National Health Council

1730 M Street NW, Suite 500, Washington, DC 20036-4561 ■ 202-785-3910 ■ www.nationalhealthcouncil.org ■ info@nhcouncil.org

June 10, 2019

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

Comments on 2020 Framework

Dear Dr. Pearson:

The National Health Council (NHC) is pleased to provide comments on the Institute for Clinical and Economic Review's (ICER) solicitation for feedback on the 2020 Value Assessment Framework. Founded in 1920, the NHC is the only organization that brings together all segments of the health community to provide a united voice for the more than 160 million people in the United States with chronic diseases and disabilities, and their family caregivers. Made up of more than 125 diverse national health-related organizations and businesses, the NHC's core membership includes the nation's leading patient advocacy organizations, which control its governance and policy-making process. Other members include health-related associations and nonprofit organizations including the provider, research, and family caregiver communities and businesses representing biopharmaceutical, device, diagnostic, generic, and payer organizations.

Both ICER and the NHC share a mutual goal of promoting increased access to affordable, high-value, sustainable health care. While important progress has been made, there is still significant work needed to fully integrate the patient voice into value assessment.

In July 2018, the NHC held a dialogue meeting of patients and patient groups with US value assessment (VA) bodies to articulate a shared vision for what marks success in patient-centered VA and to discuss what patient groups and value assessors can do, individually and together, to make value assessment more patient centered. We are pleased to note that ICER participated in that dialogue. Patient groups and VA bodies agreed: the ultimate goal of patient-centered VA is for patients to have access to treatments they need at prices they can afford. Patient-centered VA exists when patients have been engaged, heard, understood, and respected throughout the entire process, and their input is incorporated and guides decision-making. Several of our suggestions below come from the recommendations we arrived at that day, and we hope you will consider them. The full report can be found on our website.[1]

I. Understanding the Diversity of Patient Experience and of What Matters Most to Patients

ICER's current framework takes on a "population" level perspective, stating that recommendations are intended to support "broad guidelines on appropriate care, pricing, insurance coverage determinations, and payment mechanisms." While ICER recognizes the tensions this presents, it is important to acknowledge that broad-stroke recommendations have real impacts on heterogeneous patients' access to care in the real world. To mitigate this concern, we recommend that ICER provide separate recommendations for important subpopulations. These subpopulations may differ, not only in individual characteristics, but also in ideal treatment approaches. This distinction should be made clearer.

To that end, we encourage ICER to more systematically consider how diagnostic, prognostic, and predictive tests, which will become increasingly important for stratifying patient populations to receive optimal care, are incorporated into assessments.[2]

Patient engagement should inform a value assessment's PICOTS framework at the time of scoping.

Patient groups are experts on the condition they represent. They understand the heterogeneity of their constituents, and many groups have patient registries intended to capture diverse natural history of disease experiences and interactions with the health care system. As was recommended by the NHC dialogue participants, a relatively simple way to ensure that heterogeneity of patient populations is adequately incorporated into value assessment would be to engage patient groups and incorporate data from their natural-history-of-disease studies when developing the value assessment PICOTS framework (population, intervention, comparator, outcome, time, setting). ICER's use of the PICOTS framework and communicating publicly, and with patient groups from which ICER seeks information, to populate the PICOTS framework is one way of standardizing communications and conveying clearly the information patient groups could bring to the table in engaging with value assessors. This early, up-front engagement can also ensure that the value assessment (including the assessment of net clinical benefit) relies on evidence or assumptions that the patient community believes represent its lived experiences rather than a clinician or researcher's interpretation. This is especially important in defining subgroups. Agreement on the PICOTS framework as a communication tool can also contribute to ICER's decision regarding whether sufficient evidence is available to initiate an assessment. A lack of data may indicate a potential need and role for real-world evidence (RWE) and/or that additional time is needed for trial findings to become available.

Finally, to ensure that economic models align with patient-centered PICOTS frameworks, ICER should provide sufficient time for researchers to develop *de novo* models rather than rely on existing models due to time constraints.

