

SUPPLEMENTAL MATERIAL

Causal effects of sleep traits on ischemic stroke and its subtypes:
a Mendelian randomization study

Supplementary Table 1 Details of data sources in the Mendelian randomization (MR) analysis

Phenotype	Pubmed ID	Sample size (cases)	Source
Short sleep duration	30846698	411,934 (106,192)	https:// http://sleepdisordergenetics.org/
Long sleep duration	30846698	339,926 (34,184)	https:// http://sleepdisordergenetics.org/
Continuous sleep	30846698	446,118	https:// http://sleepdisordergenetics.org/
Frequent insomnia symptoms	30804566	254,767 (146,410)	https:// http://sleepdisordergenetics.org/
Any insomnia symptoms	30804566	532,378 (362,171)	https:// http://sleepdisordergenetics.org/
Chronotype	30696823	651,295 (372,765)	https:// http://sleepdisordergenetics.org/
Large artery stroke	29531354	150,765 (4,373)	http://www.megastroke.org/download.html
Small vessel stroke	29531354	198,048 (5,386)	http://www.megastroke.org/download.html
Cardioembolic stroke	29531354	211,763 (7,193)	http://www.megastroke.org/download.html
Any ischemic stroke	29531354	440,328 (34,217)	http://www.megastroke.org/download.html

Supplementary Table 2 Single nucleotide polymorphisms (SNPs) used to construct the instruments for short sleep duration

SNP	Effect allele	Other allele	EAF	β	SE	<i>p</i> value
rs2863957	C	A	0.782	0.054	0.006	2.60E-18
rs13107325	T	C	0.075	0.075	0.010	2.50E-13
rs1229762	T	C	0.665	0.037	0.005	1.10E-12
rs1380703	G	A	0.384	0.035	0.005	1.60E-11
rs12963463	C	T	0.299	0.029	0.004	1.90E-11
rs75539574	A	C	0.915	0.045	0.007	8.40E-11
rs17388803	C	A	0.106	0.053	0.009	6.50E-10
rs4585442	G	A	0.311	0.031	0.005	8.10E-10
rs1607227	G	T	0.705	0.031	0.005	1.50E-09
rs2820313	G	A	0.341	0.031	0.005	2.30E-09
rs17005118	A	G	0.265	0.030	0.005	2.50E-09
rs5757675	G	T	0.260	0.034	0.006	2.70E-09
rs12567114	G	A	0.725	0.036	0.006	4.10E-09
rs142180737	C	T	0.009	0.154	0.026	4.40E-09
rs2186122	T	A	0.562	0.024	0.004	4.80E-09
rs11763750	G	A	0.814	0.035	0.006	5.10E-09
rs12518468	C	T	0.328	0.031	0.005	8.50E-09
rs9367621	T	A	0.431	0.024	0.004	1.60E-08
rs3776864	A	C	0.667	0.031	0.006	1.70E-08
rs60882754	A	T	0.939	0.055	0.010	1.80E-08
rs59779556	T	G	0.554	0.025	0.004	2.00E-08
rs2014830	C	T	0.698	0.030	0.005	2.70E-08
rs205024	C	T	0.617	0.031	0.005	2.70E-08
rs12661667	T	C	0.263	0.028	0.005	2.80E-08
rs7939345	T	G	0.208	0.035	0.006	4.00E-08
rs9321171	C	T	0.540	0.031	0.006	4.20E-08
rs7524118	C	T	0.708	0.030	0.005	4.90E-08

SNP, single nucleotide polymorphism; EAF, effect allele frequency; SE, standard error

Supplementary Table 3 SNPs used to construct the instruments for frequent insomnia symptoms

SNP	Effect allele	Other allele	EAF	β	SE	<i>p</i> value
rs113851554	T	G	0.058	0.131	0.009	1.19E-43
rs11651809	G	C	0.296	0.030	0.004	5.48E-16
rs35881094	G	T	0.426	0.039	0.005	9.59E-16
rs1942262	A	G	0.292	0.039	0.005	4.42E-14
rs4688760	T	C	0.690	0.030	0.004	2.48E-13
rs62158170	A	G	0.784	0.049	0.007	7.76E-13
rs1923770	T	A	0.383	0.030	0.004	1.15E-12
rs7711696	T	G	0.305	0.030	0.004	2.62E-12
rs2644128	G	C	0.550	0.030	0.004	3.04E-12
rs4886860	G	C	0.234	0.039	0.006	3.08E-12
rs10156602	A	G	0.638	0.020	0.003	6.63E-12
rs12405761	A	C	0.571	0.030	0.004	1.04E-11
rs10280045	G	C	0.574	0.030	0.004	1.60E-11
rs2296580	G	T	0.702	0.030	0.004	3.54E-11
rs11184946	T	C	0.417	0.030	0.005	1.02E-10
rs1592757	C	G	0.357	0.020	0.003	1.84E-10
rs324017	A	C	0.295	0.030	0.005	2.01E-10
rs2062113	T	C	0.430	0.020	0.003	2.57E-10
rs4886140	G	A	0.668	0.030	0.005	3.75E-10
rs11673344	G	A	0.380	0.030	0.005	7.65E-10
rs314280	G	A	0.548	0.010	0.002	9.66E-10
rs11191595	A	C	0.937	0.068	0.011	9.92E-10
rs1031654	C	A	0.202	0.039	0.006	1.22E-09
rs4577309	A	G	0.468	0.030	0.005	1.22E-09
rs68094047	T	C	0.250	0.030	0.005	1.34E-09
rs10865954	T	C	0.334	0.020	0.003	1.81E-09
rs10838708	G	A	0.541	0.020	0.003	2.04E-09
rs11097861	G	A	0.715	0.030	0.005	3.66E-09
rs6593005	G	A	0.741	0.020	0.003	4.76E-09
rs9845387	C	A	0.959	0.077	0.013	5.08E-09
rs2956278	G	A	0.215	0.030	0.005	7.16E-09
rs11635495	C	T	0.515	0.020	0.003	7.46E-09
rs6932158	C	T	0.491	0.030	0.005	8.76E-09
rs17151854	T	G	0.154	0.030	0.005	9.11E-09
rs4751	T	G	0.425	0.020	0.003	9.24E-09
rs3104778	A	G	0.589	0.020	0.003	9.89E-09
rs28061	A	G	0.692	0.030	0.005	1.48E-08
rs1841625	G	A	0.432	0.020	0.004	2.20E-08
rs10947690	G	A	0.261	0.020	0.004	2.58E-08
rs3824081	T	C	0.475	0.020	0.004	2.60E-08

rs1430205	T	C	0.458	0.020	0.004	3.24E-08
rs11804386	A	G	0.332	0.030	0.005	3.48E-08
rs6664467	G	A	0.863	0.030	0.005	3.60E-08
rs17669584	G	A	0.195	0.030	0.005	4.71E-08
rs4683301	T	A	0.600	0.020	0.004	6.14E-08
rs17139246	C	T	0.389	0.020	0.004	7.46E-08
rs2192338	C	G	0.780	0.030	0.006	9.50E-08
rs2147141	G	C	0.543	0.030	0.006	1.08E-07
rs11793074	A	G	0.853	0.030	0.006	1.69E-07
rs2613503	A	C	0.802	0.030	0.006	2.64E-07
rs1544637	T	C	0.488	0.010	0.002	4.99E-07
rs11793831	G	T	0.583	0.030	0.006	2.44E-06
rs302165	G	A	0.216	0.020	0.004	5.95E-06
rs12713372	C	T	0.566	0.020	0.004	7.74E-06
rs55946513	C	T	0.934	0.039	0.009	1.47E-05
rs6785034	A	G	0.422	0.030	0.007	4.73E-05

Supplementary Table 4 Steiger tests of short sleep duration and frequent insomnia symptoms causally linked to ischemic stroke and its subtypes

Exposure and outcome	Direction of causality	Directionality <i>p</i> value
<u>Short sleep duration</u>		
Large artery stroke	Exposure causes outcome	5.67E-77
Small vessel stroke	Exposure causes outcome	2.97E-43
Cardioembolic stroke	Exposure causes outcome	1.63E-73
Any ischemic stroke	Exposure causes outcome	1.55E-83
<u>Frequent insomnia symptoms</u>		
Large artery stroke	Exposure causes outcome	7.58E-217
Small vessel stroke	Exposure causes outcome	1.34E-136
Cardioembolic stroke	Exposure causes outcome	6.98E-232
Any ischemic stroke	Exposure causes outcome	6.10E-228

Supplementary Table 5 Results and sensitivity analyses of two-sample MR of any insomnia symptoms, continuous sleep, long sleep duration, and chronotype against ischemic stroke and its subtypes

