

October 15, 2021

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 on severe asthma. Asthma impacts about 25 million Americans, and it is a condition that disproportionately impacts Black and Hispanic patients. With this in mind, it is important that ICER handle this assessment in a way that does not exacerbate health inequities that are already very prevalent in the asthma community. PIPC requests ICER consider the following comments.

ICER's model is unrepresentative of real-world settings.

ICER takes its baseline inputs from placebo rates from randomized clinical trials (RCT) not from real world data – this makes the model unrepresentative of real-world settings.

The annual probability of an exacerbation of 1.82 per year was taken from the RCT placebo arms. We know that RCT populations are typically far healthier than the actual indicated population for the treatment. In the case of asthma, this is particularly concerning as communities of color are typically underrepresented in RCTs, and there are major racial disparities in the burden of asthma in the United States. A recent report by the Asthma and Allergy Foundation of America found that non-Hispanic Black Americans are almost three times as likely to die from asthma-related causes than non-Hispanic white Americans.¹

Recent studies designed to estimate the real world rate of exacerbation in a severe asthma population have showed a much higher rate of exacerbation, ranging from 2.68-3.97 per year;²

¹ Asthma and Allergy Foundation of America, "Asthma Disparities in America" (2020). <https://www.aafa.org/asthma-disparities-burden-on-minorities.aspx#pdf>. Accessed October 4, 2021.

² Llanos JP, Ortega H, Bogart M, Packnett ER, Manjelienskaia J, Bell CF, Hahn B. Real-world effectiveness of mepolizumab in patients with severe asthma: an examination of exacerbations and costs. *Journal of asthma and allergy*. 2020;13:77.

2.195 - 2.687 per year;³ 2.7 per year;⁴ 4.92 per year;⁵ and as much as 8.3 per year.⁶ All of these studies suggest a baseline exacerbation rate of at least 50% higher than that used by ICER and some suggest a rate greater than 400% higher than that used in the ICER model.

This reliance on RCT data, which does not include a representative population of asthma patients, leads to a model that underestimates the burden of the disease and as such an underestimate of the value of any incremental treatment effect.

PIPC continues to express concern with ICER’s consistent use of the Quality-Adjusted Life Year (QALY).

PIPC has consistently voiced concern with ICER continuing to rely on the QALY in its assessments despite its discriminatory implications for people with disabilities. In addition to its discriminatory impacts for people with disabilities, traditional cost-effectiveness assessments relying on the QALY have similarly discriminatory implications for communities of color, which bear a heavier burden of disease in asthma.

Most cost-effectiveness assessments rely on data from RCTs (issues with which we have touched on above) and health utility preference weighting surveys, which rely on inputs from primarily Caucasian populations. These assessments are largely based on outcomes to the “average” patient and do not account for patient subgroups. This means key components like social determinants of health are not captured, and ultimately treatments that may be very effective for minority populations can be undervalued.⁷

The model makes the likely incorrect assumption that the reduction in risk of exacerbation at 52 weeks seen in the RCTs is the peak of the treatment’s effectiveness.

Several studies have shown that the impact of continued biologics use improves over time.⁸ Effectiveness (particularly reduced exacerbation rates) improves year after year for at least four

³ Suruki RY, Daugherty JB, Boudiaf N, Albers FC. The frequency of asthma exacerbations and healthcare utilization in patients with asthma from the UK and USA. *BMC pulmonary medicine*. 2017 Dec;17(1):1-1.

⁴ Schleich F, Graff S, Nekoe H, Moermans C, Henket M, Sanchez C, Paulus V, Guissard F, Donneau AF, Louis R. Real-world experience with mepolizumab: Does it deliver what it has promised?. *Clinical & Experimental Allergy*. 2020 Jun;50(6):687-95.

⁵ Kavanagh JE, Hearn AP, Dhariwal J, d’Ancona G, Douiri A, Roxas C, Fernandes M, Green L, Thomson L, Nanzer AM, Kent BD. Real-world effectiveness of benralizumab in severe eosinophilic asthma. *Chest*. 2021 Feb 1;159(2):496-506.

⁶ Ibrahim H, O’Sullivan R, Casey D, Murphy J, MacSharry J, Plant BJ, Murphy DM. The effectiveness of reslizumab in severe asthma treatment: a real-world experience. *Respiratory research*. 2019 Dec;20(1):1-5.

⁷ National Minority Quality Forum et al. “Traditional Value Assessment Methods Fail Communities of Color and Exacerbate Health Inequities.”

⁸ Schleich F, Graff S, Nekoe H, Moermans C, Henket M, Sanchez C, Paulus V, Guissard F, Donneau AF, Louis R. Real-world experience with mepolizumab: Does it deliver what it has promised?. *Clinical & Experimental Allergy*. 2020 Jun;50(6):687-95.

years. This is not a factor that has been incorporated into the model, which only assumes the rate achieved in the RCT at year one.⁹

The choice of disutility for exacerbations used in the ICER model is an underestimate.

ICER calculated the disutility of an exacerbation from a study undertaken in the UK, which estimated that the health state utility of an asthma patient without exacerbation was 0.89, an exacerbation that did not lead to hospitalization would have a utility of 0.57, and an exacerbation that led to hospitalization a utility of 0.33.¹⁰ This would mean the disutility of a non-hospitalized exacerbation is -0.32 (0.89-0.57) and the disutility of an exacerbation that leads to hospitalization is -0.56 (0.89-0.33).

Yet, the ICER model uses a disutility of 0.1 and 0.2 for these two states, despite referencing this study as its source. It seems the cause of this error is misinterpretation of the data. A fourth column in table 2 of Lloyd (2007) represents the mean change in utility over the course of the data collection period and the estimates for this fall over time within states was 0.1 and 0.2 respectively. We believe these data were mistakenly used as estimates of mean disutility for exacerbation without hospitalization and exacerbation with hospitalization in the model.

In addition, the study also states that these utilities represent the mean for the patients over a one-month period for which data was collected. The ICER model applies these utilities for just 2 weeks (a single model cycle), so even if the disutilities used were correct, they would be providing half of the absolute disutility associated with the exacerbations themselves.

Taking into account both of these elements, the ICER model underestimates the disutility of exacerbation, and the absolute disutility for an exacerbation in the model is approximately one sixth of what it should be. As net benefit in the model is based largely on the rate and severity of exacerbations this means the incremental gain in health utility is likely to be six times higher than those calculated by the ICER model.

Conclusion

First, PIPC urges ICER to review the technical components of the model to ensure it is providing accurate results. Second, PIPC cautions ICER about the use of a QALY-based cost-effectiveness analysis relying on RCT data to evaluate treatments for asthma. It is likely that this will underestimate their benefit for patients and people of color and continue to exacerbate health disparities already experienced by asthma patients.

⁹ Menzies-Gow A, Corren J, Bourdin A, Chupp G, Israel E, Wechsler ME, Brightling CE, Griffiths JM, Hellqvist Å, Bowen K, Kaur P. Tezepelumab in Adults and Adolescents with Severe, Uncontrolled Asthma. *New England Journal of Medicine*. 2021 May 13;384(19):1800-9.

¹⁰ Lloyd A, Price D, Brown R. The impact of asthma exacerbations on health-related quality of life in moderate to severe asthma patients in the UK. *Primary Care Respiratory Journal*. 2007 Feb;16(1):22-7.

Sincerely,



Tony Coelho
Chairman
Partnership to Improve Patient Care