



May 27, 2021

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

Dear Dr. Pearson:

On behalf of the Asthma and Allergy Foundation of America (“AAFA”), the American Academy of Allergy, Asthma & Immunology (“AAAAI”) and the Allergy & Asthma Network (“AAN”), we would like to thank the Institute for Clinical and Economic Review (“ICER”) for the opportunity to comment on ICER’s Draft Scoping Document on the comparative clinical cost effectiveness and value of tezepelumab for the treatment of severe asthma. We appreciate ICER’s ongoing willingness to engage with us and to better understand patients’ perspectives.

Because of the major racial and ethnic disparities in the burden of asthma in the U.S., we are writing today to specifically urge ICER to use this review as an opportunity to identify and address the ways in which the data informing its analyses may reflect and even perpetuate biases in the healthcare and clinical trial systems. Our concerns are outlined below.

Asthma Disparities in the U.S.

AAFA has worked to address disparities in asthma prevalence and care for years. In AAFA’s recent report *Asthma Disparities in America: A Roadmap to Reducing the Burden on Racial and Ethnic Minorities*,ⁱ we detailed the serious and persistent racial and ethnic disparities in the burden of illness, including:

- Non-Hispanic Black Americans are almost three times as likely to die from asthma-related causes than non-Hispanic whites.ⁱⁱ
- Black children under age 15 die from asthma at a rate ten times higher than non-Hispanic white children.ⁱⁱⁱ
- Black women are 20% more likely to have asthma than non-Hispanic white women.^{iv}
- Children with asthma who belong to racial or ethnic minority communities have higher rates of hospitalization, more visits to emergency rooms, and higher mortality rates from asthma than white children.^v

As discussed in the report, the disparate burdens of asthma in the U.S. are rooted in deep structural inequities, including racism, that contribute to individual and community risk and

access to care.^{vi} Asthma disparities are exacerbated by social determinants that negatively impact health and wellbeing including poverty, lack of access to quality education or employment, unhealthy housing, unfavorable work or neighborhood conditions, exposure to neighborhood violence, and the clustering of poverty in particular groups of people and in particular places.

Equity in Clinical Trials

We are particularly concerned that the underrepresentation of racial and ethnic minority populations in clinical studies – despite the higher burden of asthma they experience – creates a systematic bias in the data on which ICER relies.

As you are aware, AAFA has joined with other organizations in the past expressing concern about ICER’s reliance on QALYs.^{vii} An overarching concern is that metrics depend on averages across what may be highly heterogeneous patient populations – within which people may differ considerably in their experience of the disease and what factors they value in assessing their own quality of life. Furthermore, QALYs devalue the lives of people with chronic conditions and other disabilities compared to those considered to be in objectively “perfect” health. The use of eLYGs can mitigate some of the quality of life concerns, but still fails to capture the range of clinical and personal experiences of disease, and of treatment, across patient populations.

AAFA’s work on disparities in asthma underscore the further concern of the underlying underrepresentation of racial and ethnic minorities in clinical trials. In clinical research in the U.S., racial and ethnic minorities are broadly underrepresented. For example, from 1993-2013, only 1.9% of all studies of respiratory disease (and less than 5% of NIH-funded studies) formally reported inclusion of racial or ethnic minority subjects.^{viii} Therefore, most cost-effectiveness analyses, including those used to estimate cost per QALY, rely on data from clinical trials that disproportionately focus on Caucasian participants.

As the National Minority Quality Forum (NMQF) has described, this pattern means that the data informing cost effectiveness assessments “compromises the clinical validity of data and information regarding disease presentation and therapeutic responses and findings regarding safety and efficacy.”^{ix} For a given analysis, this results in a lack of meaningful information on which to develop an understanding of how a disease, and treatment, may affect racial and ethnic minorities. In the aggregate, the pattern creates a systematic bias that favors medications that are more effective for Caucasians and disfavors those that effective for minority populations. As NMQF explains:

For example, if a particular therapy is effective for an African American population, but less effective for a Caucasian population, but the enrolled trial cohort is dominantly Caucasian, with

African Americans under-represented, its average effect size demonstrated by the RCT will be small, and the therapy will have a lower chance of being approved.

Conversely, if a therapy is highly effective for Caucasians and less effective for African Americans, with a similar distribution of RCT participants as before, this will result in an overestimation of the effect size and increase its chance of being approved. Multiply this effect by the hundreds and thousands of trials that have evaluated the thousands of therapies that have been approved – or not – over the decades and you have a systematic bias of available therapies that favor Caucasians to the detriment of African Americans and other disenfranchised patients and communities.^x

This distortion of the data extends to cost-effectiveness analyses, which can impact payers' willingness to cover certain drugs, thereby conditioning access on racially nonrepresentative data.

