SUPPLEMENTARY INFORMATION

INDEX

1. Supplementary Tables

Study	No. Cases AS	No. Cases AIS	No. Cases LAS	No. Cases CES	No. Cases SVS	No. controls	Ethnicity
CHARGE	4,348	3,028		602		80,613	EUR
METASTROKE	10,307	10,307	1,817	1,859	1,349	19,326	EUR
SIGN	7,743	7,743	1,253	2,135	1,534	17,970	EUR
DECODE	5,520	4,483	512	1,346	615	255,213*	EUR
EPIC-CVD	4,347	2,226				7,897	EUR
Young Lacunar DNA	1,403	1,268			1,012	970	EUR
SIFAP	981	981	184	170	104	1,824	EUR
INTERSTROKE EUR	911	826	188	208	243	863	EUR
HVH1	681	577	62	92	175	1,331	EUR
Glasgow	599	599	72	105	137	1,775	EUR
CADISP	555	555	67	211	31	9,259	EUR
Barcelona	520	520	119	215		315	EUR
FINLAND	501	501	99	187	62	1,813	EUR
SAHLSIS	298	298		35	85	596	EUR
MDC	202	202				4,295	EUR
HVH2	124	103		28	39	570	EUR
ICH	1,545					1,481	
Total European	**40,585**	**34,217**	**4,373**	**7,193**	**5,386**	**406,111**	
Biobank Japan	16,256	16,256	1,256	710	4,613	27,294	EAS
HISAYAMA	1,113	1,113	370	137	483	901	EAS
RACE1	1,218	1,218	200	229	192	1,158	SAS
RACE2	1,167	1,167	155	193	122	4,035	SAS
SDS	52	52				1,514	SAS
COMPASS	5,541	5,541				11,664	AFR
SLESS**			102	173	271	868	AFR
SIGN_3**			23	77	78	361	AFR
SIGN_4**			102	118	301	2,022	AFR
INTERSTROKE AFR**			32	46	44	231	AFR
INTERSTROKE ASN	365	222	34	31	134	333	ASN
INTERSTROKE LAT	865	555	41	99	86	692	LAT
TOTAL	**67,162**	**60,341**	**6,688**	**9,006**	**11,710**	**454,450**	

Supplementary Table 1 Overview of studies included in MEGASTROKE. AS, any stroke; AIS, any ischemic stroke; LAS, large artery stroke; CES, cardioembolic stroke; SVS, small vessel stroke. * included differently sized control sets for stroke subtypes. (LAS:146,392 controls, CE:204,570 controls, SVD:192,662 controls) ** subsamples of COMPASS

Supplementary Table 2 Sample overview and genetic information of all studies. Given for each sample are the age distribution, gender distribution and risk factors distribution, if available. Further, information on genotyping platform, technique, imputation parameters and QC parameters are given, if available.

Enclosed electronic excel file

rs_ID	Gene(s)	Phenotype	log(BF)	transethnic Fixed effects	European Fixed effects	Het_pval MANTRA	Het_pval Fixed effects	Het_pval European	Mean oevar_imp transethnic	Mean oevar_imp European
rs880315	CASZ1	AS	8.09489	**3.62E-10**	6.55E-08	0.068	0.577	0.5623	0.9248	0.9990
rs12037987	WNT2B	AS	6.33614	**2.73E-08**	9.39E-07	0.135	0.6592	0.3841	0.9126	0.9188
rs12124533	TSPAN2	LAS	6.60016	**1.22E-08**	6.73E-08	0.148	0.757	0.341	0.9111	0.9560
rs1052053	PMF1- SEMA4A	AS	11.92471	**2.70E-14**	**2.25E-12**	0.062	0.6419	0.9224	0.9997	0.9997
rs146390073	RGS7	CES	NA	NA	**2.20E-08**	NA	NA	0.6137	NA	0.8952
rs12476527	KCNK3	AS	6.47247	**6.44E-08**	3.71E-04	0.755	0.02834	0.006444	0.8816	0.8730
rs7610618	TM4SF4-TM4SF1	LAS	NA	NA	**1.44E-08**	NA	NA	0.3887	NA	0.9101
rs13143308	PITX2	CES	45.10357	**1.86E-47**	**5.19E-41**	0.491	0.0143	0.02133	0.9955	0.9960
rs34311906	ANK2	AIS	5.67196	1.19E-07	**1.07E-08**	0.135	0.2377	0.2558	0.8613	0.8477
rs17612742	EDNRA	LAS	9.47422	**1.46E-11**	1.05E-06	0.138	0.3331	0.4329	0.9274	0.9329
rs6825454	FGA	AIS	7.53002	**7.43E-10**	9.23E-08	0.08	0.3185	0.4575	0.9531	0.9475
rs11957829	LOC100505841	AIS	6.67074	**7.51E-09**	7.51E-07	0.096	0.4534	0.9846	0.9266	0.9408
rs6891174	NKX2-5	CES	6.9559	**5.82E-09**	3.19E-07	0.189	0.5987	0.9462	0.9319	0.9259
rs4959130	FOXF2	AS	7.51576	**1.42E-09**	**1.13E-09**	0.107	0.6876	0.8494	0.9243	0.9336
rs16896398	SLC22A7- ZNF318	AS	6.59891	**1.30E-08**	8.62E-06	0.064	0.2401	0.422	0.9889	0.9920
rs2107595	HDAC9-TWIST1	LAS	12.99407	**3.65E-15**	**1.44E-13**	0.307	0.1365	0.02756	0.9084	0.9286
rs42039	CDK6	AIS	6.83974	**6.55E-09**	2.18E-07	0.106	0.6212	0.4498	0.9701	0.9626
rs7859727	Chr9p21	AS	8.01097	**4.22E-10**	7.18E-08	0.061	0.5571	0.689	0.9920	0.9912
rs10820405	LINC01492	LAS	4.74007	1.86E-06	**4.51E-08**	0.503	0.03186	0.6144	0.9412	0.9571
rs635634	ABO	AIS	1.24591	6.93E-03	**9.18E-09**	0.68	0.01488	0.4505	0.9941	0.9925
rs2295786	SH3PXD2A	AS	8.335	**1.80E-10**	1.43E-07	0.071	0.9895	0.1098	0.9690	0.9794
rs2005108	MMP12	AIS	6.12069	**3.33E-08**	1.74E-07	0.13	0.3794	0.3116	0.9610	0.9697
rs7304841	PDE3A	AIS	5.87141	**4.93E-08**	5.80E-04	0.104	0.2739	0.2258	0.9259	0.9271
rs3184504	SH2B3	AIS	12.04062	**2.17E-14**	**1.23E-14**	0.085	0.2964	0.4207	0.9956	0.9952
rs35436	TBX3	AS	6.29274	**2.87E-08**	3.26E-04	0.215	0.1458	0.07261	0.9437	0.9526
rs9526212	LRCH1	AS	7.97154	**5.03E-10**	**1.78E-08**	0.08	0.6197	0.912	0.9490	0.9696
rs4932370	FURIN-FES	AIS	6.05016	**2.88E-08**	6.32E-07	0.049	0.8489	0.08447	0.9123	0.9214

