Use of Patient-Centered Outcomes in ICER Assessments

Avalere and The Partnership to Improve Patient Care | 07.25.23

Table of Contents

Executive Summary

US healthcare stakeholders are increasingly expected to define the value of technology and services provided.[1] This is especially applicable to health technology manufacturers who are responsible for demonstrating the value of their treatments to payers, providers, patients, policymakers, and other stakeholders. A product's value may be considered from multiple angles, including clinical effectiveness, economic impact, patient-centered outcomes (PCOs), and broader societal value. A drug may improve clinical symptoms, leading to reduced healthcare utilization, which may increase a patient's ability to work, resulting in economic benefit to the patient through increased wages, and to the employer through increased productivity. Coverage policies may rely on the conclusions of a value assessment process, making consideration of patient centered outcomes essential if those decisions are to be centered on patients and people with disabilities. Therefore, this research was conducted to better understand the current role of PCOs in the value assessment process, utilizing select assessments from The Institute for Clinical Economic Review as a case study. Findings from this analysis highlighted that the use of PCOs in these values assessments were limited and often did not impact the quantitative assessments of value.

Unlike other countries, the U.S. does not have a designated governmental organization or process mandated to assess the value of health technologies.[2,3] The Institute for Clinical and Economic Review (ICER) has emerged as a value assessor in the US market. ICER typically reviews new treatments around the time of launch to assess their long-term value and short-term affordability, producing a "health benefit price benchmark".[4] While these results are not binding on coverage determinations or price negotiations, results are increasingly considered in payer decision-making.[5,6,7] In the process of updating its value framework in 2019, ICER noted its intention to better integrate patient input and preferences in its evidence reviews.[4] However, it is unclear the extent to which PCOs used in ICER's evidence reviews impact ICER's health benefit price benchmark calculations that payers may rely on to make decisions related to coverage and utilization management.

To assess the extent to which ICER has integrated PCOs in its assessments, The Partnership to Improve Patient Care engaged Avalere to review 4 reports released since ICER introduced its 2020–2023 value assessment framework.[8] The review covered materials across ICER's review process, from the scoping document to the final evidence report and recommendations. The review reveals that:

---

[1] Badash, I., Kleinman, N. P., Barr, S., Jang, J., Rahman, S., & Wu, B. W. (2017). Redefining health: the evolution of health ideas from antiquity to the era of value-based care. *Cureus*, *9*(2).

[2] Neumann, P. J., Willke, R. J., & Garrison Jr, L. P. (2018). A health economics approach to US value assessment frameworks—introduction: an ISPOR Special Task Force report [1]. *Value in Health*, *21*(2), 119-123.

[3] Thokala, P., Carlson, J. J., & Drummond, M. (2020). HTA's in the USA: A comparison of ICER in the United States with NICE in England and Wales. *Journal of Managed Care & Specialty Pharmacy*, *26*(9), 1162-1170.

[4] Institute for Clinical and Economic Review. 2020-2023 Value Assessment Framework. https://icer.org/wp-content/uploads/2020/10/ICER_2020_2023_VAF_102220.pdf

[5] Lising, A., Drummond, M., Barry, M., & Augustovski, F. (2017). Payers' use of independent reports in decision making–will there be an ICER effect. *Value Outcomes Spotlight*, *3*(2), 7-10.

[6] Sampsel, E., & Gladman, J. (2019). PMU96 US payer perspective on ICER reports: What is the impact on formulary reviews?. *Value in Health*, *22*, S266.

[7] ICON. ICER's impact on payer decision making. Results of ICON's third annual survey. July 2020. https://www.iconplc.com/insights/value-based-healthcare/icers-impact-on-payer-decision-making/

[8] Institute for Clinical and Economic Review. Assessments. https://icer.org/explore-our-research/assessments/

Avalere | PIPC

- ICER's use of PCOs in assessments varies widely.
- ICER's current approach often does not effectively account for disease and population level variation in patient preferences and outcomes.
- Across most of the reviewed assessments, the inclusion of PCOs was purely qualitative, and did not impact the health benefit price benchmarks.

This conclusion underscores some limitations of prevailing value assessment methodologies that influence benefit design and coverage decisions, which, in turn, may affect patient access to care. Additionally, it also highlights opportunities to make value assessment more patient centered. Introducing a patient lens in health technology and service valuation can enable healthcare decisionmakers to better understand the risks and benefits from the patient's view. Capturing patient-centric dimensions of value is crucial to properly demonstrate the value of medical innovations. Further, as methods for value assessment mature, flexible modeling approaches that can incorporate PCOs into the quantitative analysis will need to be researched, developed, and established to properly align assessment methods with the needs of patients and people with disabilities.

