patient perspective. *Health Qual Life Outcomes*;2018;16:160.

⁹ Keetharuth AD, Rowen D, Bjorner JB, Brazier J. Estimating a preference-based index for mental health from the Recovering Quality of Life Measure: valuation of Recovering Quality of Life Utility Index. *Value Health*. 2021;24(2):281-290.

¹⁰ Garau M, Shah K, Towse A, Wang Q, Drummond M, Mason A. Assessment and appraisal of oncology medicines: does NICE's approach include all relevant elements? What can be learnt from international HTA experiences? Report for the Pharmaceutical Oncology Initiative (POI) February 2009.

¹¹ van Leeuwen KM, Jansen APD, Muntinga ME, Bosmans JE, Westerman MJ, van Tulder MW, et al. Exploration of the content validity and feasibility of the EQ-5D-3L, ICECAP-O and ASCOT in older adults. *BMC Health Serv Res*. 2015;15:1–10.

¹² Cookson R, Mirelman AJ, Griffin S, et al. Using Cost-Effectiveness Analysis to Address Health Equity Concerns. *Value Health*. 2017;20(2):206-212.

¹³ Round J, Paulden M. Incorporating equity in economic evaluations: a multi-attribute equity state approach. *Eur J Health Econ*. 2018;19(4):489-498

¹⁴ Avanceña ALV, Prosser LA. Examining Equity Effects of Health Interventions in Cost-Effectiveness Analysis: A Systematic Review. *Value Health*. 2021;24(1):136-143

evaluate the downstream effects of its decisions. Ignoring this reality will continue to perpetuate the health inequities that ICER claims a desire to help remedy.

ICER should acknowledge that no patient is average.

ICER states that its framework “takes a ‘population’ level perspective as opposed to trying to serve as a shared decision-making tool to be used by individual patients and their clinicians.” This statement does not acknowledge the reality that ICER has intentionally sought to establish itself in the payer community as an arbiter of value, and as such, ICER reports are being used frequently by PBMs and payers to make formulary decisions.¹⁵

The reality is that ICERs reports give one-size-fits-all results that oversimplify the value of new drugs by assuming an archetypal patient. Payer and PBM reliance on these reports then has the implication of limiting the physician’s ability to have robust shared decision-making conversations and prescribe a drug based on an individual patient. This can lead to significant harm to patients and people with disabilities for whom the drug in question would be highly effective and, in all likelihood, a highly cost-effective use of scarce health care resources in that context.

Ultimately, individuals will be the ones receiving the treatments which ICER reviews, and all of them are different. The “average” patient defined in ICER’s report is not a reasonable proxy for a real patient. The “average” patient is quite rare, and no more common than patients and people with disabilities at the wider edges of any random distribution.¹⁶ The reality is this patient archetype is not representative of most patients in a real-world setting, which challenges ICER’s value models.

While we appreciate that ICER seeks to address at least some aspects around the issue of heterogeneity of treatment effect, patient characteristics, and disease burden, it appears to be largely limited to approaching the validity of subgroup effects using a frequentist approach and traditional methods of measuring variance and uncertainty. We would encourage ICER to evolve beyond this thinking and look to newer innovations in subgroup analysis. The science of analyzing subgroup effects has developed considerably in the last few decades amid a growing acceptance of Bayesian techniques as a more effective approach to asking more complex multi-faceted questions such as identification of variance by subgroup. Stratification of patient characteristics is now almost solely conducted using Bayesian hierarchical models¹⁷ both in

¹⁵ Chambers JD, Enright DE, Panzer AD, Cohen JT, Ollendorf DA, Neumann PJ. Examining US commercial health plans’ use of The Institute for Clinical and Economic Review’s reports in specialty drug coverage decisions. *Journal of Managed Care & Specialty Pharmacy*. 2023 Mar;29(3):257-64.

¹⁶ Feinstein AR, Horwitz RL. Problems in the “evidence” of “evidence-based medicine”. *The American journal of medicine*. 1997 Dec 1;103(6):529-35.

