Ethnicity and sex: intersectional disadvantage in cardiovascular disease risk in an ageing tri-ethnic cohort

Theoretical Focus

Despite improvements in cardiovascular outcomes in high income countries, cardiovascular disease (CVD) remains a leading cause of morbidity and mortality worldwide [1]. However, its burden is not equally distributed across ethnic and sex groups. In the United Kingdom and other high-income countries, people of South Asian and Black African or African Caribbean ethnic minority backgrounds experience disproportionate rates of certain cardiovascular outcomes compared with their White European counterparts [2]. South Asian populations have consistently shown higher rates of coronary heart disease (CHD), while African or African Caribbean populations tend to have higher rates of stroke but lower rates of CHD.

Sex differences add complexity to this area. Men are generally more likely to develop CHD, yet women are more likely to develop stroke and often experience poorer outcomes once disease occurs [3]. However, existing research is based largely on studies that either focus on single ethnic groups (in predominately White European cohorts) or examine overall CVD as a composite outcome. What remains unclear is how the associations between ethnic minority status and specific endpoints (CHD and stroke) differ by sex within the same population and, conversely, whether sex-specific risk for individual CVD outcomes is equally seen across different ethnic minority groups. Addressing these gaps is critical for refining prevention strategies, improving risk prediction models, and ensuring that clinical guidelines and public health interventions are equitably targeted across ethnic minority and sex groups.

The Southall and Brent Revisited (SABRE) study allowed us to address these drawbacks by examining the incidence of CHD and stroke across first generation South Asian and African and African Caribbean migrants as well as White Europeans over a long follow-up period. We aimed to identify sex by ethnicity differences in CHD and stroke incidence individually. We also aimed to identify common cardiovascular risk factors which may differentially contribute to CHD risk across sex and ethnicity groups.

Data

The SABRE study is a tri-ethnic community-based UK cohort [2,4,5]. Participants aged 40 to 69 years at baseline (1988-1991) were recruited from the West London districts of Southall and Brent. Baseline assessment comprised in-depth demographic, health and lifestyle questionnaires as well as a clinic visit which collected blood pressure measurements, electrocardiography, and anthropometry (n=4857). From 2008 through 2011, and 2014 through 2018, surviving participants were invited for follow-up data collection. At follow-up 1 this included a health and lifestyle questionnaire, primary care medical record review, and a clinic visit, while follow-up 2 included a health and lifestyle questionnaire, and clinic visit. Since baseline, participants have also been flagged for death by the Office for National Statistics and Hospital Episode Statistics were obtained for traced participants. At least one form of follow-up data was available for 4,797 participants (98.8%).

Methods

We identified the first CHD or stroke event in the time since baseline from a combination of follow-up data sources. The first CHD event was identified from: 1) cause of death or including angina, myocardial infarction or its sequelae, or atherosclerotic heart disease; 2) primary care record review by two senior physicians according to pre-determined criteria based on symptoms, cardiac enzymes, electrocardiography findings, and hospital discharge diagnosis [6]; 3) Hospital Episode Statistics mentioning similar conditions to 1, and interventions or rehabilitation for ischemic heart disease; or 4) self-reported myocardial infarction or related interventions. The first stroke event was identified from: 1) cause of death including cerebrovascular disease; 2) primary care record review by two senior physicians according to pre-determined criteria based on symptoms, duration of symptoms, and magnetic resonance image or computed tomography imaging; 3) Hospital Episode Statistics mentioning cerebrovascular disease; or 4) participant report of physician-diagnosed

stroke and duration of symptoms in excess of 24 h. As a competing risk, death due to unrelated reasons was identified from mortality records and GP record review.

Ethnicity was agreed on with the interviewer at baseline based on self-report, parental place of origin, and appearance: White European, South Asian, and African or Caribbean (African Caribbean). All South Asian, and African Caribbean participants were first-generation migrants. Sex was self-reported. A series of cardiovascular risk factors were also assessed at baseline. Smoking status and years of education were self-reported. Manual occupations, indicating lower socioeconomic class, were identified using the Registrar General occupational classification [7]. Area-based socioeconomic status was derived from residential postcode using the Townsend deprivation index. Hypertension was identified from self-reported doctor diagnosis or blood pressure (BP) measurements (systolic BP>140 mmHg or diastolic BP>90mmHg). Diabetes was identified according to World Health Organization criteria, self-report of doctor-diagnosed diabetes, or receipt of anti-diabetes medications. Anthropometric measures provided measures of central adiposity (waist-hip ratio) and obesity (body mass index). Fasting total cholesterol and triglycerides were assessed from collected morning blood draws.