Recommendations

The challenge of increasing representation of racial and ethnic minorities in clinical trials is longstanding and complex. As AAFA detailed in our disparities report, major steps are needed on the part of funders, industry, and academic institutions to increase representation of Black, Hispanic, and Indigenous people in clinical trials for asthma and other respiratory diseases.^{xi}

While we do not expect ICER to solve this problem, we believe it is time for ICER to more explicitly acknowledge the impact of underrepresentation in clinical trials on the entirety of the evidence that informs ICER's analyses. To that end, because of the major and unacceptable disparities in asthma prevalence and care, we urge ICER to use the tezepelumab review as an opportunity to start analyzing and reporting on key issues related to equity in trial data. Black Americans are three times more likely to die from asthma than white Americans. Black Americans are also five times more likely treated for asthma in hospital emergency rooms compared to white patients.^{xii} We encourage ICER to consider and report on information such as:

- The extent to which racial and ethnic minority populations were represented in each of the clinical trials used to inform ICER's analysis;
- Whether the data are sufficient to provide effectiveness and cost-effectiveness analyses by racial or ethnic group;
 - If the data are sufficient, whether it is feasible to develop weighted estimates that would reflect outcomes if racial and ethnic minorities were proportionately represented in the clinical trials;
 - If the data are not sufficient, what gaps this creates in understanding of the effectiveness, and cost-effectiveness, of the treatment for different populations;

- Whether disparities in the burden of a given disease mean that an “average” effectiveness has different implications for different groups. For example, if Black adults are more likely to be hospitalized for a given disease, does a drug showing reductions in hospitalization rates mean that it would be particularly important for Black populations?

This level of engaging with the data is crucial if ICER intends to meaningfully address equity in this, and future, analyses.


Conclusion

Thank you very much for your time and attention. We look forward to continuing to work with ICER to reflect the diverse patient experience among those with asthma, and to begin to address the impact of the systematic racial biases that affect healthcare and clinical trials.

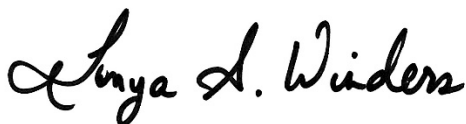
Sincerely,



Kenneth Mendez
President & CEO
Asthma and Allergy Foundation of America



Giselle Mosnaim, MD MS FAAAAI
President
American Academy of Allergy, Asthma & Immunology



Tonya A. Winders
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ⁱ Asthma and Allergy Foundation of America, “Asthma Disparities in America” (2020). Available at <https://www.aafa.org/asthma-disparities-burden-on-minorities.aspx#pdf>

ⁱⁱ *Id.*

ⁱⁱⁱ Office of Minority Health. Asthma and African Americans. U.S. Department of Health and Human Services. Available at: <https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=4&lvlid=15>

^{iv} *Id.*

^v Anna Volerman, Marshall H. Chin and Valerie G. Press. Solutions for Asthma Disparities. *Pediatrics* March 2017, 139 (3) e20162546; DOI: <https://doi.org/10.1542/peds.2016-2546>

^{vi} Asthma and Allergy Foundation of America, “Asthma Disparities in America” (2020). Available at <https://www.aafa.org/asthma-disparities-burden-on-minorities.aspx#pdf>

^{vii} Letter from Patient Groups to Dr. Steven Pearson regarding ICER 2020 Value Assessment Framework (October 19, 2019). Available at <https://www.aafa.org/media/2497/aafa-sign-on-letter-icer-proposed-updates-2020-value-assessment-framework.pdf>

^{viii} Burchard EG, Oh SS, Foreman MG, Celedón JC. Moving toward true inclusion of racial/ethnic minorities in federally funded studies. A key step for achieving respiratory health equality in the United States. *Am J Respir Crit Care Med.* 2015 Mar 1;191(5):514-21. doi: 10.1164/rccm.201410-1944PP. PMID: 25584658; PMCID: PMC4384771.

^{ix} National Minority Quality Forum, “Traditional Value Assessment Methods Fail Communities of Color and Exacerbate Health Inequities White Paper.” Available at <https://www.nmqf.org/nmqf-media/traditional-value-assessment-methods>

^x *Id.*

^{xi} Asthma and Allergy Foundation of America, “Asthma Disparities in America” (2020). Available at <https://www.aafa.org/asthma-disparities-burden-on-minorities.aspx#pdf>

^{xii} *Id.*