Supplementary documents for "Education, socioeconomic status and intelligence in childhood and stroke risk in later life: A meta-analysis"

eDocument 1: Medline Search Strategy

eTable 1a-c: Details of included studies by early life factor

eFigure 3: Quality assessment: Frequencies of scores on individual quality items

eFigure 4a. Funnel Plot for analysis of publication bias in studies reporting ORs for education and risk of stroke

eFigure 4b. Funnel Plot for analysis of publication bias in studies reporting MDs for education and risk of stroke.

eFigure 4c. Funnel Plot for analysis of publication in studies reporting HRs for education and risk of stroke.

eDocument 2. Footnotes for Figure 2a. Educational attainment (low versus high) and risk of stroke, risk ratio (OR, HR and RR), random effects model (risk ratio <1 indicates low education decreases risk of stroke; >1 = low education increases risk of stroke.

eFigure 5a. Sensitivity analysis comparing studies that included younger (mean age ≤ 65 years) vs those that included older (mean age >65 years) participants by education level and risk of stroke; OR>1= low education increases risk of stroke.

eFigure 5b. Sensitivity analysis comparing studies that included younger (mean age ≤ 65 years) vs studies that included older (mean age >65 years) participants by education level and risk of stroke; HR>1= low education increases risk of stroke.

eFigure 5c. Sensitivity analysis for comparing studies that included younger (mean age \leq 65 years) vs studies that included older (mean age >65 years) participants by education level and risk of stroke; negative mean difference = lower education decreases risk of stroke and positive mean difference = lower education increases risk of stroke.

eFigure 5d. Sensitivity analysis comparing adjusted vs unadjusted studies by education level and risk of stroke; OR>1= low education increases risk of stroke.

eFigure 5e. Sensitivity analysis comparing adjusted for vascular risk factors vs unadjusted studies by education level and risk of stroke; OR>1= low education increases risk of stroke.

eFigure 5f. Sensitivity analysis comparing population cohort studies vs hospital/outpatient studies by education level and risk of stroke; OR>1= low education increases risk of stroke.

eFigure 5g. Sensitivity analysis comparing stroke ascertainment methods (clinical examination, self-report, central health statistics) by education level and risk of stroke; OR>1= low education increases risk of stroke.

eFigure 5h. Sensitivity analysis comparing males and females by education level and risk of stroke; OR>1= low education increases risk of stroke.

eFigure 5i. Sensitivity analysis comparing males and females by education level and risk of stroke; HR>1= low education increases risk of stroke.

eFigure 5j. Sensitivity analysis comparing first only and recurrent/unspecified stroke by education level and risk of stroke; HR>1= low education increases risk of stroke.

eDocument 1: MEDLINE Search Strategy

Note we included search terms to identify studies examining early life risk factors for post-stroke cognitive impairment and depression for subsequent reviews, hence terms such as cognition – these have not been excluded if not relevant to education, SES, IQ and stroke in the present analysis.

1. cerebrovascular disorders/ or basal ganglia cerebrovascular disease/ or exp brain ischemia/ or carotid artery diseases/ or carotid artery thrombosis/ or carotid stenosis/ or cerebral small vessel diseases/ or cerebral amyloid angiopathy, familial/ or stroke, lacunar/ or intracranial arterial diseases/ or cerebral arterial diseases/ or intracranial arteriosclerosis/ or exp "intracranial embolism and thrombosis"/ or exp stroke/ or leukoencephalopathies/ or leukoaraiosis/

2. exp *brain/ and *atrophy/

3. (isch?emi\$ adj6 (stroke\$ or apoplex\$ or cerebral vasc\$ or cerebrovasc\$ or cva)).tw.

4. ((brain or cerebr\$ or cerebell\$ or vertebrobasil\$ or hemispher\$ or intraceran\$ or intracerebral or infratentorial or supratentorial or middle cerebral artery or MCA\$ or anterior circulation or posterior circulation or basilar artery or vertebral artery or space-occupying) adj6 (isch?emi\$ or infarct\$ or thrombo\$ or emboli\$ or occlus\$ or hypoxi\$)).tw.

5. ((cerebell\$ or vertebrobasil\$ or hemispher\$ or intracran\$ or intracerebral or infratentorial or supratentorial or middle cerebr\$ or MCA\$ or anterior circulation or posterior circulation or basilar artery or vertebral artery or space-occupying) adj6 stroke\$).tw.

6. ((brain or cereb\$) adj6 (vascular or microvascular) adj6 (disease\$ or disorder\$)).tw.

7. (intracranial adj6 (disease\$ or disorder\$)).tw.

8. (cerebral adj6 (small vessel disease\$ or microangiopath\$ or amyloid angiopath\$)).tw.

9. ((lacun\$ or subcortical) adj6 (stroke\$ or infarct\$)).tw.

10. (leukoencephalopath\$ or leukoaraiosis).tw.

11. (white matter adj6 (disease\$ or hyperintensit\$ or intensity\$ or change\$ or lesion\$ or damage or abnormalit\$ or integrity or tracts or infarct\$ or structure)).tw.

12. ((brain or cerebral or intracranial) adj6 (arteriosclero\$ or atherosclero\$ or atrophy\$ or microbleed\$ or microhaem\$ or microhem\$)).tw.

13. exp *intracranial hemorrhages/ and (microbleed\$ or microhaem\$ or microhem\$).tw.

14. or/1-13

15. cognition disorders/ or mild cognitive impairment/ or dementia/ or dementia, vascular/ or dementia, multiinfarct/

16. neurobehavioral manifestations/ or confusion/ or memory disorders/

17. mental processes/ or cognition/ or cognitive reserve/ or Arousal/ or Orientation/ or Attention/ or exp memory/ or perception/ or exp thinking/ or Awareness/ or Problem Solving/ or "Generalization (Psychology)"/ or "Transfer (Psychology)"/ or comprehension/ or Impulsive Behavior/ or Learning/

18. ((cogniti\$ or arous\$ or orientat\$ or attention\$ or concentrat\$ or memor\$ or recall or percept\$ or think\$ or sequenc\$ or judg?ment\$ or awareness or problem solving or generali?ation or transfer or comprehension or learning or mental process\$ or (concept adj5 formation) or executive function\$) adj6 (ability\$ or function\$ or

difficult\$ or impair\$ or process\$ or skill\$ or performance or reserve or disorder\$ or manifestation\$ or declin\$ or dysfunct\$ or deficit\$ or disabilit\$ or problem\$)).tw.

19. (cognition or confusion or dysexecutive syndrome\$ or impulsive behavio?r\$ or executive dysfunction\$).tw.20. or/15-19

21. exp intelligence/ or exp intelligence tests/

22. aptitude/ or aptitude tests/ or language tests/

23. education/ or educational status/ or exp educational measurement/

24. (intelligence or intelligent or IQ or intellectual or aptitude).tw.

25. (language adj6 (test\$ or ability)).tw.

26. (education\$ adj6 (status or attainment or measurement\$)).tw.

27. ((mental or intellect\$) adj6 (capacit\$ or capabilit\$ or abilit\$ or performance)).tw.

28. or/21-27

29. child/ or child, preschool/ or adolescent/ or adult children/

30. (child\$ or adolescen\$ or youth or early life or early adult or pre-adult or early year\$ or premorbid or premorbid).tw.

31. 29 or 30

32. 28 and 31

33. Education/ or Socioeconomic factors/ or educational status/ or educational measurement/ or psychology, educational/ or achievement/

34. (education or school\$ or preschool or college or university or literate or literacy).tw.

35. ((educat\$ or academi\$ or schola\$) adj6 (achieve\$ or attain\$ or level or qualification\$ or performance or status)).tw.

36. or/33-35

37. socioeconomic factors/ or exp poverty/ or social class/ or social mobility/ or employment/ or unemployment/ or exp family characteristics/ or exp income/ or exp occupations/

38. ((soci\$ or economic or living or family) adj6 (condition\$ or factor\$ or status or inequalit\$ or standard\$ or

characteristic\$ or size\$ or wealth or position or depriv\$ or income)).tw.

39. 37 or 38

40. child/ or child, preschool/ or adolescent/ or adult children/ or fathers/ or mothers/ or parents/

41. (child\$ or adolescen\$ or youth or early life or early adult or pre-adult or early year\$).tw

42. 40 or 41

43. 39 and 42

44. ((father\$ or mother\$ or parent\$) adj6 (income\$ or occupation\$ or job\$)).tw

45. 43 or 44

46. 14 and 20 and 32 (CVD, cog and IQ))

47. 14 and 20 and 36 (CVD, cog and education)

- 48. 14 and 20 and 45 (CVD, cog and SES)
- 49. 14 and 32 (CVD and IQ)
- 50. 14 and 36 (CVD and education)
- 51. 14 and 45 (CVD and SES)
- 52. 46 or 47 or 48 (CVD, Cog and any early life factor)
- 53. 49 or 50 or 51 (CVD and any early life factor)
- 54. 52 or

eTable 1a-c. Details of included studies by early life factor

1a Education									
Study	Setting	Total number of participants	Participants with stroke (n)	Participants without stroke (n)	Age at follow up/stroke	Measure of education	Primary outcome	Measurement of outcome	Results
				Mean year	s of education				
Tatemichi et al (1992) ¹	Hospital Outpatient clinic	500	251	249	71.9	Mean years of education	Ischaemic stroke	Clinical examination Neuroimaging	Stroke: 10.1±4.5 Non-stroke: 12.3±4.6
Sydney Stroke Study Sachdev et al (2014) ² (3-7)	Hospital	280	183	97	71.91	Mean years of education	Ischaemic stroke and TIA	Clinical examination Neuroimaging	Stroke: 10.10±2.66 Non-stroke: 11.75±3.31
Lukatela et al (2000) ⁸	Outpatient clinic	218	159 89 Single stroke 70 Multiple infarction	59	Mean age approx. 72	Mean years of education	Ischaemic and haemorrhagic stroke	Clinical examination Neuroimaging	Single stroke 11.97±2.57 Multiple infarction: 11.62±3.23 Non-stroke: 12.86±2.51

Vantaa 85+ Study	Population	553	111	442	88.5	Mean years of education	Ischaemic, haemorrhagic stroke and TIA	Clinical examination	Stroke: 3.2±2.0
Rastas et al (2007) ⁹								Centralised Health Statistics	Non-stroke: 4.3±3.0
Copstein et al (2012) ¹⁰	Population	3391	285	3106	≥20	Mean years of education	Ischaemic and haemorrhagic stroke	Self-report questionnaire	Stroke: 7.09±4.05
					44.13 (whole sample)				Non-stroke: 8.12±3.45
Honolulu- Asia Aging Study	Population	3734	147	3170	78.8	Mean years of education	Ischaemic and haemorrhagic stroke	Neuroimaging	Stroke: 9.8±3.0
Petrovitch et al (1998) ¹¹								Case note review	Non-stroke: 10.5±3.2
Mok et al (2004) ¹²	Hospital	117	75	42	71	Mean years of education	Ischaemic stroke and TIA	Clinical examination	Stroke: 4.8±4.1
								Neuroimaging	Non-stroke: 5.4±4.6
Hochstenbach et al (1998) ¹³	Hospital	262	229	33	18-70	Mean years of education	Ischaemic and haemorrhagic stroke	Clinical examination	Stroke: 4.1±1.5
					mean = 55.9			Neuroimaging	Non-stroke: 4.4±1.5

Helsinki Stroke Aging Memory (SAM) Study	Hospital	361	323	38	71.7	Mean years of education	Ischaemic stroke	Clinical examination	Stroke (other): 9.8±4.3
Jokinen et al (2006) ¹⁴			85 Subcortical ischaemic vascular disease 238 other stroke					Neuroimaging	Non-stroke: 9.4±3.5
Kastorini et al (2013) ¹⁵	Hospital	500	250	250	77/73	Mean years of education	Ischaemic stroke	Clinical examination Neuroimaging	Stroke: 8±4.6 Non-stroke: 8±4.9
Third National Health and Nutrition Survey (NHANES III)	Population	11 163	619	10 544	>40	Year of schooling	Ischaemic and haemorrhagic stroke	Self-report questionnaire	Stroke: 9.2±4.1
Bravata et al (2005) ¹⁶ ¹⁷⁻¹⁹					Average <65				Non-stroke: 10.3±4.2
Kauranen et al (2013) ²⁰	Hospital	190	140	50	52	Mean years of education	Ischaemic stroke	Clinical examination Neuroimaging	Stroke: 12.5±2.6 Non-stroke: 12.4±2.9

Reitz et al (2006) ²¹	Community	1 271	97	1 174	76.3	Mean years of education	Ischaemic, haemorrhagic stroke and TIA	Clinical examination	Stroke: 8.9±4.3
							WHO criteria	Neuroimaging	Non-stroke: 8.6±4.6
								Case note review	
								Self-report questionnaire	
Gillespie et al (2012) ²²	Hospital	112	56	56	40-88	Mean years of education	Ischaemic and haemorrhagic stroke	Clinical examination	Stroke: 10.09±1.64
					65.55			Neuroimaging	Non-stroke: 10.56±2.12
Kessels et al $(2006)^{23}$	Hospital	266	105	161	59.5	Mean years of education	Ischaemic and haemorrhagic stroke	Clinical examination	Stroke: 10.7±3.7
	Outpatient Clinic								Non-stroke: 10.3±3.2
Columbia- Presbyterian Medical Centre	Outpatient Clinic	575	334	241	≥60	Mean years of education	Ischaemic stroke	Clinical examination	Stroke: 10.7±4.9
Desmond et al $(2002)^{24}$								Neuroimaging	Non-stroke: 12.4±4.5
25									

			Fre	equencies (n=st	roke vs without	t stroke)			
Hu et al (2005) ²⁶	Population cohort	47 721	2863	44 858	Men: 49.5	0-6 years	Ischaemic and haemorrhagic stroke	Centralised Health Statistics	0-6 years = 798 vs 12 610
					Women: 52	7-9 years			≥7 years = 2065 vs 32 248 [§]
					No range	9+ years			
Japan Public Health Centre- based Prospective Study (JPHC)	Population cohort	29 134	793	28 341	50-69	Age at completion of education	Ischaemic and haemorrhagic stroke	Neuroimaging	\leq 14 years = 439 vs 13 662
Honjo et al (2009) ²⁷						\leq 14 years		Case note review	$\geq 15-17 = 354$ vs 14 679 [§]
28-30						15-17 years		Centralised health statistics	
								Self-report	
National Health Interview Survey (NHIS-1994)	Population cohort	11 925	71	11 854	All ages included	Not educated (NE)	Ischaemic and haemorrhagic stroke	Case note review	$\frac{\leq PS = 60 \text{ vs}}{5459^{\$}}$
Huang et al (1997) ³¹					Majority over 65yrs	Primary school (PS)		Self-report	\geq JS = 11 vs 6395
						≥ Junior School (JS)			
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Framingham Heart Study	Population cohort	264	132	132	77.4	< High school (<hs)< th=""><th>Ischaemic and haemorrhagic stroke</th><th>Clinical examination</th><th><hs =14="" vs<br="">10</hs></th></hs)<>	Ischaemic and haemorrhagic stroke	Clinical examination	<hs =14="" vs<br="">10</hs>
Weinstein et al $(2014)^{32}$						High school degree (HS)		Neuroimaging	$\geq HS = 118 \text{ vs}$ $122^{\$}$
33						Some college		Case-note review	
						≥ College degree		Centralised Health Statistics	
								Self-report	
Health and Aging and Body Composition (Health ABC)	Population cohort	2574	180	2394	70-75	< 12 years	Ischaemic, haemorrhagic stroke and TIA	Clinical examination	<12 years = 82 vs 1046
Koster et al (2005) ³⁴						12 years		Self-report	≥ 12 years = 98 vs 1345§
						>12 years			
REGARDS	Population cohort	27 716	2830	24 886	≥45	< High school (<hs)< td=""><td>Ischaemic, haemorrhagic stroke and TIA</td><td>Self-report</td><td><hs 611="" =="" vs<br="">2986</hs></td></hs)<>	Ischaemic, haemorrhagic stroke and TIA	Self-report	<hs 611="" =="" vs<br="">2986</hs>
Brenner et al $(2010)^{35}$					Majority over 65yrs	High school degree (HS)			\geq HS = 2 216 vs 21 924§
36						Some college (SC)			
						College graduate (CG)			

de Bruijin et al (2014) ³⁷	Hospital	157	96	61	47.3	Low: ≤ High school (HS)	Ischaemic stroke	Clinical examination	\leq HS = 35 vs 7
			94 with education		18-49	Medium: Secondary vocational education		Neuroimaging	>HS = 59 vs 54§
						High: ≥Higher professional or university			
Multi-ethnic Study of Atherosclerosis (MESA)	Outpatient clinic	6749	195	6554	68.3	<high school<br="">(<hs)< td=""><td>Ischaemic, haemorrhagic stroke and TIA</td><td>Clinical examination</td><td><hs 43="" =="" vs<br="">1171</hs></td></hs)<></high>	Ischaemic, haemorrhagic stroke and TIA	Clinical examination	<hs 43="" =="" vs<br="">1171</hs>
Everson-Rose (2014) ³⁸			147 strokes		45-84	High school or some college (HS)		Neuroimaging	≥HS = 152 vs 5383§
			48 TIA			≥College degree (≥CD)			
Uppsala Longitudinal Study of Adult Men (ULSAM)	Population cohort	919	155	764	70	Elementary school (6-8 years)	Ischaemic, haemorrhagic stroke and TIA	Centralised health Statistics	6-8 years = 53 vs 571
Wiberg et al 2012) ³⁹			72 with education	729 with education		Secondary school (12 years)		Medical records	≥12 years = 19 vs 158 [§]
40						≥College (>12 years)			

EPIC- Postdam Study	Population cohort	27 548	168	2198	55.9	≤ Vocational school (≤ 10 years)	Ischaemic stroke	Case note review	$\leq 10 \text{ years} = 72 \text{ vs } 808$
Weikert et al (2008) ⁴¹			167 with education	2196 with education	35-65	Technical school (12 years)		Self-report questionnaire	≥12 years: n = 95 vs 1389 [§]
						University (>12 years)		Death certificate	
Cardiovascular Health Study	Cohort study	4619	650	3969	≥65	<high school<br="">(<hs)< td=""><td>Ischaemic stroke</td><td>Clinical examination</td><td><hs 216="" =="" vs<br="">1125</hs></td></hs)<></high>	Ischaemic stroke	Clinical examination	<hs 216="" =="" vs<br="">1125</hs>
Yan et al (2013) ⁴²					73.57	High School or GED (HS)		Centralised Health Statistics	$\geq HS = 434 \text{ vs}$ $2844^{\$}$
						Some college (SC)		Self-report	
						College graduate (CG)			
						Graduate or Professional school (Grad)			
Diet, Cancer and Health Danish Follow up Study	Hospital	508	254	254	60.5	7 years	Ischaemic stroke	Neuroimaging	$\leq 10 \text{ years} =$ 217 vs 203 [§]
Nybo et al (2008) ⁴³					50-64	8-10 years		Centralised Health Statistics	>10 year =37 vs 51
						>10 years		Autopsy	

Engels et al (2014) ⁴⁴	Population	44 742	127	44 615	15+	0-4 years	Ischaemic and haemorrhagic stroke	Clinical examination	0-9 = 117 vs 33 716 [§]
					Majority of stroke over 65yrs	5-9 years		Neuroimaging	≥10: n=10 vs 10 899
						≥ 10 years		Self-report	
Trygged et al (2011) ⁴⁵	Population	424 281	42 026	382 255	18-64	Compulsory (9 years)	NS	Centralised Health Statistics	Compulsory = 16 642 vs 126 482
						Upper Secondary			≥ Upper secondary = 25 359 vs 255 798 [§]
						University			
Social Inequality in Cancer Cohort Study	Population cohort	68 643	3613	65 030	30-70	Low: Primary and lower Secondary	Ischaemic stroke	Centralised Health Statistics	Low = 1393 vs 67 250
Combines Copenhagen City Heart Study, 1936 Cohort Study, Monica I, II, III, Diet Cancer and Health Study and Inter 99 Study					54 at baseline (follow up 14 years)	Medium: Upper secondary, vocational or technical education			≥Medium = 2148 vs 135 066§
Nordahl et al (2014) ⁴⁶						High: University			