Background & Introduction

Assessing the Value of Treatments

The United States healthcare system is shifting away from a volume-based system to a value-based system.[i] It is increasingly common for hospitals and health systems to be reimbursed for positive health outcomes instead of a fee-for-service model. A product's 'value' is typically determined by assessing various 'attributes' which may include a combination of clinical effectiveness (the impact of the intervention on select health outcomes) and economic value (the impact of the intervention on healthcare resource use and costs), without consideration of patient-centered outcomes and societal value. Less frequently, value assessments account for outcomes that patients deem important, i.e., the impact of the intervention on patient-centered and patient-reported outcomes demonstrated to be important to patients, or the impact of the intervention for the public more broadly.

For instance, a novel therapy for spinal muscular atrophy (SMA) may improve patient mobility and increase survival (providing clinical value), which may in turn reduce healthcare resource utilization and healthcare costs related to the condition (direct economic value), both of which are salient to payers. There may also be indirect economic value from this treatment in terms of reduced workplace or school absenteeism for both the patient and caregiver. Additionally, for the patient, increased mobility may increase quality of life (QoL), reduce reliance on caregivers, allow for improved development and growth, and improve the patient's ability to reach life milestones.

Recently, there have been increased calls by stakeholders for inclusion of different types of outcomes that are important to patients in ICER's evidence reviews. For example, over 40 organizations signed a letter to ICER calling for their methods to be updated to account for the values of a represented subgroup to be incorporated into their base case cost-effectiveness analysis of COVID-19 treatments, and noted their concern that ICER's model did not sufficiently incorporate outcomes that matter to patients and their families, as well as societal concerns.[ii]

To deepen understandings of the extent to which ICER incorporates and values PCOs, this analysis reviews select value assessments conducted by ICER and considers outcomes that patients say are most important to them.

Challenges with Current Value Assessment Methodologies

Incorporation of patient-centered outcomes (PCOs) in research, value assessment, and healthcare decision-making has become a critical channel to infuse the needs of patients and caregivers into healthcare policymaking and delivery. In short, patient-centered care is high-quality care,[iii] yet value assessment may not holistically capture PCOs or patient perspectives.

Economic evaluations typically use quality-adjusted life years (QALY) as a standard summary measure to capture a health technology's impact on QoL. Health utilities or health-related quality of life (HRQoL) weights are used to generate QALYs. The concept of health utilities is anchored in preferences—utilities are correlated with the desirability (or preference) of one health state over another. Health utilities can be measured using direct elicitation measures, such as the visual analogue scale or standard gamble, or indirect methods, such as generic preference-based measures. The latter are the most widely used elicitation methods, particularly the EuroQol (EQ-5D) and Short Form 6D (SF-6D). Generic preference-based measures do not consistently account for differences across subpopulations.[iv] Healthy individuals often have different preferences than individuals with health conditions, and such measures often do not account for

socioeconomic and demographic specific preferences and impacts. Thus, use of these generic preference-based measures in value assessment may perpetuate biases favoring certain patient populations. These biases affect input parameters utilized in economic modeling as an artifact of how those utilities are estimated.

For the context of this paper, it is important to understand what makes a PCO different from broad outcomes elicited from non-disease-specific measures, tools, scales, etc.[v,vi] Patient preferences and the values that patients place on their healthcare varies due to many factors, including, but not limited to disease state, patient background and underlying socio-demographic characteristics, disease severity, etc. A generic scale, like EQ-5D,[vii] captures standardized information from patients—in this case about their quality of life. The EQ-5D measures HRQoL across five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.

However, the outcomes that patients experience across disease spaces (e.g., SMA, hypertrophic cardiomyopathy, myasthenia gravis [MG], amyotrophic lateral sclerosis [ALS]) vary significantly. Although patients may experience disease-related impacts to the 5 broad dimensions outlined in EQ-5D, they likely also experience impacts to dimensions not covered in EQ-5D dimensions as well as nuanced impacts from outcomes that could be considered sub-sets of these dimensions (e.g., ability for a patient with SMA to sit-up could be part of "mobility").[viii] There is evidence that the EQ-5D is responsive to some, but not all, health conditions and there may be ceiling effects in non-acute conditions (e.g., hearing impairment).[ix,x,xi] Further, patients with chronic conditions often develop coping mechanisms which may obscure EQ-5D results if a patient reports higher QoL before an intervention due to these established coping mechanisms. By contrast, condition-specific measures are less prone to confounding due to mediating mechanisms such as coping and are more sensitive to nuanced changes that affect patients' quality of life.

Without a nuanced, patient-driven lens, a generic scale like EQ-5D will fail to account for HRQoL impacts outside the dimensions that are included in the scale. Meanwhile, a disease-scale, like the ALSFRS-R,[xii] although not perfect, does a better job of capturing HRQoL impacts for patients with ALS compared to a non-ALS-specific scale—although it still may not be comprehensive of the entire patient experience. Failure to account for the true value of a therapy for specific patients could lead to an inaccurate measure of value. Further, the EQ-5D is based on a generic population, which may not capture distinct social, economic, and racial differences that impact patient preferences. Therefore, using generic preferences to parameterize value assessment models may have health equity implications.

