PIPC Partnership to Improve Patient Care

February 20, 2020

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

Dear Dr. Pearson,

The Partnership to Improve Patient Care (PIPC) appreciates this opportunity to comment on the Institute for Clinical and Economic Review's (ICER) draft evidence report regarding treatments for Sickle Cell Disease (SCD). SCD is a debilitating disease impacting roughly 100,000 individuals in the United States[1] and disproportionately affects racial minorities. African-Americans are particularly at risk, with SCD occurring approximately one in every 365 births. Despite the description of the disease first being formalized in 1910, there has been limited innovation for the disease until very recently. With this in mind, it is imperative that ICER act responsibly in its assessment to avoid the consequence of limiting treatments to a population that is in great need of them. PIPC encourages ICER to give serious consideration to the following comments.

The QALY is a Particularly Inappropriate Metric to Evaluate Treatments for SCD

PIPC has highlighted the discriminatory nature of the QALY, as well as the limitations of the metric as a measure of health gain, in many previous comments on ICER assessments. Given the complex nature of SCD, its severity, and the fact that the burden disproportionately falls upon specific groups within society, the QALY is a particularly inappropriate method for evaluating any value accrued from interventions aimed at its alleviation.[2]

Numerous studies have highlighted how key factors such as severity of disease,[3] pain levels, and sparse availability and limited effectiveness of alternative treatments — all relevant for SCD — are considered as key determinants of priority in health care settings.[4,5] In fact, some health technology assessment

[1] Sickle Cell Disease Coalition. About Sickle Cell Disease. Accessed February 19, 2020.
[2] Levenson JL, McClish DK, Dahman BA, Bovbjerg VE, Citero VD, Penberthy LT, Aisiku IP, Roberts JD, Roseff SD, Smith WR. Depression and anxiety in adults with sickle cell disease: the PiSCES project. Psychosomatic medicine. 2008 Feb 1;70(2):192-6.
[3] Nord E, Pinto JL, Richardson J, Menzel P, Ubel P. Incorporating societal concerns for fairness in numerical valuations of health programmes. Health Economics. 1999;8:25–39
[4] McKie J, Richardson J. Social preferences for prioritizing the treatment of severely ill patients: the relevance of severity, expected benefit, past health and lifetime health. Health Policy. 2017 Aug 1;121(8):913-22
[5] Gu Y, Lancsar E, Ghijben P, Butler JR, Donaldson C. Attributes and weights in health care priority setting: a systematic review of what counts and to what extent. Social Science & Medicine. 2015 Dec 1;146:41-52.

systems in European countries such as Norway, Sweden and the Netherlands[6] actively use information on these factors to inform approval decisions for new medicines, given the limitations and simplicity of the QALY as a measure of health gain.

Additionally, health state valuation studies that translate into QALYs are undertaken in predominantly white populations, and weighting calculations are largely constructed using linear regression which over-homogenizes weights around the mean. The selection and construction of the 'domains' that make up quality of life tools were constructed by a small group of white men twenty years ago in Switzerland.[7] No one has challenged these sets to be updated, as it would be inconvenient for the method, but it is very clear that this type of metric is highly inappropriate for ICER to use in evaluating a treatment for a disease that disproportionately impacts people of African and Hispanic descent.

If access and approval decisions around new healthcare technologies are made based on metrics that treat patients as averages like the QALY, and these averages are driven by regression towards majority populations, minorities within the population will ultimately suffer the most.

Standard of Care is a Faulty Comparator, as it Does Not Truly Exist for SCD

ICER chooses to use the comparator of "usual care," which is neither standardized nor considered comprehensive care for SCD. SCD is a syndrome of diseases and care for any two patients can look markedly different depending on disease subtypes and the unique complications experienced by each patient. ICER even acknowledges in its report that "baseline or usual care for patients with SCD is highly variable and represents a failure in the US health care system." Despite this recognition, ICER continues to utilize methods that do not adequately account for this variability.

SCD patients are a largely underserved population. There is a lack of specialists and clinicians with expertise to treat SCD, leading patients to seek care from generalists who are often not equipped to help patients manage their disease. Due to the lack of standardized care for SCD, treatment plans administered by generalists often vary drastically depending on the unique characteristics of each patient. Furthermore, non-specialists also often assume SCD is a pain condition, which can lead to inappropriate treatment for the disease's complications.

ICER Chooses to Use Claims Data Instead of Listening to Input on Standards of Care from Patient and Clinician Stakeholders

ICER's report uses claims data to determine the number of acute pain crises (APC) in SCD patients. Administrative and accounting data sets such as claims data sets have the advantage of being real-world data that are more likely to reflect 'actual' cost data than the more traditional ingredients approach.

[6] Angelis A, Lange A, Kanavos P. Using health technology assessment to assess the value of new medicines: results of a systematic review and expert consultation across eight European countries. The European Journal of Health Economics. 2018 Jan 1;19(1):123-52.
[7] Oliver A. Discovering the QALY: Or How Rachel Rosser Changed My Life. Alan Williams in Personal Histories in Health Research, ed. Adam Oliver. Nuffield Twst. London 2005.