Greater acceptance of additional research designs is needed to understand what matters most to patients.

Systematic literature reviews are conducted by ICER to identify relevant studies to perform the assessment. Importantly, these reviews are limited to studies on the intervention(s).[3] ICER should consider the role of qualitative and quantitative preference studies, and other research stemming from patient-generated data sources. For example, the methods the US Food and Drug Administration (FDA) recommends for eliciting concepts important to patients are qualitative (e.g., focus groups, interviews).[4–7] Outcomes researchers have published extensively on how qualitative methodologies should be used for concept elicitation.[8–11] Additionally, CADTH has developed and tested methods for identifying these data, for example with their perspectives and experiences of patients and caregivers (PEPC) literature search filter.[12]

In addition to endorsing qualitative research for these purposes, we recommend that ICER describe the role that preference studies and real-world evidence (RWE) can play. In addition to ICER's own RWE framework, consideration of the FDA's recent guidance on using RWE for regulatory consideration can be a useful guide to ensuring ICER captures in its work the breadth of rigorous RWE studies available, which can in turn improve patient centricity by better reflecting the breadth of patient populations and their experiences with care.[13,14] The International Society for Pharmacoeconomics and Outcomes Research and the International Society for Pharmacoepidemiology Task Force recommendations also describe approaches to ensure rigor in RWE.[15,16] Given the lack of generalizability in clinical trial populations, RWE may be the only opportunity to glean insights on the effectiveness of treatments among certain subpopulations.[17] As ICER seeks to understand the diversity of patient experiences, it is critical ICER develops a formal process for incorporating RWE into appraisals, and acknowledge when reports lack this type of evidence, so as to indicate gaps in available data and/or assumptions supporting the value assessment.

II. Incorporating Patient-Generated Evidence

Partner with patient groups to understand realistic timeframes and information needs.

It is important patient groups are contacted far enough in advance, so they have an opportunity to respond adequately. Two to three weeks does not grant enough time for any group, much less a small patient group with minimal resources, to be appropriately responsive to an ICER request. Patient groups may need to convene scientific or medical advisory boards of volunteers or engage large numbers of patients to gather sufficient data to be responsive. A few weeks is typically not sufficient timing to make this possible. Additionally, ICER should consider adapting its timeline and approaches to accommodate the real world in which voluntary health agencies operate, with lean staff numbers, limited in-house staff with related scientific expertise, and limited budgets for hiring consultants who can help them be as responsive and timely as they would like to be.

ICER can partner with patient groups to ensure that communications are optimal and are reaching the patient community effectively. Additionally, earlier awareness could be achieved through innovative approaches. For example, CADTH issues calls for patient input through Twitter. We again encourage ICER to consider these issues and the NHC stands ready to assist in implementing approaches that can help patient groups be engaged in a time-sensitive manner.

Clearly state information needs and acceptable study characteristics.

We are pleased that ICER increasingly provides opportunities for patients to engage throughout a VA and to submit data. To complement ICER's Patient Open Input Questionnaire, ICER should clearly emphasize and describe the patient-provided information that would be valuable for patient groups to collect pro-actively. The earlier that patient groups are aware of the need for surveys and other input/data collection, the better they can accommodate these requests. Data quality may also be improved. For example, it may be possible for patient groups to incorporate additional questions into existing patient registries and collect data over time rather than cross sectionally in conjunction with a VA. Identifying and providing templates and tools from past data-collection efforts that were successfully incorporated into an appraisal (e.g. copy of successful survey) could be very useful and informative to the patient community.

Additionally, informing patient groups well in advance if submitted survey data need to have been published in a peer-reviewed journal would help all patient groups begin collecting and publishing data in advance of VA. Again here, earlier is better. The NHC and its membership is open to co-developing a guide to help patient groups with this process.

Impact of patient input and patient-group-submitted data should be clearly stated.