rs12932445	ZFHX3	CES	15.48565	**6.86E-18**	**6.88E-13**	0.118	0.5875	0.09736	0.9442	0.9611
rs12445022	ZCCHC14	AS	8.57641	**1.05E-10**	1.03E-07	0.062	0.6384	0.2271	0.8970	0.9253
rs11867415	PRPF8	AIS	6.05679	**4.81E-08**	6.58E-07	0.115	0.5156	0.3308	0.9290	0.9476
rs2229383	ILF3-SLC44A2	AIS	6.02123	**4.72E-08**	3.71E-07	0.055	0.8613	0.7238	0.9719	0.9691
rs8103309	SMARCA4-LDLR	AS	5.85534	**3.40E-08**	3.70E-07	0.052	0.442	0.6725	0.8970	0.8982

Supplementary Table 3 Heterogeneity and imputation quality metrics for the MEGASTROKE lead SNPs**.** Shown are the MANTRA transethnic meta-analysis log(BF), the fixed effects transethnic meta-analysis p-value, and the fixed effects Europeans-only p-value. For both the MANTRA meta-analysis and the two fixed-effects meta-analyses, the heterogeneity p-values are shown. For each SNP, the mean imputation quality (oevar_imp) score for both the overall transethnic sample and the Europeans-only sample are shown. BF, Bayes factor; Het_pval, heterogeneity p-value; oevar_imp, imputation quality.

Supplementary Table 4 Detailed description of the genes at novel stroke loci

Chromosomal location, Lead variant, *Gene(s)*: Description of the genes at the locus.

1p36, rs880315, CASZ1: rs880315 is an intronic variant in *CASZ1*. *CASZ1* encodes Castor Zinc Finger 1, a zinc finger transcription factor, which is regulated by *PRRXL1*.(PMID 26913565) *CASZ1* is required for cardiomyocyte G1-to-S phase progression during mammalian cardiac development (PMID 25953344) and promotes vascular assembly and morphogenesis through the direct regulation of an EGFL7/RhoA-mediated pathway.(PMID 23639441) *CASZ1*-depleted human endothelial cells display marked alterations in adhesion, morphology, and sprouting. *CASZ1* is also implicated in several forms of cancer, including neuroblastoma.(PMID 21252912)

1p13, rs12037987, WNT2B: rs12037987 is an intronic variant in *WNT2B*. *WNT2B* encodes Wnt Family Member 2B, a member of the wingless-type MMTV integration site (WNT) family. *WNT2B* is implicated in the survival of intestinal stem cells and gut homeostasis.(PMID 27117411) Elevated TGF-β/Smad3 stimulates the secretion of *WNT2B* which in turn enhances vascular smooth muscle proliferation through β-catenin stabilization.(PMID 26912210) Secretion of *WNT2B* and stabilization of β-catenin upon virus infection negatively regulates expression of *IFNB1*, *IFIT1* and *TNF* in a β-catenin-dependent effector mechanism.(PMID 23785285)

1q43, rs146390073, RGS7: rs146390073 is located intronic in *RGS7*. *RGS7* encodes Regulator of G-Protein Signaling 7 which regulates G-protein-coupled receptor signaling cascades. It is highly expressed in neurons where it regulates many physiological processes. RGS7 protein contains several distinct domains and forms obligatory dimers with the atypical Gβ subunit, *Gβ5*. (PMID 10521509) *RGS7* inhibits signal transduction by increasing the GTPase activity of G protein alpha subunits, thereby driving them into their inactive GDP-bound form.(PMID 10521509, 10862767) The *RGS7*/*GNB5* dimer enhances *GNAO1* GTPase activity.(PMID 10521509) *RGS7* may play a role in synaptic vesicle exocytosis.(PMID 12659861) It modulates the activity of potassium channels that are activated by *GNAO1* in response to muscarinic acetylcholine receptor M2/CHRM2 signaling.(PMID 15897264)

