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Supplementary Methods

Ischemic strokes were classified into six etiologic subtypes: atherothrombotic, likely atherothrombotic, lacunar, cardioembolic, coexisting (atherothrombotic and lacunar), or unknown.¹

Atherogenic dyslipidemia was defined as high-density lipoprotein cholesterol ≤ 40 mg/dL and triglycerides ≥ 150 mg/dL.² Metabolic syndrome was defined, using World Health Organization and National Cholesterol Education Program Adult Treatment Panel III criteria,³⁻⁵ as ≥ 3 of: body mass index >30.0 kg/m² for non-Asians or >27.5 kg/m² for Asians,⁶ fasting blood glucose 5.6–6.9 mmol/L (100–125 mg/dL), systolic blood pressure (BP) >130 mm Hg, triglycerides >1.7 mmol/L (150 mg/dL), and high-density lipoprotein cholesterol <1.0 mmol/L (40 mg/dL) for men or <1.3 mmol/L (50 mg/dL) for women.

Supplementary References

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Supplementary Table I. Distribution of the PERFORM study population by country and region

Country	Centers, n	Patients, n
Western Europe		
Austria	16	189
Belgium	22	563
Finland	9	245
France	56	796
Germany	66	1480
Greece	5	29
Ireland	6	25
Italy	61	1098
Luxembourg	1	17
Norway	5	99
Portugal	6	262
Spain	53	1077
Sweden	8	128
Switzerland	9	204
The Netherlands	19	467
The United Kingdom	52	865
Turkey	10	78
Eastern Europe		
Bulgaria	10	467
Croatia	6	190
Czech Republic	10	787
Hungary	22	766
Lithuania	6	193
Poland	24	384
Romania	15	809
Russia	56	1594
Slovakia	14	533
Slovenia	4	157
Ukraine	7	213
North America		
Canada	32	483
South America		
Argentina	23	463
Brazil	22	1021
Chile	11	165
Mexico	12	119
Asia		
China	21	468
Hong Kong	4	224
India	14	277
Malaysia	2	61
Singapore	3	173
South Korea	11	377
Taiwan	8	255
Thailand	8	343
Oceania		
Australia	24	494
New Zealand	7	83
Africa		
Morocco	5	5
South Africa	10	130
Tunisia	7	151
Total	802	19119

Supplementary Table II. Medication use before and at randomization among patients from non-Asian and Asian countries

	Before randomization		At randomization	
	Non-Asian (n=16,922)	Asian (n=2,178)	Non-Asian (n=16,922)	Asian (n=2,178)
≥1 antiplatelet agent, n (%)	15,590 (92.1)	1,947 (89.4)*	16,922 (100.0)	2,178 (100.0)
Aspirin	14,785 (87.4)	1,912 (87.8)	8,388 (49.6)	1,174 (53.9)*
Other antiplatelet agent	5,228 (30.9)	710 (32.6)	9,549 (56.4)	1,118 (51.3)*
Aspirin and other antiplatelet agent	3,091 (18.3)	444 (20.4)*	1,015 (6.0)	114 (5.2)
Oral anticoagulant agent, n (%)	5,982 (35.3)	153 (7.0)*	1,543 (9.1)	12 (0.5)*
≥1 antihypertensive agent, n (%)	13,959 (82.5)	1,573 (72.2)*	13,636 (80.6)	1,392 (63.9)*
1 agent	4,625 (27.3)	757 (34.8)*	5,492 (32.4)	842 (38.7)*
2 agents	4,767 (28.2)	480 (22.0)	4,794 (28.3)	394 (18.1)
≥3 agents	4,567 (27.0)	336 (15.4)	3,350 (19.8)	156 (7.2)
Statin, n (%)	10,177 (60.1)	1,463 (67.2)*	10,033 (59.3)	1,424 (65.4)*

* Age- and sex-adjusted p <0.05.

Supplementary Table III. Blood pressure and lipid levels at 3, 12, and 24 months among patients from non-Asian and Asian countries

	3 months		12 months		24 months	
	Non-Asian (n=16,375)	Asian (n=2,088)	Non-Asian (n=15,630)	Asian (n=1,993)	Non-Asian (n=14,667)	Asian (n=1,822)
Blood pressure, mm Hg, mean±SD						
Systolic	137±16	138±18*	137±16	137±18	136±16	136±18
Diastolic	81±9	82±10*	80±9	81±10*	80±9	80±10
Lipid concentrations						
Total cholesterol, mg/dL, mean±SD	179±43	168±39*	184±44	176±40*	186±45	178±40*
LDL cholesterol, mg/dL, mean±SD	105±37	99±32*	106±38	102±33*	107±38	105±34*
HDL cholesterol, mg/dL, mean±SD	52±14	48±12*	52±15	49±13*	51±14	48±13*
Triglycerides, mg/dL, † median (IQR)	118 (88–163)	127 (97–172)*	120 (88–165)	127 (95–173)*	119 (88–166)	124 (93–168)
HDL ≤40 and triglycerides ≥150 mg/dL, n (%)	1,556 (9.2)	271 (12.4)*	1,805 (10.7)	282 (12.9)	1,793 (10.6)	257 (11.8)
HDL ≤35 and triglycerides ≥200 mg/dL, n (%)	458 (2.7)	84 (3.9)*	554 (3.3)	95 (4.4)*	583 (3.4)	65 (3.0)

Abbreviations: HDL, high-density lipoprotein; IQR, interquartile range; LDL, low-density lipoprotein; SD, standard deviation.

