

Supplementary Table 1: Exclusion Criteria for Cases

1	Age <18 years.
2	Patients unable to communicate because of severe stroke, aphasia, or dementia who did not have a valid proxy respondent.* *A valid proxy respondent was considered a spouse or first degree relative who was living in the same home or aware of the participant's previous medical history and current therapies.
3	Stroke symptoms lasting >120 hours from symptom onset or last seen normal.
4	Not first stroke presentation/diagnosis.
5	Non-vascular causes of acute presentation (e.g. tumour, abscess, multiple sclerosis, hypoglycaemia, seizure etc.).
6	Subdural haemorrhage.
7	Current hospitalisation for acute coronary syndromes or stroke secondary to endovascular procedure.
8	Unable to get consent.

Supplementary Table 2: Guidance to Sites for Selection of Controls

Selection of Controls for INTERSTROKE Study
<p>Controls:</p> <ol style="list-style-type: none">1. Community-based control.2. Relative of a patient from a non-cardiac ward.3. Unrelated (not first degree relative) visitor of any patient.4. Patients attending the hospital or outpatient clinic:<ul style="list-style-type: none"><u>Preferred controls from hospital settings:</u><p>Patients attending the hospital or outpatients clinic for the following reasons:</p><ol style="list-style-type: none">4.1 Refraction and cataracts (excluding those presenting with acute visual loss).4.2 Physical check-up.4.3 Routine pap smear.4.4 Routine breast exam.4.5 Elective minor surgery for conditions that are not obviously related to stroke or its risk factors.4.6 Elective orthopaedic surgery.<u>Acceptable controls from hospital settings:</u><p>Patients attending the hospital or outpatients clinic for the following reasons:</p><ol style="list-style-type: none">4.7 Outpatient fractures.4.8 Arthritic complaints.4.9 Plastic surgery.4.10 Haemorrhoids, hernias, hydroceles.4.11 Routine colon cancer screening.4.12 Endoscopy.4.13 Minor dermatological disorders.

Supplementary Table 3: Participants Included in INTERSTROKE Study by Country Income Level