¹⁷ Pennello G, Rothmann M. Bayesian subgroup analysis with hierarchical models. In *Biopharmaceutical Applied Statistics Symposium: Volume 2 Biostatistical Analysis of Clinical Trials* 2018 Aug 22 (pp. 175-192).

clinical evaluation¹⁸ or relative effectiveness^{19,20,21} and more recently in cost-effectiveness models.^{22,23}

On top of the advancement of methodological approaches to evaluating subgroup effects in evidence, multiple papers have highlighted the huge potential for subgroup analyses in economic modeling to improve overall health gain, in particular with respect to its ability to inform investment by targeting potential effects on reducing health disparities.^{24,25,26} If ICER is serious about its work helping move towards a more equitable health care system, it should be considering the concept of subgroup analyses from that perspective as well, not solely from the point of view of statistical methodology.

ICER puts significant focus on choosing model structures, calculating a utility value for a health state, or underlying mortality by age and sex. We would encourage ICER to transfer some of that effort into working in good faith to understand the variation of a drug's effectiveness in different patients.

ICER should pursue incorporation of caregiver benefits and costs in future modeling but also go further and rely on the societal perspective for its base case models.

We appreciate ICER's acknowledgement that it will incorporate caregiver benefits and costs along with productivity losses for patients and caregivers in future societal-perspective modeling. Patient groups have encouraged ICER to take this step for years and it is something that has been considered an essential component of cost-effectiveness methodology in the United States by the Second Panel on Cost-Effectiveness since the last panel in 2016.²⁷

Though we appreciate this incremental improvement, we are discouraged to see that ICER plans to continue to use the health care system perspective as its foundational perspective. The "health care system perspective" is not an accurate way to capture full value. It comes up short by failing to incorporate the values that accrue to the health care system via appropriate treatment, instead

¹⁸ Li N, Zhu W. A Bayesian approach for subgroup analysis. *Biometrical journal*. Biometrische Zeitschrift. 2023 Mar 12:e2200231-.

¹⁹ Pan J, Bunn V, Hupf B, Lin J. Bayesian Additive Regression Trees (BART) with covariate adjusted borrowing in subgroup analyses. *Journal of Biopharmaceutical Statistics*. 2022 Jul 4;32(4):613-26.

²⁰ Bunn V, Liu R, Lin J, Lin J. Flexible Bayesian subgroup analysis in early and confirmatory trials. *Contemporary Clinical Trials*. 2020 Nov 1;98:106149.

²¹ Jones HE, Ohlssen DI, Neuenschwander B, Racine A, Branson M. Bayesian models for subgroup analysis in clinical trials. *Clinical Trials*. 2011 Apr;8(2):129-43.

²² Nixon RM, Thompson SG. Methods for incorporating covariate adjustment, subgroup analysis and between-centre differences into cost-effectiveness evaluations. *Health economics*. 2005 Dec;14(12):1217-29.

²³ Burke JF, Sussman JB, Kent DM, Hayward RA. Three simple rules to ensure reasonably credible subgroup analyses. *Bmj*. 2015 Nov 4;351.

²⁴ Grutters, J.P., Sculpher, M., Briggs, A.H., Severens, J.L., Candel, M.J., Stahl, J.E., De Ruyscher, D., Boer, A., Ramaekers, B.L. and Joore, M.A., 2013. Acknowledging patient heterogeneity in economic evaluation: a systematic literature review. *Pharmacoeconomics*, 31, pp.111-123.

²⁵ Stevens, W. and Normand, C., 2004. Optimisation versus certainty: understanding the issue of heterogeneity in economic evaluation. *Social science & medicine*, 58(2), pp.315-320.

²⁶ Basu A, Grieve R, Pritchard D, Stevens W. One size does not always fit all in value assessment. *Am J Manag Care*. 2019 Nov 1;25(11):540-2.

²⁷ Sanders GD, Neumann PJ, Basu A, Brock DW, Feeny D, Krahn M, Kuntz KM, Meltzer DO, Owens DK, Prosser LA, Salomon JA. Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: second panel on cost-effectiveness in health and medicine. *Jama*. 2016 Sep 13;316(10):1093-103.

only focusing on payer benefit.²⁸ We continue to encourage ICER to move to a societal perspective for its base case models.