ICER's Role in US Value Assessment

In the United States, there are multiple payers and entities that determine value and there is no centralized approach, in contrast to countries like the United Kingdom, where NICE determines the cost-effectiveness and value of drugs.[xiii,xiv] The Institute for Clinical and Economic Review (ICER) is a non-profit that analyzes evidence, produces reports on the value of medical services, and sells access to its ICER Analytics platform to payers and P&T committees. In July 2015, ICER established the Emerging Therapy Assessment and Pricing (ETAP) Program to "transform the way new drugs are evaluated and priced in the United States."[xv]

ICER conducts assessments of novel medical innovations, with 80% of assessments targeting pharmaceutical treatments, to assess their value and produce price benchmark reports addressing clinical- and cost-effectiveness, potential budget impact, and a "health benefit price benchmark". Unlike some ex-US health technology assessment (HTA) bodies, ICER's guidance is non-binding to any US payers or providers as it uses a proprietary model that is not transparent

to the public or peer reviewed. However, recent research suggests that US payers are starting to incorporate ICER's findings in their coverage and reimbursement decision-making.[xvi, xvii, xviii]

The ICER value framework focuses on two primary domains: long-term value and short-term affordability. To assess long-term value, ICER assesses the comparative efficacy of the intervention(s) under review, as well as the comparative cost-effectiveness using a QALY measure and an equal value of life year gained measure. ICER has responded to criticism that treatment value cannot be focused solely on efficacy, safety, and cost-effectiveness, and now accommodates that sentiment by including and considering qualitative "contextual considerations" or "other benefits or disadvantages" alongside the aforementioned quantitative analyses, but these may not be included as part of the quantitative analyses.

In late 2019, ICER released its updated value framework, part of which included the development of a patient engagement program and the inclusion of a patient perspectives chapter in all of its assessment reports.[xix] Although ICER has improved its mechanisms to solicit and incorporate patient perspectives and PCOs in its value assessment framework and review process, it is unclear the extent to which PCOs are truly incorporated and utilized, and to what magnitude they impact ICER's economic modeling that assesses long-term value and short-term affordability.

Purpose of Analysis

Avalere conducted a review of select ICER assessments between 2019–2022 (the time period in which its most recent value framework was utilized) to determine the extent to which ICER considers PCOs at each point of its review process, including and up to its Final Evidence Reports and Policy Recommendations. Although not an exhaustive review of all ICER reviews, this white paper looks to utilize these case examples to discuss considerations for how ICER, and value assessment broadly, can best incorporate patient-centered outcomes.

Methodology

Avalere examined four assessments[xx] as part of this analysis:

- Spinal muscular atrophy (SMA) – completed in March 2019
- Hypertrophic cardiomyopathy – completed in October 2019
- Myasthenia gravis (MG) – completed in September 2021
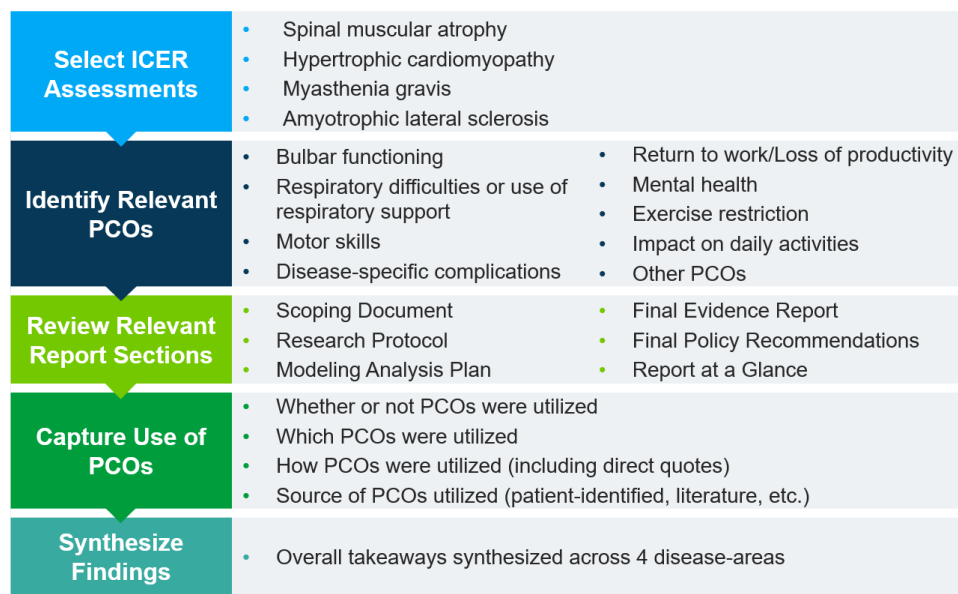- Amyotrophic lateral sclerosis (ALS) – completed in August 2022

Throughout each review, Avalere identified the inclusion of PCOs that are relevant for each disease space, by examining the methods and the Impact Inventory of each report's appendices to determine if PCOs were included in the assessment, whether they were outcomes in a modified societal co-base case, and how the PCOs were included. The Impact Inventory is a formal framework adapted from the Second Panel on Cost Effectiveness in Health and Medicine that ICER utilizes to specify the effects of an intervention included in the analysis from both the health system payer and societal perspectives. If ICER does not include an effect of treatment in its analysis, the rationale is noted in this section.