2p23, rs12476527, KCNK3: rs12476527 is located in the 5'-untranslated region of *KCNK3*. *KCNK3* encodes Potassium Two Pore Domain Channel Subfamily K Member 3, a member of the superfamily of potassium channel proteins that contain two pore-forming P domains. *KCNK3* is a pH-sensitive potassium channel characterized by the presence of four transmembrane domains and two pore domains per sub-unit.(PMID 11053038) *KCNK3*, an important determinant of background K(+) conductance and membrane potential, is regulated by diacylglycerol (PMID 25420509). The *KCNK3* channel, a nonvoltage-dependent outward rectifier potassium channel, participates in the regulation of plasma membrane resting potential (PMID 16574908, 11344164, 9113366) in several cell types including human pulmonary artery smooth muscle cells.(PMID 19188660) All pathogenic mutations currently identified in KCNK3 alter conserved residues, and electrophysiological studies demonstrated the loss of function of the potassium channel. (PMID 23883380) The decreased *KCNK3* activities due to mutations cause depolarization of the resting membrane potential, which can lead to vasoconstriction and pulmonary artery remodeling. *Endothelin-1* has been shown to inhibit the *KCNK3* channel in human pulmonary artery smooth muscle cells via rho kinase phosphorylation.(PMID 21838752)

3q25, rs7610618, TM4SF4-TM4SF1: rs7610618 is located in an intergenic region between *TM4SF1* and *TM4SF4*. *TM4SF1* and *TM4SF4* encode Transmembrane 4 L Six Family Member 1 and Transmembrane 4 L Six Family Member 4 respectively. Both are members of the transmembrane 4 superfamily, also known as the tetraspanin family. *TM4SF1* is a paralog of *TM4SF4*. *TM4SF1* is a small plasma membrane glycoprotein that regulates cell motility and proliferation. It is highly expressed in tumor cells and in activated endothelial cells (EC), including cultured ECs and in cells lining the blood vessels supplying several human cancers.(PMID 24986520) *TM4SF4* is a transcriptional target of *Nkx2.2*, which is upregulated during pancreas development.(PMID 21750032)

4q25, rs34311906, ANK2: rs34311906 is situated in an intergenic region upstream of *ANK2*. *ANK2* encodes *Ankyrin 2* or *Ankyrin-b*, a member of the ankyrin family of proteins that link the integral membrane proteins to the underlying spectrin-actin cytoskeleton. *ANK2* is ubiquitously expressed, but shows high expression in cardiac muscle. The death/C-terminal domain of *ANK2* determines both the subcellular localization as well as the activity in restoring normal inositol trisphosphate receptor (*ITR*) and ryanodine receptor (*RR*) localization and cardiomyocyte contractility.(PMID 11781319) Further studies have shown that the beta-hairpin loops within the ankyrin repeat domain of *ANK2* are required for the interaction with the ITR, and a reduction of *ANK2* in neonatal cardiomyocytes reduces the half-life of the *ITR* receptor by 3-fold and destabilizes its proper localization; all of these effects were rescued by reintroducing *ANK2*.(PMID 14722080) *Ank2* deficient mice display several electrophysiological abnormalities, including bradycardia, variable heart rate, long QT intervals, catecholaminergic polymorphic ventricular tachycardia, syncope, and sudden cardiac death.(PMID 12571597) Effects on ryanodine receptors specifically were also rescued by a potent Ca2+/calmodulin-dependent protein kinase II inhibitor, suggesting that inhibition of Ca2+/calmodulin-dependent protein kinase II may also be a potential treatment strategy.

4q31, rs17612742, EDNRA: rs17612742 is located intronic in *EDNRA*. *EDNRA* encodes Endothelin Receptor Type A, the receptor for endothelin-1, a peptide that plays a role in potent and long-lasting vasoconstriction.(PMID 8581282) Signaling via both *EDNRA* and *EDNRB* in smooth muscle cells has potent vasoconstrictive effects. *EDNRA* knockout mice share defects of the cardiac outflow tract and large vessels.(PMID 2407710) It has been shown that *EDNRA*-dependent mast cell activation can diminish both endothelin-1 levels and endothelin-1-induced pathology in vivo.(PMID 15543132)

4q31, rs6825454, FGA: rs6825454 is located in an intergenic region between *FGA* and *FGB*. *FGA*, *FGB* and *FGG* encode Fibrinogen Alpha, Beta and Gamma Chain, respectively. Fibrinogen is a hexameric protein composed of two copies of these three peptide chains. The latter are expressed and secreted as an assembled hexamer (AαBβγ)2 from hepatocytes. Next to its well-described role in clotting, physiological functions of fibrinogen also include platelet crosslinking as part of primary haemostasis, as contribution to blood viscosity, as a binding surface for a number of proteins involved in various aspects of vascular physiology (PMID 11090059, 9516457) and as an extracellular matrix component.(PMID 6752288, 2613766) *IL-6* stimulates a coordinated increase in fibrinogen mRNA and protein expression via *STAT3* activation (phosphorylation) and interaction with *IL-6*-responsive elements. This is potentiated by *IL-6*-induced miR-18a that targets *PIAS3*, a negative regulator of *STAT3*.(PMID 7592638)

5q23, rs11957829, LOC100505841: rs11957829 is located intronic in *LOC100505841*. *LOC100505841* is annotated as Zinc Finger Protein 474-like due to its vicinity to *ZNF474*. The upstream *ZNF474* gene encodes Zinc Finger Protein 474, which due to its domain structure is likely involved in transcription. *ZNF474* is ubiquitously expressed, but nothing is known about its function.

