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RESEARCH LETTER

Ethnicity-based differences in the incident risk of allergic diseases and autoimmune disorders: A UK-based retrospective cohort study of 4.4 million participants

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To the Editor,

The burden of allergic diseases (ADs) such as asthma and rhinitis and autoimmune disorders (AIDs) such as rheumatoid arthritis (RA) is relatively low/moderate in low- and low-middle-income countries,[1,2] and there is some evidence regarding higher incidence rates of these conditions amongst immigrant population settled in high-income countries.[3,4] The burden of ADs is particularly high in high-income countries such as the UK, Republic of Ireland and New Zealand.[1] Studies in immigrants have been limited by several factors including relatively small sample size, shorter duration and methodological issues such as selection bias, survey- or questionnaire-based data, focus on a single or limited number of ADs or AIDs, and some not accounting for important disease confounders such as smoking history.

Limited data sets are available on ethnicity-based comparative incident risk of AIDs such as myasthenia gravis, autoimmune thyroid disease (ATD), pernicious anaemia, vitiligo and coeliac disease in high-income countries. Knowledge of the risk of immune-mediated conditions in ethnic minority groups settled in high-income countries may yield useful clues regarding the role for genetic and environmental factors in disease pathogenesis.

In this large comprehensive population-based cohort study (e-methods & study flow diagram in Supporting Information), we performed a comparative analysis of incident risk of common ADs including asthma, allergic rhinitis/conjunctivitis (ARC) and atopic eczema (AE) and a range of AIDs (RA, Sjogren's syndrome, systemic lupus erythematosus [SLE], inflammatory bowel disease [IBD], coeliac disease, pernicious anaemia, psoriasis, vitiligo, myasthenia gravis, ATD and multiple sclerosis) in ethnic minority groups *versus* White ethnicity in the UK. Data were extracted from The Health Improvement Network (THIN, a UK primary care database). Over a 10-year study period (01 January 2006-31 December 2016), we included a very large sample size of ~4.4 million participants (baseline characteristics; Table S1) registered in primary care, of whom 602 627 belonged to ethnic minorities providing sufficient statistical power to detect differences. Our data set is generalizable[5] to the UK population and all clinical diagnoses and outcomes

Krishnarajah Nirantharakumar and Mamidipudi Thirumala Krishna are joint last authors.

were physician-documented. We determined adjusted incident rate ratios (aIRRs) of these conditions amongst three major ethnic minority groups, including South Asians, Afro-Caribbeans and mixed-race/other ethnic minorities, and compared with people in the White ethnic group, after adjusting for relevant potential confounding variables.

There were significant ethnicity-based differences in multiple ADs and AIDs, and these are summarized in Figures 1 and 2 (relevant data in Table S2).

Whilst incidence rates of ARC and AE were uniformly higher in the three ethnic minority groups, asthma was only modestly higher amongst South Asians, but lower amongst Afro-Caribbean and mixed-race/other ethnicities. Our findings are in keeping with some published evidence from high-income countries that incidence rates or risk of some ADs is higher amongst their non-native population.[6,7]

The incidence of RA and pernicious anaemia was significantly higher amongst South Asians but not in Afro-Caribbeans and mixed-race/other ethnic minority group. There is limited evidence that prevalence of RA is relatively lower in low- and low-middle-income countries.[2] This may in part be explained by confounders such as relatively lesser health education in the population, differences in health service framework and data reporting systems in these countries, although it plausible that an enhanced risk seen in this study may also be due to potential influence of environmental factors. Prevalence data on pernicious anaemia in low- and low-middle-income countries are sparse.

The incidence of Sjogren's syndrome was higher in South Asians and showed a similar trend in mixed-race/other ethnicity group. This is in alignment with a French study that reported a higher risk of primary Sjogren's syndrome amongst people of non-European race/ethnicity.[4]

Interestingly, the incidence of SLE, vitiligo and ATD was uniformly higher in all three ethnic minority groups included in the study. The highest incidence of SLE observed in Afro-Caribbean group is well recognized and provides external validity for our data set. We showed nearly a fivefold higher incidence of vitiligo in South Asians and a >2.5-fold higher incidence in Afro-Caribbeans and mixed-race/other ethnic minority group in comparison with White ethnicity. A recent meta-analysis[8] reported a relatively low prevalence of vitiligo in Asia, a relatively higher prevalence in Africa and Europe and the highest prevalence in Oceania. This however is not directly comparable to our study considering the differences in ethnic stratifications (ie, South Asians in our study versus a variety of Asians in the meta-analysis).

In contrast, the incidence of multiple sclerosis was lower across all ethnic minority groups compared with White ethnicity. As regards psoriasis, coeliac disease and IBD, the incidence was lower amongst Afro-Caribbean and mixed-race/other ethnic minority group. However, no significant differences were seen between ethnic groups and White population for myasthenia gravis.