* Age- and sex-adjusted p <0.05.

† Analyzed using logarithmic values.

Supplementary Table IV. Two-year primary, secondary, and tertiary outcomes in patients receiving aspirin from non-Asian and Asian countries

	Events, n (%) [*]		Adjusted [*] HR (95% CI)	p-value [*]	Fully-adjusted [†] HR (95% CI)	p-value [†]
	Non-Asian (n=8,388)	Asian (n=1,174)				
Primary outcome						
MACE	844 (10.3)	107 (9.8)	0.95 (0.77-1.16)	0.60	0.90 (0.73-1.10)	0.31
Nonfatal myocardial infarction	105 (1.3)	7 (0.7)	0.50 (0.23-1.07)	0.07	0.49 (0.22-1.07)	0.07
Nonfatal stroke	617 (7.6)	87 (7.9)	1.05 (0.83-1.31)	0.69	1.02 (0.81-1.27)	0.89
Cardiovascular death	150 (1.9)	18 (1.8)	0.95 (0.58-1.55)	0.83	0.82 (0.50-1.34)	0.42
Secondary outcomes						
All-cause death	401 (4.9)	49 (4.6)	0.94 (0.70-1.27)	0.70	0.87 (0.64-1.18)	0.37
Myocardial infarction	109 (1.4)	8 (0.7)	0.55 (0.26-1.13)	0.10	0.53 (0.25-1.10)	0.09
Stroke	623 (7.6)	87 (7.9)	1.04 (0.82-1.30)	0.75	1.01 (0.80-1.27)	0.94
Intracranial hemorrhage	89 (1.2)	19 (1.9)	1.55 (0.95-2.55)	0.08	1.52 (0.91-2.51)	0.10
Bleeding	1220 (16.2)	172 (16.4)	1.02 (0.86-1.20)	0.85	1.02 (0.86-1.20)	0.82
Minor bleeding	984 (13.1)	132 (12.6)	0.96 (0.80-1.16)	0.67	0.96 (0.80-1.16)	0.68
Major bleeding	303 (4.2)	50 (5.1)	1.22 (0.91-1.65)	0.19	1.22 (0.90-1.65)	0.20
Tertiary outcomes						
New-onset atrial fibrillation	147 (1.9)	14 (1.4)	0.75 (0.43-1.30)	0.30	0.82 (0.47-1.42)	0.48
MACE [‡]	24 (16.9)	1 (7.3)	0.41 (0.05-3.06)	0.38	0.37 (0.04-2.90)	0.35

Abbreviations: CI, confidence interval; HR, hazard ratio; MACE, major adverse cardiovascular events.

^{*} Adjusted for age and sex.

[†] Adjusted for age, sex, modified Rankin Scale, hypertension, statin use.

[‡] Calculated for patients with new onset atrial fibrillation.

Supplementary Table V. Two-year primary, secondary, and tertiary outcomes in patients of non-Asian and Asian ethnic origins

	Events, n (%) [*]		Adjusted [*] HR (95% CI)	p-value [*]	Fully-adjusted [†] HR (95% CI)	p-value [†]
	Non-Asian (n=16,856)	Asian (n=2,244)				
Primary outcome						
MACE	1,731 (10.6)	233 (11.3)	1.08 (0.94-1.24)	0.29	1.04 (0.90-1.19)	0.59
Nonfatal myocardial infarction	213 (1.3)	17 (0.9)	0.65 (0.39-1.07)	0.09	0.65 (0.39-1.07)	0.09
Nonfatal stroke	1,281 (7.8)	181 (8.7)	1.12 (0.95-1.30)	0.17	1.10 (0.93-1.29)	0.25
Cardiovascular death	301 (1.8)	43 (2.3)	1.23 (0.89-1.69)	0.21	1.08 (0.78-1.50)	0.64
Secondary outcomes						
All-cause death	817 (4.9)	105 (5.3)	1.08 (0.88-1.33)	0.46	0.99 (0.80-1.22)	0.89
Myocardial infarction	220 (1.4)	18 (0.9)	0.66 (0.41-1.08)	0.10	0.66 (0.40-1.06)	0.09
Stroke	1,290 (7.9)	184 (8.8)	1.13 (0.96-1.32)	0.13	1.11 (0.94-1.30)	0.20
Intracranial hemorrhage	191 (1.3)	46 (2.4)	1.88 (1.36-2.60)	<0.001	1.87 (1.34-2.59)	<0.001
Bleeding	2,224 (14.6)	318 (16.3)	1.13 (1.00-1.27)	0.05	1.11 (0.98-1.25)	0.09
Minor bleeding	1,745 (11.5)	232 (12.0)	1.04 (0.91-1.20)	0.55	1.03 (0.89-1.18)	0.72
Major bleeding	600 (4.1)	104 (5.9)	1.39 (1.12-1.71)	0.002	1.35 (1.09-1.68)	0.005
Tertiary outcomes						
New-onset atrial fibrillation	390 (2.4)	36 (1.9)	0.78 (0.55-1.10)	0.15	0.86 (0.61-1.22)	0.39
MACE [‡]	70 (18.7)	7 (19.6)	1.06 (0.48-2.32)	0.89	1.13 (0.50-2.46)	0.79