5q35, rs6891174, NKX2-5: rs6891174 is located in an intergenic region between *BNIP1* and *NKX2-5*.
NKX2-5 encodes NK2 Homeobox 5, a transcription factor involved in cardiac development. The in vitro characterization of *NKX2-5* as a master regulator of the transcriptional activity of cardiac-specific genes like Natriuretic Peptide A (*NPPA)*, and the early and broad expression of the gene in the heart suggests a role in cardiogenesis.(PMID 16510504) This is further supported by a *NKX2-5-/-* knock-out mouse model, which shows abnormal heart morphogenesis, growth retardation and embryonic lethality at embryonic stage 10.5.(PMID 7628699) Additional studies have shown a regulatory role of this gene in controlling cardiac cell specification, and chamber formation.(PMID 17604724, 21357845)

6p21, rs16896398, SLC22A7-ZNF318: rs16896398 is located in an intergenic region upstream of *SLC22A7*.
SLC22A7 encodes Solute Carrier Family 22 Member 7, which belongs to the solute carrier group of membrane transport proteins that mediate cellular uptake of numerous organic ions, including xenobiotics and endogenous substrates. *SLC22A7* expression appears to be comparable in human kidney and liver and it is a facilitative transporter for cGMP and other guanine nucleotides.(PMID 18216183)

ZNF318 encodes zinc finger protein 318, a nuclear protein with two U1-type zinc fingers found in RNA-binding proteins. *ZNF318* is essential for expression of Immunglobulin D, the alternatively spliced Immunglobulin H product made by mature B lymphocytes.(PMID 24616512)

7q21, rs42039, CDK6: rs42039 is located in the 3'-untranslated region of *CDK6*. *CDK6* encodes Cell division protein kinase 6. It is regulated by cyclins, more specifically by Cyclin D proteins and cyclin-dependent kinase inhibitor proteins. *CDK6* is a catalytic subunit of the protein kinase complex important for the G1 phase progression and G1/S transition of the cell cycle. Another important component of this complex is the activating sub-unit *cyclin D*.(PMID 23861057) In mutant knockout mice of *CDK6*, the hematopoietic function is impaired with otherwise organism normal development. This might hint at additional roles of *CDK6* in the development of blood components.(PMID 15315761) There are additional functions of *CDK6* not associated with its kinase activity. For example, *CDK6* is involved in the differentiation of T cells, acting as an inhibitor of differentiation. Even though *CDK6* and *CDK4* share 71% amino acid identity, this role in differentiation is unique to *CDK6*.(PMID 26500059) *CDK6* has further been found to be important in the development of other cultured cells, including astrocytes.(PMID 12861051)

9p21, rs7859727, Chr9p21: rs7859727 is located in a non-coding RNA *CDKN2B-AS1*, also known as ANRIL. Multiple linear as well as circular isoforms of ANRIL have been identified. It has been proposed that ANRIL influences gene expression in cis by recruiting chromatin-modifying multiprotein complexes, such as Polycomb repressive complexes (PRCs), to the Chr9p21 region. ANRIL associates with the Polycomb-group protein *CBX7*, which is part of the *PRC1* complex, and together they repress expression of *p16INK4.*(PMID 20541999) Modulation of ANRIL expression leads to the epigenetic regulation of target genes expression in both cis (PMID 21151178) and trans. (PMID 23861667, 22382030 ,20664976) Trans-regulation has recently been shown to be dependent on an Alu-DEIN motif (PMID 23861667) which marks the promoters of ANRIL target genes and is mirrored in ANRIL RNA transcripts.

9q31, rs10820405, LINC01492: rs10820405 is located in a non-coding RNA *LINC01492*. The status of this long intergenic non-protein coding RNA is verified, but there is nothing known about its function.

10q24, rs2295786, *SH3PXD2A*: rs2295786 is located intergenic between *SH3PXD2A* and *OBCF1*. *SH3PXD2A* encodes the SH3 and PX domain-containing protein 2A or Adapter protein *TKS5*, and has been shown to play an essential role in various malignancies including schwannomas.(PMID 27723760) *TKS5* interacts with Src tyrosine kinase to promote tumor growth and the formation of invadopodia resulting in degradation of extracellular matrix and invasion of cancer cells into surrounding tissue in malignancies including glioma.(PMID 26446840, 27802184, 27789576) *SH3PXD2A* has further been implicated in axonal guidance by growth cone invadosomes (PMID 25564649), neural crest migration (PMID 25259869), macrophage invasion (PMID 22021214), and the migration of microglia.(PMID 22873355)

12p12, rs7304841, PDE3A: rs7304841 is located in an intron of *PDE3A*. *PDE3A* encodes Phosphodiesterase 3A, a member of the cGMP-inhibited cyclic nucleotide phosphodiesterase family. *PDE3A* mRNA is enriched in blood vessels, heart, megakaryocytes, and oocytes.(PMID 7706458) *PDE3A* is activated by *PKC* phosphorylation on Ser(312), Ser(428), Ser(438), Ser(465), and Ser(492).(PMID 19261611) *PDE3A* is a component of the thrombin signaling pathway in platelets. Thrombin raises *PDE3A* activity through phosphorylation/activation of *PDE3A* and activated *PDE3A* participates in regulating intracellular cAMP contents through acceleration of cAMP hydrolysis.(PMID 17392505) In addition to being subject to phosphorylation-induced activation, *PDE3A* is also directly inhibited by cGMP-mediated competition for cAMP binding to the active site. This effect of cGMP can represent a significant mode of regulation of *PDE3A* in cells expressing this enzyme.(PMID 10605731) For example, incubation of *PDE3A*-expressing cells with guanylyl cyclase-activating organic nitrates, nitric oxide donors, or natriuretic peptides, results in a significant increase in both cGMP and cAMP and a synergistic increase in cAMP when these agents are combined with activators of adenylyl cyclases.(PMID 1964912, 1851703)

