Ischemic stroke in South Asians: the BRAINS study

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**Ischemic Stroke in South Asians: the BRAINS study**

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

Supplemental Appendix:

Supplementary Table SI - Comparison of Population Characteristics between ethnicities, by sex.

Supplementary Table SII - Comparison of Population Characteristics between ethnicities.
Abstract

Background: Studies on stroke in South Asians are sparse. We compared differences in age of onset of ischemic stroke in South Asians living in the UK and those in India with white British stroke patients.

Methods: We studied the UK and Indian arms of the ongoing international prospective hospital-based study of South Asian stroke (BRAINS study). BRAINS includes 4038 South Asian and white British recruits from UK and Indian sites with first-ever ischemic stroke.

Results: Of included patients, 1126 were South Asians in India (ISA); 1176 British South Asians (BSA), and: 1736 white British (WB) UK residents. ISA and BSA South Asians suffered stroke 19.5 years and 7.2 years earlier than their WB counterparts, respectively (BSA: 64.3 years IQR: 22 years, vs. ISA: 52.0 years IQR: 18 years, vs. WB: 71.5 years IQR: 19 years, P<0.001). BSA had higher rates of hypertension, diabetes-mellitus and hypercholesterolaemia than ISA and WB stroke victims. Adjusting for traditional stroke risk factors, ISA and BSA continued to display an earlier age of stroke onset of 18.9 years (P<0.001) and 8.9 years (P<0.001), respectively. Following multivariable stepwise linear regression ethnicity accounted for 24.7% of variance of early age onset.

Conclusion: South Asians living in the UK (BSA) and those living in India (ISA) suffered ischemic stroke ~9 and ~19 years earlier respectively than their white British (WB) counterparts. Ethnicity is an independent predictor of early age onset. Our study has considerable implications for public health policymakers in countries with sizable South Asian populations.
Introduction

South Asians (Indian, Pakistani, Sri Lankan, Bangladeshi origin) make up ~24% of the world’s population but account for ~40% of global stroke deaths\(^1\). South Asians in the UK make up the largest ethnic minority group with over 3 million individuals\(^2\), and ~6 million in the USA making them one of the fastest growing immigrant groups in America. Much of this large-scale migration, beginning in the 1950s, has resulted in an aging first- and second-generation population who increasingly rely on healthcare resources.

Some small studies have suggested an earlier stroke onset in South Asians and increased stroke mortality regardless of location compared to the white population\(^3,4\). Other studies have shown migration can have an adverse effect on South Asian health due to changes in living environments, differing healthcare system\(^5\), reduced exercise, and potentially changes in diet\(^6,7\) possibly compounded by genetic liabilities\(^8\). Although these negative effects could be reduced by the use of technology for improving healthcare access\(^9\), ethnic specific analysis is likely needed to identify stroke onset differences as well as novel risk factors.

We sought to investigate stroke onset differences between the white British population and South Asians residing in the UK and those in South Asia. We used the UK and India arm of the ongoing international prospective hospital-based BRAINS (Bio-Repository of DNA in Stroke \(^10,11\)) study which has recruited patients from 23 secondary healthcare sites in those two countries. To the best of our knowledge, this is the largest comparative ischemic stroke study to-date in South Asians.
Materials and Methods