PCOs could be included in the following aspects of the ICER review process:

- Scoping document
    - o Background
    - o Stakeholder Input
    - o Scope of Clinical Evidence Review/Patient, Intervention, Comparison, Outcome, and Time (PICOTs)
    - o Potential Other Benefits and Contextual Considerations
    - o Scope of Comparative Value Analyses
- Research Protocol
    - o Background
    - o PICOTs
- Modeling Analysis Plan
    - o Health State Definitions
    - o Utilities
- Final Evidence Report
    - o Background
    - o Stakeholder Input
    - o Scope of Clinical Evidence Review
    - o Economic Model (health states definitions and health state utility estimates)
    - o Contextual Considerations and Potential Other Benefits
    - o Modified Societal Perspective (if included)
    - o Supplemental Materials/Impact Inventory
- Final Policy Recommendations
- Report-at-a-Glance

For each PCO discussed or included in the ICER report, Avalere determined whether they were identified by patients (e.g., through comment letters to ICER, in cited literature, through patient outreach referenced in the report), and whether these specific outcomes were quantitatively included in ICER's economic modeling and the resulting health benefit price recommendations. Instances where ICER noted PCOs in its scoping document, but they were not quantitatively included in its modeling methodology/outcomes, or they were only discussed qualitatively in the report discussion or Impact Inventory were noted. All of this information was abstracted from each ICER assessment that was reviewed, specifically noting whether PCOs were utilized, what specific PCOs were utilized, how they were utilized, and the exact quote from ICER's text. Overall takeaways based on the four assessment case studies and disease-specific takeaways were synthesized based on the review.

Figure 1. Review Methodology

Select ICER Assessments	• Spinal muscular atrophy • Hypertrophic cardiomyopathy • Myasthenia gravis • Amyotrophic lateral sclerosis	
Identify Relevant PCOs	• Bulbar functioning • Respiratory difficulties or use of respiratory support • Motor skills • Disease-specific complications	• Return to work/Loss of productivity • Mental health • Exercise restriction • Impact on daily activities • Other PCOs
Review Relevant Report Sections	• Scoping Document • Research Protocol • Modeling Analysis Plan	• Final Evidence Report • Final Policy Recommendations • Report at a Glance
Capture Use of PCOs	• Whether or not PCOs were utilized • Which PCOs were utilized • How PCOs were utilized (including direct quotes) • Source of PCOs utilized (patient-identified, literature, etc.)	
Synthesize Findings	• Overall takeaways synthesized across 4 disease-areas	

Results

Trends Across 4 Disease Assessments

Health State Definitions and Utility Estimates

ICER often utilizes a disease-specific PRO tool (e.g., ALSFRS-R) to define the health states of its models. However, utility estimates that dictate the health benefit impacts in each defined health state are sourced from studies that rely on disease-agnostic tools like the EQ-5D or the SF-6D. Thus, PCOs that are relevant to patients may define the structure of the model, but health benefit impacts are not based on these PCOs. With these disease-agnostic tools, it is unclear to what extent the full breadth of patient burden is considered.

Generic preference-based measures intentionally collapse all of the factors related to a specific disease into a single utility measure, and therefore only assess disease-specific experiences that are related to or mediated by the function that is impacted. In the case of MG for instance, ICER only captured disease effects mediated by muscle function and therefore any disease-related effect or patient-centric outcome not mediated by muscle function were not reflected in the utility measure. If the full breadth of PCOs is not considered (which is likely based on ICER's modeling specifications), disease-specific nuances of a patient's experience (and thus, outcomes) that are important to patients may be lost and the tool (e.g., EQ-5D) may inaccurately capture the true utility of a particular health state in the model specific to the disease.

The selection of a preference elicitation measure – meaning the methodology and questions asked in order to identify the preferred outcome – will impact the utility metric and will determine the outcome of ICER's model assessing the value of a treatment. However, utility measurement is not an exact science: an identical patient population could have divergent utility measure depending on the choice of elicitation method used. In ICER's model, multi-factorial QoL domains are collapsed into a single utility measure and carried through the incremental cost effectiveness analysis that yields the cost per QALY, QALY threshold, and budget impact model. The result is

those multi-factorial, generic QoL domains dictate the health benefit modeled, leading to economic modeling results based on imperfect, non-disease specific measures.