This study has limitations. First, data on ethnicity were not available for approximately 50% of patients. However, a study on completeness and usability of primary care ethnicity data suggests that the available data are comparable to the UK 2011 census (Table S3) and supports use of primary care ethnicity data for research from 2006 onwards.[9] Second, data regarding country of birth, immigrant status and number of resident years in the UK were not available and thus not factored into our analysis. Third, serological data regarding sensitization status for ADs

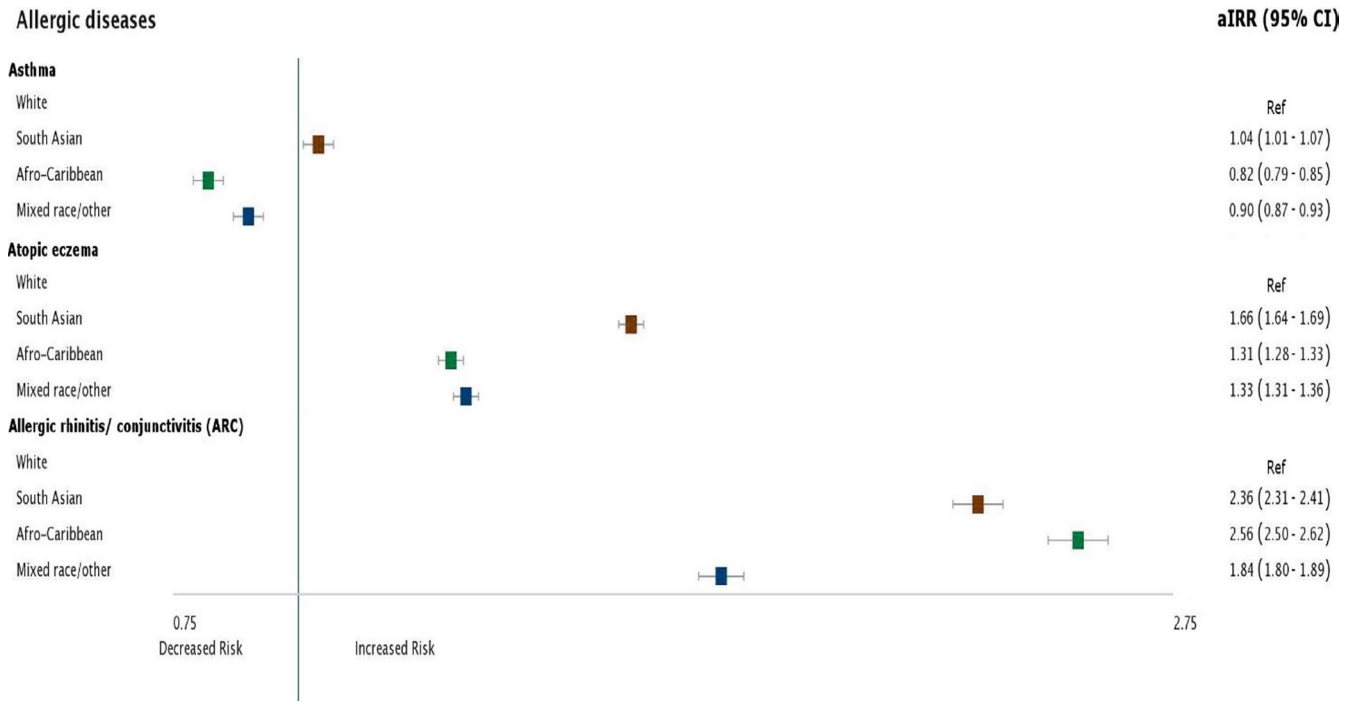

FIGURE 1 Forest plot summarizing aIRRs of allergic diseases

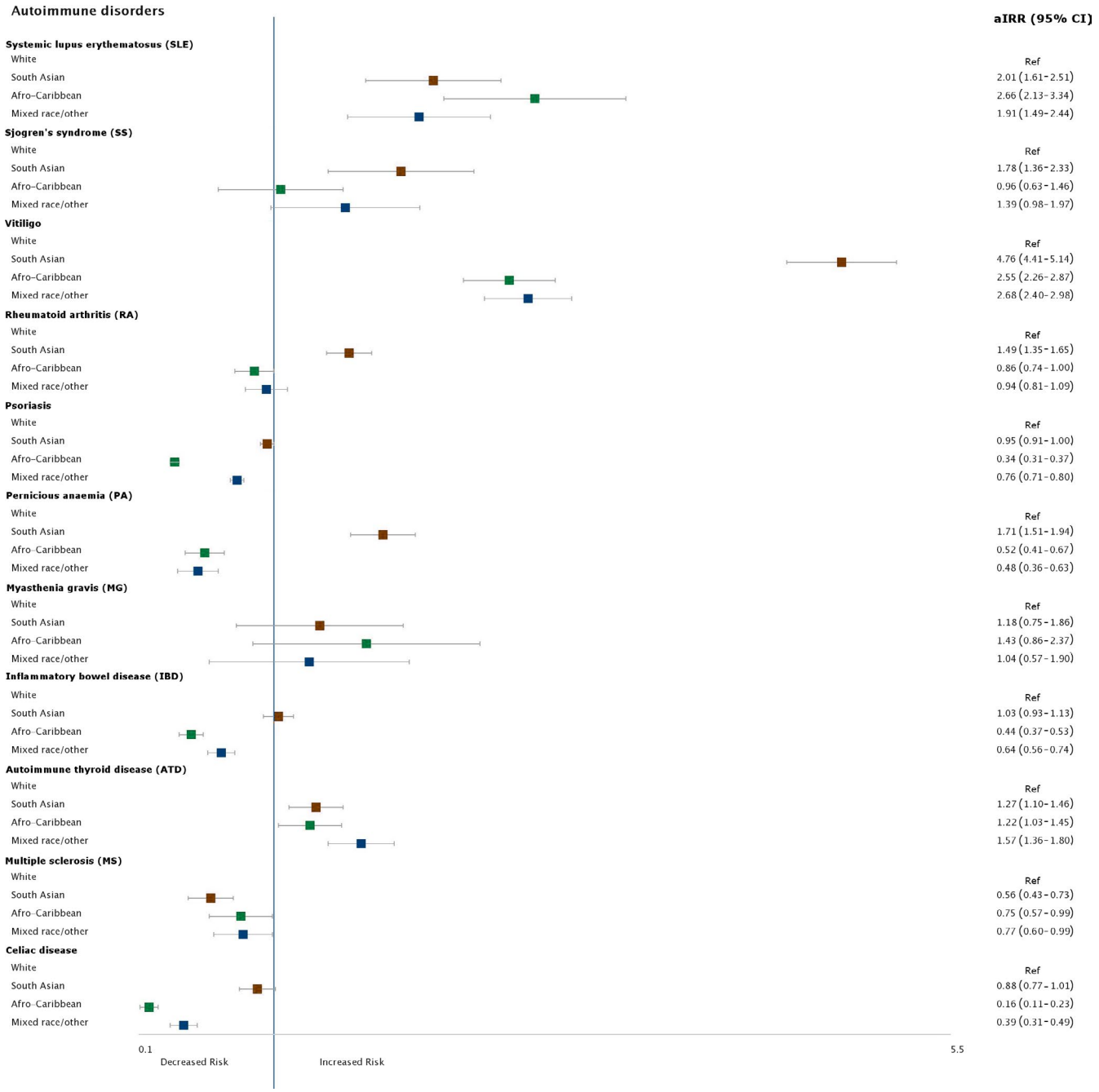

FIGURE 2 Forest plot summarizing aIRRs of autoimmune disorders

and autoimmune serology for AIDs were not captured. However, for AIDs including IBD, RA, SLE, Sjogren's syndrome, coeliac disease and myasthenia gravis, all patients would have received their diagnosis from a specialist in secondary care as per standard UK National Health Service (NHS) practice. It is, however, plausible that relatively mild or straightforward cases of ATD, vitiligo and pernicious anaemia may not have received specialist input. Fourth, the majority of ADs are managed by primary care physicians in the UK NHS, thereby raising the possibility of potential diagnostic inaccuracy and/or miscoding. Finally, exposure time before study entry was not considered in our incident rate calculation, but adjustment for age was performed and the proportion of patients with ADs and AIDs at baseline are reported in Table S1.