Data Source

We analysed the UK and Indian arms of the ongoing prospective international Bio-Repository of DNA in Stroke (BRAINS) study, the details of which have been previously published but are described again here in brief. This hospital-based study meets all ethical standards set by local institutional review boards and has received full institutional ethics approval in the UK and India. UK stroke patients were screened at 21 participating hospital sites located within London, Sussex, Surrey, West Yorkshire, West Midlands, Kent, Bedfordshire, and Lancashire. The recruitment period was between 2010 and 2019. The sites were chosen to include regions with high South Asian populations while also being representative of the white British population. The Indian arm screened stroke patients at two hospital sites located in New Delhi (All India Institute of Medical Sciences, AIIMS) and Kerala (Sree Chitra Tirunal Institute for Medical Sciences and Technology). All cases were reviewed by a pre-designated onsite neurologist/stroke physician with the diagnosis of ischemic stroke confirmed with computed tomography (CT) or magnetic resonance (MR) imaging. Stroke cases were subtyped using the TOAST (trial of ORG 10172 in acute stroke treatment) classification. Written informed consent was sought for each included case. For those unable to provide written consent, surrogate consent was taken. Extensive demographic data including age, sex, and ethnicity was collected during a nurse-led interview. All participants over 18 years of age at the time of stroke event were considered for the study to ensure a representative sample. Ethnicity was obtained via self-identification as Indian, Pakistani, Sri Lankan, or Bangladeshi origin. White British and white Irish was classified as white British. Ethnicity is classified as South Asians living in India (ISA), South Asians living in Britain UK (BSA), and white British UK stroke (WB) patients. All analyses in this study compared ISA and BSA with WB patients as the reference group.
Risk factors for cases were defined as: hypertension diagnosed at discharge (≥140/90mmHg), previous diagnosis of hypertension or pre-stroke treatment with antihypertensive; hypercholesterolemia defined by previous diagnosis or serum cholesterol >5.2 mmol/L; diabetes mellitus classified from a previous diagnosis of type I or II. Previous diagnosis of ischemic heart disease and atrial fibrillation data was collected from clinical records. Smoking and alcohol history were recorded if the patient uses/used on a regular basis. Central obesity is classified by increased waist circumference (men: >102cm, women: >88cm) or BMI (≥30)\textsuperscript{14}.

\textit{Standard Protocol Approvals, Registrations, and Patient Consents}

A not-for-profit stroke patient support group advised on the original protocol for recruitment of patients. Appropriate ethical approval for this study was obtained in both the UK and India.

\textit{Statistical Analysis}

Demographic details and categorical data between ISA, BSA and WB were compared using independent \textit{t}-test and \textit{\chi}^2 test. Prevalence of individual risk factors between ethnicity and age were analysed by linear regression. Age of onset for each TOAST subtype were compared using one-way analysis of variance (ANOVA) test. General linear model (GLM) analysis was performed to identify association between ethnicity and age adjusted for potential confounders\textsuperscript{15}. Variables likely associated with age were selected with respect to biological plausibility (sex, central obesity, smoking history, alcohol history, hypertension, diabetes mellitus, hypercholesterolemia, ischemic heart disease and atrial fibrillation). Little's MCAR test was used to assess if traditional stroke risk factors with missing values were missing completely at random\textsuperscript{16}. A \textit{P}<0.05 was considered as statistically significant. Results were analysed using SPSS v25.0 Statistical Software for Windows.
Results

The combined UK and India arm of the BRAINS study consists of 6207 patients. Of these, 4038 individuals identified with first-time ischemic stroke composing of 1126 (men: 757, women: 369) ISA: 1176 (men: 761, women: 415) BSA, and: 1736 (men: 966, women: 770) WB patients.

Demographic and clinical characteristics between ethnicity are presented in Table 1. BSA suffered from ischaemic stroke onset 7.2 years earlier, while ISA was 19.5 years earlier than their WB counterparts (BSA: 64.3 years IQR: 22 years, vs. ISA: 52.0 years IQR: 18 years, vs. WB: 71.5 years IQR: 19 years, \( P<0.001 \)). BSA patients had an increased prevalence of hypertension (BSA: 76.9% vs. ISA: 68.0% vs. WB: 66.3%, \( P<0.001 \)), diabetes mellitus (BSA: 50.3% vs. ISA: 32.9% vs. WB: 18.8%, \( P<0.001 \)), hypercholesterolaemia (BSA: 52.6% vs. ISA: 36.4% vs. WB: 34.1%, \( P<0.001 \)), and ischemic heart disease (BSA: 30.3% vs. ISA: 13.6% vs. WB: 19.5%, \( P<0.001 \)) compared to ISA and WB patients. Atrial fibrillation, smoking history and high alcohol consumption were more prevalent in WB stroke cases (Table 1).
Table 1: Population Characteristics stratified by ethnicity.