Valko et al (2008) ⁴⁷	Hospital	689	235	454	63/47	Primary school (PS)	Ischaemic stroke	NS	PS = 59 vs 43
			214 with education	447 with education	21-87	Secondary school (SS)			$\geq SS = 155 \text{ vs}$ $404^{\$}$
						College (Coll)			
						University (Uni)			
Assets and Health Dynamics among the oldest old (AHEAD)	Population	5511	545	4966	≥65	Grade school (GS)	Ischaemic and haemorrhagic stroke	Centralised Health Statistics	GS = 137 vs 1241
Wolinsky et al (2009) ⁴⁸						High school (HS)			$\geq HS = 408$ vs $3725^{\$}$
						College (Coll)			
Baune et al (2006) ⁴⁹	Hospital	336	112	224	35-69	No education	Ischaemic and haemorrhagic stroke	Clinical examination	≤ Prep = 86 vs 157
	Outpatient clinic		111 with education	223 with education	Majority under 65yrs	Primary school (PS)		Neuroimaging	\geq SS = 25 vs 66 [§]
						Preparatory school (Prep)			
						Secondary school (SS)			
						University degree (Uni)			
						Other			

Deoke et al (2012) ⁵⁰	Hospital	201	101	100	59.3	Illiterate or Primary school $(\leq PS)$	Ischaemic and haemorrhagic stroke	Clinical examination	$\leq PS = 38 vs$ 34
					Most over 60	>Primary school (>PS)		Neuroimaging	>PS = 63 vs 66
Oxford Vascular Study (OXVASC)	Population	314	207	107	71.4	<12 years	Ischaemic and haemorrhagic stroke	NS	<12 years = 119 vs 25
Oxford Project to Investigate Memory and Ageing (OPTIMA)						≥12 years			≥12 years = 88 vs 82
Pendlebury et al (2012) ⁵¹									
Kingsholem Project	Population	1301	183	1118	≥75	<8 years	Ischaemic and haemorrhagic stroke	Centralised Health Statistics	<8 years = 96 vs 559
Zhu et al (2000) ⁵²						≥8 years		Hospital register	≥8 years = 87 vs 559
Sim et al (2008) ⁵³	Outpatient clinic	479	265	214	58.87	<12 years	Ischaemic and haemorrhagic stroke	Clinical examination	<12 years = 141 vs 117
	Population				40-79	\geq 12 years			\geq 12 years = 124 vs 97

Population	1 135 383	8215	1 127 168	NS	\leq 9 years	Ischaemic and	Centralised	\leq 9 years =
1					2	haemorrhagic	Health	1945 vs 157
						stroke	Statistics	804
				28-55	> 9 years		Cause of death register	>9 years = 6270 vs 969 364
							ICD 8 : 430- 438; ICD 9: 430-435, 437; ICD10: I60, I62-I69, G45	
Out-patient clinic	219	143	74	≥45	None (0 years)	Ischaemic and haemorrhagic stroke	Clinical examination and neuroimaging	0-6 years = 60 vs 21 [§]
Hospital				60.4	Primary education (1-6 years)		WHO criteria	\geq 7 years = 83 vs 53 [§]
					Secondary education (7-12 years)			
					Tertiary education (>12 years)			
	Out-patient clinic	Out-patient 219 clinic 219	Out-patient 219 143	Out-patient 219 143 74	Out-patient 219 143 74 ≥45	Out-patient clinic 219 143 74 ≥45 None (0 years) Hospital 60.4 Primary education (1-6 years) Secondary education (7-12 years) Tertiary education (>12	Out-patient clinic 219 143 74 ≥45 None (0 years) Ischaemic and haemorrhagic stroke Hospital 143 74 ≥45 None (0 years) Ischaemic and haemorrhagic stroke Hospital 143 74 ≥45 None (0 years) Ischaemic and haemorrhagic stroke Hospital 143 74 ≥45 None (0 years) Ischaemic and haemorrhagic stroke Hospital 143 74 ≥45 None (0 years) Ischaemic and haemorrhagic stroke Hospital 143 74 ≥45 None (0 years) Ischaemic and haemorrhagic stroke Hospital 143 74 ≥45 None (0 years) Ischaemic and haemorrhagic stroke Hospital 143 74 ≥45 None (0 years) Ischaemic and haemorrhagic stroke Hospital 143 143 143 143 143 143 143 Hospital 143 143 143 143 143 143 143 Hospital 143 143 143 143 143 143 143	Out-patient clinic 219 143 74 ≥45 None (0 years) Ischaemic and haemorrhagic stroke Clinical examination and neuroimaging Health Statistics Out-patient clinic 219 143 74 ≥45 None (0 years) Ischaemic and haemorrhagic stroke Clinical examination and neuroimaging Hospital 60.4 Primary education (1-6 years) WHO criteria Secondary education (2-12 years) Secondary education (2-12 WHO criteria

Liu et al (2008) ⁵⁷	Hospital	112	60	52	73	Illiterate Primary school (PS; 0-6 years) Middle school (MS;7+ years)	Ischaemic stroke	Clinical examination Neuroimaging Chinese classification - 1995	$\leq PS = 30 vs$ $37^{\$}$ > MS = 30 vs 15
				Odd	ls Ratios				<u> </u>
Jilin Provincial Chronic Disease Survey of 2012	Population	21 435	NS	NS	18-79	≤ Primary school	"Cerebrovascul ar disease"	Self-report questionnaire	OR = 0.91 (0.78-1.07)*†
Wang et al (2015) ⁵⁸					Majority under 60yrs	Junior high school	Based on the ICD10: I60-67, I69		
						Senior high school			
						\geq College			

Chen et al (2014) ⁵⁹	Population	512 891	8884	504 007	35-74	No formal	Ischaemic,	Self-report	OR = 2.28
						school	haemorrhagic stroke and TIA	questionnaire	(2.02-2.56)*†
					61.5	Primary school (PS)			
						Middle school (MS)			
						High school (HS)			
						College/univers ity			
Hamano et al (2014) ⁶⁰	Population	326 229	4718	321 511	≥30	Compulsory school (≤ 9 years)	Ischaemic and haemorrhagic stroke	Centralised Health Statistics	OR = 1.56 (1.45-1.67)†
						High school (10-12 years)	ICD10: I60- I69		
						High school/college (>12 years)			
Strodl et al (2008) ⁶¹	Community	7839	174	8939	70-75	No formal education	Stroke	Self-report questionnaire	OR = 0.98 (0.68-1.41)*
						Primary school (PS)			
						Secondary school (SS)			
						Tertiary			

Nanjing Chronic Disease and Risk Behaviour Study (NCDRBS)	Population	29 340	453	28 887	>35	0-9 years	Stroke	Self-report questionnaire	OR = 1.08 (0.82-1.44)*†
Xu et al (2008) ⁶²					Majority of stroke >65	10-12 years >13 years	WHO MONICA	Medical records	
Medin et al (2008) ⁶³	Hospital	168	65	103	54.8	Low education (6-9 years) High education (> 9 years)	Ischaemic and haemorrhagic stroke ICD10 I61, I63, I64	NS	OR = 2.48 (1.18-5.23)†
You et al (1999) ⁶⁴	Community and hospital	904	452	452	59	No high school Some high school Completed high school Other tertiary University	Ischaemic stroke WHO classification	NS	OR = 0.83 (0.47-1.47)*†
Kisjanto et al (2005) ⁶⁵	Hospital	917	235	682	20-44	Illiterate or elementary school (ES) ≥Secondary school	Ischaemic and haemorrhagic stroke WHO classification	Clinical examination	OR= 0.72 (0.52-0.99)*

Lofmark et al	Population	55 266	457	54 809	35-85	Low education	Ischaemic	Centralised	OR: Age 35-
(2007) ⁶⁶						(maximum of 9 years compulsory school)	stroke	health Statistics	75 years = 1.09 (0.88- 1.34)†
					Split into 35- 75 and 75-85	High education (>9years compulsory school)	WHO classification		OR: Age 75- 85 years = 2.48 (1.06- 5.77)†
							ICD 10: I63.0- I63.9		
Folsom et al (1990) ⁶⁷	Population	2063	218	1845	55-69	<high school<br="">(<hs)< td=""><td>Ischaemic and haemorrhagic stroke</td><td>Centralised health Statistics</td><td>OR = 0.6 (0.4-0.8)*†</td></hs)<></high>	Ischaemic and haemorrhagic stroke	Centralised health Statistics	OR = 0.6 (0.4-0.8)*†
						High school (HS) >High school	ICD 9: 430- 438	Self-report questionnaire Contact with	
						(>HS)		GP	

The Rotterdam	Population	4274	162	3996	NS	Primary school	NS	Case note	OR: HS =
Study				(baseline)		(PS)		review	0.89 (054- 1.49)*†
Van Rossum et al (1999) ⁶⁸			105 with history of stroke (HS)	3839 (follow up)	Majority over 65yrs	Lower/intermed iate general and lower vocational education	ICD 10	Centralised Health Statistics	OR: FS = 0.86 (0.57-1.30)*†
			157 with stroke at follow up (FS)			Higher general and intermediate vocational education		Self-report	
						Higher education (vocational) and university			
Vasterbotten Intervention Program (VIP) in collaboration with WHO MONICA	Population	1148	473	945	25-74	Low (≤9 years)	Ischaemic and haemorrhagic stroke	Neuroimaging	OR: Men = 1.1 (0.7-1.8)
Emmelin et al (2003) ⁶⁹					54.7	Medium (10-12 years)			OR: Women = 1.1 (0.7- 1.9)
						High (≥ 13 years)			

Gan et al (2011) ⁷⁰	Hospital	618	309	309	61.34/61.03	\leq Junior school (\leq JS)	Ischaemic stroke	Clinical examination	OR = 0.63 (0.42-0.96)*
									, , ,
Fitzpatrick et al (2012) ⁷¹	Population	1612	401	1211	52	Mean years of education	Ischaemic, haemorrhagic stroke and TIA	Self-report questionnaire	OR: 0.98 (0.93-1.04)*
Epidemiologic studies of the Elderly (EPESE) program	Community	4034	307	3727	>65		NS	Self-report questionnaire	OR: 0.97 (0.95-1.01)*†
Fillenbaum et al (2000) ⁷²									
WHO collaborative study	Hospital	8146	2162	5984	15-49	High (>Secondary schooling)	Ischaemic and haemorrhagic stroke	Clinical examination	OR: Eastern Europe = 2.05 (0.92-4.54)†
Chang et al (2002) ⁷³						Secondary schooling	Only Ischaemic stroke results used		OR: Asia = 1.19 (0.71- 1.98)†
74						Low (Primary or no schooling)			OR: Latin American = 1.16 (0.72- 1.87)†

The Brain Attack	Population	1147	808	339	≥45	<high school<="" th=""><th>Ischaemic and</th><th>Case note</th><th>OR: NHW =</th></high>	Ischaemic and	Case note	OR: NHW =
Surveillance in						(<hs)< td=""><td>haemorrhagic</td><td>review</td><td>4.53 (2.20-</td></hs)<>	haemorrhagic	review	4.53 (2.20-
Corpus Christie							stroke and TIA		9.32)†
(BASIC) project									
Smith et al			405 Non-		70	≥High school		Centralised	OR: MA =
$(2003)^{75}$			Hispanic			(≥HS)		health Statistics	5.08 (3.17-
			whites						8.14)†
			(NHW)						
			403 Mexican						
			Americans						
			(MA)						
Jackson et al	Population	11 468	177	11 291	47-52	No formal	Ischaemic and	Self-report	OR = 1.30
$(2014)^{76}$	- I			-		education	haemorrhagic	questionnaire	(0.72-2.34)*
							stroke	-	
						School	ICD10: I60-	Centralised	
						certificate	I60.9, I61-	health Statistics	
							I61.9, I53-		
							I63.9 and I64		
						TT: 1 - 1 - 1			
						High school certificate			
						centificate			
						Trades and			
						apprentice			
						Certificate/dipl			
						oma			
						University			
						degree or			
						higher			

Grau et al (2012) ⁷⁷	Hospital	740	370	370	60.7	\geq 12 years	Ischaemic,	Clinical	OR = 0.81
							haemorrhagic stroke and TIA	examination	(0.50-1.31)*†
78-81						<12 years		Neuroimaging	
				Rela	ative Risk	•			
Andersen et al (2014) ⁸²	Population	54 048	NS	NS	71.9	Basic/High school (7-12 years)	Ischaemic stroke	Neuroimaging	RR = 0.99 (0.97-1.0)*†
						Vocational (10- 12 years)		Centralised health Statistics	
						Higher (≥13 years)			
NHANES I and NHEFS	Population	5614	802	4812	45-74	<8 years	Ischaemic and haemorrhagic stroke	Centralised health Statistics	RR: White Men =0.96 (0.73-1.27)*†
Gillum et al (2002) ⁸³					Majority of strokes >65	8-11 years	ICD 9: 431- 434.9, 436, 437-437.1		RR: White Women = 0.91 (0.69- 1.19)*†
84						12 years			RR: Black Men and Women = 0.66 (0.46- 0.96)*†
						>12 years			
Lindenstrom et al (1993) ⁸⁵	Population	13 000	696	12 304	>35	\leq 7 years	Ischaemic stroke and TIA	NS	RR = 1.3 (1.1- 1.5)†
					61.7	\geq 8 years			

The Brain Attack Surveillance in Corpus Christie (BASIC) project	Population	631	631	NS	72.7	High school (HS)	Ischaemic and haemorrhagic stroke	Neuroimaging	RR = 0.42 (0.35-0.50)*†
Lisabeth et al (2007) ⁸⁶						<high school<br="">(<hs)< td=""><td>ICD 9: 430- 432, 435-439</td><td>Case note review Centralised health Statistics</td><td></td></hs)<></high>	ICD 9: 430- 432, 435-439	Case note review Centralised health Statistics	
Hart et al (2000) ⁸⁷	Community	5765	416	5349	35-64	Age at leaving full time education: ≤ 16 Age at leaving full time education: >16	Ischaemic, haemorrhagic stroke and TIA ICD 8 & 9: 430-438; ICD 10: I60-I69, G45	Centralised health Statistics Hospital discharge records	RR = 1.28 (0.96-1.70)†
				Haza	rd Ratios			·	·
Kuopic Ischaemic Heart Disease Study (KIHD)	Population	2303	113	2190	42-60	≤ Primary school (≤ PS/6 years)	Ischaemic and haemorrhagic stroke	Centralised health Statistics	HR: 1.76 (0.87-3.55)
Everson et al (2001) ⁸⁸			90 ischaemic			< High school/some vocational training (<hs 7-8="" td="" years)<=""><td>ICD 9: 430- 438</td><td>FINMONICA stroke register</td><td></td></hs>	ICD 9: 430- 438	FINMONICA stroke register	
						Some high school or more (≥ 9 years)	Only Ischaemic stroke results used		

Malmo-Diet-and-	Population	24 944	1253	23 691	Approx.	Didn't complete	Ischaemic	Centralised	HR = 0.38
Cancer-Cohort					mean age of 58	elementary school	stroke	health Statistics	(0.23-0.62)*†
Hamrefors et al (2014) ⁸⁹						Elementary school (6-8 years)	ICD9: 430, 431, 434, 436		
						Junior school (9-10 years)	ICD10: I60, I61, I63, I64		
						Education at advanced level (12 years)			
						At least one additional year			
						University degree			
Northern	Derrulation	1840	687	1153	68.2	ciliah asha si	Ischaemic	Centralised	HR = 1.4
Manhattan Stroke Study (NOMAS)	Population	1640	087	1133	08.2	<high school<br="">(<hs)< td=""><td>stroke</td><td>health Statistics</td><td>HR = 1.4 (1.1-1.7)†</td></hs)<></high>	stroke	health Statistics	HR = 1.4 (1.1-1.7)†
Boden-Albala et al (2012) ⁹⁰						\geq High school (\geq HS)		Self-report questionnaire	
91-93									

Prevention with	Outpatient	7263	136	7126	55-80	Low education	Ischaemic and	Case note	HR = 1.83
Mediterranean Diet (PREDIMED)	clinics					(Primary school education or less)	haemorrhagic stroke	review	(1.09-3.09)†
Mejia-Lacheros et al (2014) ⁹⁴					67	High education (Secondary or university studies)		Self-report questionnaire	
								Centralised health statistics	
ARIC	Population	274 299	988	14 419	45-64	< High school	Ischaemic and haemorrhagic stroke	Neuroimaging	HR: black ethnicity = 1.79 (1.06- 3.02)†
Huxley et al (2014) ⁹⁵						High school graduate and/or vocational school		Case note review	HR: White ethnicity = 0.83 (0.56- 1.23)†
96						College		Centralised health statistics	
						Graduate or professional school		Self-report questionnaire	

Swedish	Population	44 495	592	43 903	40-55	≤9 years	Ischaemic and	Centralised	HR: 1.04
Conscription Surveys							haemorrhagic stroke	health statistics	(0.99-1.09)
Hemmingsson et al (2007) ⁹⁷						10-11 years	ICD 9: 430- 438; ICD 10: I60-I69		
						12-13 years			
						14 years			
						≥15 years			
EPESE Newhaven sample	Population	2494	260	2234	≥65	0-7 years	Ischaemic and haemorrhagic stroke	Case note review	HR =1.31 (0.66-2.65)†
Avendano et al (2006) ⁹⁸						8-9 years		Centralised health statistics	
						10-12 years		Self-report/ questionnaire	
						≥13			
Prospective population study of women in Gothenberg	Population	1460	184	1276	38-60	8 levels from elementary school to secondary school.	Ischaemic and haemorrhagic stroke	Centralised health statistics	HR = 1.17 (1.01-1.35)†
Blomstrand et al (2014) ⁹⁹							Only Ischaemic stroke results used		

Dutch National	Population	190 665	472	190 193	≥25	Low (no	Ischaemic,	Case note	HR: Men =
Survey of General Practice						schooling or solely elementary education)	haemorrhagic stroke and TIA	review	1.58 (1.07- 2.36)†
Avendano et al (2006) ¹⁰⁰					70.9 (men);76.1 (females)	Middle (Secondary schooling)	International classification of Primary care coding system		HR: Women = 1.12 (0.59- 2.14)†
						High (Post- secondary education)			
Health and Retirement Study merged with Study of Asset and Health Dynamics among the Oldest Old; Children of the Depression; War Baby; Early Baby Boomer	Population	22 847	2298	20 549	>51	Low: < High School (<9 years)	Ischaemic and haemorrhagic stroke	Self-report questionnaire	HR = 1.37 (1.17-1.59)†
Liu et al (2013) ¹⁰¹					Majority of strokes over 65yrs	Middle: High School (9-12 years)			
102;103						High: College (≥13 years)			

Kuper et al	Population	47 942	200	47 742	30-49	Total years of	Ischaemic and	Centralised	HR = 2.2
$(2007)^{104}$						education	haemorrhagic stroke	health statistics	(1.3-3.7)†
							ICD 9: 434,		
							431; ICD 10:		
							163.3-163.9,		
							I64; ICD 7:		
							332, 331; ICD 8: 433-434,		
							334		
							Only		
							Ischaemic		
							stroke results		
							used		
Jichi Medical	Population	10 640	362	10 278	NS	Age at leaving	Ischaemic and	Clinical	Males: HR:
School Cohort Study	Topulation	10 040	502	10 278	115	school: ≤ 14	haemorrhagic stroke	examination	0.92 (0.51- 1.65)*
									,
Honjo et al (2010) ¹⁰⁵						15-17 years		Neuroimaging	Females: :HR: 1.04 (0.47- 2.31)*
						\geq 18 years			

						vocational) Highest			
						Highest (University or			
						higher vocational education)			
				Preval	ence Ratio	,			
Llibre et al (2010) ¹⁰⁸	Population	3015	229	2786	≥65	≤ 6 grades	Ischaemic and haemorrhagic stroke	Neuroimaging	\geq 7 grades: Prevalence ratio: 0.90 (0.6-1.1)
						\geq 7 grades	WHO definition	Self-report questionnaire	