In conclusion, there are ethnicity-based differences in the incidence risk of immune-mediated diseases in the UK. Specifically, the risk of AE, ARC, SLE, ATD and vitiligo is uniformly higher amongst British ethnic minority groups in comparison with the White population. In contrast, risk of multiple sclerosis is higher in the White population. Further research is needed to investigate the role of genetic and environmental factors that might influence the risk of immune-mediated diseases in British ethnic minority groups and pave the way for primary prevention strategies.

CONFLICT OF INTEREST

MTK department received funds from ALK-Abello, Thermo Fisher, MEDA and other companies for PracticAllergy course. MTK received funds from ALK-Abello to attend an international conference. KN reports grants from NIHR, grants from MRC, grants from Diabetes UK, personal fees from Astra Zeneca, personal fees from Sanofi, personal fees from MSD and personal fees from BI, outside the submitted work.

AUTHOR CONTRIBUTIONS

MTK conceived the idea for the study. KN and GG contributed to refining the research question. KN and AS designed the study with contribution from MTK. MTK, AS and KN wrote the study protocol. AS, KMG and KN extracted data. AS, KN, NA and KMG performed the analyses. MTK, AS and KN drafted the manuscript, which was reviewed and revised by all authors.

ETHICAL APPROVAL

Data extraction and research using THIN were approved by the NHS South-East Multicentre Research Ethics Committee in 2003. Approval for the use of THIN data for this study was obtained independently from the Scientific Review Committee in August 2018 (SRC reference 18THIN64).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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