<table>
<thead>
<tr>
<th></th>
<th>ISA (n=1126)</th>
<th>BSA (n=1176)</th>
<th>WB (n=1736)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average age of onset, mean (IQR), years</td>
<td>52.0 (18)</td>
<td>64.3 (22)</td>
<td>71.5 (19)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Men, No. (%)</td>
<td>757 (67.2)</td>
<td>761 (64.7)</td>
<td>966 (55.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TOAST Stroke Subtype</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large-artery atherosclerosis</td>
<td>216 (25.4)</td>
<td>185 (19.1)</td>
<td>414 (33.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Small-vessel occlusion</td>
<td>170 (20.0)</td>
<td>302 (31.1)</td>
<td>261 (21.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardioembolism</td>
<td>100 (11.8)</td>
<td>157 (16.2)</td>
<td>246 (19.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Environmental Factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central obesity</td>
<td>348 (35.8)</td>
<td>358 (35.0)</td>
<td>368 (31.1)</td>
<td>0.042</td>
</tr>
<tr>
<td>Smoking history</td>
<td>492 (43.9)</td>
<td>413 (35.5)</td>
<td>915 (53.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>468 (41.8)</td>
<td>254 (23.2)</td>
<td>660 (45.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>747 (68.0)</td>
<td>890 (76.9)</td>
<td>1137 (66.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>361 (32.9)</td>
<td>582 (50.3)</td>
<td>321 (18.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>355 (36.4)</td>
<td>593 (52.6)</td>
<td>579 (34.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>147 (13.6)</td>
<td>340 (30.3)</td>
<td>300 (19.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>56 (6.1)</td>
<td>131 (11.7)</td>
<td>372 (21.9)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

n, sample size; IQR, Interquartile Range; Central obesity classified by waist circumference (men: >102 cm, women: >88 cm) or BMI (≥30 kg/m²). One-way ANOVA was used to compare age of onset with all other using Chi-square test. Stroke subtype uses the TOAST (trial of ORG 10172 in acute stroke treatment) classification. ISA: India residing South Asians. BSA: British residing South Asians. WB: White British.
Sex specific analyses are presented in Supplement SI. ISA men suffered stroke 10.7 years and 17.0 years earlier than BSA and WB men respectively. Conversely, ISA women suffered stroke 15.5 years and 23.2 years earlier than BSA and WB women. Of the environmental factors, ISA, BSA, and WB women reported greater prevalence of central obesity compared to men. Smoking history and alcohol consumption were greater in men compared to women for each ethnicity. Comparisons of traditional stroke risk factors between differing ethnicities are presented in Supplement SII.

BSA patients had a greater prevalence of small-vessel occlusion (BSA: 31.1% vs. ISA: 20.0% vs. WB: 21.0%, \( P<0.001 \)) and lower prevalence of large-artery atherosclerosis (BSA: 19.1% vs. ISA: 25.4% vs. WB: 33.4%, \( P<0.001 \)), and cardio-embolism (BSA: 16.2% vs. ISA: 11.8% vs. WB:19.8%, \( P<0.001 \)) compared to WB patients. However, despite differences in prevalence, ISA suffered stroke at a younger age across all stroke subtypes compared to their BSA and WB counterparts (Figure 1).
**Figure 1:** Average age of onset (years) among TOAST subtype, stratified by ethnicity.