				Haza	rd ratios				
Health and Retirement Study	Population Cohort	22 847	2298	20 549	61	Sum of parents education	Ischaemic or haemorrhagic stroke	Clinical examination	HR=1.35 (1.15-1.59
Liu et al (2013) ¹⁰¹ 103;109-111								Neuroimaging	
Swedish Conscript Study 1949-1951	Population	44 495	592	43 903	40-55	Father's occupation	Ischaemic or haemorrhagic stroke	Centralised health statistics	HR= 1.08 (1.03-1.09)
Hemmingsson et al (2007) ⁹⁷						Crowded housing			
Copenhagen City Heart Study	Population	9542	350	9192	NS	Financial problems in childhood	Ischaemic stroke	Centralised health statistics	HR=1.71 (1.29-2.26)*
Kornerup et al $(2010)^{112}$									
	<u> </u>		Fre	quencies (n=stı	oke vs withou	t stroke)			
ARIC	Population Cohort	5347	234	5113	51.8	Father's education	Ischaemic stroke	Centralised health statistics	Low SES= 7 vs 1736
Johnson et al (2010) ¹¹³			104 with childhood SES	2507 with childhood SES	57-79			Self-report	High SES = 30 vs 875

Hart et al (2000) ⁸⁷	Community sample	5765	416	5349	35-64	Father's occupation	Ischaemic, haemorrhagic stroke or TIA	Centralised health statistics	Low SES = 335 vs 3948
			404 with childhood SES	5,249 with childhood SES					High SES = 69 vs 1301
Nurse's Health Study Cohort	Population sample	117 006	828	116 178	30-55	Father's occupation	Ischaemic or haemorrhagic stroke	Case note review	Low SES = 463 vs 63 697
Gliksman et al (1995) ¹¹⁴			741 with childhood SES	104,644 with childhood SES				Centralised health statistics	High SES = 278 vs 40 947
British Regional Heart Study	Population cohort	5934	136	5380	40-59	Father's occupation	Stroke	Self-report	Low SES = 103 vs 3903
Wannamethee et al (1996) ¹¹⁵									High SES = 33 vs 1477
Swedish Conscript Study 1951-1976	Population cohort	1 135 383	8215	1 127 168	Approx. 36	Father's occupation	Stroke	Centralised health statistics	Low SES = 4580 vs 542 168
Wennerstad (2010) ⁵⁴									High SES = 3635 vs 585 001
116									
				Odd	ls Ratios				
Grau et al (2012) ⁷⁷	Hospital	740	370	370	60.7	Father's occupation	Ischaemic, haemorrhagic stroke or TIA	Clinical examination	OR= 0.79 (0.48-1.30)*†
					<80			Neuroimaging	

				Preva	lence Rate				
Aberdeen Children of the 1950's Lawlor et al (2006) ¹¹⁷	Population cohort	11 106	-	-	Approx. 50	Father's occupation	Ischaemic or haemorrhagic stroke	Centralised health statistics	PR per 10 000 PY: Social class I/II= 2.3 (1.0-6.9) PR per 10 000 PY: Social
1c. Childhood/ Prer	norbid IQ								class V= 7.8 (5.6-11.3)
Study	Setting	Total number of participants	Participants with stroke (n)	Participants without stroke (n)	Age at follow up/stroke	Measure of childhood/ premorbid IQ	Primary outcome	Measurement of outcome	Results
		I		Haza	rd Ratios				I
Danish Birth Cohort Study 1953	Population	6910	93	6817	≈ 47	Danish translation of the Swedish Harnquist Intelligence Test	Stroke	Centralised Health Statistics	HR=1.29 (0.75-2.25)†
Batty et al (2005) ¹¹⁸							ICD 8: 430- 438, 410-414		
							ICD 10: I60- I69, I20-25		

Swedish	Population	44 495	592	43 903	40-55	Standardised	Ischaemic and	Centralised	HR = 1.26
Conscription Study 1949-1951						global IQ score	haemorrhagic stroke	Health Statistics	(0.76-2.09) †
Hemmingsson et al (2007) ⁹⁷							ICD-9: 430– 438		
							ICD-10: I60– I69		
Swedish Conscription Study 1951-1976	Population	1 135 383	8215	1 127 168	Mean age \approx 36	Standardised global IQ score	Ischaemic or haemorrhagic stroke	Centralised Health Statistics	HR=0.94 (0.92-0.96) *†
Wennerstad et al (2010) ⁵⁴							ICD8: 430-438		
							ICD9: 433-438		
							ICD10: I60- I69, G45		
Helsinki Birth	Population	2786	131	2655	56.7	The Finnish	Ischaemic or	Centralised	HR= 0.98
Cohort Study	Cohort					Defence Forces Basic Ability Test	haemorrhagic stroke	Health Statistics	(0.75-1.27) †
Kajantie et al (2012) ¹¹⁹							ICD8: 430- 434, 436-437		
							ICD9: 430- 434, 436-438		
							ICD10: I60- I69		

Aberdeen Children of the 1950s Lawlor et al (2008) ¹²⁰	Population Cohort	11 125	56	11 069	50-55	Moray House Test aged 11	Ischaemic or haemorrhagic stroke ICD9: 430-438 ICD10: I60- I69, G45	Centralised Health Statistics	HR=0.68 (0.55-0.84) *†
-				Mean	Differences	1	1	I	
Sydney Stroke Study Brodaty et al (2010) ⁴ 3;6;7;121	Hospital	264	167	97	72.42	NART-R IQ	Ischaemic stroke WHO criteria	Clinical examination	104.31 ± 10.26 Stroke 114.09 ± 7.99 Non-stroke
Kessels et al (2006) ²³	Hospital	266	105	161	59.5	NART-R IQ	Ischaemic or haemorrhagic stroke	NS	97.1 ± 15.6 Stroke 101.1 ± 14.6 Non-stroke
Sampson et al (2002) ¹²²	Hospital	103	50	47	72.5	NART-R IQ	Stroke	NS	105 (95-114) Stroke 110 (102-116) Non-stroke

Odds Ratios

Wisconsin	Cohort	8623	276	8347	64.8	Henmon-	Stroke	NS	OR=0.85
Longitudinal Study						Nelson Test of			(0.74-0.99)*
						Mental Ability			
Jokela et al (2011) ¹²³									

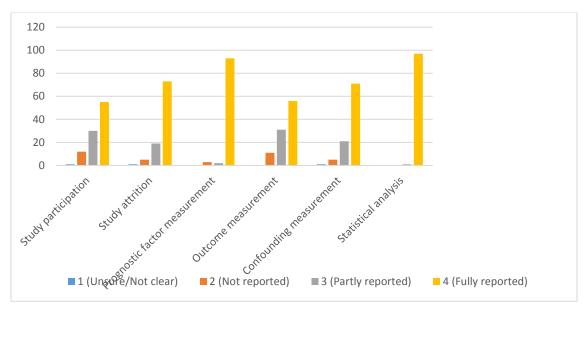
* inverted for meta-analysis to demonstrate inverse relationship

† Adjusted

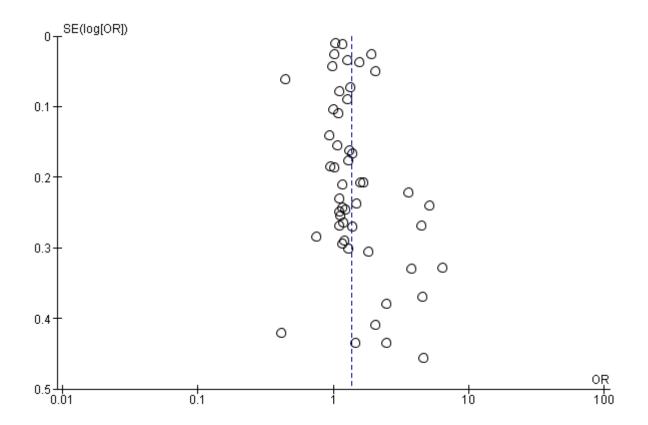
§ Sum of multiple categories to represent low and high educational level

NS= Not specified

Values in table and figures may differ due to rounding

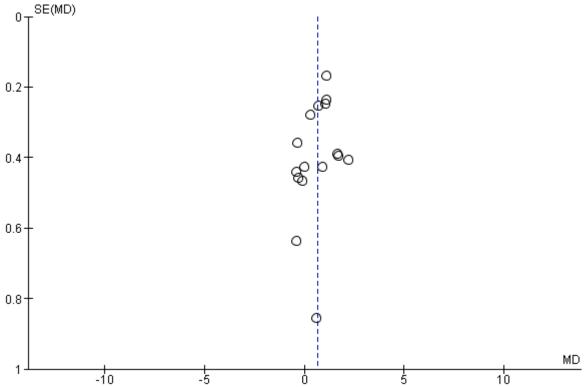


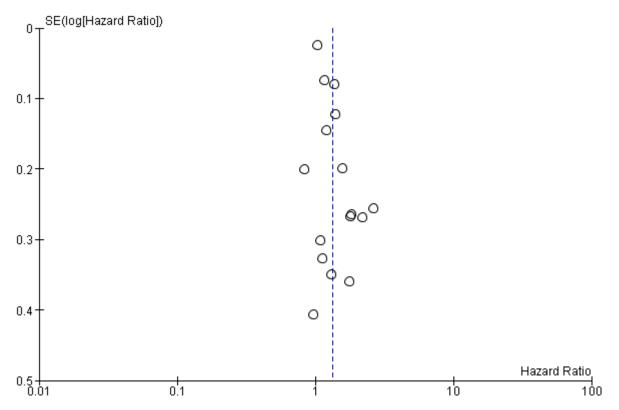
eFigure 3. Quality assessment: Frequencies of scores on individual quality items



eFigure 4a. Funnel Plot for analysis of publication bias in studies reporting ORs for education and risk of stroke.

eFigure 4b. Funnel Plot for analysis of publication bias in studies reporting MDs for education and risk of stroke.





eFigure 4c. Funnel Plot for analysis of publication in studies reporting HRs for education and risk of stroke.

eDocument 2. Footnotes for figure 2a. Educational attainment (low versus high) and risk of stroke, risk ratio (OR, HR and RR), random effects model (risk ratio <1 indicates low education decreases risk of stroke; >1 = low education increases risk of stroke.

- ^a Adjusted for age, gender and region
- ^b Adjusted for age, gender, area of residence, BMI, smoking, alcohol consumption, diabetes, high blood pressure, occupational and leisure time physical activity
- ^c Adjusted for age, sex, race
- ^d Adjusted for age and sex
- e Adjusted for age, gender, income, medical insurance, smoking and BMI
- ^f Adjusted for age, systolic BP, hypertension, drug use for hypertension, smoking, cardiovascular disease, left ventricular hypertrophy, atrial fibrillation, diabetes, fibrogen, BMI, alcohol consumption
- ^g Adjusted for history of high BP, use of oral contraceptives, marital status, number of live births, cigarette and alcohol consumption, hypertension in pregnancy, family history of premature stroke or AMI, area of residence, diabetes and abnormal blood fats
- ^h Adjusted for hypertension, heart disease, diabetes, smoking
- ⁱ Adjusted for hypertension, diabetes, hyperlipidaemia, previous stroke/TIA, and PAD, current smoking, alcohol abstinence, high alcohol consumption, leisure time sports activity
- ^j Adjusted for age, home ownership, education, smoking, BMI, alcohol, physical activity, depression, marital status, hypertension, diabetes mellitus, heart disease and hysterectomy/oophorectomy
- ^k Adjusted for CHD, hypertension, COPD, obesity, income, age and sex
- ¹Adjusted for age. Total number of strokes and controls for education categories used not specified. Total strokes and controls 218 and 1845 respectively.
- ^m Adjusted for work related factors on the Job Content Questionnaire, organisational change at the workplace and decreased participation
- ⁿ Adjusted for age, sex, income, BMI, smoking, systolic blood pressure, antihypertensive medication, diabetes, HDL-C, LDL-C, lipid medication, CHD, PAD, ECG, carotid intima thickness and physical activity
- ^o Adjusted for age, area of residence, cholesterol level, physical activity, ethanol intake, marital status, smoking, obesity, medical history of hypertension, diabetes
- ^p Adjusted for age
- ^q Adjusted for age, hypertension, BMI, smoking, physical inactivity, cholesterol, triglycerides, mental stress
- ^r Adjusted for age, sex, physical activity, smoking, alcohol consumption, diet
- ^s Adjusted for age, sex, race, sex, hypertension, smoking, diabetes, alcohol, BMI, physical activity, social networks, depression, difficult life events
- ^t Adjusted for age, race, ethnicity, gender, marital status, adult SES
- ^u Adjusted for cardiac disease, hypertension, diabetes, inactivity, social isolation, Medicaid insurance, home heath aid
- ^v Adjusted for aged, gender, smoking, alcohol consumption, BMI, hypertension, diabetes, high cholesterol, family history of CHD and diet
- ^w Adjusted for age, smoking, BMI, alcohol consumption, hypertension, diabetes, exercise
- ^x Adjusted for baseline age, smoking, history of diabetes, history of heart disease, alcohol consumption, non recreational physical activity, blood pressure medication, and systolic blood pressure
- ^y Adjusted for age, sex, calendar year and income
- ^z Adjusted for age, smoking, adjusted FEV1, diastolic and systolic blood pressure, height, alcohol consumption and pre-existing CHD.
- aa Adjusted for age, sex and ethnicity

eFigure 5a. Sensitivity analysis comparing studies that included younger (mean age ≤ 65 years) vs those that included older (mean age >65 years) participants by education level and risk of stroke; OR>1= low education increases risk of stroke.

			Stroke	Non-stroke		Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Total		Weight	IV, Random, 95% CI	IV, Random, 95% CI
2.6.1 Younger participants							
Akinyemi (2014)	0.5988	0.3055	143	74	1.5%	1.82 [1.00, 3.31]	
Baune (2006)	0.3293	0.2693	111	223	1.7%	1.39 [0.82, 2.36]	
Chang (2002) Asia (1)	0.174	0.2635	159	481	1.7%	1.19 [0.71, 1.99]	
Chang (2002) Eastern Europe (2)		0.4088	85	211	1.0%	2.05 [0.92, 4.57]	
Chang (2002) Latin America (3)		0.2433	183	477	1.8%	1.16 [0.72, 1.87]	
Chen (2014) (4)		0.0618	2810	169938	3.3%	0.44 [0.39, 0.50]	-
de Brujin (2014)		0.4549	84	61	0.9%	4.58 [1.88, 11.16]	
Emmelin (2003) Females	0.0953	0.269	114	240	1.7%	1.10 [0.65, 1.86]	
Emmelin (2003) Males		0.2306	169	348	1.9%	1.10 [0.70, 1.73]	Ţ
Fitzpatrick (2012) Folsom (1990) (5)	0.0198	0.0267 0.2069	401 0	1211 0	3.4% 2.1%	1.02 [0.97, 1.07]	
Gan (2011)		0.2069	309	309	2.1%	1.66 [1.11, 2.49] 1.59 [1.06, 2.38]	
Grau (2012) (6)		0.2461	359	365	1.8%	1.23 [0.76, 1.99]	
Hu (2005)	-0.0232		2854	44858	3.4%	0.98 [0.90, 1.06]	+
Jackson (2013) (7)		0.3015	69	5220	1.5%	1.30 [0.72, 2.35]	
Kisjanto (2003)	0.3293	0.166	235	682	2.5%	1.39 [1.00, 1.92]	
Lofmark (2007) ages 35-75 (8)		0.1092	207	48643	2.9%	1.09 [0.88, 1.35]	+-
Medin (2008) (9)	0.9083	0.379	65	103	1.1%	2.48 [1.18, 5.21]	
Nybo (2008)	0.3876	0.237	254	254	1.9%	1.47 [0.93, 2.34]	+
Sim (2008)		0.1844	265	214	2.3%	0.94 [0.66, 1.35]	+
Trygged (2011)	0.1569	0.0114	34436	284694	3.4%	1.17 [1.14, 1.20]	•
Valko (2008)		0.2217	96	447	2.0%	3.58 [2.32, 5.52]	
Wang (2015) (10)		0.0786	0	0	3.2%	1.10 [0.94, 1.28]	
Weikert (2008)		0.1624	167	2196	2.5%	1.30 [0.95, 1.79]	
Wennerstad (2010)		0.0261	8215	1127168	3.4%	1.91 [1.81, 2.01]	•
You (1999) (11) Subtotal (95% CI)	0.1823	0.2902	219 52009	97 1688514	1.5% 56.5%	1.20 [0.68, 2.12] 1.30 [1.12, 1.50]	
Heterogeneity: Tau ² = 0.10; Chi ² = 692.29, df = 25 (P < 0 Test for overall effect: Z = 3.48 (P = 0.0005) 2.6.2 Older participants							
Brenner (2010)	0.7053	0.0497	2827	24910	3.3%	2.02 [1.84, 2.23]	-
Engels (2014)	1.3303	0.3296	127	44615	1.3%	3.78 [1.98, 7.22]	
Everson-Rose (2014)	0.2627	0.1757	195	6554	2.4%	1.30 [0.92, 1.84]	
Fillenbaum (2000) (12)		0.0106	307	3727	3.4%	1.03 [1.01, 1.05]	
Hamano (2015) (13)		0.0373	3950	230927	3.4%	1.56 [1.45, 1.68]	•
Huang (1997)		0.3285	71	11854	1.3%	6.27 [3.29, 11.93]	
Koster (2005)		0.1552	180	2391	2.5%	1.08 [0.79, 1.46]	
Liu (2008)	-0.8916	0.42	60	52 6166	1.0%	0.41 [0.18, 0.93]	
Lofmark (2007) ages 75-85 (14) Pendlebury (2012)		0.4337 0.2683	250 207	107	0.9% 1.7%	2.48 [1.06, 5.80] 4.44 [2.62, 7.50]	
Smith (2003) Mexican Americans (15)		0.2003	403	339	1.9%	4.44 [2.62, 7.50] 5.08 [3.17, 8.14]	
Smith (2003) Non-Hispanic whites (16)		0.3685	405	339	1.2%	4.53 [2.20, 9.33]	
Strodi (2008)		0.1865	88	4470	2.3%	1.02 [0.71, 1.47]	
van Rossum (1999a) First stroke (17)		0.2098	129	3054	2.1%	1.16 [0.77, 1.75]	
van Rossum (1999b) History of stroke at baseline (18)		0.2549	95	3149	1.8%	1.12 [0.68, 1.85]	- -
Weinstein (2014)	0.3698		132	132	0.9%	1.45 [0.62, 3.39]	
Wiberg (2015)	-0.2896	0.2839	72	657	1.6%	0.75 [0.43, 1.31]	-+
Wolinsky (2009)	0.0079	0.104	545	4966	3.0%	1.01 [0.82, 1.24]	+
Xu (2008) (19)	-0.0726		339	24979	2.7%	0.93 [0.71, 1.22]	-
Yan (2013)		0.0904	650	3969	3.1%	1.26 [1.05, 1.50]	-
Zhu (2000)	0.0984	0.2488	183	118	1.8%	1.10 [0.68, 1.80]	
Subtotal (95% CI)			11215	377475	43.5%	1.53 [1.27, 1.84]	▼
Heterogeneity: Tau ² = 0.14; Chi ² = 417.87, df = 20 (P < 0 Test for overall effect: Z = 4.51 (P < 0.00001)	0.00001); I ² = 95%						
Total (95% CI)			63224	2065989	100.0%	1.36 [1.24, 1.50]	•
Heterogeneity: Tau ² = 0.07; Chi ² = 1146.64, df = 46 (P <	0.00001); l ² = 96%					F C	0.01 0.1 1 10 100
Test for overall effect: $Z = 6.40 (P < 0.00001)$	10 12 - 10 10						Decreased risk of stroke Increased risk of stroke
Test for subgroup differences: Chi ² = 1.94, df = 1 (P = 0.	16), I ² = 48.4%						Low education
Footnotes	these months at the	mumk -	of Buch	the electric		hel energy worker to a sta	
							ension in pregnancy, family history of premature stroke or AMI,

(2) Adjusted for history of high BP, use of oral contraceptives, marital status, number of live births, cigarette and alcohol consumption, hypertension in pregnancy, family history of premature stroke or AMI,...