Abbreviations: CI, confidence interval; HR, hazard ratio; MACE, major adverse cardiovascular events.

^{*} Adjusted for age and sex.

[†] Adjusted for age, sex, modified Rankin Scale, hypertension, statin use, and antiplatelet treatment allocation (aspirin or terutroban).

[‡] Calculated for patients with new onset atrial fibrillation.

Supplementary Table VI. Baseline characteristics associated with 2-year major adverse cardiovascular events and the interaction between patients from Asian and non-Asian countries

	Non-Asian		Asian		
	Adjusted* HR (95% CI)	p-value*	Adjusted* HR (95% CI)	p-value*	p-value†
Demographics					
Age, per 10 years	1.03 (1.03–1.04)	<0.001	1.33 (1.12–1.58)	0.001	0.61
Male	1.35 (1.22–1.50)	<0.001	1.41 (1.06–1.87)	0.02	0.74
Medical history					
Hypertension	1.20 (1.05–1.38)	0.009	1.04 (0.75–1.45)	0.81	0.42
Diabetes	1.40 (1.27–1.55)	<0.001	1.06 (0.81–1.39)	0.67	0.06
Former smoking	0.99 (0.89–1.10)	0.85	1.02 (0.71–1.44)	0.93	0.87
Current smoking	1.13 (1.01–1.27)	0.03	1.10 (0.81–1.49)	0.53	0.98
Stroke, TIA	1.54 (1.38–1.70)	<0.001	1.63 (1.23–2.17)	<0.001	0.71
Coronary artery disease	1.78 (1.61–1.96)	<0.001	1.31 (0.90–1.89)	0.16	0.11
Peripheral artery disease	1.73 (1.44–2.07)	<0.001	3.34 (0.83–13.46)	0.09	0.35
Atrial fibrillation or flutter	2.06 (1.71–2.48)	<0.001	1.73 (0.81–3.69)	0.16	0.61
Congestive heart failure	1.83 (1.55–2.16)	<0.001	1.07 (0.27–4.32)	0.92	0.44
Educational level					
0–4 years	1.00 (ref)	0.02	1.00 (ref)	0.98	–
5–8 years	0.85 (0.73–0.98)		0.97 (0.68–1.38)		0.42
9–13 years or high school diploma	0.91 (0.78–1.05)		1.01 (0.70–1.46)		0.44
College experience or higher degree	0.79 (0.67–0.94)		0.93 (0.59–1.47)		0.41
Examinations					
Body mass index, per 1 kg/m ² increase	1.00 (0.99–1.01)	0.90	0.97 (0.93–1.01)	0.15	0.20
Systolic BP, per 5 mm Hg increase	1.01 (1.01–1.03)	0.03	1.01 (0.98–1.05)	0.43	0.92
Diastolic BP, per 5 mm Hg increase	1.01 (0.98–1.03)	0.50	1.08 (1.01–1.13)	0.03	0.06
Atherogenic dyslipidemia	1.16 (1.01–1.33)	0.03	0.76 (0.51–1.13)	0.17	0.05
Metabolic syndrome	1.13 (1.02–1.26)	0.02	0.95 (0.71–1.28)	0.75	0.26
Modified Rankin Scale					
0 (no symptoms)	1.00 (ref)	<0.001	1.00 (ref)	0.001	–
1 (no significant disability)	1.26 (1.09–1.44)		1.39 (0.81–2.38)		0.71
2 (slight disability)	1.73 (1.50–2.00)		1.79 (1.02–3.15)		0.89
3 (moderate disability)	1.58 (1.32–1.88)		1.94 (1.08–3.49)		0.52
4 (moderately severe disability)	1.77 (1.44–2.18)		2.76 (1.54–4.92)		0.18

Abbreviations: BP, blood pressure; CI, confidence interval; HR, hazard ratio; TIA, transient ischemic attack.

* Adjusted for age and sex.

† p for interaction between patients from Asian and non-Asian countries.