

Correspondence and Replies

Ethnicity-based differences in asthma diagnostic thresholds



To the Editor:

We read with great interest Busby et al's¹ findings of ethnic differences in severe asthma and congratulate the authors on their robust findings. They report a disproportionate disease burden, with patients from ethnic minority groups (EMGs) compared with nonethnic minority patients (non-EMG) in severe asthma, in specialist clinics, and from primary care consultations.

Interestingly, the authors suggest that EMG patients with severe asthma have a more severe biological profile compared with their non-EMG patient counterparts, irrespective of asthma severity. The authors discuss that the proportion of EMG and non-EMG referrals to secondary care respiratory medicine specialists is not significantly different and there is no ethnicity-based bias in diagnosing severe asthma, leading us to conclude that the T2 inflammatory profile is likely to be different. Although this is a thought-provoking hypothesis, it is particularly important to address the differences in smoking rates between the EMG and non-EMG patients in this dataset. Busby et al show conclusively that there are significantly fewer smokers in the non-EMG population, despite there being no difference in UK smoking rates when adjusted for age between EMG and non-EMG populations.² Perhaps it is worth considering that a non-EMG patient is more likely to be diagnosed with severe asthma (ie, the threshold for diagnosis is lower), whereas a former smoker in the EMG population is more likely to be diagnosed with an alternative diagnosis (such as chronic obstructive pulmonary disease [COPD]), leading to a potential delay in diagnosis.

Bias in the diagnosis of asthma is well documented. In particular, women are more likely to be diagnosed with asthma than men despite presenting with similar symptoms,³ whereas adults limited by disability are less likely to be diagnosed with asthma.⁴ We propose that this may also be true for smoking and ethnicity, and this can be conceptualized in Figure 1; although the respiratory referral and severe asthma diagnosis is found to be equal between non-EMG and EMG patients, it is quite possible that the threshold to be diagnosed with asthma is different.

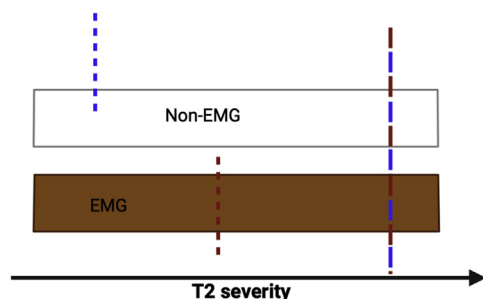


FIGURE 1. Our hypothesis of differential thresholds to diagnose asthma. The blue dotted line is non-EMG threshold for asthma. The red dotted line is EMG threshold. The red and blue dotted line is coding threshold for severe asthma. EMG, Ethnic minority group. Created with [Biorender.com](https://biorender.com).

Specifically, we note that a coding diagnosis of COPD was an exclusion in this analysis but would be interested to know if the authors have reviewed the EMG/non-EMG proportion of patients excluded from the analysis.

Christine Mwasuku, PGDip^{a,b}
Sanjay Ramakrishnan, MBBS^{a,b,c}
Mona Bafadhel, MBChB, PhD^{a,b}

^aRespiratory Medicine Unit, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, United Kingdom

^bNational Institute for Health Research (NIHR) Oxford Biomedical Research Centre (BRC), Oxford, United Kingdom

^cSchool of Medical and Health Sciences, Edith Cowan University, Perth, WA, Australia. No funding was received for this work.

Conflicts of interest: The authors declare that they have no relevant conflicts of interest. Received for publication November 12, 2021; Revised November 17, 2021; accepted for publication November 17, 2021.

Corresponding author: Christine Mwasuku, PGDip, Nuffield Department of Medicine, Old Ronald McDonald House, John Radcliffe Hospital, Oxford OX3 9DU, United Kingdom. E-mail: Christine.mwasuku@ndm.ox.ac.uk.