 (c) Adjusted for age. Total number of strokes and controls for education categories used not specified. Total strokes and controls 218 and 1845 respectively.
 (6) Adjusted for hypertension, diabetes, hyperlipidemia, previous stroke/TIA, and PAD, current smoking, alcohol abstinence, high alcohol consumption, leisure time sports activity (7) Adjusted for age, home ownership, education, smoking, BMI, alcohol, physical activity, depression, marital status, hypertension, diabetes mellitus, heart disease and hysterectomy/oophorectomy (8) Adjusted for age and sex

(a) Adjusted for work related factors on the Job Content Questionnaire, organisational change at the workplace and decreased participation
 (10) Adjusted for age, gender, income, medical insurance, smoking and BMI.
 (11) Adjusted for hypertension, heart disease, diabetes, smoking

(12) Adjusted for age, sex, race

(13) Adjusted for CHD, hypertension, COPD, obesity, income, age and sex.

(14) Adjusted for age and sex (15) Adjusted for age and sex

(16) Adjusted for age and sex

(17) Adjusted for age, systolic BP, hypertension, drug use for hypertension, smoking, cardiovascular disease, left ventricular hypertrophy, atrial fibrilation, diabetes, fibrogen, BMI, alcohol consumption (18) Adjusted for age, systolic BP, hypertension, drug use for hypertension, smoking, cardiovascular disease, left ventricular hypertrophy, atrial fibrilation, diabetes, fibrogen, BMI, alcohol consumption (19) Adjusted for age, gender, area of residence, BMI, smoking, alcohol consumption, diabetes, high blood pressure, occupational and leisure time physical activity NOTE: Studies without footnotes report unadjusted results

eFigure 5b. Sensitivity analysis comparing studies that included younger (mean age \leq 65 years) vs studies that included older (mean age >65 years) participants by education level and risk of stroke; HR>1= low education increases risk of stroke.

			Stroke I	Non-stroke		Hazard Ratio	Hazard Ratio
Study or Subgroup	log[Hazard Ratio]	SE	Total	Total	Weight	IV, Random, 95% Cl	I IV, Random, 95% CI
2.7.1 Younger participants							
Blomstrand (2014) (1)	0.157	0.075	138	0	12.2%	1.17 [1.01, 1.36]	-
Everson (2001)	0.5653	0.3595	90	2190	3.2%	1.76 [0.87, 3.56]	
Hamrefors (2014) (2)	0.967	0.2562	0	0	5.1%	2.63 [1.59, 4.35]	
Hemmingsson (2007)	0.0392	0.0251	592	43903	13.7%	1.04 [0.99, 1.09]	•
Huxley (2014a) Whites (3)	0.5822	0.2673	573	10748	4.8%	1.79 [1.06, 3.02]	
Huxley (2014b) Blacks (4)	-0.1863	0.2008	415	3671	6.8%	0.83 [0.56, 1.23]	
Kuper (2007) (5)	0.7885	0.2684	200	47942	4.8%	2.20 [1.30, 3.72]	
Mejean (2013) (6)	0.1906	0.1454	531	32575	8.9%	1.21 [0.91, 1.61]	-
Subtotal (95% CI)			2539	141029	59.5%	1.32 [1.09, 1.61]	◆
Heterogeneity: Tau ² = 0.04; Chi	i ² = 30.16, df = 7 (P <	0.0001);	² = 77%				
Test for overall effect: Z = 2.85	(P = 0.004)						
2.7.2 Older participants							
Avendano (2006) (7)	0.27	0.3498	260	2234	3.3%	1.31 [0.66, 2.60]	
Avendano (2006a) men (8)	0.4574	0.1989	253	0	6.8%	1.58 [1.07, 2.33]	
Avendano (2006a) women (9)	0.1133	0.327	219	0	3.6%	1.12 [0.59, 2.13]	
Boden-Albala (2012) (10)	0.3365	0.123	687	1153	10.0%	1.40 [1.10, 1.78]	-
Liu (2013)	0.3148	0.0805	0	0	11.9%	1.37 [1.17, 1.60]	-
Mejia-Lancheros (2014) (11)	0.6043	0.2644	135	7126	4.9%	1.83 [1.09, 3.07]	
Subtotal (95% CI)			1554	10513	40.5%	1.40 [1.25, 1.58]	•
Heterogeneity: Tau ² = 0.00; Chi	² = 1.97, df = 5 (P = 0	.85); I ² =	0%				
Test for overall effect: Z = 5.66	(P < 0.00001)						
Total (95% CI)			4093	151542	100.0%	1.36 [1.18, 1.57]	•
Heterogeneity: Tau ² = 0.04; Chi	i ² = 49.70, df = 13 (P <	< 0.0000); ² = 74	%			
Test for overall effect: Z = 4.23	(P < 0.0001)						0.01 0.1 1 10 100 Decreased risk of stroke Increased risk of stroke
Test for subgroup differences: 0	Chi ² = 0.26, df = 1 (P =	= 0.61), l ^a	= 0%				
Footnotes		,.					Low education
(1) Adjusted for one, humertanel	on DMI employe ab	unional in a	ath day also	alastaral tru		mantal atraac	

(1) Adjusted for age, hypertension, BMI, smoking, physical inactivity, cholesterol, tryglycerides, mental stress

(2) Adjusted for age and sex.

(a) Adjusted for age, sex, income, BMI, smoking, systolic blood pressure, antihypertensive medication, diabetes, HDL-C, LDL-C, lipid medication, CHD, PAD, ECG, carotid intima... (d) Adjusted for age, sex, income, BM, smalling, systolic blood pressure, antihypertensive medication, diabetes, HDL-C, LDL-C, lipid medication, CHD, PAD, ECG, carotid intima...
 (5) Adjusted for age, smoking, BMI, alcohol consumption, hypertension, diabetes, exercise

(6) Adjusted for age, sex, physical activity, smoking, alcohol consumption, diet

(7) Adjusted for age, sex, race, sex, hypertension, smoking, diabetes, alcohol, BMI, physical activity, social networks, depression, difficult life events (8) Adjusted for age

(9) Adjusted for age

(10) Adjusted for cardiac disease, hypertension, diabetes, inactivity, social isolation, Medicaid insurance, home heath aid.

(11) Adjusted for aged, gender, smoking, alcohol consumption, BMI, hypertension, diabetes, high cholesterol, family history of CHD and diet. Note:Studies without footnotes report unadjusted results

eFigure 5c. Sensitivity analysis for comparing studies that included younger (mean age ≤65 years) vs studies that included older (mean age >65 years) participants by education level and risk of stroke; negative mean difference = lower education decreases risk of stroke and positive mean difference = lower education increases risk of stroke.

	Nor	1-strok	(e	s	troke			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
2.8.1 Younger participants									
Copstein (2012)	8.12	3.45	3106	7.09	4.05	285	8.1%	1.03 [0.54, 1.52]	-
Gillespie (2012)	10.56	2.12	56	10.9	1.64	56	7.2%	-0.34 [-1.04, 0.36]	-
Hochstenbach (1998)	4.4	1.5	33	4.1	1.5	229	7.8%	0.30 [-0.25, 0.85]	-
Kaurenen (2013)	12.4	2.9	50	12.5	2.6	140	6.2%	-0.10 [-1.01, 0.81]	-
Kessels (2006)	10.3	3.2	161	10.7	3.7	105	6.4%	-0.40 [-1.26, 0.46]	-
Subtotal (95% CI)			3406			815	35.7%	0.16 [-0.43, 0.74]	◆
Heterogeneity: Tau ² = 0.32; Chi ²	= 15.09	, df = 4	4 (P = 0).005); I	² = 74 ⁹	%			
Test for overall effect: Z = 0.52 (P = 0.60)							
2.8.2 Older participants									
Desmond (2002)	12.4	4.5	242	10.7	4.9	334	6.8%	1.70 [0.93, 2.47]	
Jokinen (2006)	9.4	3.5	38	9.8	4.4	238	4.8%	-0.40 [-1.65, 0.85]	-+-
Kastorini (2002)	8	4.9	250	8	4.6	250	6.5%	0.00 [-0.83, 0.83]	+
Lukatela (2000a) Single stroke	12.86	2.51	59	11.97	2.57	89	6.5%	0.89 [0.06, 1.72]	
Mok (2004)	5.4	4.6	42	4.8	4.1	75	3.5%	0.60 [-1.07, 2.27]	- -
Petrovitch (1998)	10.5	3.2	3170	9.8	3	147	8.1%	0.70 [0.20, 1.20]	-
Rastas (2007)	4.3	3	442	3.2	2	111	8.2%	1.10 [0.63, 1.57]	-
Reitz (2006)	8.6	4.6	1174	8.9	4.3	97	6.3%	-0.30 [-1.20, 0.60]	
Sachdev (2014)	11.75	3.31	97	10.1	2.56	183	6.9%	1.65 [0.89, 2.41]	-
Tatemichi (1992)	12.3	4.6	249	10.1	4.5	251	6.7%	2.20 [1.40, 3.00]	·
Subtotal (95% CI)			5763			1775	64.3%	0.88 [0.39, 1.36]	◆
Heterogeneity: Tau ² = 0.42; Chi ²	= 34.89	, df = §	9 (P < 0).0001);	$ ^2 = 74$	1%			
Test for overall effect: Z = 3.56 (P = 0.00	04)							
Total (95% CI)			9169			2590	100.0%	0.62 [0.22, 1.01]	•
Heterogeneity: Tau ² = 0.44; Chi ²	= 61.07	, df = 1	14 (P <	0.0000	1); l ² =	77%			
Test for overall effect: Z = 3.06 (-10 -5 0 5 10 Decrease in stroke risk Increase in stroke risk
Test for subgroup differences: C		/	1 (P =	0.06), F	² = 71.	4%			Low education
		-, -,	. (,						Low education

eFigure 5d. Sensitivity analysis comparing adjusted vs unadjusted studies by education level and risk of stroke; OR>1= low education increases risk of stroke.

udy or Subgroup 9.1 Adjusted nang (2002) Asia (1) nang (2002) Eastern Europe (2) nang (2002) Latin America (3) nen (2014) (4) mmelin (2003) Females mmelin (2003) Males lenbaum (2000) (5)	0.7178 0.1484	0.2635 0.4088	Total 159	481		IV, Random, 95% CI	IV, Random, 95% Cl
nang (2002) Asia (1) nang (2002) Eastern Europe (2) nang (2002) Latin America (3) nen (2014) (4) mmelin (2003) Females nmelin (2003) Males	0.7178 0.1484		159	481	4 50/		
nang (2002) Eastern Europe (2) nang (2002) Latin America (3) nen (2014) (4) mmelin (2003) Females nmelin (2003) Males	0.7178 0.1484		159	481			
nang (2002) Latin America (3) nen (2014) (4) nmelin (2003) Females nmelin (2003) Males	0.1484	0.4088			1.5%	1.19 [0.71, 1.99]	
nen (2014) (4) nmelin (2003) Females nmelin (2003) Males			85	211	0.9%	2.05 [0.92, 4.57]	
nmelin (2003) Females nmelin (2003) Males			183	477	1.7%	1.16 [0.72, 1.87]	
nmelin (2003) Males		0.0618	2810	169938	3.0%	0.44 [0.39, 0.50]	-
	0.0953	0.269	114	240	1.5%	1.10 [0.65, 1.86]	
lenbaum (2000) (5)	0.0953	0.2306	169	348	1.7%	1.10 [0.70, 1.73]	
	0.0296	0.0106	307	3727	3.2%	1.03 [1.01, 1.05]	•
blsom (1990) (6)	0.5068	0.2069	0	0	1.9%	1.66 [1.11, 2.49]	_ - _
rau (2012) (7)	0.207	0.2461	359	365	1.6%	1.23 [0.76, 1.99]	
amano (2015) (8)	0.4447	0.0373	3950	230927	3.1%	1.56 [1.45, 1.68]	·
ckson (2013) (9)	0.2624	0.3015	69	5220	1.3%	1.30 [0.72, 2.35]	
fmark (2007) ages 35-75 (10)	0.0862	0.1092	207	48643	2.7%	1.09 [0.88, 1.35]	
ofmark (2007) ages 75-85 (11)	0.9083		250	6166	0.8%	2.48 [1.06, 5.80]	
edin (2008) (12)	0.9083	0.379	65	103	1.0%	2.48 [1.18, 5.21]	
nith (2003) Mexican Americans (13)	1.6253		403	339	1.7%	5.08 [3.17, 8.14]	
nith (2003) Non-Hispanic whites (14)			405	339	1.0%	4.53 [2.20, 9.33]	
	1.5107						
n Rossum (1999a) First stroke (15)	0.1484		129	3054	1.9%	1.16 [0.77, 1.75]	
n Rossum (1999b) History of stroke at baseline (16)		0.2549	95	3149	1.6%	1.12 [0.68, 1.85]	
ang (2015) (17)	0.0953		0	0	2.9%	1.10 [0.94, 1.28]	-
J (2008) (18)	-0.0726		339	24979	2.4%	0.93 [0.71, 1.22]	-
ou (1999) (19)	0.1823	0.2902	219	97	1.4%	1.20 [0.68, 2.12]	
ubtotal (95% CI)			10317	498803	38.8%	1.32 [1.09, 1.59]	▼
eterogeneity: Tau ² = 0.14; Chi ² = 392.35, df = 20 (P < 0 est for overall effect: Z = 2.89 (P = 0.004)	0.00001); I² = 95%						
9.2 Unadjusted							
kinyemi (2014)	0.5988	0.3055	143	74	1.3%	1.82 [1.00, 3.31]	
aune (2006)	0.3293	0.2693	111	223	1.5%	1.39 [0.82, 2.36]	
enner (2010)	0.7053	0.0497	2827	24910	3.1%	2.02 [1.84, 2.23]	-
Brujin (2014)	1.5209	0.4549	84	61	0.7%	4.58 [1.88, 11.16]	
eoke (2012)	0.1577	0.2945	101	100	1.3%	1.17 [0.66, 2.09]	
ngels (2014)	1.3303	0.3296	127	44615	1.2%	3.78 [1.98, 7.22]	
verson-Rose (2014)	0.2627		195	6554	2.2%	1.30 [0.92, 1.84]	
tzpatrick (2012)	0.01988		401	1211	3.2%	1.02 [0.97, 1.07]	-
an (2011)	0.4618		309	309	1.9%	1.59 [1.06, 2.38]	
onjo (2009)		0.2009	793	28341	3.0%		-
						1.33 [1.16, 1.54]	
J (2005)	-0.0232		2854	44858	3.1%	0.98 [0.90, 1.06]	
Jang (1997)		0.3285	71	11854	1.2%	6.38 [3.35, 12.14]	
sjanto (2003)	0.3293	0.166	235	682	2.2%	1.39 [1.00, 1.92]	· · ·
oster (2005)	0.0732		180	2391	2.3%	1.08 [0.79, 1.46]	
u (2008)	0.0862		207	48643	2.7%	1.09 [0.88, 1.35]	
ordhal (2014)	0.2313		3613	202316	3.1%	1.26 [1.18, 1.35]	-
/bo (2008)	0.3876	0.237	254	254	1.7%	1.47 [0.93, 2.34]	
endlebury (2012)	1.4896	0.2683	207	107	1.5%	4.44 [2.62, 7.50]	
m (2008)		0.1844	265	214	2.1%	0.94 [0.66, 1.35]	-+-
rodl (2008)	0.01988		88	4740	2.1%	1.02 [0.71, 1.47]	<u> </u>
ygged (2011)		0.0114	34436	284694	3.2%	1.17 [1.14, 1.20]	•
alko (2008)	1.2743		96	447	1.8%	3.58 [2.32, 5.52]	
eikert (2008)	0.2658		167	2196	2.3%	1.30 [0.95, 1.79]	↓
einstein (2004)	0.3698		132	132	0.8%	1.45 [0.62, 3.39]	
ennerstad (2010)	0.6448		8215	1127166	3.2%	1.91 [1.81, 2.01]	
iberg (2015)		0.2839	72	657	1.4%	0.75 [0.43, 1.31]	
olinsky (2009)	0.0079	0.104	545	4966	2.7%	1.01 [0.82, 1.24]	T
olinsky (2009)	0	0	0	0		Not estimable	
an (2013)	0.2297		650	3969	2.8%	1.26 [1.05, 1.50]	-
nu (2000)	0.0984	0.2488	183	1118	1.6%	1.10 [0.68, 1.80]	
ubtotal (95% CI)			57561	1847802	61.2%	1.43 [1.27, 1.60]	♦
eterogeneity: Tau² = 0.07; Chi² = 586.71, df = 28 (P < 0 est for overall effect: Z = 6.06 (P < 0.00001)	0.00001); I ² = 95%						
otal (95% CI)			67878	2346605	100 0%	1.36 [1.24, 1.48]	▲
	0.00001): 12 - 0.00/		0.010	20-10000	100.070	1.00 [1.24, 1.40]	· · · · · · · · · · · · · · · · · · ·
eterogeneity: Tau ² = 0.06; Chi ² = 1152.48, df = 49 (P <	0.00001); 1* = 96%						0.01 0.1 1 10
est for overall effect: Z = 6.82 (P < 0.00001)							Decreased risk of stroke Increased risk of stroke
est for subgroup differences: Chi ² = 0.52, df = 1 (P = 0.4							Decreased lisk of stroke increased lisk of stroke

(1) Adjusted for history of high BP, use of oral contraceptives, marital status, number of live births, cigarette and alcohol consumption, hypertension in pregnancy, family history of premature stroke or AMI,... (2) Adjusted for history of high BP, use of oral contraceptives, marital status, number of live births, cigarette and alcohol consumption, hypertension in pregnancy, family history of premature stroke or AMI... (3) Adjusted for history of high BP, use of oral contraceptives, marital status, number of live births, cigarette and alcohol consumption, hypertension in pregnancy, family history of premature stroke or AMI...