We would also encourage ICER to incorporate the caregiver health benefits accrued from reducing the burden on informal caregiving that result from more effective treatments. The United Kingdom's National Institute for Health and Care Excellence (NICE), which ICER leans heavily on for its approach to value assessment, has already included caregiver utility in its base-case cost-effectiveness models for diseases where informal caregiver burden is known to be high, such as Alzheimer's, Multiple Sclerosis and Parkinson's disease.²⁹ It is also the recommended perspective for cost-effectiveness models of the United States Second Panel on Cost-Effectiveness³⁰ and the International Society for Pharmacoeconomics and Outcomes Research.³¹

ICER continues to fall short in capturing dimensions of value that matter to patients and people with disabilities.

We were disheartened to see that, despite consistent recommendations from stakeholders including patient groups and recent exploration of the topic by respected entities like ISPOR, ICER has opted to omit “additional dimensions of value.”

ICER argues that including these additional dimensions risks double-counting. This feels like a manufactured excuse to not include dimensions of value that patient and caregiver stakeholders have shared are important to them. Many of the dimensions highlighted by ISPOR³² would certainly be immune from any double-counting concern as they are excluded from the standard measure of health benefits in standard cost or comparative effectiveness modeling.

One example is that of system effects. This is an area of investigation that tries to better reflect the true nature of complex health systems, and how improving efficiency in one area can lead to efficiency gains and resulting accrued health benefits in another area of health care since systems share key resources in practice. For example, if a new treatment for depression was both effective but also indirectly reduced the need for as much psychiatry time per patient, a known scarce resource,³³ greater access to psychiatry time would be available for a separate set of patients. This second set of patients' net health gain would rise indirectly. These types of benefits are deeply important to patients and standard modeling cannot capture them because they model all patients in a hypothetical vacuum where indirect effects are ignored by design. Capturing this

²⁸ Jena AB, Stevens W, Gonzalez YS, Marx SE, Juday T, Lakdawalla DN, Philipson TJ. The wider public health value of HCV treatment accrued by liver transplant recipients. *The American journal of managed care*. 2016 May;22(6 Spec No.):SP212-9.

²⁹ Afentou N, Jarl J, Gerdtham UG, Saha S. Economic evaluation of interventions in Parkinson's disease: a systematic literature review. *Movement disorders clinical practice*. 2019 Apr;6(4):282-90.

³⁰ Sanders GD, Neumann PJ, Basu A, Brock DW, Feeny D, Krahn M, Kuntz KM, Meltzer DO, Owens DK, Prosser LA, Salomon JA. Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: second panel on cost-effectiveness in health and medicine. *Jama*. 2016 Sep 13;316(10):1093-103.

³¹ Garrison Jr LP, Mansley EC, Abbott III TA, Bresnahan BW, Hay JW, Smeeding J. Good research practices for measuring drug costs in cost-effectiveness analyses: a societal perspective: the ispor drug cost task force report—Part II. *Value in Health*. 2010 Jan;13(1):8-13.

³² Lakdawalla DN, Doshi JA, Garrison Jr 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 in Health*. 2018 Feb 1;21(2):131-9.

³³ Satiani A, Niedermier J, Satiani B, Svendsen DP. Projected workforce of psychiatrists in the United States: a population analysis. *Psychiatric Services*. 2018 Jun 1;69(6):710-3.

deeper dimension of impact on the health care system would benefit patients as well as health care decision makers.

As a real-world example of this, a recent study looked at the impact of systematic treatment of hepatitis C on waiting lists for liver transplants, not just for hepatitis patients but also other patients with chronic liver disease.¹⁸ Successful treatment of hepatitis C led to tens of thousands of non-hepatitis patients getting access to liver transplants and living longer lives as a result. It is clear the significant net health benefit this provides both for patients and society writ large. Standard cost-effectiveness modeling cannot capture this benefit. ICER has an opportunity to expand beyond standard modeling and capture broader and more accurate dimensions of value. It is unfortunate that ICER has chosen not to do this, and we would encourage it to reconsider this decision as it is developing its final framework revisions.