In addition, the impact of patient engagement or patient-group-submitted data is often unclear. We recommend ICER clearly state why and how patient input was or was not used in each report (if contributed). This feedback to groups will result in improved data contributions in the future.

Additionally, providing case examples where patient-experience input was demonstrated to have an impact on a value assessment could also be a valuable learning tool for other groups. Examples within health technology assessment have been provided in Canada, the United Kingdom, and elsewhere.[18–22]

Debrief with patient groups after a report is complete.

Once an appraisal has been performed, it would be helpful if ICER and patient groups debrief on how submitted data were or were not useful in the end. As ICER begins the process of "re-reviews," this grants the opportunity to investigate how data collection or presentation can be improved moving forward.

III. Methods to Integrate Dimensions of Value not Captured by the QALY

Quality-adjusted life year-based approaches are insufficient for capturing value from the patient perspective – shortcomings must be clearly articulated.

Both the NHC and ICER recognize the issues and implications of the quality-adjusted life year's (QALY) limitations. Indeed, there are myriad methodological, ethical, and theoretical challenges associated with the QALY.[23–26] ICER's proposed alternative approach, the Equal Value of Life Years Gained (evLYG), is a welcome step toward addressing these important limitations. However, the evLYG is insufficient to overcome broader concerns with the QALY. Patient concerns with the QALY include but are not limited to discrimination based on quantity of life years gained. Ultimately, the evLYG is simply an additional sensitivity analysis that again does not adequately capture important components of value to the patient.[27] The NHC encourages continued methodological exploration to overcome these limitations.

In parallel to continued consideration of methods that move beyond the confines of the QALY and evLTY, ICER must clearly and adequately describe uncertainty and caveats associated with QALY-based approaches. It is essential that underlying populations, timeframe, and assumptions, from which health utilities are calculated, be transparent and clearly stated within the report.

We seek to avoid circumstances such as those that have been reported where a cost/QALY number will be used as the sole determinant of value rather than as an input to a thoughtful decision-making process. While we understand fully that ICER cannot be responsible for a user's misuse of a value assessment report's findings, we implore ICER to be responsible in how it presents findings so that intentional cherry picking of results, especially in a way that hurts patients, is clear.

Societal and public-payer perspectives are key.

ICER presents the health system perspective for its base case and has previously described that it does not intend to provide a full societal perspective despite the Second Panel on Cost Effectiveness' recommendation to do so.[28] The recent ICER draft evidence report on Oral Immunotherapy and Viaskin® Peanut for Peanut Allergy: Effectiveness and Value found that the "addition of societal costs notably decreased the incremental cost-effectiveness ratios at each

value-based price anchor point."[29] This additional context is critical for interpreting findings based on a health system perspective. It may also provide key information for certain payers, especially employers where caregivers could be the employees. Similarly, public payers should consider how investments in healthcare can help to alleviate poverty and disability more broadly. As public payers have expressed interest in using ICER reports to inform coverage decision-making, ICER should urgently consider the adequacy of a health system perspective.[30]

IV. Conclusion

The NHC appreciates the opportunity to comment on ICER's initiative and agrees that in this emerging field, methods must evolve and will need to be updated/adapted as experience in this space grows. We are excited by and hopeful that patient-focused drug development will yield clinical-trial data that is more patient centered, focusing on experiences of and outcomes important to patients. This will improve data sources for patient-centered value assessment in the future.

The recommendations made above are offered with the goal of increasing patient centricity in health technology assessment. The NHC appreciates ICER's work to more proactively involve the patient community in value assessment. Just as opportunities to engage have increased in recent years, we hope to see a greater impact of patient engagement on value assessment moving forward.

We at the NHC are happy to discuss these recommendations with you, to clarify any suggestions we've made and to hear from you about how we can be supportive of their implementation. As always, please do not hesitate to reach out to us by contacting Elisabeth Oehrlein, PhD, MS, our Senior Director of Research and Programs, at 202-973-0540 or via email at eoehrlein@nhcouncil.org.