12q24, rs35436, TBX3: rs35436 is located in an intergenic region upstream of *TBX3*. *TBX3* encodes T-box transcription factor 3. *TBX3* is a transcriptional repressor and is thought to play a role in the

anterior/posterior axis of the tetrapod forelimb. Recently, heart and conduction system defects have also been described in mice and humans with abnormal *Tbx3* (mice) and *TBX3* (humans) function.(PMID 18467625) Germline deletion of *Tbx3* in mice results in embryonic lethality with heart, limb, and mammary defects.(PMID 22203979,12668638) *Tbx3* also regulates pluripotency and cell fate in early development.(PMID 20139965,24319661) *TBX3* transcriptional repression controls expression of cell proliferation and senescence factors.(PMID 11748239) These studies highlight the important pleiotropic molecular functions of *TBX3*.

13q14, rs9526212, LRCH1: rs9526212 is located intronic in *LRCH1*. *LRCH1* encodes Leucine Rich Repeats And Calponin Homology Domain Containing 1. *LRCH1* competes with Cdc42 for interaction with DOCK8 and restrains T cell migration.(PMID 28028151) In response to chemokine stimulation, *PKCα* phosphorylates *DOCK8* at its three serine sites, promoting *DOCK8* separation from *LRCH1* and translocation to the leading edge to guide T cell migration.

15q26, rs4932370, FURIN-FES: rs4932370 is located in an intergenic region upstream of *FURIN*. *FURIN* encodes the Furin protein. *FURIN* is the most studied mammalian proprotein convertase. This ubiquitously expressed enzyme is located mainly in the trans-Golgi network (TGN) of the secretory pathway. In addition, *FURIN* cycles between TGN and the cell surface via the endosomal system, and a proportion of it is secreted to the extracellular space.(PMID 12360192) Because *FURIN* is widely expressed, its activity regulates the maturation of numerous precursor proteins. Its substrates include various growth factors and their receptors, enzymes, hormones, cytokines, serum proteins, as well as extracellular matrix proteins. In addition to *FURIN's* crucial function in the maintenance of cellular homoeostasis, it is also involved in the pathogenesis of several diseases. For example, increased *FURIN* levels are associated with aggressive cancers and metastatic activity, and it is highly expressed in chronically inflamed tissues in rheumatoid arthritis (RA) and atherosclerosis.(PMID 21889147, 22605541)

FES encodes FES Proto-Oncogene, Tyrosine Kinase. It has tyrosine-specific protein kinase activity and this activity is required for maintenance of cellular transformation. Based on its chromosomal location *FES* has been linked to a specific translocation event identified in patients with acute promyelocytic leukemia but it is also involved in normal hematopoiesis as well as growth factor and cytokine receptor signaling.(PMID 12871378 ,15003822) *FES* transduces inductive signals for terminal macrophage and granulocyte differentiation, and this biological activity is mediated through the activation of lineage-specific transcription factors.(PMID 15003822)

17p13, rs11867415, PRPF8: rs11867415 is located intronic in *PRPF8*. *PRPF8* encodes Pre-mRNA Processing Factor 8. The large ~280-kDa U5 snRNP protein is central to the dynamics of spliceosome assembly.(PMID 15840809) It not only establishes direct contacts in the RNA substrate with the 5' splice site, the branch point and the polypyrimidine tract in the 3' splice site, but also engages the U5 and U6 snRNAs.(PMID 26392272, 24968230) Mutations in human *PRPF8* that disrupt these interactions, affecting spliceosome assembly and function, are found in autosomal dominant retinitis pigmentosa, a variable-onset hereditary disease that results in a progressively decreasing field of vision due to degeneration of rods and cones. Loss-of-function mutants of human *PRPF8* delay the assembly of spliceosome components on pre-mRNA, and impair the splicing of 9 % of tested genes.(PMID 11468273)

19p13, rs2229383, ILF3-SLC44A2: rs2229383 is an exonic, synonymous variant in *ILF3*. *ILF3* encodes Interleukin Enhancer Binding Factor 3, which regulates gene expression and stabilizes mRNAs through interactions with various other molecules. *ILF3* forms a heterodimer with ILF2, which is required for T-cell expression of interleukin 2 and interleukin 12.(PMID 20051514, 15817156) The complex is known to negatively regulate microRNA processing (PMID 19398578) and in particular myogenic microRNA processing.(PMID 25918244) The upstream *SLC44A2* gene encodes Solute Carrier Family 44 Member 2 which is expressed in human brain microvascular endothelial cells.(PMID 26746385) Isoform 1 of this protein displays choline transporter activity. *SLC44A2* harbors the neutrophil alloantigen HNA-3a (5b) in its first extracellular loop (R154Q).(PMID 20040764)

19p13, rs8103309, SMARCA4-LDLR: rs8103309 is located intergenic between *SMARCA4* and *LDLR*. *SMARCA4* encodes SWI/SNF Related, Matrix Associated, Actin Dependent Regulator Of Chromatin,