(4) Adjusted for age,gender and region.(5) Adjusted for age, sex, race

(c) Adjusted for age. Total number of strokes and controls for education categories used not specified. Total strokes and controls 218 and 1845 respectively.
 (7) Adjusted for hypertension, diabetes, hyperlipidemia, previous stroke/TIA, and PAD, current smoking, alcohol abstinence, high alcohol consumption, leisure time sports activity

 (8) Adjusted for CHD, hypertension, COPD, obesity, income, age and sex.
 (9) Adjusted for age, home ownership, education, smoking, BMI, alcohol, physical activity, depression, marital status, hypertension, diabetes mellitus, heart disease and hysterectomy/oophorectomy (10) Adjusted for age and sex (11) Adjusted for age and sex

(12) Adjusted for work related factors on the Job Content Questionnaire, organisational change at the workplace and decreased participation

(13) Adjusted for age and sex

(14) Adjusted for age and sex

(15) Adjusted for age, systolic BP, hypertension, drug use for hypertension, smoking, cardiovascular disease, left ventricular hypertrophy, atrial fibrilation, diabetes, fibrogen, BMI, alcohol consumption (16) Adjusted for age, systolic BP, hypertension, drug use for hypertension, smoking, cardiovascular disease, left ventricular hypertrophy, atrial fibrilation, diabetes, fibrogen, BMI, alcohol consumption (16) Adjusted for age, systolic BP, hypertension, drug use for hypertension, smoking, cardiovascular disease, left ventricular hypertrophy, atrial fibrilation, diabetes, fibrogen, BMI, alcohol consumption

(17) Adjusted for age, gender, income, medical insurance, smoking and BMI.
 (18) Adjusted for age, gender, area of residence, BMI, smoking, alcohol consumption, diabetes, high blood pressure, occupational and leisure time physical activity

(19) Adjusted for hypertension, heart disease, diabetes, smoking Note: Studies without footnotes report unadjusted results

eFigure 5e. Sensitivity analysis comparing adjusted for vascular risk factors vs unadjusted studies by education level and risk of stroke; OR>1= low education increases risk of stroke.

tudy or Subgroup	log[Odds Ratio]	SF	Weight	Odds Ratio IV, Random, 95% C	Odds Ratio IV, Random, 95% CI
14.1 Adjusted	log[ouus Ratio]	36	weight	14, Rahuolii, 95% C	
-	0.474	0.0005	4 50/	4 40 10 74 4 001	
hang (2002) Asia (1)		0.2635	1.5%	1.19 [0.71, 1.99]	-
hang (2002) Eastern Europe (2)		0.4088	0.9%	2.05 [0.92, 4.57]	
hang (2002) Latin America (3)		0.2433	1.7%	1.16 [0.72, 1.87]	
rau (2012) (4)		0.2461	1.6%	1.23 [0.76, 1.99]	
amano (2015) (5)		0.0373	3.1%	1.56 [1.45, 1.68]	•
ackson (2013) (6)		0.3015	1.3%	1.30 [0.72, 2.35]	
an Rossum (1999a) First stroke (7)	0.1484	0.2098	1.9%	1.16 [0.77, 1.75]	
an Rossum (1999b) History of stroke at baseline (8)	0.1133	0.2549	1.6%	1.12 [0.68, 1.85]	
u (2008) (9)	-0.0726	0.1405	2.4%	0.93 [0.71, 1.22]	-
ou (1999) (10)	0.1823	0.2902	1.4%	1.20 [0.68, 2.12]	
ubtotal (95% CI)			17.4%	1.25 [1.04, 1.49]	◆
eterogeneity: Tau ² = 0.03; Chi ² = 19.00, df = 9 (P = 0.0 est for overall effect: Z = 2.44 (P = 0.01)	03); I² = 53%				
14.2 Unadjusted					
kinyemi (2014)	0.5988	0.3055	1.3%	1.82 [1.00, 3.31]	
aune (2006)	0.3293	0.2693	1.5%	1.39 [0.82, 2.36]	+
renner (2010)	0.7053	0.0497	3.1%	2.02 [1.84, 2.23]	-
hen (2014) (11)	-0.821	0.0618	3.0%	0.44 [0.39, 0.50]	-
e Brujin (2014)		0.4549	0.7%	4.58 [1.88, 11.16]	
eoke (2012)	0.1577		1.3%	1.17 [0.66, 2.09]	- -
mmelin (2003) Females	0.0953	0.269	1.5%	1.10 [0.65, 1.86]	
mmelin (2003) Males	0.0953		1.7%	1.10 [0.70, 1.73]	- -
ngels (2014)		0.3296	1.2%	3.78 [1.98, 7.22]	
verson-Rose (2014)	0.2627		2.2%	1.30 [0.92, 1.84]	
illenbaum (2000) (12)	0.0296		3.2%	1.03 [1.01, 1.05]	
itzpatrick (2012)	0.0290		3.2%		1
				1.02 [0.97, 1.07]	
olsom (1990) (13)	0.5068		1.9%	1.66 [1.11, 2.49]	
an (2011)	0.4618		1.9%	1.59 [1.06, 2.38]	
onjo (2009)		0.0724	3.0%	1.33 [1.16, 1.54]	
u (2005)	-0.0232		3.1%	0.98 [0.90, 1.06]	Ť
uang (1997)		0.3285	1.2%	6.38 [3.35, 12.14]	
isjanto (2003)	0.3293		2.2%	1.39 [1.00, 1.92]	
oster (2005)	0.0732	0.1552	2.3%	1.08 [0.79, 1.46]	+
iu (2008)	0.0862	0.1092	2.7%	1.09 [0.88, 1.35]	+
ofmark (2007) ages 35-75 (14)	0.0862	0.1092	2.7%	1.09 [0.88, 1.35]	+
ofmark (2007) ages 75-85 (15)	0.9083	0.4337	0.8%	2.48 [1.06, 5.80]	
ledin (2008) (16)	0.9083	0.379	1.0%	2.48 [1.18, 5.21]	
ordhal (2014)	0.2313	0.0345	3.1%	1.26 [1.18, 1.35]	-
ybo (2008)	0.3876	0.237	1.7%	1.47 [0.93, 2.34]	
endlebury (2012)		0.2683	1.5%	4.44 [2.62, 7.50]	
im (2008)		0.1844	2.1%	0.94 [0.66, 1.35]	-
mith (2003) Mexican Americans (17)		0.2406	1.7%	5.08 [3.17, 8.14]	
mith (2003) Non-Hispanic whites (18)		0.3685	1.0%	4.53 [2.20, 9.33]	
trodl (2008)	0.01988		2.1%	4.53 [2.20, 9.33]	
					[.
rygged (2011)		0.0114	3.2%	1.17 [1.14, 1.20]	
alko (2008)	1.2743		1.8%	3.58 [2.32, 5.52]	
/ang (2015) (19)	0.0953		2.9%	1.10 [0.94, 1.28]	Ľ_
/eikert (2008)		0.1624	2.3%	1.30 [0.95, 1.79]	
/einstein (2014)	0.3698		0.8%	1.45 [0.62, 3.39]	
/ennerstad (2010)	0.6448		3.2%	1.91 [1.81, 2.01]	•
/iberg (2015)	-0.2896		1.4%	0.75 [0.43, 1.31]	+
/olinsky (2009)	0	0		Not estimable	
/olinsky (2009)	0.0079	0.104	2.7%	1.01 [0.82, 1.24]	+
an (2013)	0.2297	0.0904	2.8%	1.26 [1.05, 1.50]	-
hu (2000)	0.0984		1.6%	1.10 [0.68, 1.80]	
ubtotal (95% CI)			82.6%	1.39 [1.26, 1.53]	•
eterogeneity: Tau ² = 0.06; Chi ² = 1080.23, df = 39 (P < est for overall effect: Z = 6.58 (P < 0.00001)	< 0.00001); l ² = 96 ⁴	%			
otal (95% CI)			100.0%	1.36 [1.24, 1.48]	•
eterogeneity: Tau ² = 0.06; Chi ² = 1152.48, df = 49 (P <	< 0.00001): l ² = 96	%			
est for overall effect: $Z = 6.82$ (P < 0.00001) est for subgroup differences: Chi ² = 1.06, df = 1 (P = 0	,.				0.01 0.1 1 10 Decreased risk of stroke Increased risk of stroke Low education

(1) Adjusted for history of high BP, use of oral contraceptives, marital status, number of live births, cigarette and alcohol consumption, hypertension in pregnancy, family history of... (2) Adjusted for history of high BP, use of oral contraceptives, marital status, number of live births, cigarette and alcohol consumption, hypertension in pregnancy, family history of... (3) Adjusted for history of high BP, use of oral contraceptives, marital status, number of live births, cigarette and alcohol consumption, hypertension in pregnancy, family history of... (4) Adjusted for hypertension, diabetes, hyperlipidemia, previous stroke/TIA, and PAD, current smoking, alcohol abstinence, high alcohol consumption, leisure time sports activity (5) Adjusted for CHD, hypertension, COPD, obesity, income, age and sex.

 (d) Adjusted for age, howe ownership, education, smoking, Bull, alcohol, physical activity, depression, marital status, hypertension, diabetes mellitus, heart disease and...
 (7) Adjusted for age, systolic BP, hypertension, drug use for hypertension, smoking, Gull, alcohol, physical activity, depression, marital status, hypertension, diabetes mellitus, heart disease and...
 (8) Adjusted for age, systolic BP, hypertension, drug use for hypertension, smoking, Gull, alcohol, physical activity, depression, disease, left ventricular hypertrophy, atrial fibrilation, diabetes, fibrogen, BMI,... (9) Adjusted for age, gender, area of residence, BMI, smoking, alcohol consumption, diabetes, high blood pressure, occupational and leisure time physical activity (10) Adjusted for hypertension, heart disease, diabetes, smoking

(11) Adjusted for age,gender and region.(12) Adjusted for age, sex, race

(13) Adjusted for age. Total number of strokes and controls for education categories used not specified. Total strokes and controls 218 and 1845 respectively.

(14) Adjusted for age and sex (15) Adjusted for age and sex

(16) Adjusted for work related factors on the Job Content Questionnaire, organisational change at the workplace and decreased participation

(17) Adjusted for age and sex

(18) Adjusted for age and sex

(19) Adjusted for age, gender, income, medical insurance, smoking and BMI. Note: Studies without footnotes report unadjusted results

eFigure 5f. Sensitivity analysis comparing population cohort studies vs hospital/outpatient studies by education level and risk of stroke; OR>1= low education increases risk of stroke.