Exposure	Large artery stroke		Small vessel stroke		Cardioembolic stroke		Any ischemic stroke	
	OR (95%CI)	<i>p</i> value	OR (95%CI)	<i>p</i> value	OR (95%CI)	<i>p</i> value	OR (95%CI)	<i>p</i> value
<u>Any insomnia symptoms</u>								
IVW	1.19 (1.00-1.42)	0.049	0.95 (0.81-1.11)	0.517	0.97 (0.85-1.11)	0.666	1.01 (0.94-1.08)	0.817
MR-PRESSO	1.25 (1.03-1.50)	0.024	-	-	-	-	-	-
MR-RAPS	1.25 (1.02-1.53)	0.032	0.96 (0.79-1.16)	0.679	0.98 (0.85-1.14)	0.827	1.01 (0.93-1.10)	0.741
WME	1.29 (0.99-1.68)	0.060	0.95 (0.74-1.23)	0.718	1.02 (0.84-1.25)	0.811	1.02 (0.91-1.14)	0.757
MR-Egger	1.09 (0.57-2.06)	0.408	1.11 (0.62-1.99)	0.339	1.24 (0.78-1.96)	0.178	1.07 (0.83-1.38)	0.313
<u>Continuous sleep</u>								
IVW	0.74 (0.50-1.11)	0.143	0.86 (0.59-1.24)	0.410	1.11 (0.81-1.51)	0.524	0.93 (0.79-1.09)	0.364
MR-RAPS	0.74 (0.47-1.16)	0.188	0.83 (0.55-1.26)	0.394	1.20 (0.86-1.68)	0.290	0.98 (0.82-1.16)	0.773
WME	0.91 (0.48-1.71)	0.767	0.85 (0.47-1.54)	0.581	1.23 (0.76-1.97)	0.395	0.98 (0.76-1.25)	0.857
MR-Egger	0.93 (0.22-3.97)	0.457	0.47 (0.13-1.71)	0.125	1.15 (0.44-3.00)	0.392	0.84 (0.48-1.48)	0.277
<u>Long sleep duration</u>								
IVW	1.17 (0.87-1.56)	0.291	1.04 (0.79-1.36)	0.789	1.23 (0.98-1.55)	0.073	0.98 (0.87-1.10)	0.723
MR-RAPS	1.17 (0.86-1.59)	0.319	1.03 (0.78-1.38)	0.816	1.23 (0.96-1.56)	0.101	0.98 (0.86-1.11)	0.733
WME	1.05 (0.72-1.52)	0.812	1.01 (0.72-1.41)	0.967	1.18 (0.90-1.56)	0.233	0.99 (0.85-1.15)	0.850
MR-Egger	0.78 (0.40-1.53)	0.249	0.99 (0.54-1.81)	0.501	1.13 (0.69-1.83)	0.323	0.93 (0.69-1.24)	0.303
<u>Chronotype (morningness)</u>								
IVW	1.02 (0.95-1.09)	0.679	1.01 (0.94-1.08)	0.796	1.01 (0.96-1.07)	0.604	1.00 (0.97-1.03)	0.824
MR-PRESSO	1.02 (0.94-1.11)	0.602	-	-	1.02 (0.96-1.08)	0.519	1.00 (0.97-1.03)	0.954
MR-RAPS	1.01 (0.93-1.10)	0.787	1.00 (0.94-1.08)	0.930	1.02 (0.95-1.08)	0.591	1.00 (0.97-1.04)	0.778
WME	1.02 (0.91-1.14)	0.769	1.04 (0.94-1.15)	0.485	1.01 (0.93-1.10)	0.801	1.00 (0.96-1.05)	0.903
MR-Egger	1.04 (0.83-1.31)	0.367	1.00 (0.81-1.24)	0.504	0.98 (0.82-1.16)	0.371	0.98 (0.89-1.08)	0.349

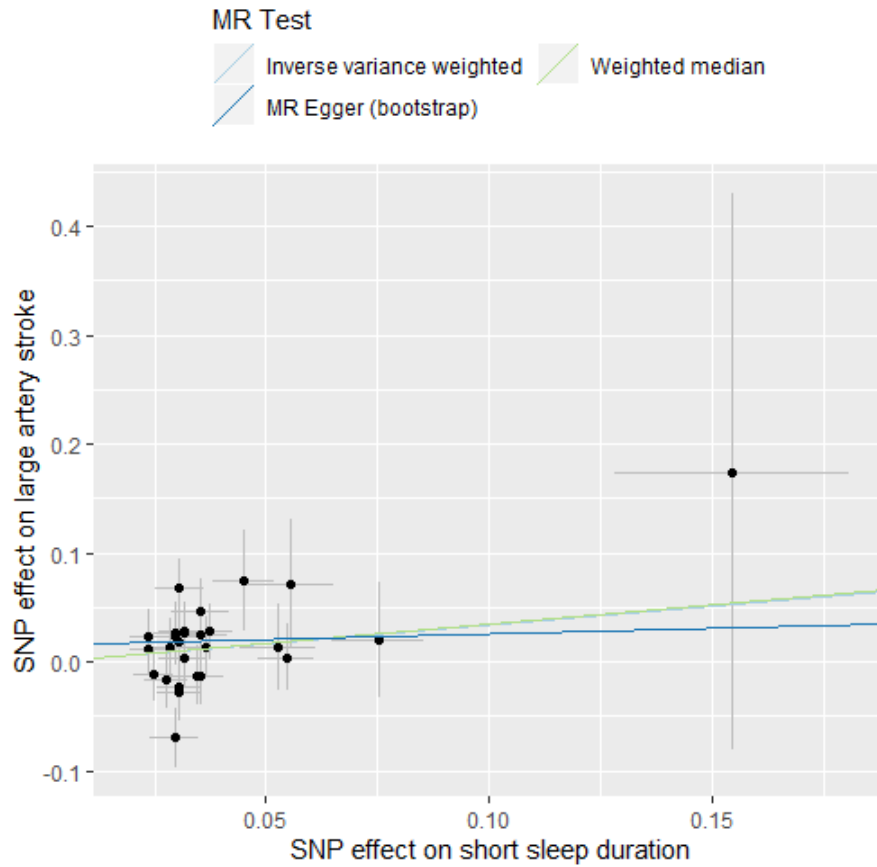
MR-PRESSO results are not showed if no outlier is identified. OR, odds ratio; CI, confidence interval; IVW, inverse-variance weighted; MR-PRESSO, MR-Pleiotropy Residual Sum and Outlier; MR-RAPS, MR-Robust Adjusted Profile Score; WME, weighted median estimate

Supplementary Table 6 Heterogeneity tests of sleep traits causally linked to ischemic stroke and its subtypes

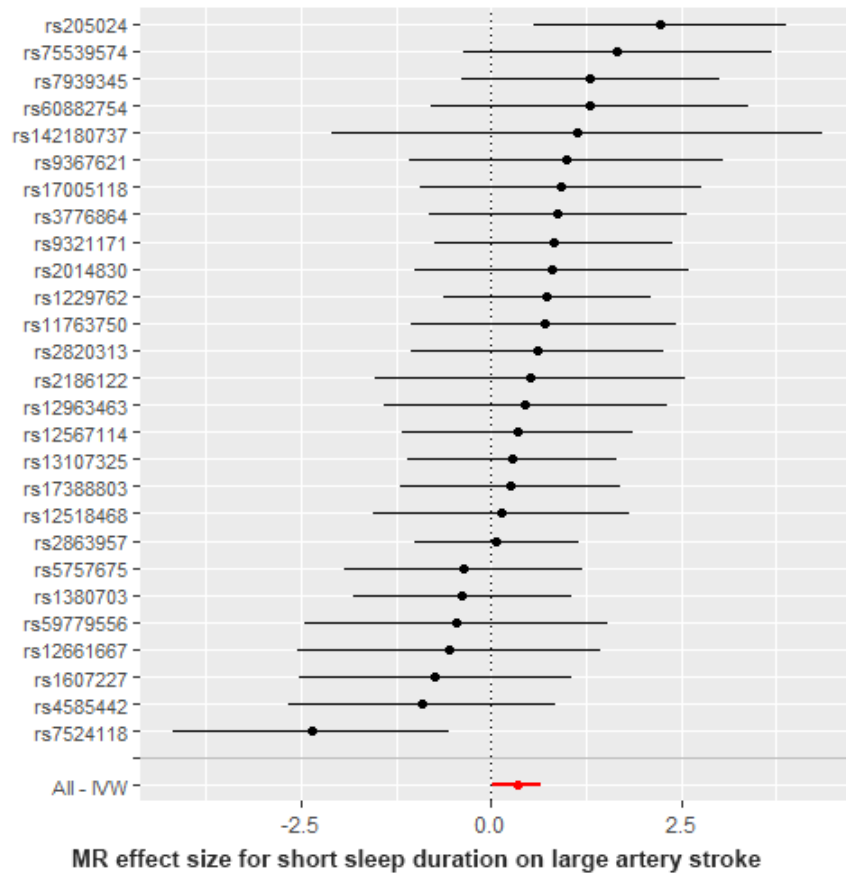
Exposure	Large artery stroke		Small vessel stroke		Cardioembolic stroke		Any ischemic stroke	
	Cochran's Q	<i>p</i> value	Cochran's Q	<i>p</i> value	Cochran's Q	<i>p</i> value	Cochran's Q	<i>p</i> value
Short sleep duration	26.47	0.438	24.19	0.508	32.20	0.152	18.15	0.836
Long sleep duration	3.69	0.594	1.96	0.854	2.02	0.846	2.36	0.797
Continuous sleep	90.32	0.095	79.23	0.318	80.59	0.281	85.73	0.166
Frequent insomnia symptoms	76.02	0.032	68.84	0.099	52.84	0.558	74.34	0.042
Any insomnia symptoms	76.08	0.031	68.79	0.100	52.82	0.558	74.34	0.042
Chronotype	431.08	1.72E-04	340.91	0.342	396.23	0.008	511.40	6.87E-10