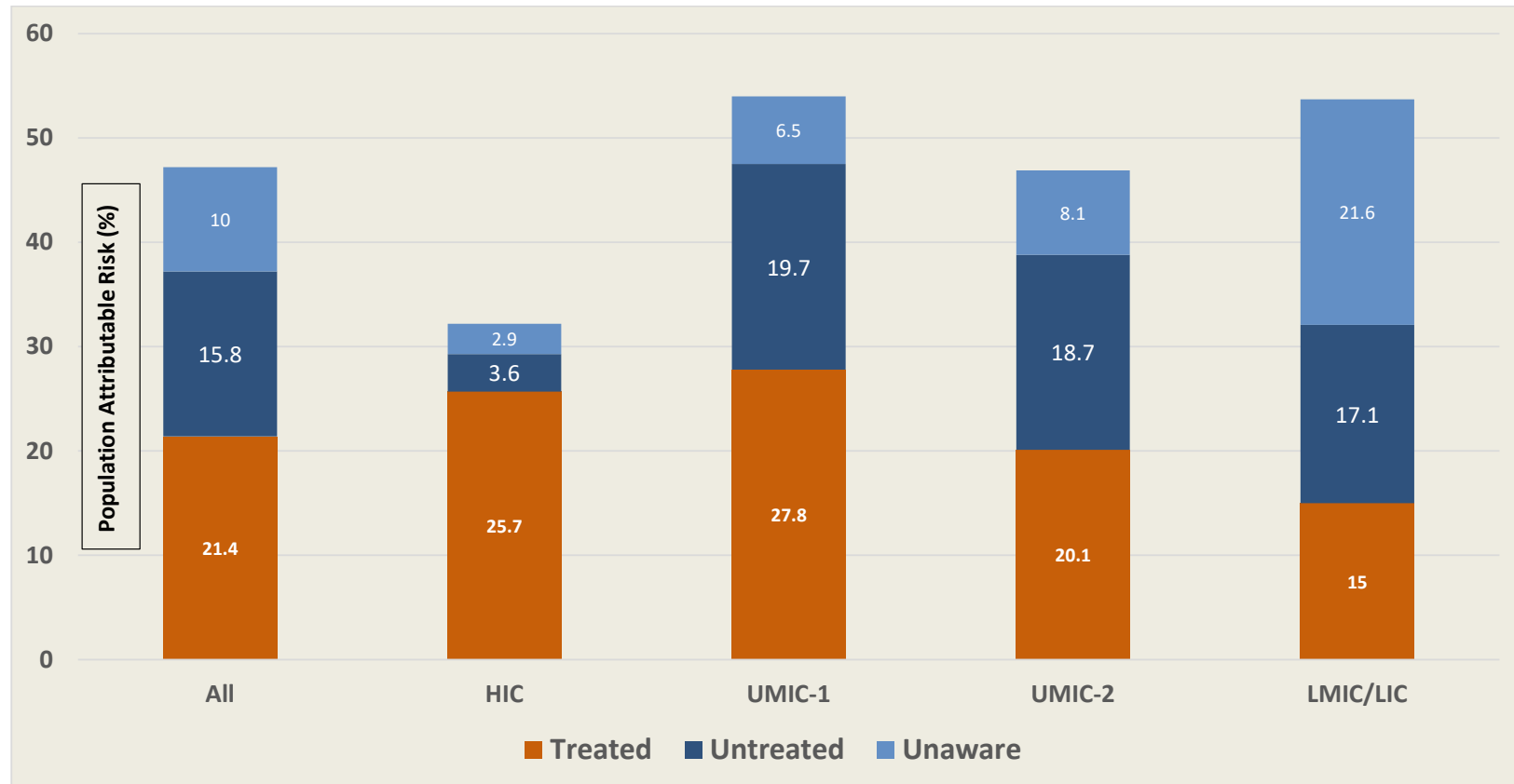
Country	GNI	%	GNI%	n	
1. Australia	64680	9.4	6080	238	HIC
2. Sweden	61600	9.7	5975	324	
3. Denmark	61310	10.6	6499	70	
4. Kuwait	55470	2.9	1609	1	
5. Canada	51690	10.9	5479	591	
6. Germany	47660	11.3	5386	666	
7. Ireland	44660	8.9	3975	44	
8. UAE	43480	3.2	1391	406	
9. UK	42,690	9.1	3885	1903	
10. Saudi Arabia	26,340	3.2	843	74	
11. Chile	14,900	7.7	1147	208	UMIC-1
12. Argentina	14,500	7.3	1059	286	
13. Poland	13,730	6.7	920	828	
14. Russia	13,210	6.5	857	536	
15. Croatia	13,020	7.3	951	118	
16. Brazil	11,760	9.7	1141	734	
17. Turkey	10,850	5.6	607	592	
18. Malaysia	10,660	4.0	426	540	UMIC-2
19. Colombia	7,780	6.8	529	542	
20. China	7,380	5.6	413	7974	
21. South Africa	6,800	8.9	605	197	
22. Peru	6410	5.3	340	276	
23. Iran	6820	6.7	512	230	
24. Ecuador	6040	7.5	450	913	
25. Thailand	5410	4.6	249	44	LMIC/LIC
26. Philippines	3440	4.4	151	1126	
27. Nigeria	2950	3.9	115	90	
28. Sudan	1740	6.5	113	606	
29. India	1610	4.0	64	4940	
30. Pakistan	1410	2.8	40	764	
31. Uganda	660	9.8	65	516	
32. Mozambique	630	6.8	43	540	

Supplementary Table 4: Association Between History of Hypertension and Stroke, By Pre-admission Use of Antihypertensive Therapy – Full Model