As discussed more below, it is important to note that disease-specific tools that do incorporate PCOs are not often able to be mapped to utilities as easily as a disease-agnostic tool like EQ-5D or SF-6D—both of which have well-established crosswalks to utilities or QALYs.[xxi] With those considerations in mind, if ICER's reviews are scoped to include PCOs relevant to the disease of interest, the utility estimates used to represent the net health benefit should reflect that. If these disease-specific tools do not map to utilities, ICER or other research bodies could conduct additional research to develop disease-specific estimates or mapping.

Qualitative Mentions of Patient Experience

ICER often mentions or references PCOs that align with patient experiences in its Contextual Considerations and Other Benefits and Disadvantages sections. However, this inclusion is qualitative in nature, and it does not translate to inclusion of PCOs in its economic modeling methodology. While the contextual considerations section of ICER's review may include discussion of PCOs, the reader must read these contextual considerations along model results. Contextual considerations are not often mentioned or relayed in report conclusions, the report-at-a-glance, policy recommendations, media coverage, etc. Unless the reader spends time in the report beyond the health benefit price benchmark and cost/QALY results, the contextual considerations would be omitted from discussion of key takeaways. This could result in an incomplete understanding of value drivers for patients and the impact of treatments on them.

Disease-Specific Takeaways

PCO use was similar across the disease-areas of interest, but there were a few differences. Figure 2 summarizes the extent of patient-centered approaches across sections in each assessment. For the purposes of this analysis, "significant" refers to a quantitative inclusion of PCOs that impact modeling results, and "limited" refers to qualitative mentions of PCOs that do not impact modeling or analysis results.

- **Disease-specific PCOs were not effectively incorporated into the modeled clinical benefit.** PCOs were only used to define health states for 2 of the 4 reports, ALS and hypertrophic cardiomyopathy. Yet, across all reports, the disease-agnostic EQ-5D was used for health state utility estimates that were used to model clinical benefit, potentially limiting the patient-centered and disease-specific perspective of clinical benefit.

- **None of the reports reviewed utilized PCOs as a contributor to health state utility estimates in the base case analysis** (i.e., the part of the assessment of costs borne by third-party payers or integrated health systems),[xxii] **and only 1 of the assessed reports included quantitative use of PCOs to model clinical benefit or value.** The SMA report included PCOs quantitatively in the modified societal perspective as a second scenario analysis, or co-base case analysis. Payers may not be aware when a value assessment's health state utility estimates fail to incorporate PCOs, meaning the value assessment does not reflect outcomes that matter to patients and people with disabilities, yet may rely on its conclusions to make coverage decisions.

- **PCO use in the MG assessment was arguably the most limited, as the inclusion of PCOs was limited to measuring QoL impact on symptom scales.** Health states were based on quantitative MG tools focused on muscle strength and endurance (e.g., MG-ADL), and did not reflect other important domains to MG patients.

- **Policy recommendations for 2 of the 4 assessments recommended patient-centered work to strengthen future assessments.** For Hypertrophic Cardiomyopathy, ICER provided a recommendation for future research to assess treatment benefits related to productivity, caregiver burden, and other patient-centered benefits so they can be included in future models. The MG report contained a recommendation for additional evidence generation on the impact of MG on patients and caregivers to allow for better modeling of healthcare and societal impacts of novel therapeutics. Lastly, the ALS assessment contained a qualitative policy recommendation to consider a benefit structure for ALS that covers necessary ancillary home health services (e.g., assistive devices, home modifications, caregiving), but this was not a patient-centered recommendation related to value assessment.

Figure 2. Disease-Level Differences in PCO Use

	Spinal Muscular Atrophy	Hypertrophic Cardiomyopathy	Myasthenia Gravis	Amyotrophic Lateral Sclerosis
Scoping Document	None	None	None	None
Research Protocol	Limited	Limited	None	Limited
Modeling Analysis Plan	Limited	Limited	None	Limited
Final Evidence Report and Meeting Summary	Limited	None	None	None
Final Policy Recommendations	N/A	Significant	Significant	Limited
Report-at-a-Glance	None	Limited	Limited	None

Extent of Patient-Centeredness
- Significant (e.g., quantitative) - Limited (e.g., qualitative mention) - None

Overall Findings

Overall, there is a disconnect between ICER statements about patient-centeredness and the actual use of PCOs in their reviews. ICER acknowledges the importance of PCOs in qualitative descriptions throughout its assessments, but does not integrate PCOs quantitatively into modeling, resulting in final valuations with limited incorporation of the patient perspective. ICER's stated preference for generic preference-based measures, especially EQ-5D, often ignores or undervalues patient-relevant outcomes. Preference measures are used to calculate the utilities that are captured in the QALY, which sits at the heart of ICER's model and carries through the resulting analyses, diminishing the patient-centered aspects of the reports. Although ICER's value framework notes that patient-reported data may be used where available, there is limited guidance on how to map patient-reported outcomes to QALYs (as they are utilized in ICER's modeling), nor is there a requirement to discuss how the model might change if different utilities were used.