study or Subgroup	log[Odds Ratio]	SF	Weight	Odds Ratio IV, Random, 95% C	Odds Ratio IV, Random, 95% CI
.11.1 Population cohorts	ground ratio				
Brenner (2010)	0.7053 0	0497	3.3%	2.02 [1.84, 2.23]	-
Chen (2014) (1)	-0.821 0		3.2%	0.44 [0.39, 0.50]	-
mmelin (2003) Females		0.269	1.7%	1.10 [0.65, 1.86]	
mmelin (2003) Males	0.0953 0		2.0%	1.10 [0.70, 1.73]	
ingels (2014)	1.3303 0		1.4%	3.78 [1.98, 7.22]	
itzpatrick (2012)	0.0198 0		3.4%	1.02 [0.97, 1.07]	•
olsom (1990) (2)	0.5068 0		2.2%	1.66 [1.11, 2.49]	
łamano (2015) (3)	0.4447 0		3.3%	1.56 [1.45, 1.68]	-
	0.287 0		3.3%		-
łonjo (2009)				1.33 [1.16, 1.54]	1
łu (2005)	-0.0232 0		3.3%	0.98 [0.90, 1.06]	
luang (1997)	1.853 0		1.4%	6.38 [3.35, 12.14]	
ackson (2013) (4)	0.2624 0		1.5%	1.30 [0.72, 2.35]	
(oster (2005)	0.0732 0		2.6%	1.08 [0.79, 1.46]	Ť
ofmark (2007) ages 35-75 (5)	0.0862 0		2.9%	1.09 [0.88, 1.35]	T
ofmark (2007) ages 75-85 (5)	0.9083 0		1.0%	2.48 [1.06, 5.80]	
lordhal (2014)	0.2313 0		3.3%	1.26 [1.18, 1.35]	*
Pendlebury (2012)	1.4896 0		1.7%	4.44 [2.62, 7.50]	
Smith (2003) Mexican Americans (5)	1.6253 0		1.9%	5.08 [3.17, 8.14]	
mith (2003) Non-Hispanic whites (5)	1.5107 0		1.2%	4.53 [2.20, 9.33]	
rygged (2011)	0.1569 0	.0114	3.4%	1.17 [1.14, 1.20]	•
an Rossum (1999a) First stroke (6)	0.1484 0	.2098	2.1%	1.16 [0.77, 1.75]	
an Rossum (1999b) History of stroke at baseline (6)	0.1133 0	.2549	1.8%	1.12 [0.68, 1.85]	
Vang (2015) (7)	0.0953 0	.0786	3.1%	1.10 [0.94, 1.28]	-
Veikert (2008)	0.2658 0	.1624	2.5%	1.30 [0.95, 1.79]	
Veinstein (2014)	0.3698 0	.4337	1.0%	1.45 [0.62, 3.39]	
Viberg (2015)	-0.2896 0	.2839	1.6%	0.75 [0.43, 1.31]	
Volinsky (2009)	0.0079	0.104	3.0%	1.01 [0.82, 1.24]	+
(u (2008) (8)	-0.0726 0		2.7%	0.93 [0.71, 1.22]	-
'an (2013)	0.2297 0		3.1%	1.26 [1.05, 1.50]	-
(hu (2000)	0.0984 0		1.9%	1.10 [0.68, 1.80]	
Subtotal (95% CI)	0.000.0		70.6%	1.34 [1.19, 1.50]	•
leterogeneity: Tau ² = 0.07; Chi ² = 614.05, df = 29 (F est for overall effect: Z = 4.86 (P < 0.00001) .11.2 Hospital/outpatient clinics					
		2055			
kinyemi (2014)	0.5988 0	.3055	1.5%	1.82 [1.00. 3.31]	
kinyemi (2014) Baune (2006)	0.5988 0 0.3293 0		1.5% 1.7%	1.82 [1.00, 3.31] 1.39 [0.82, 2.36]	
Baune (2006)	0.3293 0	.2693	1.7%	1.39 [0.82, 2.36]	
Baune (2006) Chang (2002) Asia (9)	0.3293 0 0.174 0	.2693 .2635	1.7% 1.8%	1.39 [0.82, 2.36] 1.19 [0.71, 1.99]	
Baune (2006) Chang (2002) Asia (9) Chang (2002) Eastern Europe (9)	0.3293 0 0.174 0 0.7178 0	.2693 .2635 .4088	1.7% 1.8% 1.0%	1.39 [0.82, 2.36] 1.19 [0.71, 1.99] 2.05 [0.92, 4.57]	
Baune (2006) Chang (2002) Asia (9) Chang (2002) Eastern Europe (9) Chang (2002) Latin America (9)	0.3293 0 0.174 0 0.7178 0 0.1484 0	.2693 .2635 .4088 .2433	1.7% 1.8% 1.0% 1.9%	1.39 [0.82, 2.36] 1.19 [0.71, 1.99] 2.05 [0.92, 4.57] 1.16 [0.72, 1.87]	
laune (2006))hang (2002) Asia (9))hang (2002) Eastern Europe (9))hang (2002) Latin America (9) le Brujin (2014)	0.3293 0 0.174 0 0.7178 0 0.1484 0 1.5209 0	.2693 .2635 .4088 .2433 .4549	1.7% 1.8% 1.0% 1.9% 0.9%	1.39 [0.82, 2.36] 1.19 [0.71, 1.99] 2.05 [0.92, 4.57] 1.16 [0.72, 1.87] 4.58 [1.88, 11.16]	
laune (2006) hang (2002) Asia (9) chang (2002) Eastern Europe (9) chang (2002) Latin America (9) e Brujin (2014) Deoke (2012)	0.3293 0 0.174 0 0.7178 0 0.1484 0 1.5209 0 0.1577 0	.2693 .2635 .4088 .2433 .4549 .2945	1.7% 1.8% 1.0% 1.9% 0.9% 1.6%	1.39 [0.82, 2.36] 1.19 [0.71, 1.99] 2.05 [0.92, 4.57] 1.16 [0.72, 1.87] 4.58 [1.88, 11.16] 1.17 [0.66, 2.09]	
Jaune (2006) Chang (2002) Asia (9) Chang (2002) Eastern Europe (9) Chang (2002) Latin America (9) e Brujin (2014) Jeoke (2012) Everson-Rose (2014)	0.3293 0 0.174 0 0.7178 0 0.1484 0 1.5209 0 0.1577 0 0.2627 0	.2693 .2635 .4088 .2433 .4549 .2945 .1757	1.7% 1.8% 1.0% 1.9% 0.9% 1.6% 2.4%	1.39 [0.82, 2.36] 1.19 [0.71, 1.99] 2.05 [0.92, 4.57] 1.16 [0.72, 1.87] 4.58 [1.88, 11.16] 1.17 [0.66, 2.09] 1.30 [0.92, 1.84]	
Baune (2006) Chang (2002) Asia (9) Chang (2002) Eastern Europe (9) Chang (2002) Latin America (9) le Brujin (2014) Pooke (2012) Everson-Rose (2014) San (2011)	0.3293 0 0.174 0 0.7178 0 0.1484 0 1.5209 0 0.1577 0 0.2627 0 0.4618 0	.2693 .2635 .4088 .2433 .4549 .2945 .1757 .2069	1.7% 1.8% 1.0% 1.9% 0.9% 1.6% 2.4% 2.2%	1.39 [0.82, 2.36] 1.19 [0.71, 1.99] 2.05 [0.92, 4.57] 1.16 [0.72, 1.87] 4.58 [1.88, 11.16] 1.17 [0.66, 2.09] 1.30 [0.92, 1.84] 1.59 [1.06, 2.38]	
Jaune (2006) Chang (2002) Asia (9) Chang (2002) Latin America (9) Le Brujin (2014) Jeoke (2012) Everson-Rose (2014) San (2011) Grau (2012) (10)	0.3293 0 0.174 0 0.7178 0 0.1484 0 1.5209 0 0.1577 0 0.2627 0 0.4618 0 0.207 0	.2693 .2635 .4088 .2433 .4549 .2945 .1757 .2069 .2461	1.7% 1.8% 1.0% 1.9% 0.9% 1.6% 2.4% 2.2% 1.9%	1.39 [0.82, 2.36] 1.19 [0.71, 1.99] 2.05 [0.92, 4.57] 1.16 [0.72, 1.87] 4.58 [1.88, 11.16] 1.17 [0.66, 2.09] 1.30 [0.92, 1.84] 1.59 [1.06, 2.38] 1.23 [0.76, 1.99]	
Jaune (2006) hang (2002) Asia (9) chang (2002) Eastern Europe (9) chang (2002) Latin America (9) e Brujin (2014) Deoke (2012) iverson-Rose (2014) San (2011) frau (2012) (10) Gisjanto (2003)	0.3293 0 0.174 0 0.7178 0 0.144 0 1.5209 0 0.1577 0 0.2627 0 0.4618 0 0.207 0 0.3293	.2693 .2635 .4088 .2433 .4549 .2945 .1757 .2069 .2461 0.166	1.7% 1.8% 1.0% 1.9% 0.9% 1.6% 2.4% 2.2% 1.9% 2.5%	1.39 [0.82, 2.36] 1.19 [0.71, 1.99] 2.05 [0.92, 4.57] 1.16 [0.72, 1.87] 4.58 [1.88, 11.16] 1.17 [0.66, 2.09] 1.30 [0.92, 1.84] 1.59 [1.06, 2.38] 1.23 [0.76, 1.99] 1.39 [1.00, 1.92]	
Jaune (2006) Chang (2002) Asia (9) Chang (2002) Eastern Europe (9) Chang (2002) Latin America (9) e Brujin (2014) Deoke (2012) Everson-Rose (2014) San (2011) Srau (2012) (10) Siglanto (2003) iu (2008)	0.3293 0 0.174 0 0.7178 0 0.148 0 1.5209 0 0.1577 0 0.2627 0 0.2627 0 0.2627 0 0.3293 - -0.8916	.2693 .2635 .4088 .2433 .4549 .2945 .1757 .2069 .2461 0.166 0.42	1.7% 1.8% 1.9% 0.9% 1.6% 2.4% 2.2% 1.9% 2.5% 1.0%	1.39 [0.82, 2.36] 1.19 [0.71, 1.99] 2.05 [0.92, 4.57] 1.16 [0.72, 1.87] 4.58 [1.88, 11.16] 1.17 [0.66, 2.09] 1.30 [0.92, 1.84] 1.59 [1.06, 2.38] 1.23 [0.76, 1.99] 1.39 [1.00, 1.92] 0.41 [0.18, 0.93]	
laune (2006) hang (2002) Asia (9) chang (2002) Eastern Europe (9) hang (2002) Latin America (9) le Brujin (2014) le Brujin (2014) verson-Rose (2014) san (2011) frau (2012) (10) (sisjanto (2003) lu (2008) fedin (2008) (11)	0.3293 0 0.174 0 0.1748 0 0.1484 0 1.5209 0 0.4577 0 0.4618 0 0.207 0 0.3293 -0.8916 0.9083	.2693 .2635 .4088 .2433 .4549 .2945 .1757 .2069 .2461 0.166 0.42 0.379	1.7% 1.8% 1.0% 1.9% 0.9% 1.6% 2.4% 2.2% 1.9% 2.5% 1.0% 1.2%	$\begin{array}{c} 1.39 \ [0.82, 2.36] \\ 1.19 \ [0.71, 1.99] \\ 2.05 \ [0.92, 4.57] \\ 1.16 \ [0.72, 1.87] \\ 4.58 \ [1.88, 11.16] \\ 1.17 \ [0.66, 2.09] \\ 1.30 \ [0.92, 1.84] \\ 1.59 \ [1.06, 2.38] \\ 1.23 \ [0.76, 1.99] \\ 1.39 \ [1.00, 1.92] \\ 0.41 \ [0.18, 0.93] \\ 2.48 \ [1.18, 5.21] \end{array}$	
Jaune (2006) Chang (2002) Asia (9) Chang (2002) Latin America (9) Le Brujin (2014) Jeoke (2012) Everson-Rose (2014) San (2011) Grau (2012) (10) Sigianto (2003) Liu (2008) Hedin (2008) (11) Lybo (2008)	0.3293 0 0.174 0 0.7178 0 0.184 0 1.5209 0 0.4577 0 0.4618 0 0.207 0 0.3293 -0.8916 0.9083 0.3876	.2693 .2635 .4088 .2433 .4549 .2945 .1757 .2069 .2461 0.166 0.42 0.379 0.237	1.7% 1.8% 1.0% 1.9% 0.9% 1.6% 2.2% 1.9% 2.5% 1.0% 1.2% 1.9%	1.39 [0.82, 2.36] 1.19 [0.71, 1.99] 2.05 [0.92, 4.57] 1.16 [0.72, 1.87] 4.58 [1.88, 11.16] 1.17 [0.66, 2.09] 1.30 [0.92, 1.84] 1.59 [1.06, 2.38] 1.23 [0.76, 1.99] 1.39 [1.00, 1.92] 0.41 [0.18, 0.93] 2.48 [1.18, 5.21] 1.47 [0.93, 2.34]	
laune (2006) chang (2002) Asia (9) chang (2002) Lastern Europe (9) chang (2002) Latin America (9) le Brujin (2014) vecke (2012) iverson-Rose (2014) San (2011) Gana (2012) (10) (isjanto (2003) iu (2008) Medin (2008) (11) tybo (2008)	0.3293 0 0.174 0 0.1748 0 1.5209 0 0.1577 0 0.2627 0 0.2627 0 0.3293 -0.8916 0.3083 0.3876 -0.359 0	.2693 .2635 .4088 .2433 .4549 .2945 .1757 .2069 .2461 0.166 0.42 0.379 0.237 .1844	1.7% 1.8% 1.0% 1.9% 0.9% 1.6% 2.2% 1.9% 2.5% 1.0% 1.2% 1.9% 2.3%	1.39 [0.82, 2.36] 1.19 [0.71, 1.99] 2.05 [0.92, 4.57] 1.16 [0.72, 1.87] 4.58 [1.88, 11.16] 1.17 [0.66, 2.09] 1.30 [0.92, 1.84] 1.59 [1.06, 2.38] 1.23 [0.76, 1.99] 1.39 [1.00, 1.92] 0.41 [0.18, 0.93] 2.48 [1.18, 5.21] 1.47 [0.93, 2.34] 0.94 [0.66, 1.35]	
Jaune (2006) Chang (2002) Asia (9) Chang (2002) Eastern Europe (9) Chang (2002) Latin America (9) e Brujin (2014) Deoke (2012) Everson-Rose (2014) San (2011) Gisjanto (2003) iu (2008) fedin (2008) fedin (2008) im (2008) (alko (2008)	0.3293 0 0.174 0 0.7178 0 1.5209 0 0.1577 0 0.2627 0 0.2627 0 0.2627 0 0.3293 -0.8916 0.3876 -0.9083 0.3876 -0.59 0 1.2743 0	.2693 .2635 .4088 .2433 .4549 .2945 .1757 .2069 .2461 0.462 0.42 0.379 0.237 .1844 .2217	1.7% 1.8% 1.0% 1.9% 0.9% 2.4% 2.2% 1.9% 2.5% 1.0% 1.2% 2.3% 2.3%	1.39 [0.82, 2.36] 1.19 [0.71, 1.99] 2.05 [0.92, 4.57] 1.16 [0.72, 1.87] 4.58 [1.88, 11.16] 1.17 [0.66, 2.09] 1.30 [0.92, 1.84] 1.59 [1.06, 2.38] 1.23 [0.76, 1.99] 1.39 [1.00, 1.92] 0.41 [0.18, 0.93] 2.48 [1.18, 5.21] 1.47 [0.93, 2.34] 0.94 [0.66, 1.35] 3.58 [2.32, 5.52]	
Jaune (2006) Chang (2002) Asia (9) Chang (2002) Eastern Europe (9) Chang (2002) Latin America (9) le Brujin (2014) Jeoke (2012) Everson-Rose (2014) San (2011) Srau (2012) (10) Srau (2012) (10) Srau (2012) (10) Isjanto (2003) Liu (2008) Idedin (2008	0.3293 0 0.174 0 0.1748 0 1.5209 0 0.1577 0 0.2627 0 0.2627 0 0.3293 -0.8916 0.3083 0.3876 -0.359 0	.2693 .2635 .4088 .2433 .4549 .2945 .1757 .2069 .2461 0.462 0.42 0.379 0.237 .1844 .2217	1.7% 1.8% 1.0% 1.9% 2.4% 2.2% 1.9% 2.5% 1.0% 1.2% 2.3% 2.3% 2.0%	$\begin{array}{c} 1.39 & [0.82, 2.36] \\ 1.19 & [0.71, 1.99] \\ 2.05 & [0.92, 4.57] \\ 1.16 & [0.72, 1.87] \\ 4.58 & [1.88, 11.16] \\ 1.17 & [0.66, 2.09] \\ 1.30 & [0.92, 1.84] \\ 1.59 & [1.06, 2.38] \\ 1.23 & [0.76, 1.99] \\ 1.39 & [1.00, 1.92] \\ 0.41 & [0.18, 0.93] \\ 2.48 & [1.18, 5.21] \\ 1.47 & [0.93, 2.34] \\ 0.94 & [0.66, 1.35] \\ 3.58 & [2.32, 5.52] \\ 1.20 & [0.68, 2.12] \end{array}$	
laune (2006) chang (2002) Asia (9) chang (2002) Lastern Europe (9) chang (2002) Latin America (9) le Brujin (2014) verson-Rose (2014) San (2011) Gan (2014) San (2011) Gan (2014) Gan (2008) Medin (2008) Medin (2008) Silm (2008)	0.3293 0 0.174 0 0.7178 0 0.184 0 1.5209 0 0.4518 0 0.2627 0 0.4618 0 0.207 0 0.3293 -0.8916 0.983 0.3876 -0.059 0 1.2743 0 0.1823 0	.2693 .2635 .4088 .2433 .4549 .2945 .1757 .2069 .2461 0.462 0.42 0.379 0.237 .1844 .2217	1.7% 1.8% 1.0% 1.9% 0.9% 2.4% 2.2% 1.9% 2.5% 1.0% 1.2% 2.3% 2.3%	1.39 [0.82, 2.36] 1.19 [0.71, 1.99] 2.05 [0.92, 4.57] 1.16 [0.72, 1.87] 4.58 [1.88, 11.16] 1.17 [0.66, 2.09] 1.30 [0.92, 1.84] 1.59 [1.06, 2.38] 1.23 [0.76, 1.99] 1.39 [1.00, 1.92] 0.41 [0.18, 0.93] 2.48 [1.18, 5.21] 1.47 [0.93, 2.34] 0.94 [0.66, 1.35] 3.58 [2.32, 5.52]	
Haune (2006) Shang (2002) Asia (9) Shang (2002) Lastern Europe (9) Shang (2002) Latin America (9) le Brujin (2014) Jeoke (2012) Everson-Rose (2014) San (2011) Srau (2012) (10) Sigjanto (2003) Liu (2008) Idedin (2008) (11) Lybo (2008) Idedin (2008) (2008) Valko (2008) (2008) Valko (2008) Solution (1999) (12) Lybtotal (95% CI) leterogeneity: Tau ² = 0.11; Chi ² = 44.12, df = 16 (P leterogeneity: Tau ² = 0.11; Chi ² = 44.12, df = 16 (P	0.3293 0 0.174 0 0.7178 0 0.184 0 1.5209 0 0.4518 0 0.2627 0 0.4618 0 0.207 0 0.3293 -0.8916 0.983 0.3876 -0.059 0 1.2743 0 0.1823 0	.2693 .2635 .4088 .2433 .4549 .2945 .1757 .2069 .2461 0.462 0.42 0.379 0.237 .1844 .2217	1.7% 1.8% 1.9% 0.9% 1.6% 2.4% 2.2% 1.9% 2.5% 1.0% 2.3% 2.0% 2.3% 2.0% 2.9%	$\begin{array}{c} 1.39 & [0.82, 2.36] \\ 1.19 & [0.71, 1.99] \\ 2.05 & [0.92, 4.57] \\ 1.16 & [0.72, 1.87] \\ 4.58 & [1.88, 11.16] \\ 1.17 & [0.66, 2.09] \\ 1.30 & [0.92, 1.84] \\ 1.59 & [1.06, 2.38] \\ 1.23 & [0.76, 1.99] \\ 1.39 & [1.00, 1.92] \\ 0.41 & [0.18, 0.93] \\ 2.48 & [1.18, 5.21] \\ 1.47 & [0.93, 2.34] \\ 0.94 & [0.66, 1.35] \\ 3.58 & [2.32, 5.52] \\ 1.20 & [0.68, 2.12] \\ 1.45 & [1.19, 1.78] \end{array}$	
laune (2006) chang (2002) Asia (9) chang (2002) Lastern Europe (9) chang (2002) Latin America (9) le Brujin (2014) le Brujin (2014) le Verson-Rose (2014) san (2011) Grau (2012) (10) (sigianto (2003) iu (2008) fedin (2008) (11) lybo (2008) (alko (2008) (alko (2008) (ou (1999) (12) Subtotal (95% CI) leterogeneity: Tau ² = 0.11; Chi ² = 44.12, df = 16 (P fest for overall effect: Z = 3.61 (P = 0.0003) (otal (95% CI)	0.3293 0 0.174 0 0.7178 0 0.144 0 1.5209 0 0.4618 0 0.2627 0 0.4618 0 0.207 0 0.3293 -0.8916 0.9083 0.3876 1.2743 0 1.2743 0 0.1823 0 = 0.0002); l ² = 64%	2693 2635 4088 2433 4549 22945 1757 2069 2.2461 0.166 0.42 0.379 0.237 1.1844 2.217 2.2902	1.7% 1.8% 1.0% 1.9% 2.4% 2.2% 1.9% 2.5% 1.0% 1.2% 2.3% 2.3% 2.0%	$\begin{array}{c} 1.39 & [0.82, 2.36] \\ 1.19 & [0.71, 1.99] \\ 2.05 & [0.92, 4.57] \\ 1.16 & [0.72, 1.87] \\ 4.58 & [1.88, 11.16] \\ 1.17 & [0.66, 2.09] \\ 1.30 & [0.92, 1.84] \\ 1.59 & [1.06, 2.38] \\ 1.23 & [0.76, 1.99] \\ 1.39 & [1.00, 1.92] \\ 0.41 & [0.18, 0.93] \\ 2.48 & [1.18, 5.21] \\ 1.47 & [0.93, 2.34] \\ 0.94 & [0.66, 1.35] \\ 3.58 & [2.32, 5.52] \\ 1.20 & [0.68, 2.12] \end{array}$	
laune (2006) chang (2002) Asia (9) chang (2002) Lastern Europe (9) chang (2002) Latin America (9) le Brujin (2014) verson-Rose (2014) San (2011) srau (2012) (10) (isjanto (2003) iu (2008) Medin (2008) (2	0.3293 0 0.174 0 0.7178 0 0.144 0 1.5209 0 0.4618 0 0.2627 0 0.4618 0 0.207 0 0.3293 -0.8916 0.9083 0.3876 1.2743 0 1.2743 0 0.1823 0 = 0.0002); l ² = 64%	2693 2635 4088 2433 4549 22945 1757 2069 2.2461 0.166 0.42 0.379 0.237 1.1844 2.217 2.2902	1.7% 1.8% 1.9% 0.9% 1.6% 2.4% 2.2% 1.9% 2.5% 1.0% 2.3% 2.0% 2.3% 2.0% 2.9%	$\begin{array}{c} 1.39 & [0.82, 2.36] \\ 1.19 & [0.71, 1.99] \\ 2.05 & [0.92, 4.57] \\ 1.16 & [0.72, 1.87] \\ 4.58 & [1.88, 11.16] \\ 1.17 & [0.66, 2.09] \\ 1.30 & [0.92, 1.84] \\ 1.59 & [1.06, 2.38] \\ 1.23 & [0.76, 1.99] \\ 1.39 & [1.00, 1.92] \\ 0.41 & [0.18, 0.93] \\ 2.48 & [1.18, 5.21] \\ 1.47 & [0.93, 2.34] \\ 0.94 & [0.66, 1.35] \\ 3.58 & [2.32, 5.52] \\ 1.20 & [0.68, 2.12] \\ 1.45 & [1.19, 1.78] \end{array}$	
laune (2006) chang (2002) Asia (9) chang (2002) Lastern Europe (9) chang (2002) Latin America (9) e Brujin (2014) beoke (2012) iverson-Rose (2014) San (2011) frau (2012) (10) Gisjanto (2003) iu (2008) Medin (2008) Medin (2008) falko (2008)	0.3293 0 0.174 0 0.7178 0 0.144 0 1.5209 0 0.464 0 0.2627 0 0.2627 0 0.3293 -0.8916 0.3876 0.3876 -0.059 0 1.2743 0 0.1823 0 = 0.0002); I ² = 64%	2693 2635 4088 2433 4549 22945 1757 2069 2.2461 0.166 0.42 0.379 0.237 1.1844 2.217 2.2902	1.7% 1.8% 1.9% 0.9% 1.6% 2.4% 2.2% 1.9% 2.5% 1.0% 2.3% 2.0% 2.3% 2.0% 2.9%	$\begin{array}{c} 1.39 & [0.82, 2.36] \\ 1.19 & [0.71, 1.99] \\ 2.05 & [0.92, 4.57] \\ 1.16 & [0.72, 1.87] \\ 4.58 & [1.88, 11.16] \\ 1.17 & [0.66, 2.09] \\ 1.30 & [0.92, 1.84] \\ 1.59 & [1.06, 2.38] \\ 1.23 & [0.76, 1.99] \\ 1.39 & [1.00, 1.92] \\ 0.41 & [0.18, 0.93] \\ 2.48 & [1.18, 5.21] \\ 1.47 & [0.93, 2.34] \\ 0.94 & [0.66, 1.35] \\ 3.58 & [2.32, 5.52] \\ 1.20 & [0.68, 2.12] \\ 1.45 & [1.19, 1.78] \end{array}$	0.01 0.1 10 Decreased risk of stroke
laune (2006) thang (2002) Asia (9) thang (2002) Lastern Europe (9) thang (2002) Latin America (9) e Brujin (2014) leoke (2012) tiverson-Rose (2014) san (2011) risrau (2012) (10) isjanto (2003) leddin (2008) fedin (2008) falko (2008) im (2008) im (2008) latko (2008) im (2008) latko (2008) lat	0.3293 0 0.174 0 0.7178 0 0.144 0 1.5209 0 0.464 0 0.2627 0 0.2627 0 0.3293 -0.8916 0.3876 0.3876 -0.059 0 1.2743 0 0.1823 0 = 0.0002); I ² = 64%	2693 2635 4088 2433 4549 22945 1757 2069 2.2461 0.166 0.42 0.379 0.237 1.1844 2.217 2.2902	1.7% 1.8% 1.9% 0.9% 1.6% 2.4% 2.2% 1.9% 2.5% 1.0% 2.3% 2.0% 2.3% 2.0% 2.9%	$\begin{array}{c} 1.39 & [0.82, 2.36] \\ 1.19 & [0.71, 1.99] \\ 2.05 & [0.92, 4.57] \\ 1.16 & [0.72, 1.87] \\ 4.58 & [1.88, 11.16] \\ 1.17 & [0.66, 2.09] \\ 1.30 & [0.92, 1.84] \\ 1.59 & [1.06, 2.38] \\ 1.23 & [0.76, 1.99] \\ 1.39 & [1.00, 1.92] \\ 0.41 & [0.18, 0.93] \\ 2.48 & [1.18, 5.21] \\ 1.47 & [0.93, 2.34] \\ 0.94 & [0.66, 1.35] \\ 3.58 & [2.32, 5.52] \\ 1.20 & [0.68, 2.12] \\ 1.45 & [1.19, 1.78] \end{array}$	

(2) Adjusted for age. Total number of strokes and controls for education categories used not specified. Total strokes and controls 218 and 1845 respectively.

(3) Adjusted for CHD, hypertension, COPD, obesity, income, age and sex.

(4) Adjusted for age, home ownership, education, smoking, BMI, alcohol, physical activity, depression, marital status, hypertension, diabetes mellitus, heart disease and... (5) Adjusted for age and sex

(6) Adjusted for age, spetiolic BP, hypertension, drug use for hypertension, smoking, cardiovascular disease, left ventricular hypertrophy, atrial fibrilation, diabetes, fibrogen, BMI,... (7) Adjusted for age, spender, income, medical insurance, smoking and BMI.

(8) Adjusted for age, gender, area of residence, BMI, smoking, alcohol consumption, diabetes, high blood pressure, occupational and leisure time physical activity

(9) Adjusted for history of high BP, use of oral contraceptives, marital status, number of live births, cigarette and alcohol consumption, hypertension in pregnancy, family history... (10) Adjusted for hypertension, diabetes, hyperlipidemia, previous stroke/TIA, and PAD, current smoking, alcohol abstinence, high alcohol consumption, leisure time sports...