	All stroke
	Odds Ratio (95% CI)
Current Smoking (versus Never/Former)	1.66 (1.52-1.82)
Waist-to-hip ratio	
Tertile 2 (versus tertile 1)	1.25 (1.14-1.36)
Tertile 3 (versus tertile 1)	1.45 (1.32-1.60)
Alternate Healthy Eating Index	
Tertile 1 (versus tertile 3)	1.67 (1.52-1.83)
Tertile 2 (versus tertile 3)	1.27 (1.17-1.39)
Physical Inactivity	
Mainly Inactive (versus mainly active)	1.70 (1.51-1.91)
History of self-reported diabetes or HbA1c\geq6.5%	1.13 (1.03-1.25)
Alcohol (versus Never/Former)	
- Low or Moderate Intake	1.17 (1.06-1.28)
- High Intake or Binge-pattern intake	2.15 (1.78-2.59)
Psychosocial Factors	
General (Several/Permanent)	1.35 (1.22-1.49)
Financial	1.17 (1.08-1.26)
Life events	1.08 (0.99-1.17)
Locus of Control	1.06 (0.96 – 1.16)
Depression	1.20 (1.08 – 1.34)
Cardiac Causes	3.17 (2.79 – 3.60)
ApoB/A1 Ratio	
- Tertile 2 (versus Tertile 1)	1.26 (1.16 – 1.37)
- Tertile 3 (versus Tertile 1)	1.81 (1.67 – 1.98)
History of Hypertension	
Treated	2.60 (2.38-2.83)
Untreated	5.25 (4.69-5.88)
Blood pressure \geq 140/90mmHg (without history of hypertension)	1.91(1.74-2.09)

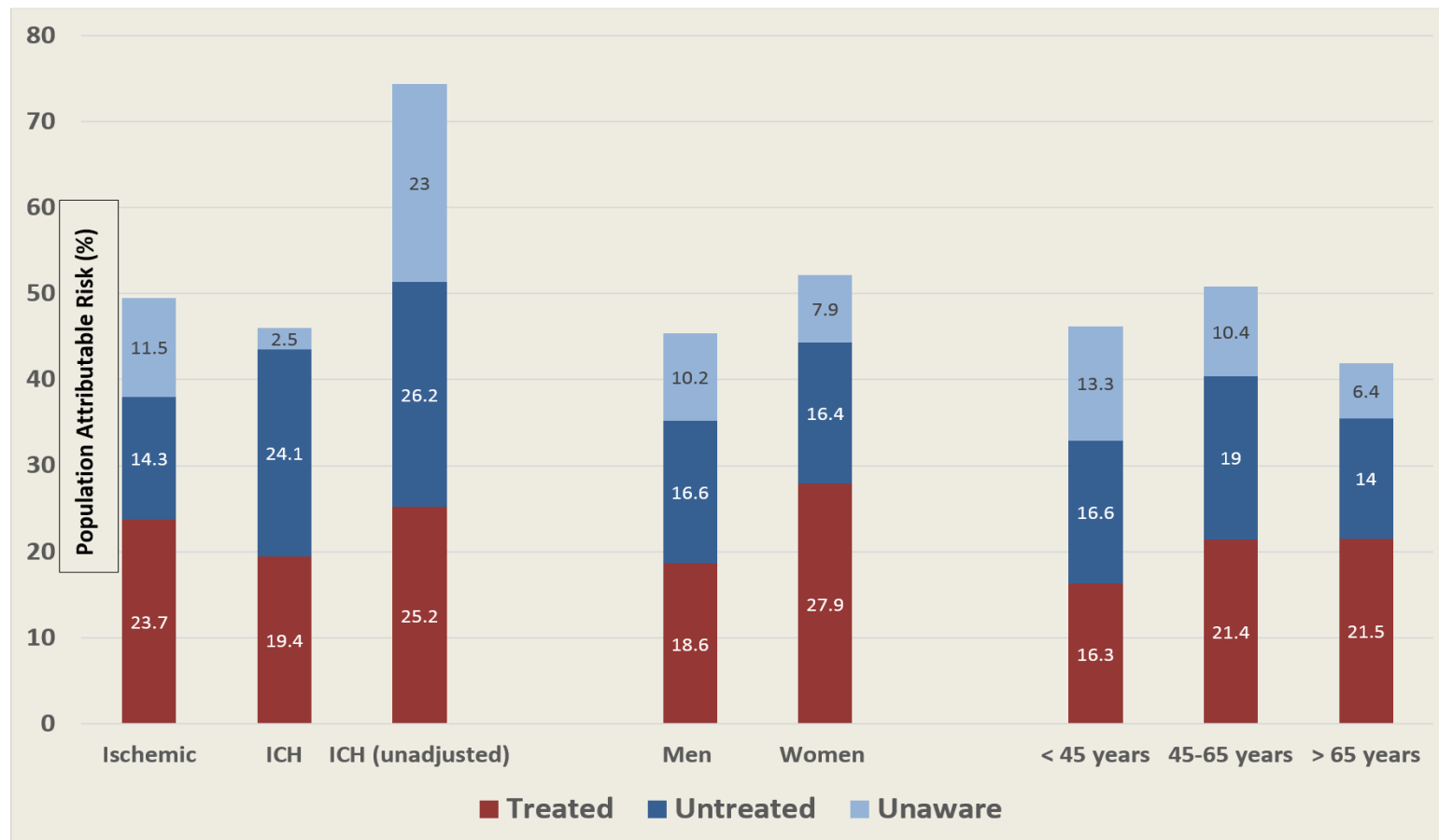
Model includes age as a continuous variable. Cardiac sources include atrial fibrillation or flutter, previous myocardial infarction, rheumatic valve disease, or prosthetic heart valve.

