PIPC Partnership to Improve Patient Care

March 18, 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) is writing to comment on the Institute for Clinical and Economic Review's (ICER) draft evidence report regarding treatments for Cystic Fibrosis (CF). CF is a rare and chronic genetic disease which causes persistent lung infections and limits the ability for people to breathe over time. Living with and managing cystic fibrosis can be physically, emotionally, and financially taxing for both patients and their caregivers. For this reason, it is imperative that ICER take a comprehensive approach when evaluating new treatments so that all aspects of value and quality of life improvements are considered during the assessment process.

The QALY is an inappropriate tool to measure the value of treatments for cystic fibrosis.

As PIPC has previously stated, the QALY is both a discriminatory metric and a poor measure of health benefits for health care interventions. This is particularly true with respect to a disease such as CF, as patients experience significant disabling effects over time.

We have noted in the past that the QALY disservices those with chronic and disabling conditions, as it is fundamentally designed to undervalue what may be deemed clinically small improvements. The ability of novel treatments to bring improvements through increased efficacy or the reduction of side effects, regardless of whether they are perceived as clinically significant, can substantially improve quality of life for patients with CF. This is particularly applicable to CF patients in regard to lung function. Even small improvements in lung function can increase a CF patient's endurance and ability to participate in day-to-day activities, such as attending work or school. The QALY undervalues these improvements and thus does not paint an accurate picture of the value of these treatments to patients.

The use of this limited metric also presents an incredibly narrow view to measure CF progression over time. ICER's model only measures the treatments' effects on lung function, weight, and acute pulmonary exacerbations, when we know there are many other outcomes that matter to patients with CF. There are tools and data available to capture a more robust picture of disease progression and quality of life for CF patients. If ICER's goal is truly to capture the value of these treatments, it should not use the EQ-5D as the patient-reported outcome tool for this assessment. The quality of life of patients with CF is better measured with the Cystic Fibrosis Questionnaire – Revised (CFQ-R), which assesses 13 domains relevant to patients living with

CF, compared to a mere five domains associated with the EQ-5D. Most importantly, given that QOL in the ICER model is linked directly to a measure of lung function, studies have shown both considerable variance in quality of life across stages and severity of disease, but also across the many aspects of QOL that the disease affects beyond lung function, in particular nutrition,[1] depression[2] and anxiety.[3] It is imperative that ICER utilize the CFQ-R or other disease-specific instruments when assessing these treatments. Furthermore, ICER should ensure that *all* outcomes are mapped back to the QALY.

We have concerns about ICER's willingness to prioritize financial savings over patient life and well-being.

PIPC has consistently voiced our discomfort with the use of the QALY in measuring health outcomes as it devalues health gains for the disabled, chronically ill, and elderly. We would like to go a step further regarding ICER's CF report and make the point that not only is the QALY discriminatory, it does not accurately represent society's values in relation to health care. ICER's use of the metric is callous and out of touch with the goal of bringing better health to individuals, which should *always* be the primary function of the health care system.

ICER's CF report makes the incredibly concerning assessment that **even if Trikafta were found to be curative, it would still not be cost-effective**. In saying this, ICER makes clear that it is very willing to put a price on a human life, which is devastating to the patient community, and which we believe would be incredibly troubling to society writ large. We do not disagree that prices should be set in a reasonable manner and that we should be having a robust discussion about what that looks like in an era of disease-modifying and curative therapies. We also feel that finances being prioritized over a patient's life is an inappropriate starting place for this conversation.

The purpose of innovation in health care is to treat and cure patients. From an ethical standpoint, society chooses to spend resources on those that need them most. Studies have shown that when asked to quantify their preferences for providing care to different patients, people will frequently choose to allocate resources to those who are most in need of help.[4] CF is a horrific disease that drastically shortens lives. Taking the societal view spelled out above, we should be prioritizing access to care for those who are chronically ill, not limiting it.

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[1] Sawicki GS, Rasouliyan L, McMullen AH, Wagener JS, McColley SA, Pasta DJ, Quittner AL. Longitudinal assessment of health-related quality of life in an observational cohort of patients with cystic fibrosis. Pediatric pulmonology. 2011 Jan;46(1):36-44.

[2] Knudsen KB, Pressler T, Mortensen LH, Jarden M, Skov M, Quittner AL, Katzenstein T, Boisen KA. Associations between adherence, depressive symptoms and health-related quality of life in young adults with cystic fibrosis. SpringerPlus. 2016 Dec;5(1):1-8.

[3] Bregnballe V, Thastum M, Lund LD, Hansen CR, Preissler T, Schiøtz PO. Validation of the Danish version of the revised cystic fibrosis quality of life questionnaire in adolescents and adults (CFQ-R14+). Journal of Cystic Fibrosis. 2008 Nov 1;7(6):531-6.

[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.

Societal and economic benefits should be included in ICER's cost-effectiveness model.

