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Title:

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Date:

2021-06-01

Citation:

Pham, J., Hew, M. & Dharmage, S. C. (2021). Is ethnicity a 'treatable trait' in asthma?. *Respirology*, 26 (6), pp.529-531. <https://doi.org/10.1111/resp.14058>.

Persistent Link:

<https://hdl.handle.net/11343/298442>

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Editorial Office Notes:

RES-21-220.R1

COMMENTARY

Publication Fee Waiver: NO

Volume number: 26

Author Manuscript

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: [10.1111/resp.14058](https://doi.org/10.1111/resp.14058)

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Is ethnicity a ‘treatable trait’ in asthma?

Key words: Asthma, ethnicity, phenotype

Asthma is a global health problem but certain ethnic groups exhibit substantially poorer outcomes than other populations.(1-3) Research in such ethnic minorities is limited, so traditional treatment approaches are predominantly based on data derived from Caucasian individuals – applying, in short, a one-size-fits-all model.(4-8) However, there is growing evidence that asthma phenotypes and treatment responses may vary considerably between ethnicities.(9-11) Understanding these interactions has the potential to refine and even re-define personalised asthma care.

When investigating the link between ethnicity and asthma, the first challenge encountered is that of defining ethnicity. An individual’s ethnicity may be categorised in a variety of ways, and these categorisations may not be interchangeable: (1) nationality – where one resides and/or the country to which one has a sense of belonging; (2) cultural affiliation – the cultural norms which the individual has adopted and the ethnic community to which they belong; (3) genetic ancestry – the genetic composition of an individual that is inherited from ancestors of a certain geographic location (eg. Africa or Europe). In essence, these represent environmental, behavioural and genetic factors, as shown in Figure 1.

Ecological studies have been a cost-effective way to investigate the association between ethnicity and asthma. However, comparisons of asthma prevalence across countries can be difficult owing to differences in how symptoms are reported, and variability in the way objective measures such as spirometry (when available) are performed. Data from the World Health Survey in 2002 using self-reported doctor diagnosis, showed that Australia and many countries in Europe had the highest prevalence of asthma in adults (in the order of 20%) compared to countries in Asia, of which the vast majority had a prevalence between 0% and 10%.(3) Notably however, this study was unable to collect

any data from the United States and Canada, representing a major gap in the global picture. Even with more complete datasets, simply reporting a single asthma prevalence for each country assumes a homogenous population with one risk profile for asthma, and overlooks potential variation between host population and indigenous or migrant/ethnic minority groups.

More informative have been comparisons of asthma outcomes between ethnic groups within a single country. In the United States, African American children have more than double the incidence of asthma than the Caucasian host-population.(1) African Americans also have higher rates of hospitalisation and mortality related to asthma than any other ethnic group in the United States.(2) In Australia, Asian migrants are more susceptible to asthma and allergy compared to Caucasian Australians. Descriptive studies have shown an increase in the prevalence of asthma and hay fever in Asian migrants and their offspring, increasing with duration of residence in Australia.(12, 13) Individuals of South-East Asian and Indian descent were disproportionately affected during the 2016 Melbourne thunderstorm asthma epidemic, and represented the majority of deaths that occurred from this environmental phenomenon.(14)

Childhood microbial exposure may explain some of the differences in asthma prevalence observed between ethnic groups. A study by *Stein et al.* compared Amish and Hutterite communities in the United States, both traditional farming-based cultures with similar European genetic ancestry.(15) Amish children had a profoundly lower prevalence of asthma, possibly related to higher airborne endotoxins exposure from farm animal dander, and specific to cultural farming practices. Conversely, exposure to other environmental microbes may be a risk factor for asthma. The increased prevalence of asthma amongst African Americans may be a consequence of socio-economic disadvantage, via sub-standard housing which predisposes to household cockroach and mould exposure and sensitisation, commonly found amongst asthmatics living in urban settings.(16)

While culture and genetics are both expressions of ethnicity, their individual associations with asthma may differ. In the United States, each decile increase in European genetic ancestry had a 0.85-fold risk of recurrent childhood wheeze when compared to an equivalent increase in African genetic ancestry – that is, compared to African ancestry, European ancestry is protective of asthma.⁽¹⁷⁾ A similar trend was found using self-reported ‘White’ ethnicity instead of genetic ancestry, but the results were not statistically significant due to a wide confidence interval, suggesting lack of study power. There are two possible explanations for this; (i) genetic ancestry has a true effect on asthma risk, whereas self-identified ethnicity, as a proxy for cultural behaviours, does not; (ii) there is more variation in the (subjective) reporting of self-identified ethnicity than in the (objective and more precise) measurement of genetic ancestry. It is also conceivable that both phenomena occur in tandem.