Supplementary Figure 1 Partitioned Population Attributable Risk of Hypertension (Unaware of Hypertension, Aware but untreated and Aware and Treated) Using Community Controls Only



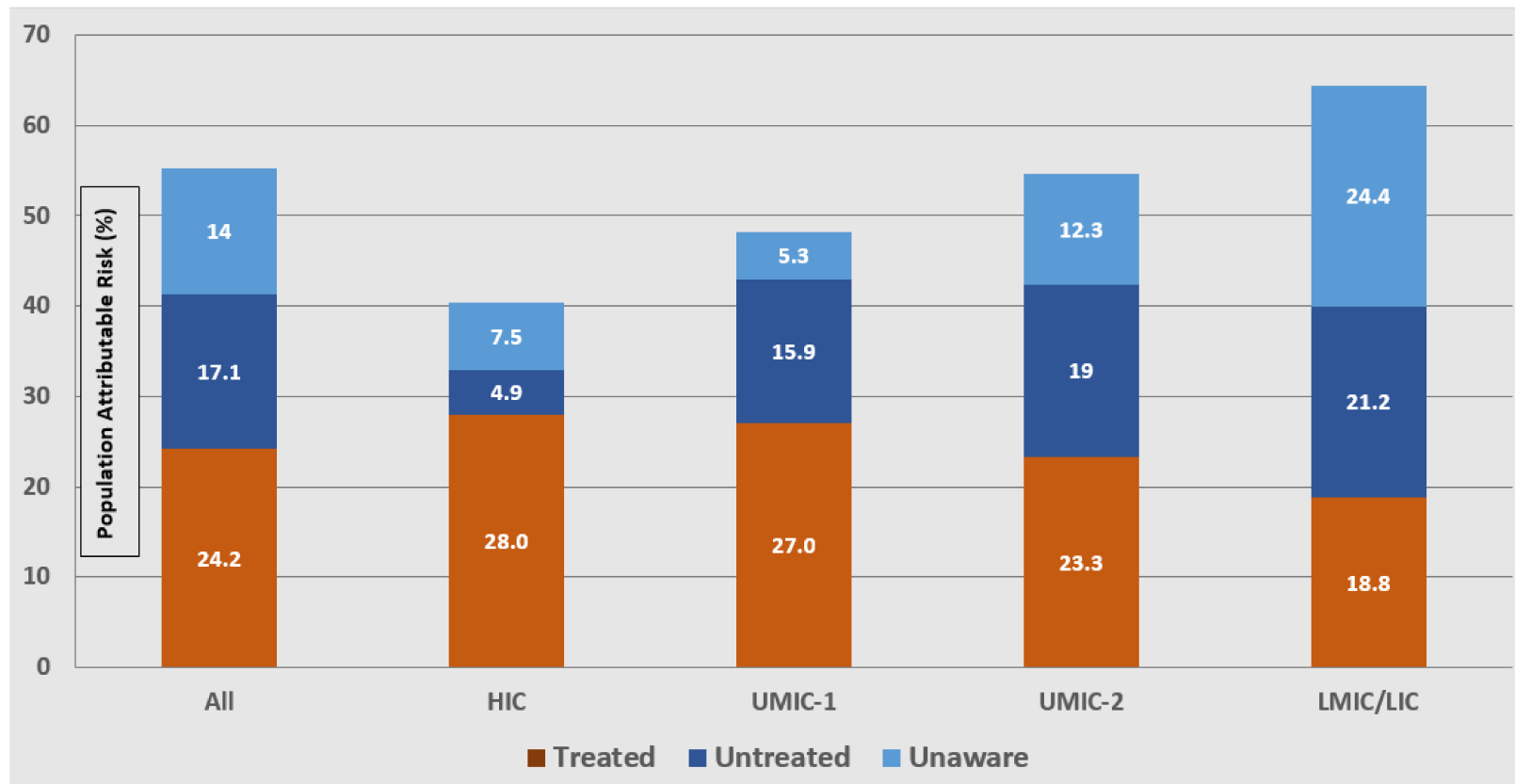
Legend. Figure reports partitioned PAR, by awareness and treatment status (i.e. subdivided into proportion due to treated hypertension, known hypertension but untreated and undiagnosed hypertension). Data are shown overall and in GNI-level groups, GNI-1=GNI >20,000; GNI-2=10,000-19,999; GNI-3=5,000-9,999; GNI-4=<5,000. Figure demonstrates a reduction in proportion of PAR associated with treated hypertension by income-category, with highest PAR for treated hypertension in HIC, and an increase in proportion of PAR associated with untreated hypertension in lower income countries.