(11) Adjusted for work related factors on the Job Content Questionnaire, organisational change at the workplace and decreased participation

(12) Adjusted for hypertension, heart disease, diabetes, smoking Note: Studies without footnotes report unadjusted results

eFigure 5g. Sensitivity analysis comparing stroke ascertainment methods (clinical examination, self-report, central health statistics) by education level and risk of stroke; OR>1= low education increases risk of stroke.

tudy or Subgroup	log[Odds Ratio] S	E Weight	Odds Ratio IV, Random, 95% C	Odds Ratio IV, Random, 95% CI
.10.1 Clinical examination and neuroimaging	<u></u>			
kinyemi (2014)	0.5988 0.305	5 0.8%	1.82 [1.00, 3.31]	
aune (2006)	0.3293 0.269	3 1.0%	1.39 [0.82, 2.36]	+
hang (2002) Asia (1)	0.174 0.263		1.19 [0.71, 1.99]	
hang (2002) Eastern Europe (1)	0.7178 0.408		2.05 [0.92, 4.57]	
hang (2002) Latin America (1)	0.1484 0.243		1.16 [0.72, 1.87]	
Brujin (2014)	1.5209 0.454		4.58 [1.88, 11.16]	
eoke (2012)	0.1577 0.294		1.17 [0.66, 2.09]	
mmelin (2003) Females	0.0953 0.26		1.10 [0.65, 1.86]	
mmelin (2003) Males ngels (2014)	0.0953 0.230 1.33 0.329		1.10 [0.70, 1.73] 3.78 [1.98, 7.21]	
verson-Rose (2014)	0.2627 0.175		1.30 [0.92, 1.84]	
an (2011)	0.4618 0.206		1.59 [1.06, 2.38]	
Grau (2012) (2)	0.207 0.246		1.23 [0.76, 1.99]	
onjo (2009)	0.287 0.072		1.33 [1.16, 1.54]	-
isjanto (2003)	0.3293 0.16	6 1.6%	1.39 [1.00, 1.92]	
oster (2005)	0.0732 0.155	2 1.7%	1.08 [0.79, 1.46]	+
iu (2008)	-0.8916 0.4	2 0.5%	0.41 [0.18, 0.93]	
ybo (2008)	0.3876 0.23		1.47 [0.93, 2.34]	
im (2008)	-0.059 0.184		0.94 [0.66, 1.35]	
'alko (2008)	1.2743 0.221		3.58 [2.32, 5.52]	
an Rossum (1999a) First stroke (3)	0.1484 0.209		1.16 [0.77, 1.75]	
an Rossum (1999b) History of stroke at baseline (3)			1.12 [0.68, 1.85]	
Veinstein (2014)	0.3698 0.433		1.45 [0.62, 3.39]	
an (2013) ubtotal (95% CI)	0.2297 0.090	4 2.2% 27.5%	1.26 [1.05, 1.50] 1.37 [1.20, 1.57]	
leterogeneity: Tau ² = 0.06; Chi ² = 56.99, df = 23 (P	= 0.0001): 12 = 60%	21.0%	1.57 [1.20, 1.57]	▼
est for overall effect: $Z = 4.59$ (P < 0.00001)	- 0.00017,1 = 00%			
.10.2 Self-report				
Irenner (2010)	0.7053 0.049	7 2.5%	2.02 [1.84, 2.23]	-
Chen (2014) (4)	-0.821 0.061		0.44 [0.39, 0.50]	- I
ingels (2014)	1.3303 0.329		3.78 [1.98, 7.22]	
illenbaum (2000) (5)	0.0296 0.010		1.03 [1.01, 1.05]	•
itzpatrick (2012)	0.0198 0.026		1.02 [0.97, 1.07]	+
olsom (1990) (6)	0.5068 0.206		1.66 [1.11, 2.49]	
lonjo (2009)	0.287 0.072	4 2.3%	1.33 [1.16, 1.54]	-
luang (1997)	1.853 0.328	5 0.7%	6.38 [3.35, 12.14]	
ackson (2013) (7)	0.2624 0.301	5 0.8%	1.30 [0.72, 2.35]	
loster (2005)	0.0732 0.155		1.08 [0.79, 1.46]	+
strodl (2008)	0.0198 0.186		1.02 [0.71, 1.47]	
'alko (2008)	1.2743 0.221		3.58 [2.32, 5.52]	
an Rossum (1999a) First stroke (3)	0.1484 0.209		1.16 [0.77, 1.75]	
an Rossum (1999b) History of stroke at baseline (3)	0.1133 0.254		1.12 [0.68, 1.85]	
Vang (2015) (8)	0.0953 0.078		1.10 [0.94, 1.28]	Ľ.
Veikert (2008)	0.2658 0.162		1.30 [0.95, 1.79]	
Veinstein (2014)	0.3698 0.433		1.45 [0.62, 3.39]	
(u (2008) (9) (an (2013)	-0.0726 0.140 0.2297 0.090		0.93 [0.71, 1.22] 1.26 [1.05, 1.50]	
ubtotal (95% CI)	0.2297 0.090	4 2.2% 31.0%	1.31 [1.12, 1.54]	•
leterogeneity: Tau ² = 0.10; Chi ² = 476.82, df = 18 (F	<pre>< 0.00001); I² = 96%</pre>			
est for overall effect: Z = 3.29 (P = 0.0010)				
.10.3 Centralised health statistics				
illenbaum (2000) (5)	0.0296 0.010		1.03 [1.01, 1.05]	1
itzpatrick (2012)	0.0198 0.026		1.02 [0.97, 1.07]	t
olsom (1990) (6)	0.5068 0.206		1.66 [1.11, 2.49]	
San (2011)	0.4618 0.206		1.59 [1.06, 2.38]	
lamano (2015) (10)	0.4447 0.037		1.56 [1.45, 1.68]	
lonjo (2009)	0.287 0.072		1.33 [1.16, 1.54]	1-
lu (2005)	-0.0232 0.043		0.98 [0.90, 1.06]	1
ackson (2013) (11) ofmark (2007) ages 35-75 (12)	0.2624 0.301		1.30 [0.72, 2.35]	
	0.0862 0.109		1.09 [0.88, 1.35]	
	0.0000 0.400	7 0.5%	2.48 [1.06, 5.80]	· · · ·
ofmark (2007) ages 75-85 (12)	0.9083 0.433	5 2 50/		
ofmark (2007) ages 75-85 (12) Iordhal (2014)	0.2313 0.034		1.26 [1.18, 1.35]	
ofmark (2007) ages 75-85 (12) lordhal (2014) lybo (2008)	0.2313 0.034 0.3876 0.23	7 1.1%	1.47 [0.93, 2.34]	<u>+</u> −−
ofmark (2007) ages 75-85 (12) lordhal (2014) lybo (2008) mith (2003) Mexican Americans (12)	0.2313 0.034 0.3876 0.23 1.6253 0.240	7 1.1% 6 1.1%	1.47 [0.93, 2.34] 5.08 [3.17, 8.14]	
ofmark (2007) ages 75-85 (12) lordhal (2014) lybo (2008) mith (2003) Mexican Americans (12) imith (2003) Non-Hispanic whites (12)	0.2313 0.034 0.3876 0.23 1.6253 0.240 1.5107 0.368	7 1.1% 6 1.1% 5 0.6%	1.47 [0.93, 2.34] 5.08 [3.17, 8.14] 4.53 [2.20, 9.33]	
ofmark (2007) ages 75-85 (12) lordhal (2014) lybo (2008) imith (2003) Mexican Americans (12) imith (2003) Non-Hispanic whites (12) rygged (2011)	0.2313 0.034 0.3876 0.23 1.6253 0.240 1.5107 0.368 0.1569 0.011	7 1.1% 6 1.1% 5 0.6% 4 2.6%	1.47 [0.93, 2.34] 5.08 [3.17, 8.14] 4.53 [2.20, 9.33] 1.17 [1.14, 1.20]	
ofmark (2007) ages 75-85 (12) lordhal (2014) lybo (2008) mith (2003) Mexican Americans (12) imith (2003) Non-Hispanic whites (12)	0.2313 0.034 0.3876 0.23 1.6253 0.240 1.5107 0.368	7 1.1% 6 1.1% 5 0.6% 4 2.6% 8 1.3%	1.47 [0.93, 2.34] 5.08 [3.17, 8.14] 4.53 [2.20, 9.33] 1.17 [1.14, 1.20] 1.16 [0.77, 1.75]	
ofmark (2007) ages 75-85 (12) lordhal (2014) with (2003) with (2003) Mexican Americans (12) mith (2003) Non-Hispanic whites (12) rygged (2011) an Rossum (1999a) First stroke (³)	0.2313 0.034 0.3876 0.23 1.6253 0.240 1.5107 0.368 0.1569 0.011 0.1484 0.209	7 1.1% 6 1.1% 5 0.6% 4 2.6% 8 1.3% 9 1.0%	1.47 [0.93, 2.34] 5.08 [3.17, 8.14] 4.53 [2.20, 9.33] 1.17 [1.14, 1.20]	
ofmark (2007) ages 75-85 (12) lordhal (2014) lybo (2008) mith (2003) Mexican Americans (12) mith (2003) Non-Hispanic whites (12) rygged (2011) an Rossum (1999a) First stroke (³) an Rossum (1999b) History of stroke at baseline (3)	0.2313 0.034 0.3876 0.23 1.6253 0.240 1.5107 0.368 0.1569 0.011 0.1484 0.209 0.1133 0.254	7 1.1% 6 1.1% 5 0.6% 4 2.6% 8 1.3% 9 1.0% 4 1.6%	1.47 [0.93, 2.34] 5.08 [3.17, 8.14] 4.53 [2.20, 9.33] 1.17 [1.14, 1.20] 1.16 [0.77, 1.75] 1.12 [0.68, 1.85]	
ofmark (2007) ages 75-85 (12) lordhal (2014) imith (2003) Mexican Americans (12) imith (2003) Non-Hispanic whites (12) rygged (2011) an Rossum (1999a) First stroke (³) an Rossum (1999b) History of stroke at baseline (3) Veikert (2008)	0.2313 0.034 0.3876 0.23 1.6253 0.240 1.5107 0.368 0.1569 0.011 0.1484 0.209 0.1133 0.254 0.2658 0.162	7 1.1% 6 1.1% 5 0.6% 4 2.6% 8 1.3% 9 1.0% 4 1.6% 7 0.5%	1.47 [0.93, 2.34] 5.08 [3.17, 8.14] 4.53 [2.20, 9.33] 1.17 [1.14, 1.20] 1.16 [0.77, 1.75] 1.12 [0.68, 1.85] 1.30 [0.95, 1.79]	
ofmark (2007) ages 75-85 (12) lordhal (2014) mith (2003) Mexican Americans (12) imith (2003) Non-Hispanic whites (12) rygged (2011) an Rossum (1999b) First stroke (3) an Rossum (1999b) History of stroke at baseline (3) Veikert (2008) Veinstein (2014) Vennerstad (2010)	0.2313 0.034 0.3876 0.23 1.6253 0.240 1.5107 0.366 0.1569 0.011 0.1484 0.209 0.1133 0.254 0.2658 0.162 0.3698 0.433	7 1.1% 6 1.1% 5 0.6% 4 2.6% 8 1.3% 9 1.0% 4 1.6% 7 0.5% 1 2.6%	1.47 [0.93, 2.34] 5.08 [3.17, 8.14] 4.53 [2.20, 9.33] 1.17 [1.14, 1.20] 1.16 [0.77, 1.75] 1.12 [0.68, 1.85] 1.30 [0.95, 1.79] 1.45 [0.62, 3.39]	
ofmark (2007) ages 75-85 (12) lordhal (2014) lybo (2008) mith (2003) Mexican Americans (12) mith (2003) Non-Hispanic whites (12) rygged (2011) an Rossum (1999a) First stroke ⁽³⁾ an Rossum (1999b) History of stroke at baseline (3) Veikert (2008) Veinstein (2014) Vennerstad (2010)	0.2313 0.034 0.3676 0.23 1.6253 0.240 1.5107 0.368 0.1569 0.011 0.1484 0.209 0.1133 0.254 0.2658 0.162 0.3698 0.433 0.6448 0.026	$\begin{array}{cccc} 7 & 1.1\% \\ 6 & 1.1\% \\ 5 & 0.6\% \\ 4 & 2.6\% \\ 8 & 1.3\% \\ 9 & 1.0\% \\ 4 & 1.6\% \\ 7 & 0.5\% \\ 1 & 2.6\% \\ 9 & 0.9\% \end{array}$	1.47 [0.93, 2.34] 5.08 [3.17, 8.14] 4.53 [2.20, 9.33] 1.17 [1.14, 1.20] 1.16 [0.77, 1.75] 1.12 [0.68, 1.85] 1.30 [0.95, 1.79] 1.45 [0.62, 3.39] 1.91 [1.81, 2.01]	
ofmark (2007) ages 75-85 (12) lordhal (2014) mith (2003) Mexican Americans (12) imith (2003) Non-Hispanic whites (12) rygged (2011) an Rossum (1999b) First stroke (3) an Rossum (1999b) History of stroke at baseline (3) Veikert (2008) Veinstein (2014) Vennerstad (2010)	0.2313 0.034 0.3876 0.23 1.6253 0.240 1.5107 0.368 0.1569 0.011 0.1484 0.209 0.1133 0.254 0.2658 0.162 0.3698 0.433 0.6448 0.026 -0.2996 0.283	$\begin{array}{cccc} 7 & 1.1\% \\ 6 & 1.1\% \\ 5 & 0.6\% \\ 4 & 2.6\% \\ 8 & 1.3\% \\ 9 & 1.0\% \\ 9 & 1.0\% \\ 4 & 1.6\% \\ 4 & 1.6\% \\ 1 & 2.6\% \\ 9 & 0.9\% \\ 4 & 2.1\% \end{array}$	$\begin{array}{c} 1.47 & [0.93, 2.34] \\ 5.08 & [3.17, 8.14] \\ 4.53 & [2.20, 9.33] \\ 1.17 & [1.14, 1.20] \\ 1.16 & [0.77, 1.75] \\ 1.12 & [0.68, 1.85] \\ 1.30 & [0.95, 1.79] \\ 1.45 & [0.62, 3.39] \\ 1.91 & [1.81, 2.01] \\ 0.75 & [0.43, 1.31] \end{array}$	
ofmark (2007) ages 75-85 (12) lordhal (2014) mith (2003) Mexican Americans (12) imith (2003) Non-Hispanic whites (12) rygged (2011) an Rossum (1999b) First stroke (3) an Rossum (1999b) History of stroke at baseline (3) Veikert (2008) Veinstein (2014) Vennerstad (2010) Viblerg (2015) Volinsky (2009) iu (2008)(9) an (2013)	0.2313 0.034 0.3876 0.23 1.6253 0.240 1.5107 0.368 0.1569 0.011 0.1484 0.209 0.1133 0.254 0.2658 0.162 0.3698 0.433 0.6448 0.026 -0.296 0.283 0.0079 0.10 -0.0726 0.140 0.2297 0.000	$\begin{array}{cccc} 7 & 1.1\% \\ 6 & 1.1\% \\ 5 & 0.6\% \\ 4 & 2.6\% \\ 8 & 1.3\% \\ 9 & 1.0\% \\ 4 & 1.6\% \\ 7 & 0.5\% \\ 1 & 2.6\% \\ 9 & 0.9\% \\ 4 & 2.1\% \\ 5 & 1.8\% \\ 4 & 2.2\% \end{array}$	1.47 [0.93, 2.34] 5.08 [3.17, 8.14] 4.53 [2.20, 9.33] 1.17 [1.14, 1.20] 1.16 [0.77, 1.75] 1.12 [0.68, 1.85] 1.30 [0.95, 1.79] 1.45 [0.62, 3.39] 1.91 [1.81, 2.01] 0.75 [0.43, 1.31] 1.01 [0.82, 1.24] 0.93 [0.71, 1.22] 1.26 [1.05, 1.50]	
ofmark (2007) ages 75-85 (12) lordhal (2014) Wybo (2008) imith (2003) Moxican Americans (12) imith (2003) Non-Hispanic whites (12) rygged (2011) an Rossum (1999a) First stroke (3) an Rossum (1999b) History of stroke at baseline (3) Veikert (2008) Veinstein (2014) Vennerstad (2010) Viberg (2015) Volinsky (2009) iu (2008) (9) an (2013) hu (2000)	0.2313 0.034 0.3676 0.23 1.625 0.240 1.5107 0.368 0.1569 0.011 0.1484 0.209 0.1133 0.254 0.2658 0.433 0.6448 0.026 -0.2896 0.433 0.6448 0.026 -0.2896 0.283 0.0079 0.100	$\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$	1.47 [0.93, 2.34] 5.08 [3.17, 8.14] 4.53 [2.20, 9.33] 1.17 [1.14, 1.20] 1.16 [0.77, 1.75] 1.12 [0.68, 1.85] 1.30 [0.95, 1.79] 1.45 [0.62, 3.39] 1.91 [1.81, 2.01] 0.75 [0.43, 1.31] 1.01 [0.82, 1.24] 0.93 [0.71, 1.22] 1.26 [1.05, 1.50] 1.10 [0.68, 1.80]	
ofmark (2007) ages 75-85 (12) lordhal (2014) imith (2003) Mexican Americans (12) imith (2003) Non-Hispanic whites (12) rygged (2011) an Rossum (1999a) First stroke (3) an Rossum (1999b) History of stroke at baseline (3) Veikert (2008) Veinserstad (2014) Veinnerstad (2014) Veinnerstad (2010) Viberg (2015) Volinsky (2009) u (2008)(9) fan (2013) hu (2000) utbotad [95% CI)	0.2313 0.034 0.3876 0.23 1.6253 0.244 1.5107 0.368 0.1569 0.011 0.1484 0.209 0.1133 0.254 0.2658 0.162 0.3698 0.433 0.6448 0.022 -0.2896 0.233 0.0079 0.10 -0.0726 0.144 0.2297 0.090	$\begin{array}{cccc} 7 & 1.1\% \\ 6 & 1.1\% \\ 5 & 0.6\% \\ 4 & 2.6\% \\ 8 & 1.3\% \\ 9 & 1.0\% \\ 4 & 1.6\% \\ 7 & 0.5\% \\ 1 & 2.6\% \\ 9 & 0.9\% \\ 4 & 2.1\% \\ 5 & 1.8\% \\ 4 & 2.2\% \end{array}$	1.47 [0.93, 2.34] 5.08 [3.17, 8.14] 4.53 [2.20, 9.33] 1.17 [1.14, 1.20] 1.16 [0.77, 1.75] 1.12 [0.68, 1.85] 1.30 [0.95, 1.79] 1.45 [0.62, 3.39] 1.91 [1.81, 2.01] 0.75 [0.43, 1.31] 1.01 [0.82, 1.24] 0.93 [0.71, 1.22] 1.26 [1.05, 1.50]	
ofmark (2007) ages 75-85 (12) lordhal (2014) imith (2003) Mexican Americans (12) imith (2003) Non-Hispanic whites (12) rygged (2011) an Rossum (1999b) History of stroke at baseline (3) Veikert (2008) Veinstein (2014) Vennerstad (2010) iviberg (2015) Volinsky (2009) iu (2008)(9) an (2013) hu (2000) iubtotal (95% CI) leterogeneity: Tau ² = 0.04; Chi ² = 667.38, df = 24 (F	0.2313 0.034 0.3876 0.23 1.6253 0.244 1.5107 0.368 0.1569 0.011 0.1484 0.209 0.1133 0.254 0.2658 0.162 0.3698 0.433 0.6448 0.022 -0.2896 0.233 0.0079 0.10 -0.0726 0.144 0.2297 0.090	$\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$	1.47 [0.93, 2.34] 5.08 [3.17, 8.14] 4.53 [2.20, 9.33] 1.17 [1.14, 1.20] 1.16 [0.77, 1.75] 1.12 [0.68, 1.85] 1.30 [0.95, 1.79] 1.45 [0.62, 3.39] 1.91 [1.81, 2.01] 0.75 [0.43, 1.31] 1.01 [0.82, 1.24] 0.93 [0.71, 1.22] 1.26 [1.05, 1.50] 1.10 [0.68, 1.80]	
ofmark (2007) ages 75-85 (12) lordhal (2014) with (2003) Mexican Americans (12) with (2003) Non-Hispanic whites (12) tygged (2011) an Rossum (1999b) History of stroke at baseline (3) Veikert (2008) Veinerstad (2010) Veinerstad (2010) Viberg (2015) Volinsky (2009) u (2008)(9) 'an (2013) hu (2000) uibtotal (95% CI) leterogeneity: Tau ² = 0.04; Chi ² = 667.38, df = 24 (F est for overall effect: Z = 5.16 (P < 0.00001)	0.2313 0.034 0.3876 0.23 1.6253 0.244 1.5107 0.368 0.1569 0.011 0.1484 0.209 0.1133 0.254 0.2658 0.162 0.3698 0.433 0.6448 0.022 -0.2896 0.233 0.0079 0.10 -0.0726 0.144 0.2297 0.090	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	1.47 [0.93, 2.34] 5.08 [3.17, 8.14] 4.53 [2.20, 9.33] 1.17 [1.14, 1.20] 1.16 [0.77, 1.75] 1.12 [0.68, 1.85] 1.30 [0.95, 1.79] 1.45 [0.62, 3.39] 1.91 [1.81, 2.01] 0.75 [0.43, 1.31] 1.01 [0.82, 1.24] 0.93 [0.71, 1.22] 1.26 [1.05, 1.50] 1.10 [0.68, 1.80] 1.30 [1.18, 1.44]	
ofmark (2007) ages 75-85 (12) lordhal (2014) lybo (2008) imith (2003) Moxican Americans (12) imith (2003) Non-Hispanic whites (12) rygged (2011) an Rossum (1999a) First stroke (3) an Rossum (1999b) History of stroke at baseline (3) Veinkert (2008) Veinstein (2014) Vennerstad (2014) Vennerstad (2014) Volinsky (2009) iu (2008) (9) 'an (2013) hu (2001) Libtotal (95% CI) leterogeneity: Tau ² = 0.04; Chi ² = 667.38, df = 24 (F est for overall effect: Z = 5.16 (P < 0.00001) 'otal (95% CI)	0.2313 0.034 0.3876 0.23 1.6253 0.240 1.5107 0.366 0.1569 0.011 0.1484 0.200 0.1133 0.254 0.2658 0.162 0.3698 0.433 0.6448 0.026 -0.2696 0.283 0.0079 0.100 -0.0726 0.140 0.227 0.000 0.0984 0.248	$\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$	1.47 [0.93, 2.34] 5.08 [3.17, 8.14] 4.53 [2.20, 9.33] 1.17 [1.14, 1.20] 1.16 [0.77, 1.75] 1.12 [0.68, 1.85] 1.30 [0.95, 1.79] 1.45 [0.62, 3.39] 1.91 [1.81, 2.01] 0.75 [0.43, 1.31] 1.01 [0.82, 1.24] 0.93 [0.71, 1.22] 1.26 [1.05, 1.50] 1.10 [0.68, 1.80]	
ofmark (2007) ages 75-85 (12) lordhal (2014) lybo (2008) imith (2003) Mexican Americans (12) imith (2003) Non-Hispanic whites (12) rygged (2011) an Rossum (1999a) First stroke (3) an Rossum (1999b) History of stroke at baseline (3) Veikert (2008) Veinstein (2014) Veinarestad (2010) Viberg (2015) Volinsky (2009) u (2008)(9) an (2013) hu (2000) iubtotal (95% Cl) leterogeneity: Tau ² = 0.04; Chi ² = 667.38, df = 24 (F leterogeneity: Tau ² = 0.04; Chi ² = 1289.33, df = 67 (0.2313 0.034 0.3876 0.23 1.6253 0.240 1.5107 0.366 0.1569 0.011 0.1484 0.200 0.1133 0.254 0.2658 0.162 0.3698 0.433 0.6448 0.026 -0.2696 0.283 0.0079 0.100 -0.0726 0.140 0.227 0.000 0.0984 0.248	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	1.47 [0.93, 2.34] 5.08 [3.17, 8.14] 4.53 [2.20, 9.33] 1.17 [1.14, 1.20] 1.16 [0.77, 1.75] 1.12 [0.68, 1.85] 1.30 [0.95, 1.79] 1.45 [0.62, 3.39] 1.91 [1.81, 2.01] 0.75 [0.43, 1.31] 1.01 [0.82, 1.24] 0.93 [0.71, 1.22] 1.26 [1.05, 1.50] 1.10 [0.68, 1.80] 1.30 [1.18, 1.44]	
ofmark (2007) ages 75-85 (1 2) lordhal (2014) ybo (2008) mith (2003) Mexican Americans (12) mith (2003) Non-Hispanic whites (12) rygged (2011) an Rossum (1999b) History of stroke at baseline (3) /eikert (2008) /einstein (2014) /einstein (2014) /einstein (2014) /olinsky (2009) u (2008)(9) an (2013) hu (2000) leterogeneity: Tau ² = 0.04; Chi ² = 667.38, df = 24 (F est for overall effect: Z = 5.16 (P < 0.00001) otal (95% CI)	0.2313 0.034 0.3876 0.23 1.6253 0.240 1.5107 0.368 0.1569 0.011 0.1484 0.209 0.1133 0.254 0.2658 0.162 0.3698 0.433 0.6448 0.026 -0.296 0.283 0.0079 0.10 -0.0726 0.140 0.2297 0.090 0.0984 0.248 P < 0.00001); I ² = 96%	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	1.47 [0.93, 2.34] 5.08 [3.17, 8.14] 4.53 [2.20, 9.33] 1.17 [1.14, 1.20] 1.16 [0.77, 1.75] 1.12 [0.68, 1.85] 1.30 [0.95, 1.79] 1.45 [0.62, 3.39] 1.91 [1.81, 2.01] 0.75 [0.43, 1.31] 1.01 [0.82, 1.24] 0.93 [0.71, 1.22] 1.26 [1.05, 1.50] 1.10 [0.68, 1.80] 1.30 [1.18, 1.44]	0.01 0.1 10 Decreased risk of stroke