![Bar chart showing age of onset for different stroke subtypes](image)

*Error bars denotes standard deviation. Average age for all stroke is the combined stroke subtype. Stroke subtype uses the TOAST (trial of ORG 10172 in acute stroke treatment) classification. ISA: South Asians residing in India. BSA: UK residing South Asians. WB: White British.*
To evaluate the association of age with ethnicity, a linear regression model was performed adjusted for the following variables: sex, central obesity, alcohol consumption, smoking history, hypertension, atrial fibrillation, and ischemic heart disease. In a simple linear regression, both BSA and ISA were associated with an earlier age of onset ($\beta=-9.61$, SE=0.27) and accounted for 24.6% of the total variance ($R^2=0.246$). A forward stepwise linear regression was performed adjusting for traditional stroke risk factors (Table 2). In this model, South Asian ethnicity, regardless of ethnicity, continued to show a negative association with age of onset of stroke ($\beta=-9.31$, SE=0.31). This model overall predicted 33.7% ($R^2=0.337$) of the variation of age of onset of ischemic stroke, with ethnicity accounting for 24.7% ($R^2=0.247$). The results of the missing value analysis indicate that missing values occur completely at random (MCAR) ($P=0.69$).
Table 2: Stepwise multivariable linear regression analysis predicting age of onset of ischemic stroke (years) with traditional risk factor.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Effect size (β), years</th>
<th>SE</th>
<th>P-value</th>
<th>R²</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ethnicity:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Reference group: WB, 1 = BSA, 2 = ISA)</td>
<td>-9.31</td>
<td>0.31</td>
<td>&lt;0.001</td>
<td>0.247</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>7.64</td>
<td>0.54</td>
<td>&lt;0.001</td>
<td>0.057</td>
</tr>
<tr>
<td><strong>Atrial fibrillation</strong></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>5.41</td>
<td>0.74</td>
<td>&lt;0.001</td>
<td>0.016</td>
</tr>
<tr>
<td><strong>Ischemic heart disease</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.28</td>
<td>0.63</td>
<td>&lt;0.001</td>
<td>0.006</td>
</tr>
<tr>
<td><strong>Alcohol Consumption</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-2.02</td>
<td>0.53</td>
<td>&lt;0.001</td>
<td>0.005</td>
</tr>
<tr>
<td><strong>Central obesity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-2.04</td>
<td>0.52</td>
<td>&lt;0.001</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>Sex (reference group: Women)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-1.93</td>
<td>0.53</td>
<td>&lt;0.001</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Effect size (β-coefficients), degree of change in age of onset of Ischemic stroke (dependent variable) for every 1-unit of change in the predictor variable. SE, standard error. R², percent of variance in age of onset of Ischemic stroke that is explained by the set of predictor variables. Constant for the gradient (B)=67.9. Diabetes mellitus (P=0.06), smoking history (P=0.15) and Hypercholesterolemia (P=0.05) were excluded from the model. High significance of the F-test=191.9, P<0.001 indicates a linear relationship between the variables in the model. Total R²=0.337. ISA: India residing South Asians. BSA: British residing South Asians. WB: White British.
To assess the independent association of age with ethnicity among stroke patients, the analyses were repeated on the basic model (i.e., adjusted for ethnicity and sex only model) with separate adjustments for each predictor in Table 3. Both BSA and ISA patients continued to display earlier age of stroke onset regardless of the traditional risk factor being adjusted suggesting that ethnicity was independently associated with age of onset. Adjusting for these traditional risk factors of stroke, ISA and BSA showed an even more pronounced earlier age of stroke onset of 18.9 years (ISA: 52.8 years vs. WB: 71.7 years, \( P < 0.001 \)) and 8.9 years (BSA: 62.8 years vs. WB: 71.7 years, \( P < 0.001 \)), respectively.
**Table 3**: Simple linear regression analysis predicting age of onset of ischemic stroke (years) adjusting for each traditional risk factor.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>ISA (WB reference group)</th>
<th>BSA (WB reference group)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Effect size ($\beta$), years</td>
<td>SE</td>
</tr>
<tr>
<td>Central obesity</td>
<td>-19.60</td>
<td>0.56</td>
</tr>
<tr>
<td>Smoking history</td>
<td>-19.29</td>
<td>0.52</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>-19.36</td>
<td>0.54</td>
</tr>
<tr>
<td><strong>Comorbidities</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>-19.37</td>
<td>0.50</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>-19.63</td>
<td>0.52</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>-19.12</td>
<td>0.54</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>-18.94</td>
<td>0.53</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>-18.27</td>
<td>0.55</td>
</tr>
<tr>
<td><strong>Multivariate Model</strong></td>
<td>-18.77</td>
<td>0.65</td>
</tr>
</tbody>
</table>