Subfamily A, Member 4. The encoded protein is part of the large ATP-dependent chromatin remodeling complex SNF/SWI, which is required for transcriptional activation of genes normally repressed by chromatin. *SMARCA4* is a target gene of the *BACH1* transcription factor according to ChIP-seq analysis in HEK 293 cells.(PMID 21555518) It has been suggested that *SMARCA4* and *SMARCA2* integrate various proinflammatory cues into cell adhesion molecule transactivation in endothelial injury.(PMID 23963727) Additionally, the interaction of *RUNX1* with *SMARCA4* and *INI1* controls hematopoietic-specific gene expression.(PMID 20506188)

LDLR encodes the low density lipoprotein receptor. LDL is cleared from plasma by binding to the cell-surface *LDLR* and is internalized by *LDLR*-mediated endocytosis.(PMID 25222343) After internalization, the receptors dissociate from their ligands upon exposure to lower pH in endosomes. (PMID 6299572) *PCSK9* has been shown to play a major role in regulating plasma LDL cholesterol levels through its ability to mediate intracellular degradation of the LDLR.

Lead SNP	Locus	Phenotype	p-value in Europeans-only analysis	p-value in East Asians-only analysis
rs10820405	LINC01492	LAS	4.51E-08	0.263
rs146390073	RGS7	CES	2.20E-08	NA*
rs7610618	TM4SF4-TM4SF1	LAS	1.44E-08	0.3456
rs635634	ABO	AIS	9.18E-09	0.9904
rs34311906	ANK2	AIS	1.07E-08	0.4078
rs9526212	LRCH1	AS	1.78E-08	0.416

Supplementary Table 5 Population specific associations with stroke. Shown are loci reaching genome-wide significant association ($p < 5.0x10^{-8}$) in the Europeans-only meta-analysis while showing no association in the East Asian ancestry meta-analysis ($p > 0.05$ or MAF < 0.01). * MAF < 0.01

Supplementary Table 6 Variance explained by the 32 lead SNPs. Shown are the lead SNPs of the 32 risk loci for stroke and the phenotypic variance explained as estimated by the method of So et al. Variances are given for the Europeans-only and the East Asian-only meta-analysis. If a SNP was not available in the analysis, variance explained was set to zero.

Enclosed electronic excel file

Supplementary Table 7 Results from the Gene-based tests using VEGAS2. Data were analyzed for each ethnicity and a meta-analysis was calculated using Stouffer's Z. Genome-wide results are displayed in bold ($p<2.02E-6$ for Bonferroni correction for the number of genes).

Enclosed electronic excel file

rsID	Chr	Gene(s)	Location relative to gene	Risk allele/ reference allele	Risk allele frequency, %	Phenotype*	Analysis	OR	95% CI	P-value	log10 (BF)
rs6695915	1p34	***PTPRF***	Intronic	A/G	86	AS	TRANS	1.07	1.04-1.10	4.25E-07	4.94§
rs638704	1q24	***PRRX1***	Intergenic	C/T	43	CES	TRANS	1.09	1.06-1.13	1.47E-07	5.41
rs188186531	2q33	***ICA1L-WDR12***	Intronic	A/T	89	SVS	TRANS	1.21	1.12-1.30	3.69E-07	5.11
rs10017904	4q26	***CAMK2D***	Intronic	A/G	14	SVS	TRANS	1.17	1.10-1.25	7.22E-07	4.80§
rs4444878	4q35	***F11***	Intronic	A/C	39	CES	TRANS	1.10	1.06-1.14	5.17E-08	5.80
rs762624	6p21	***CDKN1A***	Intronic	A/C	63	AIS	TRANS	1.05	1.03-1.07	2.36E-07	5.30
rs35276016	6p22	***C6orf62***	Intergenic	T/C	8	AS	EUR	1.10	1.06-1.14	1.30E-07	5.56
rs56393506	6q25	***LPA***	Intergenic	T/C	16	LAS	TRANS	1.17	1.10-1.24	1.33E-07	5.57
rs4727833	7q31	***CAV1/2***	3'-UTR	G/C	51	CES	TRANS	1.09	1.06-1.13	2.45E-07	5.28
rs16939239	8q21	***Chr8q21***	Intergenic	A/G	12	CES	TRANS	1.15	1.09-1.22	4.08E-07	5.24
rs11596587	10q22	***HK1***	Intronic	T/C	10	CES	TRANS	1.22	1.14-1.31	7.58E-08	5.69
rs74154533	10q24	***NEURL1***	Intronic	G/A	18	CES	TRANS	1.12	1.07-1.17	6.08E-07	5.27
rs60401382	10q26	***HTRA1***	Intronic	C/T	70	AS	TRANS	1.05	1.03-1.07	6.76E-08	5.88
rs360139	11p15	***SWAP70***	Downstream	G/A	56	AIS	TRANS	1.05	1.03-1.07	1.57E-07	5.41
rs1564454	13q32	***FARP1***	Intronic	G/A	42	LAS	TRANS	1.11	1.07-1.16	1.22E-07	5.71
rs9515201	13q34	***COL4A2***	Intronic	A/C	29	SVS	TRANS	1.11	1.07-1.16	1.05E-07	5.33
rs9521634	13q34	***COL4A1***	Intronic	C/T	34	AS	TRANS	1.04	1.03-1.06	1.42E-07	5.47
rs339800	13q21	***DACH1***	Intergenic	T/C	28	AS	TRANS	1.06	1.04-1.08	7.11E-08	5.87
rs12442374	15q21	***NEDD4***	Intergenic	G/C	14	AS	TRANS	1.06	1.04-1.09	3.70E-07	5.15
rs8028726	15q26	***Chr15q26***	Intergenic	T/G	44	AIS	TRANS	1.04	1.03-1.06	4.37E-07	5.15
rs2632512	17q22	***RNF43***	Intronic	T/C	20	AS	TRANS	1.06	1.04-1.08	2.21E-07	5.36

Supplementary Table 8 Subthreshold loci reaching the more liberal threshold for suggestive evidence of association in the transethnic meta-analysis (MANTRA log(BF) > 5). * denotes phenotype reaching the lowest p-value in fixed effects meta-analyses. § $p<5 \times 10^{-6}$ in the fixed effects analysis. Chr, chromosome; TRANS, MANTRA transethnic meta-analysis; EUR, Europeans-only fixed-effects meta-analysis; OR, odds ratio; CI, confidence interval; BF, Bayes factor; NA, not assessed because of low allele frequency or poor imputation quality in non-European ethnicities.