Supplementary Table 7 Horizontal pleiotropy tests of sleep traits causally linked to ischemic stroke and its subtypes

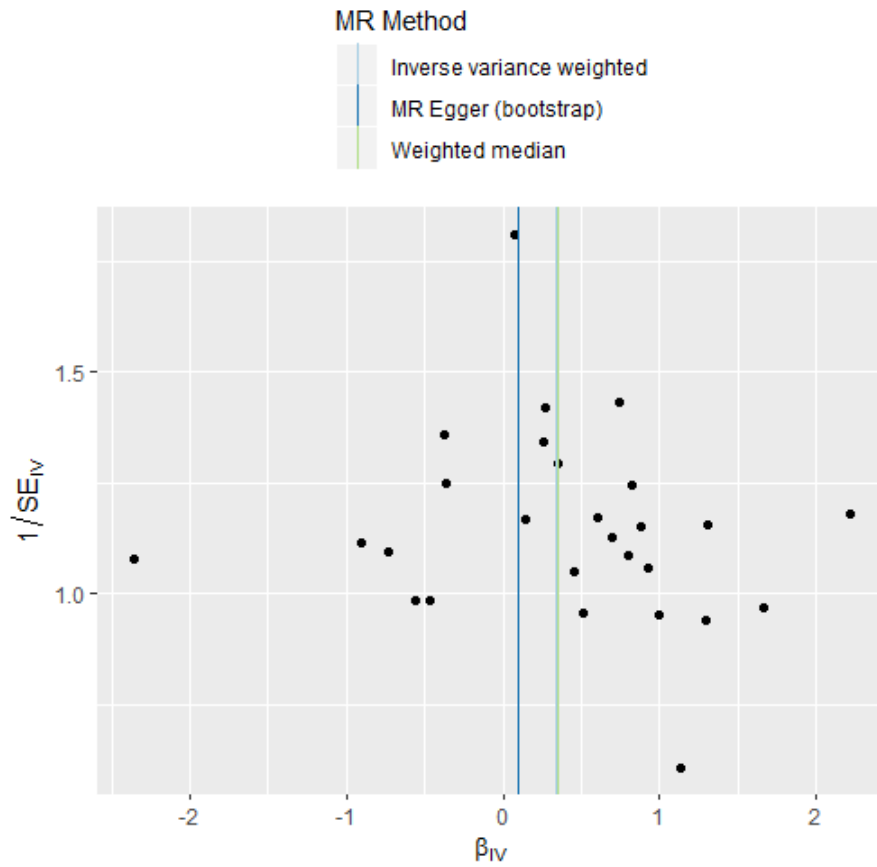
Exposure	Large artery stroke			Small vessel stroke			Cardioembolic stroke			Any ischemic stroke		
	Intercept	SE	<i>p</i> value	Intercept	SE	<i>p</i> value	Intercept	SE	<i>p</i> value	Intercept	SE	<i>p</i> value
Short sleep duration	-0.011	0.022	0.618	0.015	0.021	0.480	-0.008	0.021	0.705	-0.002	0.009	0.813
Long sleep duration	-0.047	0.038	0.290	-0.015	0.036	0.691	-0.011	0.030	0.734	-0.006	0.015	0.708
Continuous sleep	0.006	0.014	0.670	-0.008	0.012	0.530	-0.009	0.010	0.362	-0.001	0.006	0.850
Frequent insomnia symptoms	-0.005	0.012	0.692	0.004	0.011	0.736	-2.60E-04	0.008	0.974	0.004	0.005	0.445
Any insomnia symptoms	-0.004	0.012	0.725	0.005	0.011	0.666	2.34E-04	0.008	0.976	0.004	0.005	0.448
Chronotype	-0.005	0.005	0.336	-0.006	0.004	0.191	-5.57E-05	0.004	0.990	-3.95E-04	0.002	0.865



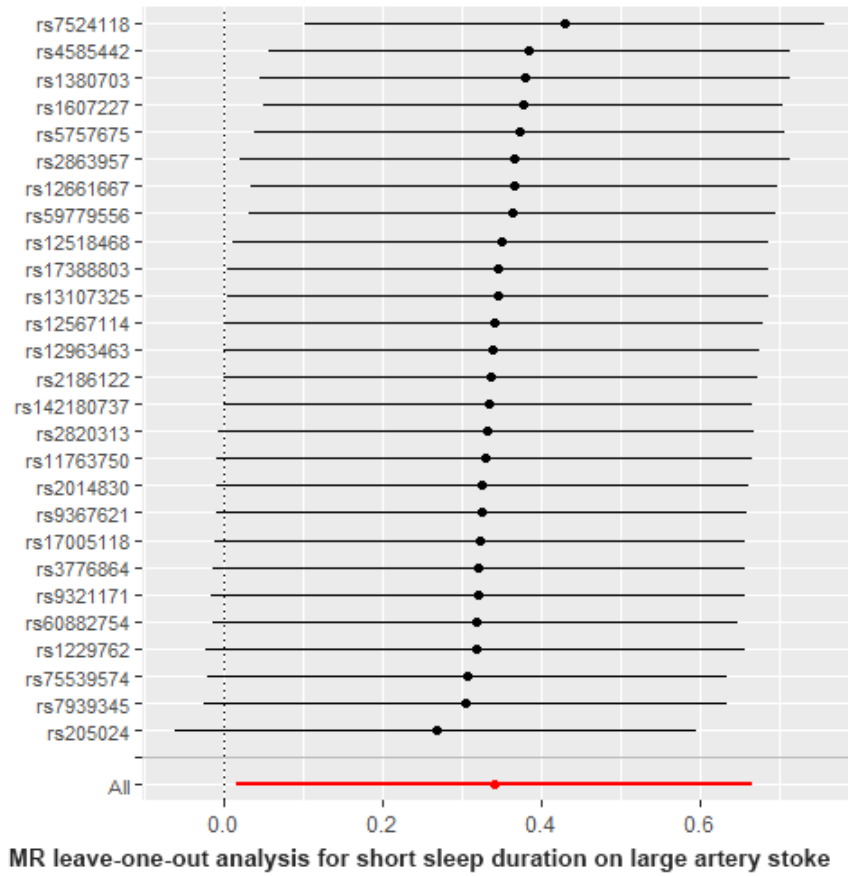
Supplementary Figure 1 Scatterplot of SNP potential effects on short sleep duration vs large artery stroke, with the slope of each line corresponding to estimated MR effect per method. MR, Mendelian randomization; SNP, single nucleotide polymorphism



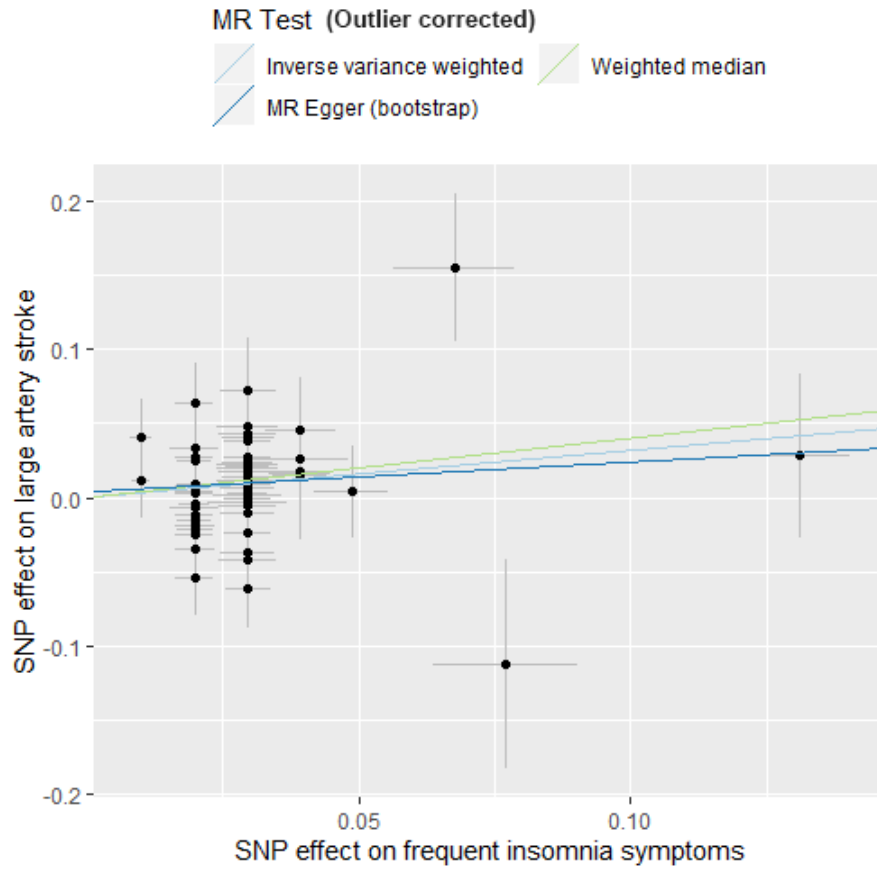
Supplementary Figure 2 Forest plot of individual and combined SNP MR-estimated effects sizes for short sleep duration on large artery stroke. Data is displayed as regression coefficient (β) and 95% CI. CI, confidence interval; IVW, inverse variance-weighted method