Importance of Patient-Centered Value Assessment

In a system where payer coverage and reimbursement decisions drive patient access, infusing PCOs and preferences for care into value assessment ensures that aspects of care or treatments that matter to patients are considered in decision-making. In today's U.S. healthcare system, patient-centered care is increasingly recognized as a key element of high-quality care,[xxiii,xxiv] and HTA organizations and value frameworks have recently begun to engage patients and incorporate preferences more explicitly in their approaches.[xxv] Doing so would allow providers, payers, and policymakers to better understand the benefits and risks of medical innovations from a patient's perspective – leading to personalized care tailored to the needs of individual patients.[xxiv] With more focus on patient-centered value assessment, shared decision-making between providers and patients may be promoted and emphasized. When patients engage in their decision-making process, they are more likely to be engaged in their care and adhere to their treatment plans, leading to better outcomes and lower costs over time.[xxiii]

However, the methodologies used in standard cost-effectiveness analyses are not flexible enough to effectively include the patient perspective, typically excluding them from the quantitative assessment of the value of a medical innovation and health benefit price recommendations.[xxvi] ICER's value assessments are conducted from a health system and payer perspective, relying on standardized patient quality of life scales (e.g., EQ-5D) across different disease states and patient populations. A limitation of this approach is that there is variation in the PCOs that are important to different patient populations and disease spaces, and thus utilizing a standard scale may exclude inclusion of PCOs that are particularly salient for patients in a specific disease space.[xxvii]

For instance, a patient with cancer may place a higher value on the ability to live without pain, but a patient with ALS may place a higher value on the ability to maintain a certain level of mobility and bulbar function. By using utility estimates based on non-disease specific scales, ICER's approach does not consistently take into consideration disease-specific differences in patient preferences and outcomes. Additionally, patient centered utility estimates may vary across different patient populations and medical conditions. For instance, the utility estimate for a particular health state may differ between a patient with cancer and a patient with diabetes, even if the health state is the same. This variability increases the difficulty of utilizing utility estimates across different patient groups and disease spaces.

As methods for value assessment mature, malleable modeling approaches that can handle infusing PCOs and additional complexities will need to be researched, developed, and established to properly align assessment methods with patient needs.[xxviii,xxix] The data needed to develop disease-specific estimates may not be readily available for all diseases and therefore would need time to collect. More accurate utility estimates would measure patients' preferences for different health states as done in patient preference information studies. These preferences can be influenced by a variety of factors, including their past experiences, their background, and their personal beliefs. Measuring these preferences accurately requires specific research, utilizing techniques such as time-tradeoff or standard gamble studies.[xxx] Obtaining disease-specific utility estimates requires significant resources, including time and funding—conducting surveys or interviews with patients to measure their preferences. ICER could conduct this research ahead of its assessments or partner with other entities already doing this kind of work, if ICER is willing to elongate its review timelines.

Lastly, patient-centered value assessment can help reduce healthcare disparities by accounting for the unique needs, preferences, and values of different patient populations with differing underlying socio-demographic characteristics. Leading HTAs and policymakers have taken steps

to address implicit biases and prioritize equity in their analyses and decision-making (e.g., the CMS Innovation Center recently published an analysis of implicit bias in its model portfolio), but more work is needed to fully integrate patient- and equity-centered values into HTA processes.[xxxi] A patient-centered approach to the value assessment process could incorporate these differences and nuances, improving payer and policy decisions related to treatment, coverage, and reimbursement decision-making across a heterogenous patient population.[xxxii]

Conclusion

ICER's use of PCOs in assessments examined as part of this analysis is varied but limited in their impact on ICER's quantitative health economic modeling results. Patient-centered value assessment is crucial to properly demonstrate the value of medical innovations and thus ICER could strive to quantitatively include PCOs in its assessments. As methods for value assessment mature, flexible modeling approaches that can incorporate PCOs and other complexities will need to be researched, developed, and established to properly align assessment methods with patient needs.