		Transethnic meta-analysis										Europeans only meta-analysis				
SNP	**locus**	**AS**		**AIS**		**LAS**		**CES**		**SVS**		**AS**	**AIS**	**LAS**	**CES**	**SVS**
		MANTRA (BF)	**Fixed effects p-value**	**MANTRA (BF)**	**Fixed effects p-value**	**MANTRA (BF)**	**Fixed effects p-value**	**MANTRA (BF)**	**Fixed effects p-value**	**MANTRA (BF)**	**Fixed effects p-value**	**p-value**	**p-value**	**p-value**	**p-value**	**p-value**
rs880315	CASZ1	**8.09489**	**3.62E-10**	**6.86767**	**5.51E-09**	-0.42721	4.18E-01	0.48014	1.64E-02	4.30326	2.59E-06	6.55E-08	9.99E-07	9.70E-01	1.07E-01	1.03E-04
rs12037987	WNT2B	**6.33614**	**2.73E-08**	4.47639	2.16E-06	-0.42041	5.67E-01	1.402	3.45E-03	1.22482	5.13E-03	9.39E-07	1.52E-04	7.52E-01	2.68E-02	5.48E-02
rs12124533	TSPAN2	-0.23427	1.73E-01	-0.12896	9.77E-02	**6.60016**	**1.22E-08**	-0.39256	3.28E-01	-0.19473	2.94E-01	1.88E-01	9.75E-02	6.73E-08	3.27E-01	8.17E-01
rs1052053	PMF1 -SEMA4A	**11.92471**	**2.70E-14**	**9.02067**	**4.48E-11**	1.41473	2.97E-03	2.74953	1.22E-04	4.54696	1.17E-06	**2.25E-12**	**5.26E-09**	1.24E-02	6.69E-04	2.67E-04
rs146390073	RGS7	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	9.68E-05	9.18E-05	4.22E-03	**2.20E-08**	4.76E-01
rs12476527	KCNK3	**6.47247**	6.44E-08	4.96502	1.30E-06	0.14805	6.63E-02	-0.22283	2.40E-01	2.7522	1.71E-04	3.71E-04	2.96E-03	3.35E-01	4.75E-01	1.49E-02
rs7610618	TM4SF4-TM4SF1	-0.5132	4.09E-01	-0.15424	3.02E-01	NA	NA	-0.61247	1.79E-01	0.24181	8.57E-02	1.88E-01	6.62E-02	**1.44E-08**	8.35E-01	4.63E-02
rs13143308	PITX2	**12.72695**	**1.69E-15**	**13.41447**	**1.11E-15**	-1.19688	9.89E-01	**45.10357**	**1.86E-47**	-0.53951	5.37E-01	**1.61E-13**	**4.88E-14**	5.34E-01	**5.19E-41**	9.96E-01
rs34311906	ANK2	4.82127	9.66E-07	5.67196	1.19E-07	0.55937	2.61E-02	0.61442	3.59E-02	0.59037	1.89E-02	3.64E-07	**1.07E-08**	5.37E-03	7.13E-03	2.94E-02
rs17612742	EDNRA	0.96463	9.26E-03	1.80238	1.88E-04	**9.47422**	**1.46E-11**	-0.55219	9.52E-01	-0.3206	2.01E-01	4.59E-01	3.70E-02	1.05E-06	7.71E-01	3.70E-01
rs6825454	FGA	**7.10875**	**2.62E-09**	**7.53002**	**7.43E-10**	2.59115	1.61E-04	3.10296	3.11E-05	-0.25554	3.04E-01	1.78E-07	9.23E-08	8.48E-04	7.32E-05	9.83E-01
rs11957829	LOC100505841	**6.47058**	**1.62E-08**	**6.67074**	**7.51E-09**	-0.16806	2.56E-01	-0.60635	8.23E-01	5.1146	3.92E-07	1.51E-06	7.51E-07	6.99E-01	8.16E-01	1.46E-04
rs6891174	NKX2-5	0.2037	2.00E-02	0.8818	1.33E-02	0.21853	7.98E-02	**6.9559**	**5.82E-09**	-0.32097	4.46E-01	8.16E-02	5.81E-02	7.36E-02	3.19E-07	2.34E-01
rs4959130	FOXF2	**7.51576**	**1.42E-09**	**7.31532**	**2.83E-09**	0.06236	7.40E-02	0.58771	3.56E-02	NA	NA	**1.13E-09**	**1.87E-09**	9.18E-02	3.16E-02	3.05E-06
rs16896398	SLC22A7-ZNF318	**6.59891**	**1.30E-08**	4.16814	2.42E-06	0.05632	6.95E-02	1.31094	5.10E-03	1.06055	1.18E-02	8.62E-06	7.17E-04	7.94E-01	3.95E-03	5.94E-01
rs2107595	HDAC9-TWIST1	**11.72902**	**4.86E-14**	**11.58508**	**9.25E-14**	**12.99407**	**3.65E-15**	-0.41059	3.12E-01	0.5171	2.46E-02	**3.59E-11**	**2.33E-11**	**1.44E-13**	9.86E-02	6.63E-02
rs42039	CDK6	**6.84288**	**7.32E-09**	**6.83974**	**6.55E-09**	0.26155	3.97E-02	1.24424	5.46E-03	0.5482	2.91E-02	1.65E-07	2.18E-07	1.10E-01	2.16E-02	2.22E-02
rs7859727	Chr9p21	**8.01097**	**4.22E-10**	**7.55562**	**1.05E-09**	3.03657	4.46E-05	-0.34512	4.21E-01	1.89019	9.91E-04	7.18E-08	1.76E-07	6.42E-05	6.07E-01	2.32E-02
rs10820405	LINC01492	-0.08706	1.99E-01	-0.07438	1.82E-01	4.74007	1.86E-06	-0.40161	3.21E-01	-1.05236	7.31E-01	1.00E-01	9.28E-02	**4.51E-08**	1.53E-01	8.69E-01
rs635634	ABO	4.23964	4.40E-06	4.98759	1.79E-06	1.24591	6.93E-03	4.98822	6.21E-07	-0.40477	9.12E-01	6.03E-08	**9.18E-09**	3.90E-04	3.31E-07	4.30E-01
rs2295786	SH3PXD2A	**8.335**	1.80E-10	5.35464	2.00E-07	0.82757	5.06E-03	1.08368	6.78E-03	4.14845	4.18E-06	1.43E-07	8.19E-05	2.72E-02	4.97E-03	2.51E-03
rs2005108	MMP12	5.92423	6.43E-08	**6.12069**	**3.33E-08**	5.38734	1.69E-07	0.99334	7.91E-03	NA	NA	3.37E-07	1.74E-07	1.61E-06	5.26E-03	7.29E-01
rs72983521	MMP12 *	2.72415	1.17E-04	3.11816	3.96E-05	**6.05514**	**3.38E-08**	-0.2067	2.46E-01	NA	NA	6.42E-05	1.72E-05	**4.82E-08**	1.96E-01	2.73E-01
rs7304841	PDE3A	5.45988	1.60E-07	5.87141	**4.93E-08**	0.65851	1.96E-02	0.59629	3.43E-02	0.90914	8.42E-03	1.40E-03	5.80E-04	8.78E-01	1.36E-01	3.78E-01