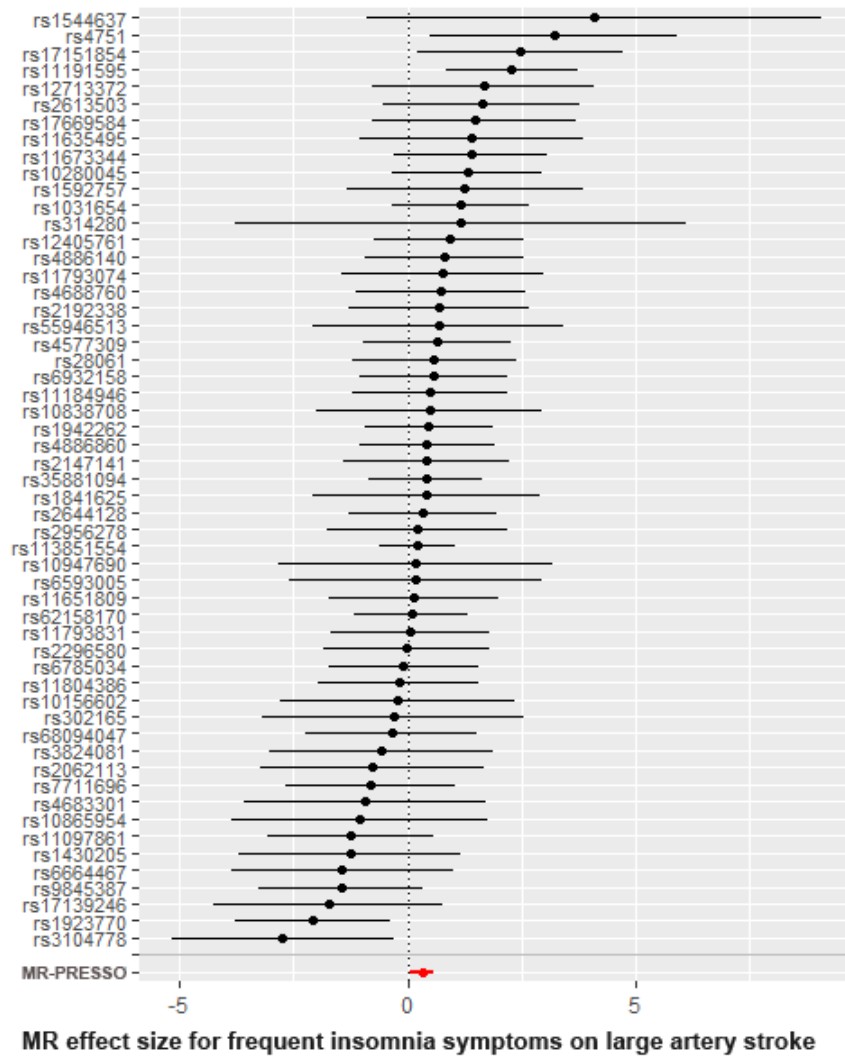
Supplementary Figure 3 Funnel plot related to the short sleep duration genetic instrument with respect to large artery stroke. Funnel plot reports the contribution of each variant (effect size on the x-axis, 1/SE on the y-axis) to MR estimate



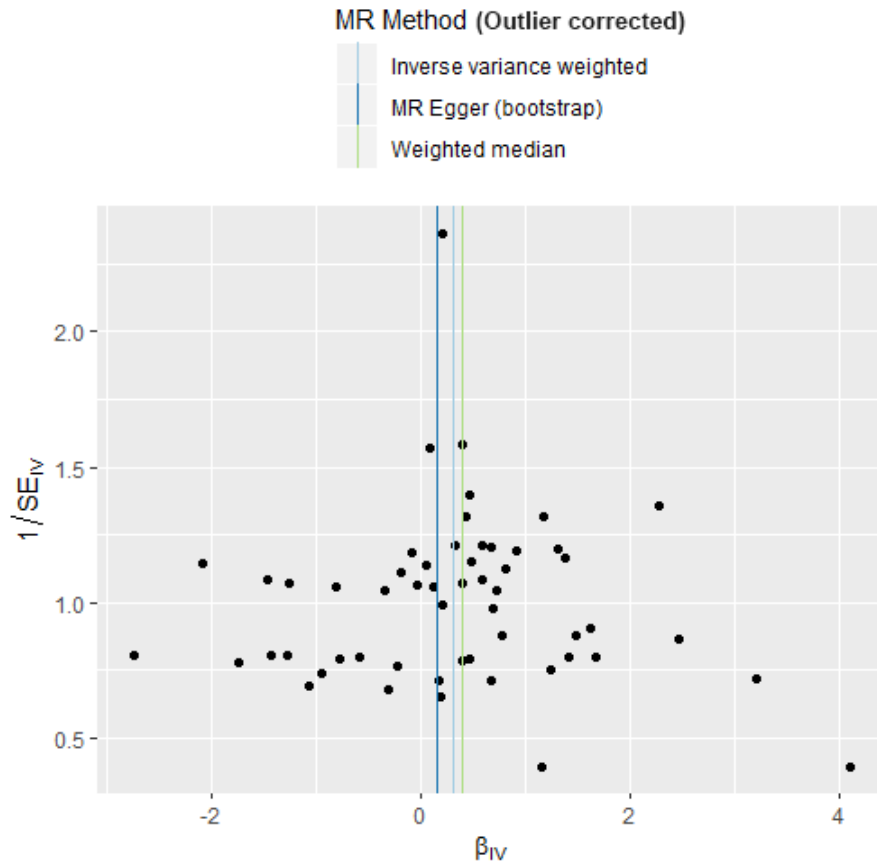
Supplementary Figure 4 Leave-one-out analysis related to the short sleep duration genetic instrument with respect to large artery stroke. Leave-one-out plot reports the MR estimate excluding one variant at a time from the genetic instrument



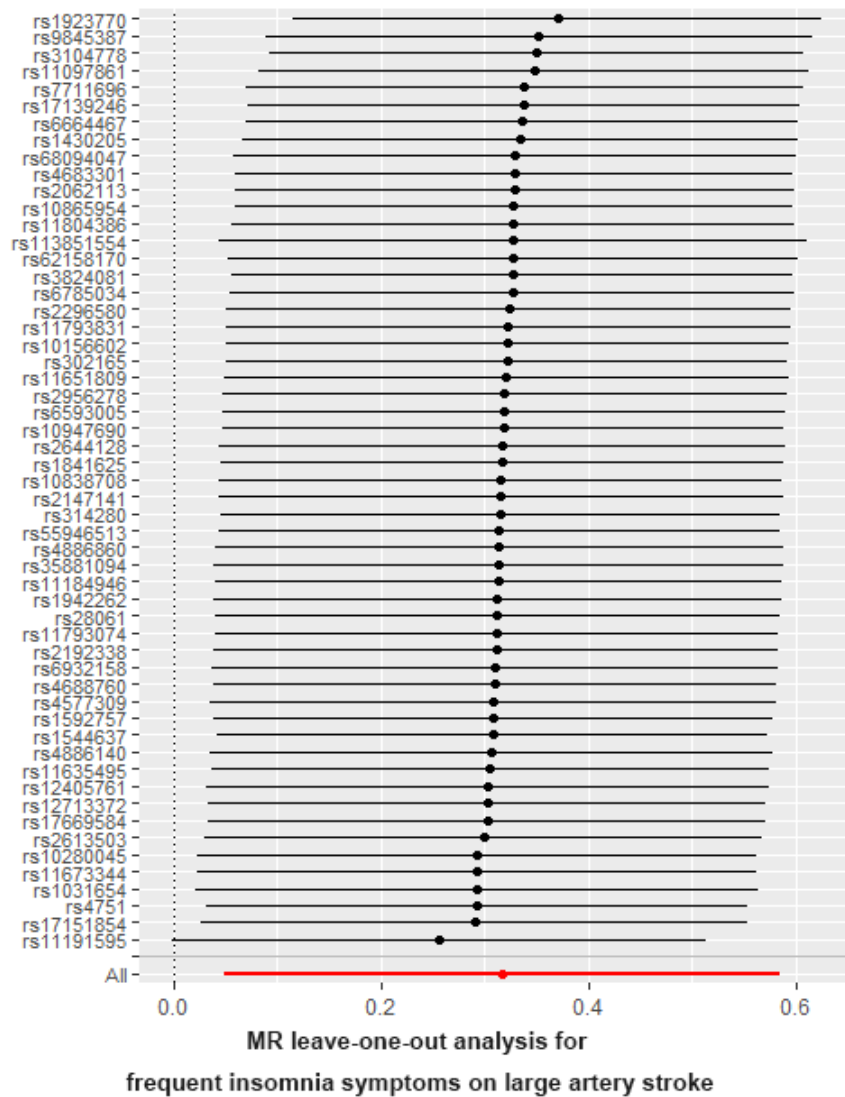
Supplementary Figure 5 Scatterplot of SNP potential effects on frequent insomnia symptoms vs large artery stroke, with the slope of each line corresponding to estimated MR effect per method after removing the outlier SNP rs324017