REFERENCES

1. Busby J, Heaney LG, Brown T, Chaudhuri R, Dennison P, Gore R, et al. Ethnic differences in severe asthma clinical care and outcomes: an analysis of United Kingdom primary and specialist care. *J Allergy Clin Immunol Pract* 2022;10:495-505.
2. Read UM, Karamanos A, João Silva M, Molaodi OR, Enayat ZE, Cassidy A, et al. The influence of racism on cigarette smoking: longitudinal study of young people in a British multiethnic cohort. *PLoS One* 2018;13:e0190496.
3. Chapman KR, Tashkin DP, Pye DJ. Gender bias in the diagnosis of COPD. *Chest* 2001;119:1691-5.
4. Bellia V, Battaglia S, Catalano F, Scichilone N, Incalzi RA, Imperiale C, et al. Aging and disability affect misdiagnosis of COPD in elderly asthmatics: the SARA study. *Chest* 2003;123:1066-72.

<https://doi.org/10.1016/j.jaip.2021.11.036>

Reply to "Ethnicity-based differences in asthma diagnostic thresholds"



To the Editor:

We have read with interest the correspondence by Mwasuku et al¹ in response to our paper exploring ethnic differences in severe asthma within UK primary and specialist care.² With regard to the specific issue of the elevated T2 biomarker profile in ethnic minority group (EMG) patients, and whether this may be a result of bias for/against asthma diagnosis by smoking status, we think this is unlikely. In particular, our analysis of T2 biomarkers (total IgE, fractional exhaled nitric oxide [FeNO], and blood eosinophil count) demonstrated significantly elevated levels among EMGs even after adjustment for body mass index and smoking status (Figure E2). Furthermore, we have now repeated our analyses but restricted to patients who had never smoked, where this bias should be largely mitigated due to the much lower prevalence of chronic obstructive pulmonary disease (COPD).³ This did not alter our conclusions, and we found higher levels of uncontrolled asthma among EMGs in both primary (65% vs 48%) and specialist (84% vs 79%) care when compared with White patients. Within specialist care, we also found substantially higher median blood eosinophils (400 vs 300 cells/ μ L) and FeNO (45

vs 36 ppb) among EMG patients, consistent with our overall results.

We believe that a potentially important driver of the higher inflammatory profile among EMG patients reported in our study is less effective use of asthma treatment, as it is known that T2 biomarkers are highly corticosteroid responsive.⁴ Consistent with our results, recent evidence from the RASP-UK program has demonstrated that minority ethnicity was associated with a lower likelihood of following treatment advice, even within the strict confines of a randomized controlled trial.⁵ This is perhaps unsurprising given that patient self-management strategies are often designed from the perspective of the majority population without tailoring to the health and cultural beliefs of EMGs.⁶

However, with regard to the general issue of ethnicity as a potential cause for bias or delay in asthma diagnosis, we wholeheartedly agree that this is an important question. Ultimately, there are a series of steps in the patient journey in severe asthma before initiation of appropriate treatment. First, a patient must recognize that he or she has ill-health requiring medical assessment, and secondly, he or she must be able to access health services. Thirdly, a correct diagnosis of asthma must be made. Fourthly, its severity must be recognized and referral made to a severe asthma center, and fifthly, specialist therapies such as biologics commenced. In our recent paper, we aimed to specifically address the later steps and would agree with Mwasuku et al¹ that potential inequalities by ethnicity in the earlier steps of this patient journey require further investigation.

We agree that bias by ethnicity in the diagnosis of asthma versus COPD is of particular interest given that they share many treatable traits. Although inhaled therapies are similar between asthma and COPD, in most health care systems, only patients with a diagnostic label of asthma have access to biologic therapies (although there is emerging evidence that they may also be beneficial in COPD). Delays in diagnosis are also of underappreciated importance for our patients. Although delays are not known to affect T2 biomarkers, they may result in long-term lung function decline and increased levels of steroid-related morbidity. We agree that there is much further research to do.

John Busby, PhD^a

Liam G. Heaney, MRCP, MD^{a,b}

Paul E. Pfeffer, MRCP, PhD^c

on behalf of the UK Severe Asthma Registry

^aSchool of Medicine, Dentistry and Biomedical Sciences, Queen's University, Belfast, United Kingdom

^bBelfast Health & Social Care NHS Trust, Belfast, United Kingdom

^cBarts Health NHS Trust, London, United Kingdom.

No funding was received for this work.