The financial burden of CF is very high, both in direct medical costs and indirect costs, such as lost productivity and caregiving costs. Annual medical costs alone incurred by adult patients with severe CF can run upwards of $200,000 whereas younger patients with severe CF can incur even higher OOP costs.[5] Direct medical costs do not even begin to capture the full financial burden of this disease. CF requires consistent care and caregiving, which places a huge emotional and financial burden on families. Very frequently when a child is diagnosed with CF, one parent will need to leave the workforce and become a full-time caregiver. CF patients also are very easily prone to infections and frequently require special accommodations in schooling and work. Several studies have shown that some of the largest costs of CF come from direct non-health care costs and indirect costs attributable to productivity losses.[6] If ICER's goal is to truly capture the value of these treatments from a societal perspective, these costs must be included in the base case.

ICER fails to capture heterogeneity of the patient population.

CF is a complex disease with considerable heterogeneity in both its severity and the degree to which therapies are effective. If ICER's aim is to produce actionable and accurate data for policymakers, then this heterogeneity must be incorporated in the model.

Unfortunately, the ranges of the sensitivity analysis are the only tool within the report to convey the impact of this patient diversity, and ICER's choices for input ranges around its sensitivity analysis are unjustifiably narrow. The range for sensitivity in the analysis are just 0.002 – 0.005. This is an incredibly small variance given the choice for the base case is already very shallow.

Additionally, given the heterogeneity, even within subgroups of CF patients, we believe it would be more appropriate to produce ranges, rather than means, for cost-effectiveness for a disease as diverse as CF. Averages are not consensus; they are just poor proxies for highly heterogeneous outcomes.

ICER's decision not to model with dynamic pricing leads to consistently flawed assessments.

ICER claims that it chooses not to incorporate the fact that drug prices change over time, as it would lead to a layer of uncertainty. However, it also states that numerous recently published models measuring the cost-effectiveness of cystic fibrosis drugs have indeed used dynamic pricing, suggesting ICER is willing to deviate from conventional methodologies often accepted by researchers and value assessors.

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[5] Becker CC, Clements K, Delong K, Harrow B, and O'Sullivan A (2011) "Economic Burden on Cystic Fibrosis in the U.S.: Costs of Care by Disease Severity and Age" Value in Health 14.

[6] Angelis, Aris et al. "Social and economic costs and health-related quality of life in non-institutionalised patients with cystic fibrosis in the United Kingdom." *BMC health services research* vol. 15 428. 28 Sep. 2015, doi:10.1186/s12913-015-1061-3

The relevance of dynamic pricing is heightened in conditions where consequences accrue over an extended period of time. CF is an obvious example of this. In fact, the ICER model assumes treatment continues for up to fifty years. This is in stark contrast to many other interventions which are either evaluated over a short time period, or for which the consequences of intervention only accrue over a short period of time.

Using static pricing in this context misunderstands how health care spending as well as uptake and integration of new technologies into health systems work. Uptake of new technologies does not happen overnight and does not begin at 100 percent utilization but rather happens slowly over time. When providing data for value attribution of a new technology within a living, evolving health system, the dynamic understanding of value is far more relevant than the static version. This point was made very clearly by Harvard researcher David Grabowski in a 2012 study of statins.[7]

Numerous studies have shown that using static prices in cost-effectiveness models make little sense when developing lifetime models.[8,9,10] While it is not impossible, it is highly unlikely that the price of these drugs will be the same in ten or twenty years, let alone fifty. The price pattern for the vast majority of drugs is that of significant decline following 5-7 years of relative stability and on average results in prices close to 10-20% of launch price after ten years.[11] This means that over the course of fifty years, relying on the launch price for the entire lifespan of each patient will likely overestimate costs between 300% and 400%.

We know ICER's reports have an impact on payer decisions and ultimately patient access. With that responsibility it is imperative ICER make every attempt to present accurate and unbiased information. Relying on static pricing runs counter to ICER's intention of painting a complete value picture.

Conclusion

ICER needs to reconsider its use of the QALY and model construction to ensure it is capturing an accurate picture of the value of treatments to patients. We are also very disturbed by ICER's statement that a drug for a devastating disease, even if curative, may not be worth the cost. We

[7] Grabowski DC, Lakdawalla DN, Goldman DP, Eber M, Liu LZ, Abdelgawad T, Kuznik A, Chernew ME, Philipson T. The large social value resulting from use of statins warrants steps to improve adherence and broaden treatment. Health Affairs. 2012 Oct 1;31(10):2276-85.
[8] 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.
[9] Healy P, Pugatch M. Capturing value: Why dynamic efficiency should be considered in the pricing and reimbursement of medicines. Stockholm: Stockholm Network. 2012.
[10] Vondeling GT, Cao Q, Postma MJ, Rozenbaum MH. The impact of patent expiry on drug prices: a systematic literature review. Applied health economics and health policy. 2018 Oct 1;16(5):653-60.
[11] Lichtenberg, F. R., & Duflos, G. (2009). The effect of patent expiration on US drug prices, marketing, and utilization by the public. Manhattan Institute for Policy Research.

disagree, as do the patients and families impacted by your analysis, that ICER should have the authority to determine the value of a patient with cystic fibrosis.

Sincerely.

Tony Coelho
Chairman
Partnership to Improve Patient Care