Supplementary Figure 6 Forest plot of individual and combined SNP MR-estimated effects sizes for frequent insomnia symptoms on large artery stroke after removing the outlier SNP rs324017. Data is displayed as β and 95% CI. MR-PRESSO, MR-Pleiotropy Residual Sum and Outlier method



Supplementary Figure 7 Funnel plot related to the frequent insomnia symptoms genetic instrument with respect to large artery stroke after removing the outlier SNP rs324017. Funnel plot reports the contribution of each variant (effect size on the x-axis, 1/SE on the y-axis) to MR estimate



Supplementary Figure 8 Leave-one-out analysis related to the frequent insomnia symptoms genetic instrument with respect to large artery stroke after removing the outlier SNP rs324017. Leave-one-out plot reports the MR estimate excluding one variant at a time from the genetic instrument

MEGASTROKE CONSORTIUM

Rainer Malik ¹, Ganesh Chauhan ², Matthew Traylor ³, Muralidharan Sargurupremraj ^{4,5}, Yukinori Okada ^{6,7,8}, Aniket Mishra ^{4,5}, Loes Rutten-Jacobs ³, Anne-Katrin Giese ⁹, Sander W van der Laan ¹⁰, Solveig Gretarsdottir ¹¹, Christopher D Anderson ^{12,13,14,14}, Michael Chong ¹⁵, Hieab HH Adams ^{16,17}, Tetsuro Ago ¹⁸, Peter Almgren ¹⁹, Philippe Amouyel ^{20,21}, Hakan Ay ^{22,13}, Traci M Bartz ²³, Oscar R Benavente ²⁴, Steve Bevan ²⁵, Giorgio B Boncoraglio ²⁶, Robert D Brown, Jr. ²⁷, Adam S Butterworth ^{28,29}, Caty Carrera ^{30,31}, Cara L Carty ^{32,33}, Daniel I Chasman ^{34,35}, Wei-Min Chen ³⁶, John W Cole ³⁷, Adolfo Correa ³⁸, Ioana Cotlarciuc ³⁹, Carlos Cruchaga ^{40,41}, John Danesh ^{28,42,43,44}, Paul IW de Bakker ^{45,46}, Anita L DeStefano ^{47,48}, Marcel den Hoed ⁴⁹, Qing Duan ⁵⁰, Stefan T Engelter ^{51,52}, Guido J Falcone ^{53,54}, Rebecca F Gottesman ⁵⁵, Raji P Grewal ⁵⁶, Vilmundur Gudnason ^{57,58}, Stefan Gustafsson ⁵⁹, Jeffrey Haessler ⁶⁰, Tamara B Harris ⁶¹, Ahamad Hassan ⁶², Aki S Havulinna ^{63,64}, Susan R Heckbert ⁶⁵, Elizabeth G Holliday ^{66,67}, George Howard ⁶⁸, Fang-Chi Hsu ⁶⁹, Hyacinth I Hyacinth ⁷⁰, M Arfan Ikram ¹⁶, Erik Ingelsson ^{71,72}, Marguerite R Irvin ⁷³, Xueqiu Jian ⁷⁴, Jordi Jim énez-Conde ⁷⁵, Julie A Johnson ^{76,77}, J Wouter Jukema ⁷⁸, Masahiro Kanai ^{6,7,79}, Keith L Keene ^{80,81}, Brett M Kissela ⁸², Dawn O Kleindorfer ⁸², Charles Kooperberg ⁶⁰, Michiaki Kubo ⁸³, Leslie A Lange ⁸⁴, Carl D Langefeld ⁸⁵, Claudia Langenberg ⁸⁶, Lenore J Launer ⁸⁷, Jin-Moo Lee ⁸⁸, Robin Lemmens ^{89,90}, Didier Leys ⁹¹, Cathryn M Lewis ^{92,93}, Wei-Yu Lin ^{28,94}, Arne G Lindgren ^{95,96}, Erik Lorentzen ⁹⁷, Patrik K Magnusson ⁹⁸, Jane Maguire ⁹⁹, Ani Manichaikul ³⁶, Patrick F McArdle ¹⁰⁰, James F Meschia ¹⁰¹, Braxton D Mitchell ^{100,102}, Thomas H Mosley ^{103,104}, Michael A Nalls ^{105,106}, Toshiharu Ninomiya ¹⁰⁷, Martin J O'Donnell ^{15,108}, Bruce M Psaty ^{109,110,111,112}, Sara L Pulit ^{113,45}, Kristiina Rannikmäe ^{114,115}, Alexander P Reiner ^{65,116}, Kathryn M Rexrode ¹¹⁷, Kenneth Rice ¹¹⁸, Stephen S Rich ³⁶, Paul M Ridker ^{34,35}, Natalia S Rost ^{9,13}, Peter M Rothwell ¹¹⁹, Jerome I Rotter ^{120,121}, Tatjana Rundek ¹²², Ralph L Sacco ¹²², Saori Sakaue ^{7,123}, Michele M Sale ¹²⁴, Veikko Salomaa ⁶³, Bishwa R Sapkota ¹²⁵, Reinhold Schmidt ¹²⁶, Carsten O Schmidt ¹²⁷, Ulf Schminke ¹²⁸, Pankaj Sharma ³⁹, Agnieszka Slowik ¹²⁹, Cathie LM Sudlow ^{114,115}, Christian Tanislav ¹³⁰, Turgut Tatlisumak ^{131,132}, Kent D Taylor ^{120,121}, Vincent NS Thijs ^{133,134}, Gudmar Thorleifsson ¹¹, Unnur Thorsteinsdottir ¹¹, Steffen Tiedt ¹, Stella Trompet ¹³⁵, Christophe Tzourio ^{5,136,137}, Cornelia M van Duijn ^{138,139}, Matthew Walters ¹⁴⁰, Nicholas J Wareham ⁸⁶, Sylvia Wassertheil-Smoller ¹⁴¹, James G Wilson ¹⁴², Kerri L Wiggins ¹⁰⁹, Qiong Yang ⁴⁷, Salim Yusuf ¹⁵, Najaf Amin ¹⁶, Hugo S Aparicio ^{185,48}, Donna K Arnett ¹⁸⁶, John Attia ¹⁸⁷, Alexa S Beiser ^{47,48}, Claudine Berr ¹⁸⁸, Julie E Buring ^{34,35}, Mariana Bustamante ¹⁸⁹, Valeria Caso ¹⁹⁰, Yu-Ching Cheng ¹⁹¹, Seung Hoan Choi ^{192,48}, Ayesha Chowhan ^{185,48}, Natalia Cullell ³¹, Jean-Fran çois Dartigues ^{193,194}, Hossein Delavaran ^{95,96}, Pilar Delgado ¹⁹⁵, Marcus Dörr ^{196,197}, Gunnar Engström ¹⁹, Ian Ford ¹⁹⁸, Wander S Gurpreet ¹⁹⁹, Anders Hamsten ^{200,201}, Laura Heitsch ²⁰², Atsushi Hozawa ²⁰³, Laura Ibanez ²⁰⁴, Andreea Ilinca ^{95,96}, Martin Ingelsson ²⁰⁵, Motoki Iwasaki ²⁰⁶, Rebecca D Jackson ²⁰⁷,