Additionally, ICER is now indicating that it accepts the importance of adjusting utility weights for the severity of the condition being treated, in response to a push from stakeholders that all conditions should not be treated equally and severity does matter.³⁴ Despite ICER acknowledging this reality, it is not proposing any real changes to its models. ICER solely plans to measure this level of severity for each disease it addresses using an evLYG shortfall but is not taking the further step of adjusting for relative severity in its modeling. Without incorporation in the actual models, the shortfall measures are simply paying lip service to the issue of severity weighting without actually incorporating it into ICER's methodology. This is also not in line with many health technology assessment systems in Europe that have begun to incorporate severity into modeling to make a more context-relevant case for any new technology,^{35,36} including NICE.³⁷ We encourage ICER to take the additional step of incorporating severity in its modeling, versus merely acknowledging it as an issue.

Conclusion

Thank you for your consideration of our suggestions on ways in which ICER can make its value assessments more fair and more equitable to patients. Please feel free to reach out to Sara van Geertruyden (sara@pipcpatients.org) in response to our recommendations above.

Sincerely,

ACMCRN Arachnoiditis & Chronic Meningitis Collaborative Research
Allergy & Asthma Network

³⁴ Sund B, Svensson M. Estimating a constant WTP for a QALY—a mission impossible? *The European Journal of Health Economics*. 2018 Jul;19(6):871-80.

³⁵ Barra, M. and K. Rand-Hendriksen, *A missing cornerstone in the Norwegian Priority Commission's weighting scheme—Sub-treatment balancedness is a necessary property for priority setting criteria*. *Nordic Journal of Health Economics*, 2016. 4(2): p. pp. 8-23.

³⁶ Swedish Parliamentary Priorities Commission, *Priorities in health care: ethics, economy, implementation*. 1995, Stockholm: Swedish Government.

³⁷ Collins C, Cheng J, Taylor I, Mumford A. HTA73 Evaluation of NICE Severity Modifiers. *Value in Health*. 2022 Dec 1;25(12):S310.

Allfocus Technologies, Inc.
Alliance for Aging Research
Alliance for Patient Access
Allies for Independence
ALS Association
American Association of Kidney Patients
American Association on Health and Disability
American Behcet's Disease Association (ABDA)
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Celiac Disease Foundation
Center for Autism and Related Disorders
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Congenital Hyperinsulinism International
Crohn's & Colitis Foundation
Cutaneous Lymphoma Foundation
Cystic Fibrosis Research Institute
Davis Phinney Foundation for Parkinson's
Derma Care Access Network
Diabetes Leadership Council
Diabetes Patient Advocacy Coalition
Disability Rights Oregon
Emily's Entourage
Epilepsy Alliance America
Epilepsy Foundation
Epilepsy Foundation New England
Familia Unida Living with MS
Family Voices of California
Genetic Alliance
Global Liver Institute
GO2 for Lung Cancer
Health Hats
HealthHIV
Hermansky-Pudlak Syndrome Network
Huntington's Disease Society of America
Hypertrophic Cardiomyopathy Association
ICAN, International Cancer Advocacy Network
International Pemphigus Pemphigoid Foundation
Lakeshore Foundation
Mary Vought, Former NCD Member

Miles for Cystic Fibrosis
MLD Foundation
Multiple Sclerosis Foundation
National Alliance for Hispanic Health
National Center for Parent Leadership, Advocacy, and Community Empowerment (National PLACE)
National Disability Rights Network (NDRN)
National Organization of Nurses with Disabilities
Not Dead Yet
Partnership to Fight Chronic Disease (PFCD)
Partnership to Improve Patient Care
Patients' Rights Action Fund
Preparedness and Treatment Equity Coalition
PXE International
Rare New England
RASopathies Network
Rosie Bartel
Second Thoughts MA: Disability Rights Advocates against Assisted Suicide
SYNGAP1 Foundation
The Bonnell Foundation: living with cystic fibrosis
The Coelho Center for Disability Law, Policy and Innovation
The Headache & Migraine Policy Forum
The Hepatitis C Mentor and Support Group-HCMSG
TSC Alliance
United Spinal Association
Usher 1F Collaborative
Usher Syndrome Coalition
Whistleblowers of America