Sincerely,

Marc Boutin, JD
Chief Executive Officer
National Health Council

References

1. A Dialogue on Patient-Centered Value Assessment: Overcoming Barriers to Amplify the Patient Voice. National Health Council. https://www.nationalhealthcouncil.org/dialogue-patient-centered-value-assessment-overcoming-barriers-amplify-patient-voice. Published November 30, 2018. Accessed March 11, 2019.

2. Pritchard D. Personalized Medicine Coalition Comments on Proposed Updates to the Value Assessment Framework. http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PMC-ICER-Proposed-Updates-4.3.17.pdf. Accessed May 30, 2019.

3. Institute for Clinical and Economic Review. A Guide to ICER's Methods for Health Technology Assessment. http://icer-review.org/wp-content/uploads/2018/08/ICER-HTA-Guide_082018.pdf. Published August 2018. Accessed May 29, 2019.

4. Research C for DE and. Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. U.S. Food and Drug Administration. http://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-reported-outcome-measures-use-medical-product-development-support-labeling-claims. Published April 21, 2019. Accessed May 29, 2019.

5. Research C for DE and. Patient-Focused Drug Development: Collecting Comprehensive and Representative Input. U.S. Food and Drug Administration. http://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-focused-drug-development-collecting-comprehensive-and-representative-input. Published December 1, 2018. Accessed May 29, 2019.

6. Food and Drug Administration. *Methods to Identify What Is Important to Patients & Select, Develop or Modify Fit-for-Purpose Clinical Outcomes Assessments*. White Oak, MD; 2018. https://www.fda.gov/media/116276/download. Accessed May 29, 2019.

7. Food and Drug Administration. Roadmap to Patient-Focused Outcome Measurement in Clinical Trials. https://www.fda.gov/media/87004/download. Accessed May 29, 2019.

8. Patrick DL, Burke LB, Gwaltney CJ, et al. Content validity--establishing and reporting the evidence in newly developed patient-reported outcomes (PRO) instruments for medical product evaluation: ISPOR PRO good research practices task force report: part 1--eliciting concepts for a new PRO instrument. *Value Health*. 2011;14(8):967-977. doi:10.1016/j.jval.2011.06.014

9. Brédart A, Marrel A, Abetz-Webb L, Lasch K, Acquadro C. Interviewing to develop Patient-Reported Outcome (PRO) measures for clinical research: eliciting patients' experience. *Health Qual Life Outcomes*. 2014;12:15. doi:10.1186/1477-7525-12-15

10. Lasch KE, Marquis P, Vigneux M, et al. PRO development: rigorous qualitative research as the crucial foundation. *Qual Life Res*. 2010;19(8):1087-1096. doi:10.1007/s11136-010-9677-6

11. Humphrey L, Willgoss T, Trigg A, et al. A comparison of three methods to generate a conceptual understanding of a disease based on the patients' perspective. *Journal of Patient-Reported Outcomes*. 2017;1(1):9. doi:10.1186/s41687-017-0013-6

12. Rader T, Farrah K, Kaunelis D. Things Go Better with PEPC: Testing the Performance of Patient-Related Literature Search Filters. Presented at the: 2016 CADTH Symposium; April 11, 2016; Ottawa, ON.

13. Health C for D and R. Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices. U.S. Food and Drug Administration. http://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-real-world-evidence-support-regulatory-decision-making-medical-devices. Published April 9, 2019. Accessed May 29, 2019.