Katarina Jood ²⁰⁸, Pekka Jousilahti ⁶³, Sara Kaffashian ^{4,5}, Lalit Kalra ²⁰⁹, Masahiro Kamouchi ²¹⁰, Takanari Kitazono ²¹¹, Olafur Kjartansson ²¹², Manja Kloss ²¹³, Peter J Koudstaal ²¹⁴, Jerzy Krupinski ²¹⁵, Daniel L Labovitz ²¹⁶, Cathy C Laurie ¹¹⁸, Christopher R Levi ²¹⁷, Linxin Li ²¹⁸, Lars Lind ²¹⁹, Cecilia M Lindgren ^{220,221}, Vasileios Lioutas ^{222,48}, Yong Mei Liu ²²³, Oscar L Lopez ²²⁴, Hirata Makoto ²²⁵, Nicolas Martinez-Majander ¹⁷², Koichi Matsuda ²²⁵, Naoko Minegishi ²⁰³, Joan Montaner ²²⁶, Andrew P Morris ^{227,228}, Elena Muiño ³¹, Martina Müller-Nurasyid ^{229,230,231}, Bo Norrving ^{95,96}, Soichi Ogishima ²⁰³, Eugenio A Parati ²³², Leema Reddy Peddareddygar ⁵⁶, Nancy L Pedersen ^{98,233}, Joanna Pera ¹²⁹, Markus Perola ^{63,234}, Alessandro Pezzini ²³⁵, Silvana Pileggi ²³⁶, Raquel Rabionet ²³⁷, Iolanda Riba-Llena ³⁰, Marta Ribas és ²³⁸, Jose R Romero ^{185,48}, Jaume Roquer ^{239,240}, Anthony G Rudd ^{241,242}, Antti-Pekka Sarin ^{243,244}, Ralhan Sarju ¹⁹⁹, Chloe Sarnowski ^{47,48}, Makoto Sasaki ²⁴⁵, Claudia L Satizabal ^{185,48}, Mamoru Satoh ²⁴⁵, Naveed Sattar ²⁴⁶, Norie Sawada ²⁰⁶, Gerli Sibolt ¹⁷², Ásgeir Sigurdsson ²⁴⁷, Albert Smith ²⁴⁸, Kenji Sobue ²⁴⁵, Carolina Soriano-Tárraga ²⁴⁰, Tara Stanne ²⁴⁹, O Colin Stine ²⁵⁰, David J Stott ²⁵¹, Konstantin Strauch ^{229,252}, Takako Takai ²⁰³, Hideo Tanaka ^{253,254}, Kozo Tanno ²⁴⁵, Alexander Teumer ²⁵⁵, Liisa Tomppo ¹⁷², Nuria P Torres-Aguila ³¹, Emmanuel Touze ^{256,257}, Shoichiro Tsugane ²⁰⁶, Andre G Uitterlinden ²⁵⁸, Einar M Valdimarsson ²⁵⁹, Sven J van der Lee ¹⁶, Henry Völzke ²⁵⁵, Kenji Wakai ²⁵³, David Weir ²⁶⁰, Stephen R Williams ²⁶¹, Charles DA Wolfe ^{241,242}, Quenna Wong ¹¹⁸, Huichun Xu ¹⁹¹, Taiki Yamaji ²⁰⁶, Dharambir K Sanghera ^{125,169,170}, Olle Melander ¹⁹, Christina Jern ¹⁷¹, Daniel Strbian ^{172,173}, Israel Fernandez-Cadenas ^{31,30}, W T Longstreth, Jr ^{174,65}, Arndt Rolfs ¹⁷⁵, Jun Hata ¹⁰⁷, Daniel Woo ⁸², Jonathan Rosand ^{12,13,14}, Guillaume Pare ¹⁵, Jemma C Hopewell ¹⁷⁶, Danish Saleheen ¹⁷⁷, Kari Stefansson ^{11,178}, Bradford B Worrall ¹⁷⁹, Steven J Kittner ³⁷, Sudha Seshadri ^{180,48}, Myriam Fornage ^{74,181}, Hugh S Markus ³, Joanna MM Howson ²⁸, Yoichiro Kamatani ^{6,182}, Stephanie Dobbie ^{4,5}, Martin Dichgans ^{1,183,184}

1 Institute for Stroke and Dementia Research (ISD), University Hospital, LMU Munich, Munich, Germany

2 Centre for Brain Research, Indian Institute of Science, Bangalore, India

3 Stroke Research Group, Division of Clinical Neurosciences, University of Cambridge, UK

4 INSERM U1219 Bordeaux Population Health Research Center, Bordeaux, France

5 University of Bordeaux, Bordeaux, France

6 Laboratory for Statistical Analysis, RIKEN Center for Integrative Medical Sciences, Yokohama, Japan

7 Department of Statistical Genetics, Osaka University Graduate School of Medicine, Osaka, Japan

8 Laboratory of Statistical Immunology, Immunology Frontier Research Center (WPI-IFReC), Osaka University, Suita, Japan.

9 Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

- 10 Laboratory of Experimental Cardiology, Division of Heart and Lungs, University Medical Center Utrecht, University of Utrecht, Utrecht, Netherlands
- 11 deCODE genetics/AMGEN inc, Reykjavik, Iceland
- 12 Center for Genomic Medicine, Massachusetts General Hospital (MGH), Boston, MA, USA
- 13 J. Philip Kistler Stroke Research Center, Department of Neurology, MGH, Boston, MA, USA
- 14 Program in Medical and Population Genetics, Broad Institute, Cambridge, MA, USA
- 15 Population Health Research Institute, McMaster University, Hamilton, Canada
- 16 Department of Epidemiology, Erasmus University Medical Center, Rotterdam, Netherlands
- 17 Department of Radiology and Nuclear Medicine, Erasmus University Medical Center, Rotterdam, Netherlands
- 18 Department of Medicine and Clinical Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
- 19 Department of Clinical Sciences, Lund University, Malmö, Sweden
- 20 Univ. Lille, Inserm, Institut Pasteur de Lille, LabEx DISTALZ-UMR1167, Risk factors and molecular determinants of aging-related diseases, F-59000 Lille, France
- 21 Centre Hosp. Univ Lille, Epidemiology and Public Health Department, F-59000 Lille, France
- 22 AA Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA
- 23 Cardiovascular Health Research Unit, Departments of Biostatistics and Medicine, University of Washington, Seattle, WA, USA
- 24 Division of Neurology, Faculty of Medicine, Brain Research Center, University of British Columbia, Vancouver, Canada
- 25 School of Life Science, University of Lincoln, Lincoln, UK
- 26 Department of Cerebrovascular Diseases, Fondazione IRCCS Istituto Neurologico "Carlo Besta", Milano, Italy
- 27 Department of Neurology, Mayo Clinic Rochester, Rochester, MN, USA
- 28 MRC/BHF Cardiovascular Epidemiology Unit, Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK
- 29 The National Institute for Health Research Blood and Transplant Research Unit in Donor Health and Genomics, University of Cambridge, UK
- 30 Neurovascular Research Laboratory, Vall d'Hebron Institut of Research, Neurology and Medicine Departments-Universitat Autònoma de Barcelona, Vall d'Hebrón Hospital, Barcelona, Spain
- 31 Stroke Pharmacogenomics and Genetics, Fundacio Docència i Recerca MutuaTerrassa, Terrassa, Spain
- 32 Children's Research Institute, Children's National Medical Center, Washington, DC, USA

33 Center for Translational Science, George Washington University, Washington, DC, USA

34 Division of Preventive Medicine, Brigham and Women's Hospital, Boston, MA, USA

35 Harvard Medical School, Boston, MA, USA

36 Center for Public Health Genomics, Department of Public Health Sciences, University of Virginia, Charlottesville, VA, USA

37 Department of Neurology, University of Maryland School of Medicine and Baltimore VAMC, Baltimore, MD, USA

38 Departments of Medicine, Pediatrics and Population Health Science, University of Mississippi Medical Center, Jackson, MS, USA

39 Institute of Cardiovascular Research, Royal Holloway University of London, UK & Ashford and St Peters Hospital, Surrey UK

40 Department of Psychiatry, The Hope Center Program on Protein Aggregation and Neurodegeneration (HPAN), Washington University, School of Medicine, St. Louis, MO, USA

41 Department of Developmental Biology, Washington University School of Medicine, St. Louis, MO, USA

42 NIHR Blood and Transplant Research Unit in Donor Health and Genomics, Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK

43 Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge, UK

44 British Heart Foundation, Cambridge Centre of Excellence, Department of Medicine, University of Cambridge, Cambridge, UK

45 Department of Medical Genetics, University Medical Center Utrecht, Utrecht, Netherlands

46 Department of Epidemiology, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, Netherlands

47 Boston University School of Public Health, Boston, MA, USA

48 Framingham Heart Study, Framingham, MA, USA

49 Department of Immunology, Genetics and Pathology and Science for Life Laboratory, Uppsala University, Uppsala, Sweden

50 Department of Genetics, University of North Carolina, Chapel Hill, NC, USA

51 Department of Neurology and Stroke Center, Basel University Hospital, Switzerland

52 Neurorehabilitation Unit, University and University Center for Medicine of Aging and Rehabilitation Basel, Felix Platter Hospital, Basel, Switzerland