Effect size ($\beta$-coefficients), degree of change in age of onset of Ischemic stroke (dependent variable) for every 1-unit of change in the predictor variable. SE, standard error. Each model was adjusted for sex and specific stroke risk factor. Multivariate Model includes all risk factors. ISA: India residing South Asians. BSA: British residing South Asians. WB: White British.
Discussion

In this study, compared to their WB stroke counterparts, BSA and ISA suffer from an earlier ischemic stroke onset of ~9 and ~19 years respectively following adjustment for traditional risk factors. In both men and women, ISA continued to suffer from an earlier ischemic stroke compared to BSA and WB patients. For each stroke subtype (including the commonest small vessel), ISA patients continued to exhibit significantly earlier age of onset compared to their WB counterparts. Ethnicity explained approx. 25% of the variance of the age of onset, with traditional risk factors of hypertension, atrial fibrillation, ischemic heart disease, alcohol consumption, central obesity, and sex accounting for only about 8% of the variance.

The significantly later age of onset of ischemic stroke in BSA patients compared to their ISA counterpart suggests an improvement in stroke prevention associated with a UK environment. Our study is the first migration-related study focusing on age of first onset of ischemic stroke of South Asians in the UK and India, making comparisons to previous studies limited. Earlier age of stroke onset in South Asians, regardless of location, is consistent with findings from other smaller studies both in south Asia and the UK, though these do not focus on first-time stroke events. Notwithstanding the health benefits of the UK, the BSA population has not standardized with WB, although are improved compared with ISA. Gunarathe et al found an 8-year earlier onset compared to WB patients with data collected between 1997 and 2005, suggesting that little improvement in stroke prevention has been achieved in this migrant demographic over the intervening decades.

This study is also the first to report age of event for each stroke subtype in this demographic. ISA patients consistently had earlier stroke onset than their BSA and WB counterparts regardless of TOAST classification. We also report stark differences between the prevalence
of stroke subtype, with of small-vessel occlusion ~1.5 fold higher in BSA. A possible reason for this age discrepancy may be from the high prevalence of traditional risk factors in BSA\textsuperscript{4,23–26}. We report significantly higher rates of hypertension, diabetes mellitus and hypercholesterolaemia in BSA patients consistent with some\textsuperscript{4,25–31} but not all previous studies\textsuperscript{29}. After adjusting for these risk factors, South Asian ethnicity explained 24.7\% of the earlier onset seen in this study and was associated with an earlier age of onset of stroke. Appropriate clinical management of these comorbidities may also play a part in determining age of stroke\textsuperscript{32,33}.

Central obesity (a known ischemic stroke risk factor) has a greater prevalence in the South Asian community\textsuperscript{34–36}. Though our study reports a significantly higher prevalence of central obesity in BSA, similar prevalence among ISA, when compared to the WB population, was also present. This highlights the possible changes in lifestyle/environmental factors associated with migrating to the UK such as diet and exercise. Traditional South Asian diet consisting of carbohydrate rich foods including rice and bread is more tailored to a physically demanding rural environment\textsuperscript{37}. But this carbohydrate rich diet continues in the UK\textsuperscript{38} partnered with lower physical activity compared with the WB population\textsuperscript{6,39,40}. A predisposition to visceral adiposity in the truncal region has resulted in the WHO recommending South Asians specific thresholds for determinators of obesity\textsuperscript{41}.