14. Pearson SD, Dreitlein WB, Towse A, Hampson G, Henshall C. A framework to guide the optimal development and use of real-world evidence for drug coverage and formulary decisions. *Journal of Comparative Effectiveness Research*. 2018;7(12):1145-1152. doi:10.2217/cer-2018-0059

15. Berger ML, Sox H, Willke RJ, et al. Good practices for real-world data studies of treatment and/or comparative effectiveness: Recommendations from the joint ISPOR-ISPE Special Task Force on real-world evidence in health care decision making. *Pharmacoepidemiol Drug Saf*. 2017;26(9):1033-1039. doi:10.1002/pds.4297

16. Wang SV, Schneeweiss S, Berger ML, et al. Reporting to Improve Reproducibility and Facilitate Validity Assessment for Healthcare Database Studies V1.0. *Pharmacoepidemiol Drug Saf*. 2017;26(9):1018-1032. doi:10.1002/pds.4295

17. Hampson G, Towse A, Dreitlein WB, Henshall C, Pearson SD. Real-world evidence for coverage decisions: opportunities and challenges. *Journal of Comparative Effectiveness Research*. 2018;7(12):1133-1143. doi:10.2217/cer-2018-0066

18. Facey KM. As health technology assessment evolves so must its approach to patient involvement. *Journal of Comparative Effectiveness Research*. May 2019. doi:10.2217/cer-2019-0039

19. Facey KM, Bedlington N, Berglas S, Bertelsen N, Single ANV, Thomas V. Putting Patients at the Centre of Healthcare: Progress and Challenges for Health Technology Assessments. *Patient*. 2018;11(6):581-589. doi:10.1007/s40271-018-0325-5

20. Facey K, Hansen HP, Single A, eds. *Patient Involvement in Health Technology Assessment*. ADIS; 2017. https://www.springer.com/gp/book/9789811040672. Accessed May 29, 2019.

21. Abelson J, Bombard Y, Gauvin F-P, Simeonov D, Boesveld S. Assessing the impacts of citizen deliberations on the health technology process. *Int J Technol Assess Health Care*. 2013;29(3):282-289. doi:10.1017/S0266462313000299

22. Staley K, Doherty C. It's not evidence, it's insight: bringing patients' perspectives into health technology appraisal at NICE. *Res Involv Engagem*. 2016;2. doi:10.1186/s40900-016-0018-y

23. Neumann PJ, Cohen JT. QALYs in 2018—Advantages and Concerns. *JAMA*. 2018;319(24):2473-2474. doi:10.1001/jama.2018.6072

24. Pettitt DA, Raza S, Naughton B, et al. The limitations of QALY: a literature review. *Journal of Stem Cell Research and Therapy*. 2016;6(4). https://ora.ox.ac.uk/objects/uuid:d22a9b1b-c2f0-4f6c-83ee-fdc320e4af61. Accessed March 15, 2019.

25. Whitehead SJ, Ali S. Health outcomes in economic evaluation: the QALY and utilities. *Br Med Bull*. 2010;96:5-21. doi:10.1093/bmb/ldq033

26. Prieto L, Sacristán JA. Problems and solutions in calculating quality-adjusted life years (QALYs). *Health Qual Life Outcomes*. 2003;1:80. doi:10.1186/1477-7525-1-80

27. Will ICER's Response to Attacks on the QALY Quiet the Critics? - Center for the Evaluation of Value and Risk in Health. https://cevr.tuftsmedicalcenter.org/news/2018/will-icers-response-to-attacks-on-the-qaly-quiet-the-critics. Accessed May 29, 2019.

28. ICER-value-assessment-framework-Updated-050818.pdf. http://icer-review.org/wp-content/uploads/2017/06/ICER-value-assessment-framework-Updated-050818.pdf. Accessed May 29, 2019.

29. Institute for Clinical and Economic Review. Oral Immunotherapy and Viaskin® Peanut for Peanut Allergy: Effectiveness and Value Draft Evidence Report (April 9, 2019). https://icer-review.org/wp-content/uploads/2018/10/ICER_PeanutAllergy_Draft_Evidence_Report_040919.pdf. Published April 9, 2019. Accessed May 30, 2019.

30. Thomas K. A Drug Costs $272,000 a Year. Not So Fast, Says New York State. *The New York Times*. https://www.nytimes.com/2018/06/24/health/drug-prices-orkambi-new-york.html. Published June 25, 2018. Accessed May 30, 2019.