53 Department of Neurology, Yale University School of Medicine, New Haven, CT, USA

54 Program in Medical and Population Genetics, The Broad Institute of Harvard and MIT, Cambridge, MA, USA

55 Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, USA

56 Neuroscience Institute, SF Medical Center, Trenton, NJ, USA
57 Icelandic Heart Association Research Institute, Kopavogur, Iceland
58 University of Iceland, Faculty of Medicine, Reykjavik, Iceland
59 Department of Medical Sciences, Molecular Epidemiology and Science for Life Laboratory, Uppsala University, Uppsala, Sweden
60 Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA, USA
61 Laboratory of Epidemiology and Population Science, National Institute on Aging, National Institutes of Health, Bethesda, MD, USA
62 Department of Neurology, Leeds General Infirmary, Leeds Teaching Hospitals NHS Trust, Leeds, UK
63 National Institute for Health and Welfare, Helsinki, Finland
64 FIMM - Institute for Molecular Medicine Finland, Helsinki, Finland
65 Department of Epidemiology, University of Washington, Seattle, WA, USA
66 Public Health Stream, Hunter Medical Research Institute, New Lambton, Australia
67 Faculty of Health and Medicine, University of Newcastle, Newcastle, Australia
68 School of Public Health, University of Alabama at Birmingham, Birmingham, AL, USA
69 Department of Biostatistical Sciences, Wake Forest School of Medicine, Winston-Salem, NC, USA
70 Aflac Cancer and Blood Disorder Center, Department of Pediatrics, Emory University School of Medicine, Atlanta, GA, USA
71 Department of Medicine, Division of Cardiovascular Medicine, Stanford University School of Medicine, CA, USA
72 Department of Medical Sciences, Molecular Epidemiology and Science for Life Laboratory, Uppsala University, Uppsala, Sweden
73 Epidemiology, School of Public Health, University of Alabama at Birmingham, USA
74 Brown Foundation Institute of Molecular Medicine, University of Texas Health Science Center at Houston, Houston, TX, USA
75 Neurovascular Research Group (NEUVAS), Neurology Department, Institut Hospital del Mar d'Investigació Mèdica, Universitat Autònoma de Barcelona, Barcelona, Spain
76 Department of Pharmacotherapy and Translational Research and Center for Pharmacogenomics, University of Florida, College of Pharmacy, Gainesville, FL, USA
77 Division of Cardiovascular Medicine, College of Medicine, University of Florida, Gainesville, FL, USA
78 Department of Cardiology, Leiden University Medical Center, Leiden, the Netherlands
79 Program in Bioinformatics and Integrative Genomics, Harvard Medical School, Boston, MA, USA
80 Department of Biology, East Carolina University, Greenville, NC, USA

- 81 Center for Health Disparities, East Carolina University, Greenville, NC, USA
- 82 University of Cincinnati College of Medicine, Cincinnati, OH, USA
- 83 RIKEN Center for Integrative Medical Sciences, Yokohama, Japan
- 84 Department of Medicine, University of Colorado Denver, Anschutz Medical Campus, Aurora, CO, USA
- 85 Center for Public Health Genomics and Department of Biostatistical Sciences, Wake Forest School of Medicine, Winston-Salem, NC, USA
- 86 MRC Epidemiology Unit, University of Cambridge School of Clinical Medicine, Institute of Metabolic Science, Cambridge Biomedical Campus, Cambridge, UK
- 87 Intramural Research Program, National Institute on Aging, National Institutes of Health, Bethesda, MD, USA
- 88 Department of Neurology, Radiology, and Biomedical Engineering, Washington University School of Medicine, St. Louis, MO, USA
- 89 KU Leuven – University of Leuven, Department of Neurosciences, Experimental Neurology, Leuven, Belgium
- 90 VIB Center for Brain & Disease Research, University Hospitals Leuven, Department of Neurology, Leuven, Belgium
- 91 Univ.-Lille, INSERM U 1171. CHU Lille. Lille, France
- 92 Department of Medical and Molecular Genetics, King's College London, London, UK
- 93 SGDP Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK
- 94 Northern Institute for Cancer Research, Paul O'Gorman Building, Newcastle University, Newcastle, UK
- 95 Department of Clinical Sciences Lund, Neurology, Lund University, Lund, Sweden
- 96 Department of Neurology and Rehabilitation Medicine, Skåne University Hospital, Lund, Sweden
- 97 Bioinformatics Core Facility, University of Gothenburg, Gothenburg, Sweden
- 98 Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden
- 99 University of Technology Sydney, Faculty of Health, Ultimo, Australia
- 100 Department of Medicine, University of Maryland School of Medicine, MD, USA
- 101 Department of Neurology, Mayo Clinic, Jacksonville, FL, USA
- 102 Geriatrics Research and Education Clinical Center, Baltimore Veterans Administration Medical Center, Baltimore, MD, USA
- 103 Division of Geriatrics, School of Medicine, University of Mississippi Medical Center, Jackson, MS, USA
- 104 Memory Impairment and Neurodegenerative Dementia Center, University of Mississippi Medical Center, Jackson, MS, USA
- 105 Laboratory of Neurogenetics, National Institute on Aging, National Institutes of Health, Bethesda, MD, USA

106 Data Tecnica International, Glen Echo MD, USA
107 Department of Epidemiology and Public Health, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
108 Clinical Research Facility, Department of Medicine, NUI Galway, Galway, Ireland
109 Cardiovascular Health Research Unit, Department of Medicine, University of Washington, Seattle, WA, USA
110 Department of Epidemiology, University of Washington, Seattle, WA
111 Department of Health Services, University of Washington, Seattle, WA, USA
112 Kaiser Permanente Washington Health Research Institute, Seattle, WA, USA
113 Brain Center Rudolf Magnus, Department of Neurology, University Medical Center Utrecht, Utrecht, The Netherlands
114 Usher Institute of Population Health Sciences and Informatics, University of Edinburgh, Edinburgh, UK
115 Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, UK
116 Fred Hutchinson Cancer Research Center, University of Washington, Seattle, WA, USA
117 Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA
118 Department of Biostatistics, University of Washington, Seattle, WA, USA
119 Nuffield Department of Clinical Neurosciences, University of Oxford, UK
120 Institute for Translational Genomics and Population Sciences, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA, USA
121 Division of Genomic Outcomes, Department of Pediatrics, Harbor-UCLA Medical Center, Torrance, CA, USA
122 Department of Neurology, Miller School of Medicine, University of Miami, Miami, FL, USA
123 Department of Allergy and Rheumatology, Graduate School of Medicine, the University of Tokyo, Tokyo, Japan
124 Center for Public Health Genomics, University of Virginia, Charlottesville, VA, USA
125 Department of Pediatrics, College of Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA
126 Department of Neurology, Medical University of Graz, Graz, Austria
127 University Medicine Greifswald, Institute for Community Medicine, SHIP-KEF, Greifswald, Germany
128 University Medicine Greifswald, Department of Neurology, Greifswald, Germany
129 Department of Neurology, Jagiellonian University, Krakow, Poland
130 Department of Neurology, Justus Liebig University, Giessen, Germany
131 Department of Clinical Neurosciences/Neurology, Institute of Neuroscience and Physiology, Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden
132 Sahlgrenska University Hospital, Gothenburg, Sweden

133 Stroke Division, Florey Institute of Neuroscience and Mental Health, University of Melbourne, Heidelberg, Australia

134 Austin Health, Department of Neurology, Heidelberg, Australia

135 Department of Internal Medicine, Section Gerontology and Geriatrics, Leiden University Medical Center, Leiden, the Netherlands

136 INSERM U1219, Bordeaux, France

137 Department of Public Health, Bordeaux University Hospital, Bordeaux, France

138 Genetic Epidemiology Unit, Department of Epidemiology, Erasmus University Medical Center Rotterdam, Netherlands

139 Center for Medical Systems Biology, Leiden, Netherlands

140 School of Medicine, Dentistry and Nursing at the University of Glasgow, Glasgow, UK

141 Department of Epidemiology and Population Health, Albert Einstein College of Medicine, NY, USA

142 Department of Physiology and Biophysics, University of Mississippi Medical Center, Jackson, MS, USA

143 A full list of members and affiliations appears in the Supplementary Note

144 Department of Human Genetics, McGill University, Montreal, Canada

145 Department of Pathophysiology, Institute of Biomedicine and Translation Medicine, University of Tartu, Tartu, Estonia

146 Department of Cardiac Surgery, Tartu University Hospital, Tartu, Estonia

147 Clinical Gene Networks AB, Stockholm, Sweden

148 Department of Genetics and Genomic Sciences, The Icahn Institute for Genomics and Multiscale Biology Icahn School of Medicine at Mount Sinai, New York, NY , USA

149 Department of Pathophysiology, Institute of Biomedicine and Translation Medicine, University of Tartu, Biomeedikum, Tartu, Estonia

150 Integrated Cardio Metabolic Centre, Department of Medicine, Karolinska Institutet, Karolinska Universitetssjukhuset, Huddinge, Sweden.