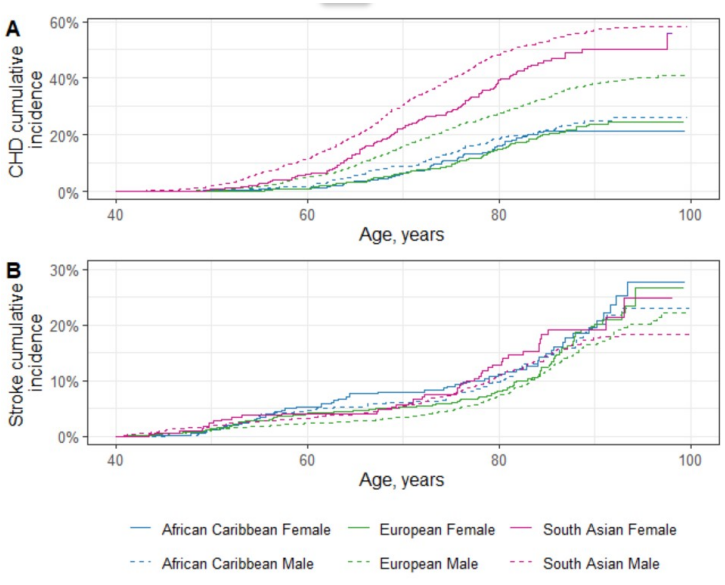
All analyses were performed in sub-populations with follow-up data who had not experienced an event at baseline (n=4,569 without CHD; n=4,790 without stroke). We estimated the cumulative incidence of CHD and stroke separately using the cumulative incidence function, treating death from other causes as a competing event. Competing risks regression based on the methods of Fine and Gray [8] were used to evaluate sex and ethnicity differences in CHD or stroke. *A priori* testing revealed significant interactions between ethnicity and sex on the incidence of CHD, therefore we also examined how ethnic differences in CHD differed across sex groups and *vice versa* using stratified analyses. All regression analyses adjusted for age at baseline. All cumulative incidence analyses and competing risk regressions were performed on complete case datasets as sex, age and ethnicity data were complete.

Preliminary methods

Population attributable fractions (PAFs) were used to examine the relative contribution of common cardiovascular risk factors to the development of CHD across sex-ethnicity groups. These reflect the relative prevalence of the risk factor as well as the strength of its association with the outcome. PAFs were calculated from subhazard ratios for each risk factor across the six sex-ethnicity strata [9]. Models only adjusted for age at baseline, therefore may be confounded and should not be considered to represent the causal contribution of the risk factor to CHD. All PAFs were performed on complete case datasets. While sex, age and ethnicity data were complete, baseline risk factors had small amounts of missingness (<5%).

Findings

Figure 1 depicts the cumulative incidence of CHD and stroke across sex and ethnicity groups. Clear group differences in CHD incidence were evident over an average follow-up time of 23.8 years (SD=10.3). By age 90, the cumulative incidence of CHD in South Asian men was 57.0% and 50.0% in South Asian women. At the same age, the cumulative incidence of CHD in European men was 38.1%, while the remaining groups had similar cumulative incidences of 21.3-25.1%. In contrast, the cumulative incidence of stroke was lower and more consistent across groups over an average follow-up time of 25.7 years (SD=10.2). By age 90, the highest cumulative incidence was observed for both European women and African Caribbean men (20.2%), while the lowest cumulative incidence was seen in European men (16.5%).