Nevertheless, there are many variables for which administrative data are noted as being poor proxies. Data not reflecting service over- or underutilization and ineffective coding procedures are common flaws in administrative data.[8,9,10]

This issue holds particularly true in evaluating APC for SCD. When you speak to SCD patients or clinicians they will tell you that the standard of care is to handle most APC in a home setting, not through hospital admission. The American Society of Hematology (ASH) noted this to ICER in its first comment letter, stating that "many patients manage both their acute pain and chronic pain at home. Adequate management of acute and chronic pain associated with SCD is an ongoing challenge both for patients and the clinicians responsible for their care." This assertion from the patient and clinician community is backed up by studies that show patients managed the majority of their APC at home versus in a hospital setting.[11] With this in mind, claims data will drastically underestimate the typical prevalence of APC events for SCD patients.

The Assessment Fails to Capture Outcomes that Truly Matter to SCD Patients.

As is typical in ICER assessments, both of the trials undertaken to evaluate quality of life effects and the studies from which the model utilities are sourced were undertaken using generic patient-reported outcome (PRO) tools, the EQ5D and the SF36, rather than disease specific tools.

SCD carries a large disease burden that is not adequately captured using generic PRO tools. As a group of SCD stakeholders shared with ICER in their initial letter, "[t]he debilitating nature of SCD impacts social relationships, employment, and the educational attainment goals of patients….Likewise, there are notable financial and emotional burdens on the caregivers and families of patients with SCD." Given the massive disease burden of SCD, specific PROs should have been used and an attempt should have been made to capture other cost factors — hospitalization, lost productivity, caregiver burden, etc. — in the base case, not just the contextual considerations.

There have been numerous studies suggesting that generic PRO tools such as EQ5D are poor at measuring marginal changes in quality of life effects across health states,[12] and that they are particularly

[8] Whittle J, Steinberg EP, Anderson GF, Herbert R. Accuracy of Medicare claims data for estimation of cancer incidence and resection rates among elderly Americans. Medical care. 1991 Dec 1:1226-36.
[9] Rhee C, Dantes R, Epstein L, Murphy DJ, Seymour CW, Iwashyna TJ, Kadri SS, Angus DC, Danner RL, Fiore AE, Jernigan JA. Incidence and trends of sepsis in US hospitals using clinical vs claims data, 2009-2014. Jama. 2017 Oct 3;318(13):1241-9.
[10] Abbas S, Ihle P, Köster I, Schubert I. Estimation of Disease Incidence in Claims Data Dependent on the Length of Follow-Up: A Methodological Approach. Health services research. 2012 Apr;47(2):746-55.
[11] Smith WR, Penberthy LT, Bovbjerg VE, McClish DK, Roberts JD, Dahman B, Aisiku IP, Levenson JL, Roseff SD. Daily assessment of pain in adults with sickle cell disease. Annals of internal medicine. 2008 Jan 15;148(2):94-101.
[12] Payakachat N, Ali MM, Tilford JM. Can The EQ-5D Detect Meaningful Change? A Systematic Review. Pharmacoeconomics. 2015;33:1137–1154.

poor measures of quality of life in SCD.[13] This brings us back to our previous point about the QALY. It is imperative when evaluating treatments for a disease as complex as SCD that disease-specific metrics are used.

ICER Makes Faulty Assumptions About Lifetime Cost of Treatment

ICER's model makes the assumption that patients will be using these new drugs under optimal prescribing conditions non-stop from the age of 24 years through to death. This is highly unrealistic.[14] It is typical in drugs taken for chronic conditions for patients to take treatment holidays, often when the treatment is effective, and at times when it is ineffective, as agreed by their physicians.[15] It is also true that drug use — especially of specialized drugs — falls away later in life when pain relief and symptom management become more common. In addition, ICER assumes that the price of these treatments will remain the same for the next 20 years, which is very unlikely.[16] What is more likely is that generic substitutes will enter the market, driving down prices. If you factor in this steep drop in price after 10-15 years, ICER's cost estimates would drop dramatically. ICER also does not factor in savings from reducing the incidence of expensive hospital care, which would impact the assumed lifetime cost of treatment.

Conclusion

ICER risks doing the SCD community a disservice by using the QALY, a metric highly inappropriate for the assessment of SCD treatments, and by failing to listen to the community about factors like standard of care and outcomes that matter to patients that should be meaningfully incorporated into its model. We strongly encourage ICER to listen closely to the SCD community and amend its model accordingly.

Sincerely,

Tony Coelho
Chairman
Partnership to Improve Patient Care

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[13] Keller S, Yang M, Treadwell MJ, Hassell KL. Sensitivity of alternative measures of functioning and wellbeing for adults with sickle cell disease: comparison of PROMIS® to ASCQ-Me℠. Health and quality of life outcomes. 2017 Dec;15(1):117.
[14] Abrahamowicz M, Tamblyn R. Drug utilization patterns. Wiley StatsRef: Statistics Reference Online. 2014 Apr 14.
[15] Alpert A. The anticipatory effects of Medicare Part D on drug utilization. Journal of health economics. 2016 Sep 1;49:28-45.
[16] Lichtenberg FR, Duflos G. The effect of patent expiration on US drug prices, marketing, and utilization by the public. Manhattan Institute for Policy Research. 2009.