Appendix

Table 1. Detailed Disease Level Differences in PCO Use

	Spinal Muscular Atrophy	Hypertrophic Cardiomyopathy	Myasthenia Gravis	Amyotrophic Lateral Sclerosis
Scoping Document	*Qualitative mention of PCOs that does not affect modeling* *PCOs reviewed are not disease specific nor comprehensive* *Productivity and other indirect costs included as data allows*	*Qualitative mention of PCOs that does not affect modeling* *Focused on QoL tools, likely not capturing PCOs holistically* *Model implies PCO integration but does not include patient financial burden*	*Qualitative mention of PCOs that does not affect modeling* *PCOs included in review scoping but are mostly symptom-focused* *Productivity and other indirect costs included as data allows*	*Qualitative mention of PCOs that does not affect modeling* *Missing important disease specific PCOs noted by patients* *Productivity and other indirect costs included as data allows*
Research Protocol	*Qualitative mention of PCOs that does not affect modeling* *Disease-specific PCOs missing*	*Unclear extent PCOs included in QoL tools that impact modeling* *Lists disease specific PCOs important to patients*	*Qualitative mention of PCOs that does not affect modeling* *PCOs described are focused on symptoms*	*Qualitative mention of PCOs that does not affect modeling* *Listed outcomes missing some important PCOs*
Modeling Analysis Plan	*Health states extrapolated based on modeling, rather than disease specific PRO tool* *Health utilities extrapolated based on modeling, does not use disease specific PRO tool*	*Health states defined using disease specific NYHA class, but excludes 2 PCOs due to data limitations* *NYHA class used to define health utilities; scores based on EQ-5D*	*Health states not patient centered. Defined using one disease specific symptom focused score* *EQ-5D used to define health utilities. MG-ADL used to define myasthenic crisis utilities.*	*Health states defined using disease specific PCOs* *EQ-5D used to define health utilities, does not use disease specific PRO tool*
Final Evidence Report & Meeting Summary	*Typically uses descriptive mentions of*	*Descriptive mentions of*	*Descriptive mentions of*	*Descriptive mentions of*

	Spinal Muscular Atrophy	Hypertrophic Cardiomyopathy	Myasthenia Gravis	Amyotrophic Lateral Sclerosis
	PCOs that do not impact modeling *Modified societal perspective includes quantitative use of PCOs that impact modeling*	*PCOs that do not impact modeling* *Missing important disease specific PCOs* *Assumption based modeling of PCOs in modified societal perspective*	*PCOs that do not impact modeling* *Symptom focused outcomes used, not patient centered* *Modified societal perspective not included in review*	*PCOs that do not impact modeling* *Missing some important disease specific PCOs* *Notes inclusion of PCOs in modified societal perspective but unclear how*
Final Policy Recommendations	*No final policy recommendations published*	*Recommends research to assess patient and caregiver treatment benefit, and inclusion of this data in future models*	*Recommends further research on gMG-specific PCOs*	*Qualitative policy recommendation related to patient-centered coverage, not value assessment*
Report-at-a-Glance	*Limited inclusion of PCOs, only mentioned in context of disease burden*	*Acknowledges that value price benchmark produced is not inclusive of value to patients, caregivers, and society*	*Calls for specific evidence related to MG PCOs*	*Limited inclusion of PCOs, only mentioned in context of disease burden*

References

i Badash, I., Kleinman, N. P., Barr, S., Jang, J., Rahman, S., & Wu, B. W. (2017). Redefining health: the evolution of health ideas from antiquity to the era of value-based care. *Cureus*, *9*(2).

ii http://www.pipcpatients.org/uploads/1/2/9/0/12902828/letter_to_icer_on_covid_model.pdf

iii Edgman-Levitan, S., & Schoenbaum, S. C. (2021). Patient-centered care: achieving higher quality by designing care through the patient's eyes. *Israel Journal of Health Policy Research*, *10*, 1-5.

iv Sarah J. Whitehead, Shehzad Ali, Health outcomes in economic evaluation: the QALY and utilities, *British Medical Bulletin*, Volume 96, Issue 1, December 2010, Pages 5–21, https://doi.org/10.1093/bmb/ldq033

v Lin, F. J., Longworth, L., & Pickard, A. S. (2013). Evaluation of content on EQ-5D as compared to disease-specific utility measures. *Quality of Life Research*, *22*, 853-874.

vi Zhou, T., Guan, H., Wang, L., Zhang, Y., Rui, M., & Ma, A. (2021). Health-related quality of life in patients with different diseases measured with the EQ-5D-5L: a systematic review. *Frontiers in Public Health*, *9*, 675523.

vii Zhou, T., Guan, H., Wang, L., Zhang, Y., Rui, M., & Ma, A. (2021). Health-related quality of life in patients with different diseases measured with the EQ-5D-5L: a systematic review. *Frontiers in Public Health*, *9*, 675523.

viii Efthymiadou, O., Mossman, J., & Kanavos, P. (2019). Health related quality of life aspects not captured by EQ-5D-5L: results from an international survey of patients. *Health Policy*, *123*(2), 159-165.

ix Yang Y, Longworth L, Brazier J. An assessment of validity and responsiveness of generic measures of health-related quality of life in hearing impairment. *Qual Life Res.* 2013;22(10):2813–28

x Payakachat N, Ali MM, Tilford JM. Can The EQ-5D Detect Meaningful Change? A Systematic Review. Pharmacoeconomics. 2015 Nov;33(11):1137-54. doi: 10.1007/s40273-015-0295-6. PMID: 26040242; PMCID: PMC4609224.