Due to the observed group differences in CHD incidence, we further investigated how these differed across both ethnicity and sex. South Asians were more likely to have a CHD event over the follow-up period compared to Europeans (*SHR=2.03, 95% CI:*

1.83, 2.26, p<0.001), while African Caribbeans were less likely *(SHR=0.65, 95% CI: 0.54, 0.77, p<0.001).* However, these findings were not completely consistent across men and women (*Figure 2B*). In men, CHD risk was higher in South Asians compared to White Europeans (*SHR=1.86, 95% CI: 1.66, 2.08*), and lower in African Caribbeans (*SHR=0.60, 95% CI: 0.49, 0.75*). However, in women, this South Asian excess was even greater (*SHR=2.71, 95% CI: 2.08, 3.55*), while African Caribbeans no longer benefitted from the relative protection of their male counterparts compared to White Europeans (*SHR=1.03, 95% CI: 1.01, 1.05*).

Similarly, while sex differences in CHD were evident, (*Female v male: SHR=0.57, 95% CI: 0.50, 0.65, p<0.001)* these were not consistent across the ethnic groups (*Figure 2A*). In Europeans, women had this lower risk of CHD compared to males (*SHR=0.51, 95% CI: 0.41, 0.63*). However, in South Asians this sex difference was diminished (*SHR=0.74, 95% CI: 0.61, 0.90*) and in African Caribbeans no longer significant (*SHR=0.83, 95% CI: 0.60, 1.15*).

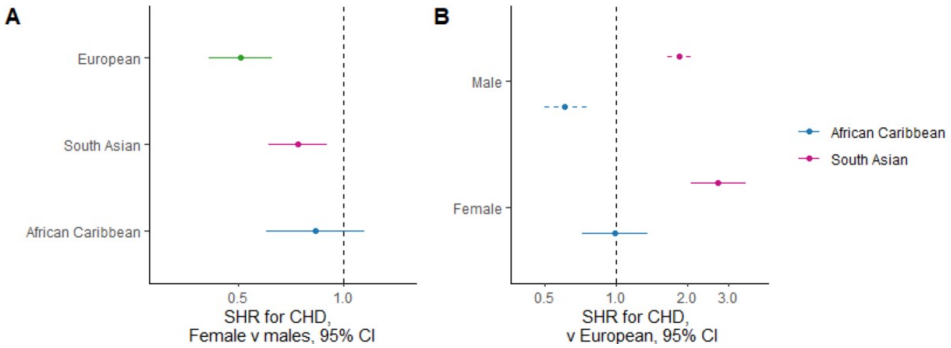


Figure 2. A) Subhazard ratios for ethnicity on CHD events stratified by sex. B) Subhazard ratios (95% CIs) for sex on CHD events stratified by ethnicity. Comparisons are made against the European group. All analyses control for age at baseline.

Preliminary findings

PAFs were used to identify cardiovascular risk factors that may contribute differently to CHD outcomes across sex and ethnicity groups, either via underlying differences in prevalence or the relative risk they confer. Initial findings suggest several common risk factors with varying PAFs across groups. For example, PAFs for diabetes suggested a moderate contribution to CHD in most groups (4.0-14.8%), however this rose to 20.8% in South Asian women.

Interpretation

Our analyses showed that incidence of different CVD events were not experienced equally across ethnic minority and sex groups in this ageing tri-ethnic UK-based cohort. While sex and ethnic differences in the incidence of stroke were minimal, CHD incidence showed vast differences across groups indicative of individual and combined effects of both ethnicity and sex. Ethnic minority men showed both increased (South Asian) and decreased (African Caribbean) CHD compared with White Europeans men in line with previous reports of sex-combined sample [2]. However African Caribbean women did not experience this same relative protection, and South Asian women experienced a greater incidence of CHD over their White European counterparts. Similarly, increased incidence of CHD was observed in White European men compared to women in line with previous reports[3], however these sex differences were largely diminished in ethnic minority groups. These relationships manifest in a particularly high incidence of CHD in South Asian women, above even above that experienced by White European men.

Intersectional approaches to health research frequently observe poorer health outcomes for ethnic minority women [10], emphasising the importance of considering multiple characteristics simultaneously. However, it should be noted that this study only considered two grouping factors (ethnicity and sex) and further factors may interact to lead to further inequalities in CVD outcome. Future research, with larger cohorts, should aim to examine these intersectional states.

Preliminary PAF analyses indicate some risk factors may potentially contribute to the sex-ethnicity differences in CHD incidence. Future work should aim to test whether identified risk factors explain the excess risk for CHD seen in South Asian men and women, and White European men.

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