Appendix 2. INTERSTROKE (methods, risk factor measurement)

Analysis was performed in Canada using the Beckman coulter Unicel® DxC600 Synchron® Clinical System and Beckman reagents All reagents were manufactured by Beckman Coulter (Brea, CA, USA). The Beckman cholesterol method is a colorimetric assay using cholesterol esterase, cholesterol oxidase, peroxidase, 4-aminoantipyrine and phenol. The Beckman high-density lipoprotein (HDL) method is a direct, colorimetric assay using a detergent to selectively solubilize HDL lipoprotein particles. The HDL cholesterol released reacts with cholesterol esterase and cholesterol oxidase in the presence of chromogens. The Beckman apolipoprotein A1 (apoA1) and apoB methods are Immunoturbidimetric assay using goat antibody monospecific for human apoA or human apoB. In order to standardize the results quality control samples and reference pools that had previously been analysed in the central core laboratory in Canada were sent to India, China, and Turkey.

Waist and hip circumference were measured in the standing and supine positions in cases and controls. If cases were unable to stand, these measurements were then completed in the supine position only. Standing waist and hip measurements were used in analyses when available. For cases with only supine estimates, we used the supine measures in the matched control. For waist-to-hip ratio and body mass index, tertiles by sex were calculated based on the overall control data. Physically active individuals were defined as being regularly involved in moderate leisure activity (walking, cycling, or gardening) or strenuous exercise (jogging, football, and vigorous swimming) for 4 hours or more a week. Alcohol use was categorized into never/former, low intake (1 to 7/week), moderate intake (7 to 14/week for women and 7 to 21/week for men), high intake (>14/month for women and >21/week for men), and episodic heavy drinking (>5 drinks a day at least once a month). For psychosocial factors, we used a combined measure of psychosocial stress employed in INTERHEART,[37] which combines measures of stress (home and work), life events and depression (defined as feeling sad, blue or depressed for 2 or more consecutive weeks over the past 12 months).

Blood pressure of cases were recorded at three time-points in the acute phase of stroke: at the time of admission (from patient's medical notes), the morning after admission (from patient's medical notes), and at the time of interview (conducted by research personnel). Hypertension was defined by self-reported history of hypertension or the composite of self-reported hypertension or blood pressure of 140/90 mm Hg or higher. We selected blood pressure measured at interview in cases and controls, as it was completed in a standardized manner in cases and control, by trained research personnel at site and required lower adjustment that admission blood pressure (as only intracerebral hemorrhage cases required adjustment). To estimate preadmission blood pressure in cases, we used adjusted blood pressure readings at the time of interview; the adjustment was based on data reported in the Oxford Vascular Study (OXVASC) and Oxfordshire Community Stroke Project (OCSP) prospective cohort studies,[37] which evaluated the relationship between premorbid blood pressure and acute post-stroke blood pressure. We calculated 'estimated' preadmission systolic blood pressure in cases with adjusted blood pressure at the time of interview, adjusted for the ratio of mean pre-morbid systolic blood pressure (most recent) to mean first post-event systolic blood pressure by study neurologist (median time from symptom onset to blood pressure measurement was 2 days) reported in OCSP cohort (adjusted for intracerebral hemorrhage only, as there was no difference in pre-morbid and post-event mean values for ischemic stroke reported).[37] In our primary report, we used adjusted blood pressure at the time of admission. We calculated the agreement between these two approaches for diagnosis of hypertension (blood pressure ≥140/90 mm Hg), which was 88.4% (95% confidence interval [CI], 87.9 to 89.0). However, for the current analysis of blood pressure, we identified a clustering of systolic blood pressure measurements at 120, 130, and 140 mm Hg, and for diastolic blood pressure at 80 and 90 mm Hg, which was due to a rounding-up or rounding-down issue, and was more common in lower income regions, likely due to higher use of manual sphygmomanometers. Applying the adjustment of blood pressure on admission resulted in an imbalance between cases and controls, which was minimised when using the blood pressure at time of admission in cases. However, estimates for odds ratios and population attributable risks (PARs) were consistent using both estimates. For hypertension definition used in primary analyses, compared to definition used in current analyses, we derived dds ratios (ORs) for hypertension of 2.98 versus 2.68 overall, 2.28 versus 1.92 for high income countries (HIC), 2.43 versus 2.29 for upper middle income countries-1 (UMIC-1), 3.01 versus 2.76 for UMIC-2, and 3.79 versus 3.27 for lower middle income countries (LMIC)/lower income countries (LIC). For PAR, we derived PARs for hypertension of 47.9% versus 47.6% overall, 42.1% versus 36.3% for HIC, 47.4% versus 46.3% for UMIC-1, 47.4% versus 47.2% for UMIC-2, and 49.8% versus 52.5% for LMIC/LICs.

To ensure standardized measurements, and high quality of

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data, we used a comprehensive operations manual, periodical training workshops, and regular communication with study personnel. We entered all data in a customized database programmed with range and consistency checks and transmitted electronically to the Project Office at the Population Health Research Institute in Hamilton (ON, Canada) where further quality control measures were implemented.

Reagent manufacturer and instrumentation

Country lab	Reagent manufacturer	Instrumentation
Canada	Beckman Coulter Synchron®Systems	Beckman Coulter DXC600
China	Roche Diagnostics	Hitachi 7060c (2009–2010) Hitachi 7100 (2014)
India	Roche Diagnostics, Switzerland method	C311, ROCHE
Turkey	Roche Diagnostics	Cobas 6000 C501