151 Clinical Gene Networks AB, Stockholm, Sweden

152 Sorbonne Universit es, UPMC Univ. Paris 06, INSERM, UMR_S 1166, Team Genomics & Pathophysiology of Cardiovascular Diseases, Paris, France

153 ICAN Institute for Cardiometabolism and Nutrition, Paris, France

154 Department of Biomedical Engineering, University of Virginia, Charlottesville, VA, USA

155 Group Health Research Institute, Group Health Cooperative, Seattle, WA, USA

156 Seattle Epidemiologic Research and Information Center, VA Office of Research and Development, Seattle, WA, USA

157 Cardiovascular Research Center, Massachusetts General Hospital, Boston, MA, USA

158 Department of Medical Research, B arum Hospital, Vestre Viken Hospital Trust, Gjøttem, Norway

159 Saw Swee Hock School of Public Health, National University of Singapore and National University Health System, Singapore

160 National Heart and Lung Institute, Imperial College London, London, UK

161 Department of Gene Diagnostics and Therapeutics, Research Institute, National Center for Global Health and Medicine, Tokyo, Japan

162 Department of Epidemiology, Tulane University School of Public Health and Tropical Medicine, New Orleans, LA, USA

163 Department of Cardiology, University Medical Center Groningen, University of Groningen, Netherlands

164 MRC-PHE Centre for Environment and Health, School of Public Health, Department of Epidemiology and Biostatistics, Imperial College London, London, UK

165 Department of Epidemiology and Biostatistics, Imperial College London, London, UK

166 Department of Cardiology, Ealing Hospital NHS Trust, Southall, UK

167 National Heart, Lung and Blood Research Institute, Division of Intramural Research, Population Sciences Branch, Framingham, MA, USA

168 A full list of members and affiliations appears at the end of the manuscript

169 Department of Pharmaceutical Sciences, College of Pharmacy, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA

170 Oklahoma Center for Neuroscience, Oklahoma City, OK, USA

171 Department of Pathology and Genetics, Institute of Biomedicine, The Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden

172 Department of Neurology, Helsinki University Hospital, Helsinki, Finland

173 Clinical Neurosciences, Neurology, University of Helsinki, Helsinki, Finland

174 Department of Neurology, University of Washington, Seattle, WA, USA

175 Albrecht Kossel Institute, University Clinic of Rostock, Rostock, Germany

176 Clinical Trial Service Unit and Epidemiological Studies Unit, Nuffield Department of Population Health, University of Oxford, Oxford, UK

177 Department of Genetics, Perelman School of Medicine, University of Pennsylvania, PA, USA

178 Faculty of Medicine, University of Iceland, Reykjavik, Iceland

179 Departments of Neurology and Public Health Sciences, University of Virginia School of Medicine, Charlottesville, VA, USA

180 Department of Neurology, Boston University School of Medicine, Boston, MA, USA

181 Human Genetics Center, University of Texas Health Science Center at Houston, Houston, TX, USA

182 Center for Genomic Medicine, Kyoto University Graduate School of Medicine, Kyoto, Japan

183 Munich Cluster for Systems Neurology (SyNergy), Munich, Germany

184 German Center for Neurodegenerative Diseases (DZNE), Munich, Germany

185 Boston University School of Medicine, Boston, MA, USA

186 University of Kentucky College of Public Health, Lexington, KY, USA

187 University of Newcastle and Hunter Medical Research Institute, New Lambton, Australia

188 Univ. Montpellier, Inserm, U1061, Montpellier, France

189 Centre for Research in Environmental Epidemiology, Barcelona, Spain

190 Department of Neurology, Università degli Studi di Perugia, Umbria, Italy

191 Department of Medicine, University of Maryland School of Medicine, Baltimore, MD, USA

192 Broad Institute, Cambridge, MA, USA

193 Univ. Bordeaux, Inserm, Bordeaux Population Health Research Center, UMR 1219, Bordeaux, France

194 Bordeaux University Hospital, Department of Neurology, Memory Clinic, Bordeaux, France

195 Neurovascular Research Laboratory. Vall d'Hebron Institut of Research, Neurology and Medicine Departments-Universitat Autònoma de Barcelona. Vall d'Hebrón Hospital, Barcelona, Spain

196 University Medicine Greifswald, Department of Internal Medicine B, Greifswald, Germany

197 DZHK, Greifswald, Germany

198 Robertson Center for Biostatistics, University of Glasgow, Glasgow, UK

199 Hero DMC Heart Institute, Dayanand Medical College & Hospital, Ludhiana, India

200 Atherosclerosis Research Unit, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden

201 Karolinska Institutet, Stockholm, Sweden

202 Division of Emergency Medicine, and Department of Neurology, Washington University School of Medicine, St. Louis, MO, USA

203 Tohoku Medical Megabank Organization, Sendai, Japan

204 Department of Psychiatry, Washington University School of Medicine, St. Louis, MO, USA

205 Department of Public Health and Caring Sciences / Geriatrics, Uppsala University, Uppsala, Sweden

206 Epidemiology and Prevention Group, Center for Public Health Sciences, National Cancer Center, Tokyo, Japan

207 Department of Internal Medicine and the Center for Clinical and Translational Science, The Ohio State University, Columbus, OH, USA

208 Institute of Neuroscience and Physiology, the Sahlgrenska Academy at University of Gothenburg, Goteborg, Sweden

209 Department of Basic and Clinical Neurosciences, King's College London, London, UK

210 Department of Health Care Administration and Management, Graduate School of Medical Sciences, Kyushu University, Japan

211 Department of Medicine and Clinical Science, Graduate School of Medical Sciences, Kyushu University, Japan

212 Landspítali National University Hospital, Departments of Neurology & Radiology, Reykjavik, Iceland

213 Department of Neurology, Heidelberg University Hospital, Germany

214 Department of Neurology, Erasmus University Medical Center

215 Hospital Universitari Mutua Terrassa, Terrassa (Barcelona), Spain

216 Albert Einstein College of Medicine, Montefiore Medical Center, New York, NY, USA

217 John Hunter Hospital, Hunter Medical Research Institute and University of Newcastle, Newcastle, NSW, Australia

218 Centre for Prevention of Stroke and Dementia, Nuffield Department of Clinical Neurosciences, University of Oxford, UK

219 Department of Medical Sciences, Uppsala University, Uppsala, Sweden

220 Genetic and Genomic Epidemiology Unit, Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK

221 The Wellcome Trust Centre for Human Genetics, Oxford, UK

222 Beth Israel Deaconess Medical Center, Boston, MA, USA

223 Wake Forest School of Medicine, Wake Forest, NC, USA

224 Department of Neurology, University of Pittsburgh, Pittsburgh, PA, USA

225 BioBank Japan, Laboratory of Clinical Sequencing, Department of Computational biology and medical Sciences, Graduate school of Frontier Sciences, The University of Tokyo, Tokyo, Japan

226 Neurovascular Research Laboratory, Vall d'Hebron Institut of Research, Neurology and Medicine Departments-Universitat Autònoma de Barcelona. Vall d'Hebrón Hospital, Barcelona, Spain

227 Department of Biostatistics, University of Liverpool, Liverpool, UK

228 Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK

229 Institute of Genetic Epidemiology, Helmholtz Zentrum München - German Research Center for Environmental Health, Neuherberg, Germany

230 Department of Medicine I, Ludwig-Maximilians-Universität, Munich, Germany

231 DZHK (German Centre for Cardiovascular Research), partner site Munich Heart Alliance, Munich, Germany

232 Department of Cerebrovascular Diseases, Fondazione IRCCS Istituto Neurologico "Carlo Besta", Milano, Italy

233 Karolinska Institutet, MEB, Stockholm, Sweden

234 University of Tartu, Estonian Genome Center, Tartu, Estonia, Tartu, Estonia

235 Department of Clinical and Experimental Sciences, Neurology Clinic, University of Brescia, Italy

236 Translational Genomics Unit, Department of Oncology, IRCCS Istituto di Ricerche Farmacologiche Mario Negri, Milano, Italy

237 Department of Genetics, Microbiology and Statistics, University of Barcelona, Barcelona, Spain

238 Psychiatric Genetics Unit, Group of Psychiatry, Mental Health and Addictions, Vall d'Hebron Research Institute (VHIR), Universitat Autònoma de Barcelona, Biomedical Network Research Centre on Mental Health (CIBERSAM), Barcelona, Spain

239 Department of Neurology, IMIM-Hospital del Mar, and Universitat Autònoma de Barcelona, Spain

240 IMIM (Hospital del Mar Medical Research Institute), Barcelona, Spain

241 National Institute for Health Research Comprehensive Biomedical Research Centre, Guy's & St. Thomas' NHS Foundation Trust and King's College London, London, UK

242 Division of Health and Social Care Research, King's College London, London, UK

243 FIMM-Institute for Molecular Medicine Finland, Helsinki, Finland

244 THL-National Institute for Health and Welfare, Helsinki, Finland

245 Iwate Tohoku Medical Megabank Organization, Iwate Medical University, Iwate, Japan

246 BHF Glasgow Cardiovascular Research Centre, Faculty of Medicine, Glasgow, UK

247 deCODE Genetics/Amgen, Inc., Reykjavik, Iceland

248 Icelandic Heart Association, Reykjavik, Iceland

249 Institute of Biomedicine, the Sahlgrenska Academy at University of Gothenburg, Goteborg, Sweden

250 Department of Epidemiology, University of Maryland School of Medicine, Baltimore, MD, USA

251 Institute of Cardiovascular and Medical Sciences, Faculty of Medicine, University of Glasgow, Glasgow, UK

252 Chair of Genetic Epidemiology, IBE, Faculty of Medicine, LMU Munich, Germany

253 Division of Epidemiology and Prevention, Aichi Cancer Center Research Institute, Nagoya, Japan

254 Department of Epidemiology, Nagoya University Graduate School of Medicine, Nagoya, Japan

255 University Medicine Greifswald, Institute for Community Medicine, SHIP-KEF, Greifswald, Germany

256 Department of Neurology, Caen University Hospital, Caen, France

257 University of Caen Normandy, Caen, France

258 Department of Internal Medicine, Erasmus University Medical Center, Rotterdam, Netherlands

259 Landspítali University Hospital, Reykjavik, Iceland

260 Survey Research Center, University of Michigan, Ann Arbor, MI, USA

261 University of Virginia Department of Neurology, Charlottesville, VA, USA