Though the increased prevalence of traditional stroke risk factors in South Asians were seen in the UK and India, the effect of migration on environmental and lifestyle factors are likely another possible cause in differing stroke risk and outcome. Accessing healthcare is an important area in stroke prevention which is often overlooked in migration studies. Though BSA have access to preventable healthcare services, knowledge about risk factors and
contribution to disease is also demonstrably poor. Many BSA are not aware of the common complications associated with diabetes mellitus, the importance of screening clinics and the need to engage with chiropodists. Furthermore, sociocultural and religious factors can exaggerate this decreased awareness with the distorted perceptions of failure at self-care and social stigma. Sex differences also can determine environmental and comorbidity factor prevalence. Of interest was the ~10% increase in ischemic heart disease among BSA men compared to women. In general, ischemic heart disease is more likely to develop at an earlier age in men who usually have a greater prevalence of cardiovascular risk factors and is likely the reason for the difference.

In common with previous literature, stroke of undetermined aetiology was the most common TOAST subtype in ISA. To be considered for small vessel occlusion the lesion diameter is required to be <15mm. More so, to be considered large artery atherosclerosis patients are required to have stenosis of >50%. If either of these criteria are not met, then patients with mild stenosis or those with small vessel occlusion but increased lesion size will be classified as undetermined.

**Limitations**

Like all studies, several limitations need to be noted. BRAINS is a long running study and thresholds for risk factors and their management have changed over the intervening years. However, such transitions would have resulted in a non-differential ethnic bias and not likely affect the significance of the results in this study. Comorbidity prevalence is recorded at the time of the event. Though we are unable to comment on the length of time these comorbidities were present prior the stroke event, much of the prevalence data collected was through treatment regimens recorded on the patient’s clinical record. Although this may lead to an
underestimating of the real effect size on the age of stroke event of the included stroke risk variables, our large sample size (n=4038) reflects the current impact of these risk variables on stroke in the South Asian population. Ethnicity was defined by grandparent origin. While this was self-reported, previous studies have demonstrated the accuracy of this methodology\textsuperscript{48,49}. Socioeconomic status which may influence morbidity and mortality was not collected so we are unable to assess its influence on age of stroke onset. This is a prospective hospital-based study so conclusions cannot be extrapolated for overall or community-based age differences. Further, older stroke patients may choose not to seek medical advice compared to younger victims which could influence this hospital-based study. However, it is likely that this limitation would apply to either ethnic group or location. Though we did not collect detailed data on the numbers of those who chose not to participate in this prospective study, those numbers were small and broadly similar across all studied groups. To assess the representation of the ISA and BSA within our study we utilised the broader BRAINS dataset, which consists of both ischemic and haemorrhagic events and found similar stroke subtype prevalence across the three groups in our study\textsuperscript{4,50}. This includes BSA in BRAINS reporting 84.5% of ischemic events which is similar to previous reported prevalence\textsuperscript{4}. Further, we are unable to report specific effects of migration and how they develop as long-term follow-up was not undertaken.

Both the UK and India recruitment sites were chosen to ensure a representative sample. In the UK we identified 21 hospital sites with high number of South Asians. India, with a geographical land mass similar to the US, is significantly more challenging to recruit a representative sample. The two hospital sites chosen, All India Institute of Medical Sciences and Sree Chitra Tirunal Institute for Medical Sciences and Technology, were identified as they are located in the north and south of the country. Furthermore, both offer free access to medical services and thus more likely attracting a wide population from varying socioeconomic
backgrounds. Finally, this is a hospital-based study and is dependent on recruitment for patients attending hospital. Different cultures have different responses and access to seeking emergency healthcare support services. While stroke usually presents with disabling symptoms, not all afflicted patients attend hospital which could lead to recruitment bias.

**Conclusion**

British South Asians (BSA) and South Asians in India (ISA) suffered from stroke ~9 and ~19 years, respectively, earlier than their white British (WB) counterparts. Ethnicity accounted for around 25% of the variance of early of age of onset. Our work has considerable implications for public health policymakers in countries with sizable South Asian populations.
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