Compounding the differential risk profiles for the development of asthma in ethnic populations, there is also emerging evidence for differential responses to treatment amongst these populations. For decades, the mainstay of asthma management has been a generic step-up model of care, based largely on research in Caucasian populations.⁽⁵⁻⁸⁾ Now, in a study of children in the United States with asthma refractory to first-line inhaled corticosteroid (ICS) therapy, Hispanic and non-Hispanic white children tended to respond better to the addition of a long acting beta agonist (LABA) rather than escalating to high-dose ICS alone, consistent with international guidelines.⁽⁴⁾ However, in the same study, African American children had equally favourable responses to either ICS-LABA or high-dose ICS alone.⁽⁴⁾ This data presents a strong argument against the one-size-fits-all treatment algorithms used in traditional clinical practice.

Personalised medicine represents a new paradigm in asthma management, with great potential to improve health care in vulnerable ethnic groups. Rather than grouping all asthmatics together, this approach involves identifying key characteristics in an individual (commonly referred to in airways

disease as ‘treatable traits’) that can then be targeted for treatment. Of note, mainstream approaches are yet to include ethnicity in assessment matrices. Research has also identified specific clusters of characteristics or phenotypes that can predict disease severity, clinical course and treatment response. However, such phenotypes can be present in one ethnic group but absent in others. Appreciating the nuances of disease expression among ethnic groups is therefore of paramount importance in the management of asthma. For example, in Caucasians populations, an adult onset, obese, female phenotype has been identified.(9) Individuals of this phenotype typically exhibit frequent exacerbations and resistance to corticosteroid therapy.(18, 19) However, cluster analysis of the Singaporean population has demonstrated that, while a similar phenotype exists in indigenous Malays, it is absent in Chinese individuals.(10)

In light of the above discussion, the following strategies are needed to fully examine the effects of ethnicity on asthma; (i) large study cohorts with sufficient representation across ethnicities, in order to provide sufficient statistical power for analysis; (ii) examination of a wide range of variables, to help tease out true causal pathways and avoid making spurious associations, and; (iii) advanced statistical methods, to elucidate complex relationships between health, genetics, environment, behavioural factors and socio-economics. Such undertakings will yield a multitude of benefits to both science and clinical medicine. Understanding what cultural behaviours or genetic factors mediate asthma expression would aid in risk factor modification for primary and secondary prevention strategies. Understanding how asthma phenotypes are exhibited in ethnic populations would also assist clinicians to predict the clinical course of disease and response to treatment in select individuals, and may even help to identify new targets for therapeutic intervention. Ultimately, advances in this area of asthma research should enhance the provision of individualised and effective treatment for vulnerable ethnic groups.

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Acknowledgements: This work is supported by the National Health and Medical Research Council of Australia grant 2005237.

Conflict of Interest Statement: The authors declare that they have no conflicts of interest