 Footnotes
 Low education

 (1) Adjusted for history of high BP, use of oral contraceptives, marital status, number of live births, cigarette and alcohol consumption, hypertension in pregnancy, family histor...

 (2) Adjusted for hypertension, diabetes, hypertipidemia, previous stroke/TIA, and PAD, current smoking, alcohol abstinence, high alcohol consumption, leisure time sports activity

 (3) Adjusted for age, systolic BP, hypertension, drug use for hypertension, smoking, cardiovascular disease, left ventricular hypertrophy, atrial fibrilation, diabetes, fibrogen, BMI....

 (4) Adjusted for age, sex, race

 (6) Adjusted for age, sex, race

 (8) Adjusted for age, ender, income, medical insurance, smoking, alcohol, physical activity, depression, marital status, hypertension, diabetes mellitus, heart disease and...

 (8) Adjusted for age, ender, income, medical insurance, smoking, alcohol consumption, diabetes, high blood pressure, occupational and leisure time physical activity

 (9) Adjusted for age, gender, area of residence, BMI, smoking, alcohol physical activity, depression, marital status, hypertension, diabetes mellitus, heart disease and...

 (11) Adjusted for age, nome ownership, education, smoking, alcohol physical activity, depression, marital status, hypertension, diabetes mellitus, heart disease and....

 (11) Adjusted for age, one ownership, education, smoking, alcohol physical activity, depression, marital status, hypertension, diabetes mellitus, heart disease and....

 (12) Adjusted for age, nome ownership, education, smoking, BMI, alcohol, physical activity, depression, marital status, hype

eFigure 5h. Sensitivity analysis comparing males and females by education level and risk of stroke; OR>1= low education increases risk of stroke.

				Odds Ratio		Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Random, 95% Cl		IV, Random, 95% CI
2.12.1 Males						
Emmelin (2003) Males	0.0953		2.8%	1.10 [0.65, 1.86]		
Honjo (2009) Males	0.2632	0.0903	6.3%	1.30 [1.09, 1.55]		-
Hu (2005)	0.0529	0.0605	7.0%	1.05 [0.94, 1.19]		*
Nordhal (2014)	-0.0915	0.0486	7.2%	0.91 [0.83, 1.00]		-
Trygged (2011) Males	0.2338	0.0136	7.6%	1.26 [1.23, 1.30]		•
Wennerstad (2010)	0.6448	0.0261	7.5%	1.91 [1.81, 2.01]		•
Wiberg (2015)	-0.3011	0.278	2.7%	0.74 [0.43, 1.28]		
Subtotal (95% CI)			41.0%	1.18 [0.94, 1.48]		•
Heterogeneity: Tau ² = 0.08; Chi ² = 283.91, df = 6 (P	< 0.00001); I ² = 98	3%				
Test for overall effect: Z = 1.45 (P = 0.15)						
2.12.2 Females						
Chang (2002) Asia (1)	0.174	0.2635	2.9%	1.19 [0.71, 1.99]		
Chang (2002) Eastern Europe (1)	0.7178	0.4088	1.5%	2.05 [0.92, 4.57]		
Chang (2002) Latin America (1)	0.1484	0.2433	3.1%	1.16 [0.72, 1.87]		
Emmelin (2003) Males	0.0953	0.269	2.8%	1.10 [0.65, 1.86]		
Folsom (1990) (2)	0.5068	0.2069	3.8%	1.66 [1.11, 2.49]		
Honjo (2009)	0.4815	0.1244	5.5%	1.62 [1.27, 2.07]		-
Hu (2005)	-0.0558	0.0612	7.0%	0.95 [0.84, 1.07]		-
Jackson (2013) (3)	0.2624	0.3015	2.4%	1.30 [0.72, 2.35]		
Kisjanto (2003)	0.3293	0.166	4.6%	1.39 [1.00, 1.92]		
Nordhal (2014) Females	0.6031	0.0504	7.2%	1.83 [1.66, 2.02]		-
Strodl (2008)	0.0198	0.1865	4.1%	1.02 [0.71, 1.47]		+
Trygged (2011)	0.3655	0.0168	7.5%	1.44 [1.39, 1.49]		•
van Rossum (1999a) First stroke (4)	0.1484	0.2098	3.7%	1.16 [0.77, 1.75]		
van Rossum (1999b) History of stroke at baseline (4)	0.1133	0.2549	3.0%	1.12 [0.68, 1.85]		
Subtotal (95% CI)			59.0%	1.33 [1.15, 1.53]		◆
Heterogeneity: Tau ² = 0.04; Chi ² = 79.36, df = 13 (P	< 0.00001); I ² = 84	%				
Test for overall effect: Z = 3.85 (P = 0.0001)	,,					
Total (95% CI)			100.0%	1.27 [1.14, 1.42]		•
Heterogeneity: Tau ² = 0.04; Chi ² = 377.15, df = 20 (F	$P < 0.00001$); $I^2 = 9$	5%			<u> </u>	i
Test for overall effect: $Z = 4.27$ (P < 0.0001)					0.01	0.1 1 10 10
Test for subgroup differences: $Chi^2 = 0.72$, df = 1 (P	= 0.39), l ² = 0%					Lower education Higher education
Footnotes	0.00/,1 - 070					Low education

Footnotes

(1) Adjusted for history of high BP, use of oral contraceptives, marital status, number of live births, cigarette and alcohol consumption, hypertension in pregnancy,...

(2) Adjusted for age. Total number of strokes and controls for education categories used not specified. Total strokes and controls 218 and 1845 respectively.

(3) Adjusted for age, home ownership, education, smoking, BMI, alcohol, physical activity, depression, marital status, hypertension, diabetes mellitus, heart...

(d) Adjusted for age, none ownersnip, education, smoking, bin, accinet, prysical activity, depression, manaristatus, rypertension, diabetes mentus, near ... (d) Adjusted for age, systolic BP, hypertension, drug use for hypertension, smoking, cardiovascular disease, left ventricular hypertrophy, atrial fibrilation, diabetes,... Note: Studies without footnotes report unadjusted results

eFigure 5i. Sensitivity analysis comparing males and females by education level and risk of stroke; HR>1= low education increases risk of stroke.

				Hazard Ratio	Hazard Ratio
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI
2.13.1 Males					
Avendano (2006a) men (1)	0.4574 (0.1989	11.5%	1.58 [1.07, 2.33]	
Everson (2001)	0.5653 (0.3595	4.6%	1.76 [0.87, 3.56]	—
Hemmingsson (2007)	0.0392 (0.0251	33.9%	1.04 [0.99, 1.09]	+
Honjo (2010a) Men	0.0862	0.301	6.2%	1.09 [0.60, 1.97]	
Subtotal (95% CI)			56.3%	1.23 [0.94, 1.63]	◆
Heterogeneity: Tau ² = 0.04; C	hi ² = 6.45, df = 3 (P =	0.09); l ^a	² = 53%		
Test for overall effect: Z = 1.5	. ,	,,,			
2.13.2 Females					
Avendano (2006a) women (1)	0.1133	0.327	5.4%	1.12 [0.59, 2.13]	_ _
Blomstrand (2014) (2)		0.075	27.2%	1.17 [1.01, 1.36]	-
Honjo (2010b) Women	-0.0408 (0.4052	3.7%	0.96 [0.43, 2.12]	
Kuper (2007) (3)	0.7885 0	0.2684	7.4%	2.20 [1.30, 3.72]	
Subtotal (95% CI)			43.7%	1.30 [0.95, 1.79]	◆
Heterogeneity: Tau ² = 0.05; C	hi ² = 5.54, df = 3 (P =	0.14); l ^a	² = 46%		
Test for overall effect: Z = 1.6		,,,			
Total (95% CI)			100.0%	1.23 [1.04, 1.44]	•
Heterogeneity: Tau ² = 0.02; C	hi² = 15.75. df = 7 (P -	= 0.03):	$ ^2 = 56\%$		
Test for overall effect: Z = 2.4	. ,			0.0	
Test for subgroup differences	· /	P = 0.81). I ² = 0%		Low education High education
Footnotes		5.61)	,,. 0,0		Low education
(d) Adverted for our					

(1) Adjusted for age

(2) Adjusted for age, hypertension, BMI, smoking, physical inactivity, cholesterol, tryglycerides, mental stress

(3) Adjusted for age, smoking, BMI, alcohol consumption, hypertension, diabetes, exercise Note: Studies without footnotes report unadjusted results

eFigure 5j. Sensitivity analysis comparing first only and recurrent/unspecified stroke by education level and risk of stroke; HR>1= low education increases risk of stroke.

tudy or Subgroup	log[Hazard Ratio]	65	Weight	Hazard Ratio IV, Random, 95% C	Hazard Ratio IV, Random, 95% CI
15.1 First stroke only	iog[Hazaru Katio]	эE	weight	iv, Random, 95% C	
-	1.5209	0 4540	0.9%	4 50 11 00 11 161	
e Brujin (2014) mmolia (2003) Econolog				4.58 [1.88, 11.16]	
mmelin (2003) Females	0.0953	0.269	1.8%	1.10 [0.65, 1.86]	-
mmelin (2003) Males		0.2306	2.0%	1.10 [0.70, 1.73]	
an (2011)		0.2069	2.2%	1.59 [1.06, 2.38]	
amano (2015) (1)	0.4447		3.6%	1.56 [1.45, 1.68]	•
u (2005)	-0.0232		3.6%	0.98 [0.90, 1.06]	Ť
ackson (2013) (2)	0.2624		1.6%	1.30 [0.72, 2.35]	
isjanto (2003)	0.3293	0.166	2.6%	1.39 [1.00, 1.92]	-
ofmark (2007) ages 35-75 (3)	0.0862		3.1%	1.09 [0.88, 1.35]	+
ofmark (2007) ages 75-85 (3)	0.9083	0.4337	1.0%	2.48 [1.06, 5.80]	
trodl (2008)	0.0198	0.1865	2.4%	1.02 [0.71, 1.47]	
rygged (2011)	0.1569	0.0114	3.7%	1.17 [1.14, 1.20]	•
/eikert (2008)	0.2658	0.1624	2.6%	1.30 [0.95, 1.79]	
/ennerstad (2010)	0.6448	0.0261	3.7%	1.91 [1.81, 2.01]	•
/iberg (2015)	-0.2896	0.2839	1.7%	0.75 [0.43, 1.31]	
ou (1999) (4)	0.1823	0.2902	1.6%	1.20 [0.68, 2.12]	
ubtotal (95% CI)			38.2%	1.31 [1.11, 1.54]	◆
eterogeneity: Tau ² = 0.07; Chi ² = 380.03, df = 15 (est for overall effect: $Z = 3.21$ (P = 0.001)	P < 0.00001); I ² = 96	%			
.15.2 First and recurrent stroke					
kinyemi (2014)	0.5988	0 3055	1.5%	1.82 [1.00, 3.31]	— <u> </u>
aune (2006)	0.3293		1.8%	1.39 [0.82, 2.36]	
()					-
renner (2010)	0.7053		3.6%	2.02 [1.84, 2.23]	-
hen (2014) (5)		0.0618	3.5%	0.44 [0.39, 0.50]	
eoke (2012)	0.1577		1.6%	1.17 [0.66, 2.09]	
ngels (2014)		0.3296	1.4%	3.78 [1.98, 7.22]	
illenbaum (2000) (6)	0.0296		3.7%	1.03 [1.01, 1.05]	1
itzpatrick (2012)	0.0198		3.7%	1.02 [0.97, 1.07]	
olsom (1990) (7)	0.5068		2.2%	1.66 [1.11, 2.49]	
irau (2012) (8)		0.2461	1.9%	1.23 [0.76, 1.99]	
onjo (2009)		0.0724	3.4%	1.33 [1.16, 1.54]	-
uang (1997)	1.853	0.3285	1.4%	6.38 [3.35, 12.14]	
oster (2005)	0.0732	0.1552	2.7%	1.08 [0.79, 1.46]	+-
ledin (2008) (9)	0.9083	0.379	1.2%	2.48 [1.18, 5.21]	
ordhal (2014)	0.2313	0.0345	3.6%	1.26 [1.18, 1.35]	•
ybo (2008)	0.3876	0.237	2.0%	1.47 [0.93, 2.34]	
endlebury (2012)	1.4896	0.2683	1.8%	4.44 [2.62, 7.50]	
im (2008)	-0.059	0.1844	2.4%	0.94 [0.66, 1.35]	
mith (2003) Mexican Americans(3)	1.6253	0.2406	2.0%	5.08 [3.17, 8.14]	
mith (2003) Non-Hispanic whites (3)		0.3685	1.2%	4.53 [2.20, 9.33]	
alko (2008)		0.2217	2.1%	3.58 [2.32, 5.52]	
an Rossum (1999a) First stroke (10)	0.1484		2.2%	1.16 [0.77, 1.75]	- -
an Rossum (1999b) History of stroke at baseline (1			1.9%	1.12 [0.68, 1.85]	- -
/einstein (2014)	0.3698		1.0%	1.45 [0.62, 3.39]	
/olinsky (2009)	0.0079	0.4337	3.2%	1.01 [0.82, 1.24]	+
u (2008) (11)	-0.0726		2.9%		
			2.9%	0.93 [0.71, 1.22]	
nu (2000) ubtotal (95% CI)	0.0984		61.8%	1.10 [0.68, 1.80] 1.48 [1.29, 1.71]	•
eterogeneity: Tau ² = 0.10; Chi ² = 596.06, df = 26 (est for overall effect: Z = 5.43 (P < 0.00001)	P < 0.00001); l ² = 96	%			
otal (95% CI)			100.0%	1.39 [1.26, 1.53]	•
eterogeneity: Tau ² = 0.07; Chi ² = 1148.49, df = 42	(P < 0.00001); I ² = 9	6%			0.01 0.1 1 10 1
est for overall effect: Z = 6.65 (P < 0.00001)					
					Decreased risk of stroke Increased risk of stroke
est for subgroup differences: Chi ² = 1.26, df = 1 (P	$= 0.26$), $l^2 = 20.7\%$				Low education

(1) Adjusted for CHD, hypertension, COPD, obesity, income, age and sex.

(2) Adjusted for age, home ownership, education, smoking, BMI, alcohol, physical activity, depression, marital status, hypertension, diabetes mellitus, heart disease and... (3) Adjusted for age and sex

(4) Adjusted for hypertension, heart disease, diabetes, smoking

(5) Adjusted for age,gender and region.(6) Adjusted for age, sex, race

(7) Adjusted for age. Total number of strokes and controls for education categories used not specified. Total strokes and controls 218 and 1845 respectively.

(8) Adjusted for hypertension, diabetes, hyperlipidemia, previous stroke/TIA, and PAD, current smoking, alcohol abstinence, high alcohol consumption, leisure time sports activity
 (9) Adjusted for work related factors on the Job Content Questionnaire, organisational change at the workplace and decreased participation
 (10) Adjusted for age, systolic BP, hypertension, drug use for hypertension, smoking, cardiovascular disease, left ventricular hypertrophy, atrial fibrilation, diabetes, fibrogen, BMI,...

(11) Adjusted for age, gender, area of residence, BMI, smoking, alcohol consumption, diabetes, high blood pressure, occupational and leisure time physical activity Note: Studies without footnotes report unadjusted results

Supplementary 2 References

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