Supplementary Figure 2 Partitioned Population Attributable Risk of Hypertension (Unaware of Hypertension, Aware but untreated and Aware and Treated) by Primary Stroke Subtype, Sex and Age Groups



Legend: Figure reports higher proportion of PAR for intracerebral haemorrhage association with untreated hypertension, compared to ischemic stroke, and higher PAR for treated hypertension in women compared to men, and similar PARs for age subgroups.

Supplementary Figure 3 Partitioned Population Attributable Risk of Hypertension (Unaware of Hypertension, Aware but untreated and Aware and Treated) Using Unadjusted Interview Blood Pressure for Cases



APPENDIX 1 - INTERSTROKE (Methods, Risk Factor Measurement)

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 (WHR) and body mass index (BMI), 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 (1-7/week), moderate intake (7-14/week for women and 7-21/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 INTERHEART³, which combines measures of stress (home and work), life events and depression (defined as feeling sad, blue or depressed for two 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 than admission blood pressure (as only intracerebral haemorrhage 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 studies¹, 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 haemorrhage only, as there was no difference in pre-morbid and post-event mean

values for ischemic stroke reported).¹ In our primary report, we used adjusted blood pressure at the time of admission, as detailed in the supplementary appendix of that paper. We calculated the agreement between these 2 approaches for diagnosis of hypertension (blood pressure $\geq 140/90$ mmHg), which was 88.4% (95%CI 87.9-89.0). However, for the current analysis of blood pressure, we identified a clustering of systolic blood pressure measurements at 120, 130, and 140mmHg, and for diastolic blood pressure at 80mmHg and 90mmHg, 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 PARs were consistent using both estimates. For hypertension definition used in primary analyses, compared to definition used in current analyses, we derived ORs for hypertension of 2.98 versus 2.68 overall, 2.28 versus 1.92 for HIC, 2.43 versus 2.29 for UMIC-1, 3.01 versus 2.76 for UMIC-2, and 3.79 versus 3.27 for LMIC/LICs. 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 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.

Estimation of Population Attributable Risk Percentage

PAR/F was calculated according to the formula:

$$PAF = 1 - E_{A,C|Y=1}(1/OR(A|C))$$

where $A \in \{0,1\}$ is the presence of hypertension, $Y \in \{0,1\}$ is an indicator for disease, C is a random vector consisting of the set of variables assumed to confound the risk factor disease relationship. $OR(a|c)$ is the odds ratio comparing risk factor levels a and 0, when the confounders are set to level c . Note that as a function of A and C , $OR(A|C)$ is a random variable that takes the value 1, when $A=0$.

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