Conflicts of interest: J. Busby declares no relevant conflicts of interest. L. G. Heaney is Academic Lead for the Medical Research Council Stratified Medicine UK Consortium in Severe Asthma, which involves industrial partnerships with a number of pharmaceutical companies. P. Pfeffer has attended advisory board for Novartis; has given lectures at meetings with/without lecture honoraria supported by AstraZeneca and GlaxoSmithKline; has taken part in clinical trials sponsored by AstraZeneca, GlaxoSmithKline, and Novartis; and is conducting research funded by GlaxoSmithKline for which his institution receives remuneration.

Received for publication January 14, 2022; accepted for publication January 14, 2022.

Corresponding author: John Busby, PhD, Centre for Public Health, Royal Victoria Hospital, Belfast BT12 6BA, United Kingdom. E-mail: john.busby@qub.ac.uk.

REFERENCES

1. Mwasuku C, Ramakrishnan S, Bafadhel M. Ethnicity-based differences in asthma diagnostic thresholds. *J Allergy Clin Immunol Pract* 2022;10:1124-5.
2. Busby J, Heaney L, Brown T, Chaudhuri R, Dennison P, Gore R, et al. Ethnic differences in severe asthma clinical care and outcomes: an analysis of United Kingdom primary and specialist care. *J Allergy Clin Immunol Pract* 2022;10:495-505.
3. Lamprecht B, McBurnie MA, Vollmer WM, Gudmundsson G, Welte T, Nizankowska-Mogilnicka E, et al. COPD in never smokers: results from the population-based burden of obstructive lung disease study. *Chest* 2011;139:752-63.
4. Busby J, Khoo E, Pfeffer PE, Mansur AH, Heaney LG. The effects of oral corticosteroids on lung function, type-2 biomarkers and patient-reported outcomes in stable asthma: a systematic review and meta-analysis. *Respir Med* 2020;173:106156.
5. Busby J, Matthews JG, Chaudhuri R, Pavord ID, Hardman TC, Arron JR, et al. Factors affecting adherence with treatment advice in a clinical trial of patients with severe asthma. *Eur Respir J*. Published online September 24, 2021. <https://doi.org/10.1183/13993003.00768-2021>
6. Ahmed S, Pinnock H, Steed E. Developing theory-based asthma self-management interventions for South Asians and African Americans: a systematic review. *Br J Health Psychol* 2021;26:1040-68.

<https://doi.org/10.1016/j.jaip.2022.01.027>

Severe topical corticosteroid withdrawal syndrome or enigmatic drug eruption?



To the Editor:

We recently read with great interest the report authored by Nguyen et al¹ regarding a possible severe topical corticosteroid (TCS) withdrawal syndrome (TCWS) case presenting in an adult with chronic atopic dermatitis using low-dose topical corticosteroids. TCWS is a rare entity, with the current literature remaining sparse and exhibiting low quality of evidence. As discussed in the National Eczema Association systematic review of topical corticosteroid withdrawal, this distinct clinical adverse event is likely correlated to the improper use of TCSs.²

As with the use of any medication, common and rare adverse events are important points of discussion. TCSs consistently demonstrate efficacy in improving skin lesion severity and quality of life in patients with inflammatory skin conditions.³ They are considered the first-line therapy for patients with atopic dermatitis and with appropriate step-up and step-down approaches have an excellent safety profile—this is especially true for low-potency TCSs such as class VII hydrocortisone used in the highlighted case.

In spite of TCWS being a poorly characterized disorder, there is a growing presence in social media. Importantly, there is a need to mitigate the spread of misinformation, which can lead to unnecessary avoidance of an important treatment mainstay of several dermatologic conditions and delay in diagnoses and increase unnecessary anxiety. Importantly as stated above, TCWS is a rare disorder lacking clear diagnostic criteria and should be considered a diagnosis of exclusion. Indeed, it is a diagnosis that requires careful consideration because overdiagnosis may lead to health care professionals avoiding prescribing safe and inexpensive TCSs and negatively impact patient adherence and acceptance of an important therapeutic option.

Clinically, TCWS tends to present predominantly with burning/stinging as the primary symptom, rather than the intense pruritis with oozing and crusting, fever, and malaise as described