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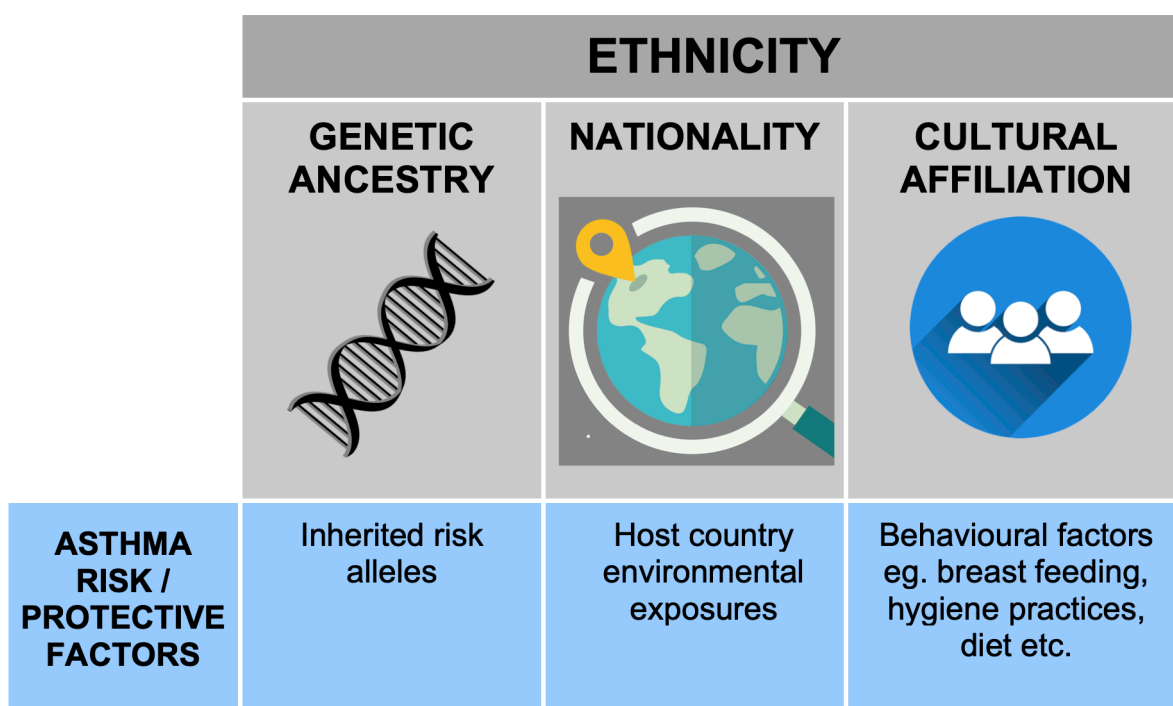
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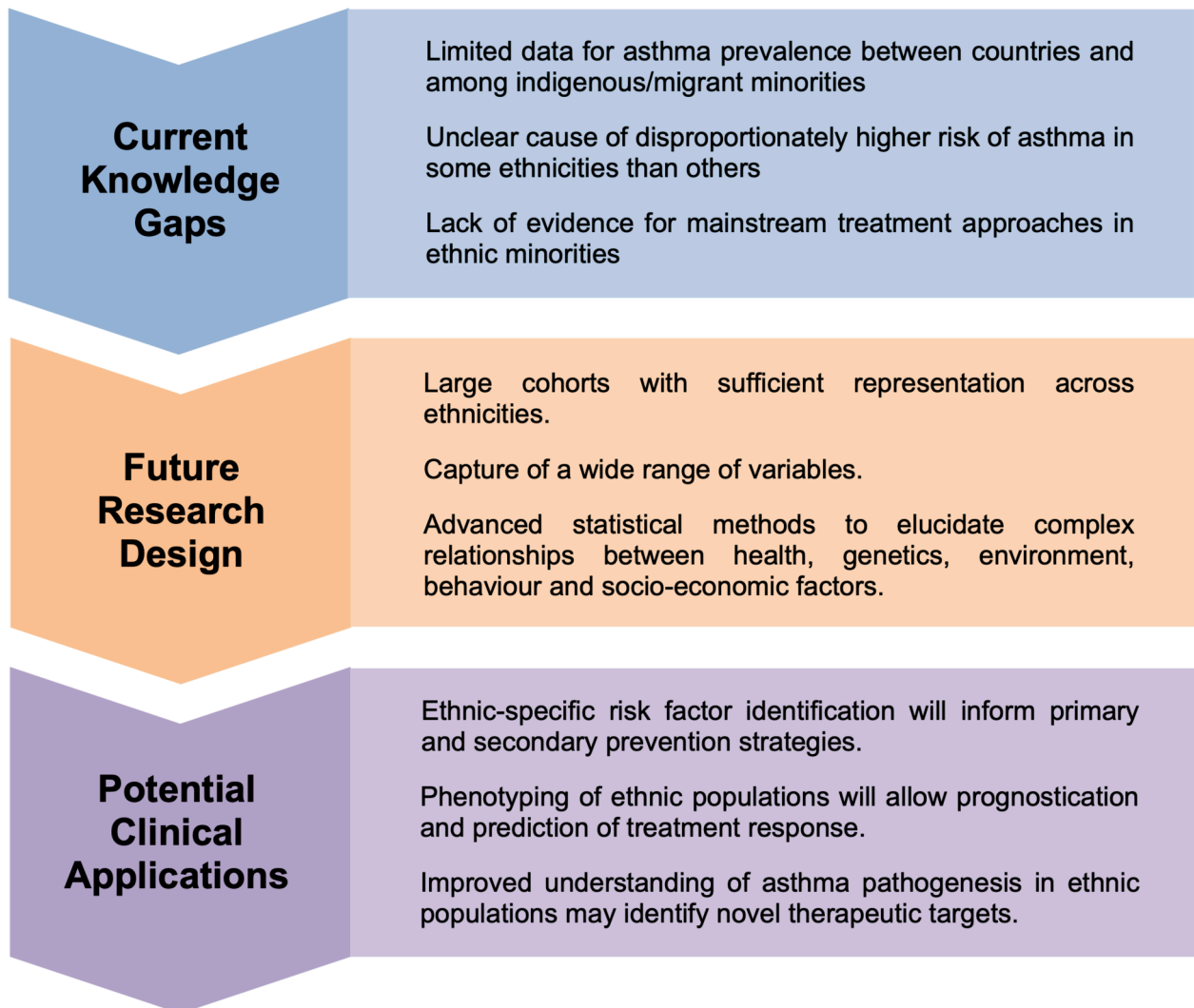
Figure Legend

Figure 1. The determinants of ethnicity can predispose to or protect against asthma.

Figure 2. Translating research in ethnic populations into clinical management of asthma.



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RESP_14058_Figure 2 ethnicity asthma 200321.tiff