xi Lorgelly PK, Doble B, Rowen D, Brazier J; Cancer 2015 investigators. Condition-specific or generic preference-based measures in oncology? A comparison of the EORTC-8D and the EQ-5D-3L. Qual Life Res. 2017 May;26(5):1163-1176. doi: 10.1007/s11136-016-1443-y. Epub 2016 Nov 9. PMID: 27830513; PMCID: PMC5376391.

xii Cedarbaum, J. M., Stambler, N., Malta, E., Fuller, C., Hilt, D., Thurmond, B., ... & 1A complete listing of the BDNF Study Group. (1999). The ALSFRS-R: a revised ALS functional rating scale that incorporates assessments of respiratory function. *Journal of the neurological sciences*, *169*(1-2), 13-21.

xiii Neumann, P. J., Willke, R. J., & Garrison Jr, L. P. (2018). A health economics approach to US value assessment frameworks—introduction: an ISPOR Special Task Force report [1]. *Value in Health*, *21*(2), 119-123.

xiv Thokala, P., Carlson, J. J., & Drummond, M. (2020). HTA's in the USA: A comparison of ICER in the United States with NICE in England and Wales. *Journal of Managed Care & Specialty Pharmacy*, *26*(9), 1162-1170.

xv Institute for Clinical and Economic Review. History & Impact. https://icer.org/who-we-are/history-impact/

xvi Lising, A., Drummond, M., Barry, M., & Augustovski, F. (2017). Payers' use of independent reports in decision making–will there be an ICER effect. *Value Outcomes Spotlight*, *3*(2), 7-10.

xvii Sampsel, E., & Gladman, J. (2019). PMU96 US payer perspective on ICER reports: What is the impact on formulary reviews?. Value in Health, 22, S266.

xviii ICON. ICER's impact on payer decision making. Results of ICON's third annual survey. July, 2020

xix Institute for Clinical and Economic Review. 2020-2023 Value Assessment Framework. https://icer.org/wp-content/uploads/2020/11/ICER_2020_2023_VAF_02032022.pdf

xx Institute for Clinical and Economic Review. Assessments. https://icer.org/explore-our-research/assessments/

xxi Ben, Â.J., van Dongen, J.M., Finch, A.P. *et al.* To what extent does the use of crosswalks instead of EQ-5D value sets impact reimbursement decisions?: a simulation study. *Eur J Health Econ* (2022). https://doi.org/10.1007/s10198-022-01539-6

[xxii] Institute for Clinical and Economic Review. ICER's Reference Case for Economic Evaluations: Principles and Rationale. https://icer.org/wp-content/uploads/2020/10/ICER_Reference_Case_013120.pdf (p12).

[xxiii] Baker, A. (2001). *Crossing the quality chasm: a new health system for the 21st century* (Vol. 323, No. 7322, p. 1192). British Medical Journal Publishing Group.

[xxiv] Epstein, R. M., Fiscella, K., Lesser, C. S., & Stange, K. C. (2010). Why the nation needs a policy push on patient-centered health care. *Health affairs*, *29*(8), 1489-1495.

[xxv] Institute for Clinical and Economic Review. ICER's New Patient Engagement Program: Amplifying the Patient Voice Before, During, and After a Value Assessment. https://icer.org/news-insights/commentaries/icers-new-patient-engagement-program-amplifying-the-patient-voice-before-during-and-after-a-value-assessment/

[xxvi] Weintraub, W. S., & Cohen, D. J. (2009). The limits of cost-effectiveness analysis. *Circulation: Cardiovascular Quality and Outcomes*, *2*(1), 55-58.

[xxvii] Morel, T., & Cano, S. J. (2017). Measuring what matters to rare disease patients–reflections on the work by the IRDiRC taskforce on patient-centered outcome measures. *Orphanet journal of rare diseases*, *12*(1), 1-13.

[xxviii] Armstrong, M. J., & Mullins, C. D. (2017). Value assessment at the point of care: incorporating patient values throughout care delivery and a draft taxonomy of patient values. *Value in Health*, *20*(2), 292-295.

[xxix] Linda Bohannon, M. S. M., & Franklin, E. (2022). Value Assessment That Puts Patients at the Forefront. *Signal*, 08.

[xxx] Wolowacz, S. E., Briggs, A., Belozeroff, V., Clarke, P., Doward, L., Goeree, R., & Norman, R. (2016). Estimating health-state utility for economic models in clinical studies: an ISPOR good research practices task force report. *Value in Health*, *19*(6), 704-719.

[xxxi] IVI & Sick Cells. *Finding Equity in Value: Racial and Health Equity Implications of U.S. HTA Processes.* Available here*: https://sickcells.org/wp-content/uploads/2022/10/IVI_Sick-Cells_Equity-in-Value_2022.pdf

[xxxii] Diaby, V., Ali, A., Babcock, A., Fuhr, J., & Braithwaite, D. (2021). Incorporating health equity into value assessment: frameworks, promising alternatives, and future directions. *Journal of managed care & specialty pharmacy*, *27*(9-a Suppl), S22-S29.