rs3184504	SH2B3	**9.60311**	**8.63E-12**	**12.04062**	**2.17E-14**	3.80111	4.17E-06	1.86958	1.24E-03	3.98372	6.36E-06	**5.89E-12**	**1.23E-14**	3.72E-05	2.46E-03	1.78E-05
rs35436	TBX3	**6.29274**	**2.87E-08**	**6.05786**	**3.21E-08**	0.2817	6.14E-02	1.75669	1.36E-03	2.49468	2.44E-04	3.26E-04	4.85E-04	1.70E-01	1.82E-02	7.55E-02
rs9526212	LRCH1	**7.97154**	**5.03E-10**	**7.7099**	**9.19E-10**	2.08625	7.67E-04	0.23922	8.08E-02	-0.01014	5.09E-02	**1.78E-08**	**3.56E-08**	7.31E-04	6.83E-02	6.13E-02
rs4932370	FURIN-FES	5.14661	3.12E-07	**6.05016**	**2.88E-08**	2.19732	3.36E-04	1.41818	4.07E-03	-0.43993	3.32E-01	1.15E-05	6.32E-07	2.97E-04	2.32E-03	4.46E-01
rs12932445	ZFHX3	5.27628	2.23E-07	4.49034	1.77E-06	0.67441	2.26E-02	**15.48565**	**6.86E-18**	-0.25885	2.17E-01	4.99E-06	4.67E-05	1.46E-02	**6.88E-13**	9.88E-01
rs12445022	ZCCHC14	**8.57641**	**1.05E-10**	**8.49181**	**1.28E-10**	1.0356	8.61E-03	-1.54037	9.82E-01	**6.48023**	**2.55E-09**	1.03E-07	1.81E-07	1.17E-02	9.92E-01	9.26E-08
rs11867415	PRPF8	3.91513	4.50E-06	**6.05679**	**4.81E-08**	1.24755	4.77E-03	0.12259	1.00E-01	-0.26081	2.26E-02	1.75E-04	6.58E-07	1.87E-02	5.68E-02	3.01E-01
rs2229383	ILF3-SLC44A2	5.47686	1.38E-07	**6.02123**	**4.72E-08**	2.25928	4.70E-04	1.78543	8.50E-04	-0.26099	3.51E-01	8.67E-07	3.71E-07	3.40E-03	9.26E-03	7.98E-01
rs8103309	SMARCA4-LDLR	5.85534	**3.40E-08**	5.76797	8.35E-08	2.75608	8.53E-05	1.52959	2.64E-03	-0.0932	2.11E-01	3.70E-07	1.07E-06	5.74E-04	1.27E-03	8.33E-01

Supplementary Table 9 Association results for the 32 genome-wide significant loci in AS, AIS and AIS subtypes. Displayed are the MANTRA log(Bayes' factor. BF) and fixed effects p-values from the transethnic meta-analysis and the Europeans-only meta-analysis. Associations reaching genome-wide significance (BF > 6 and p-values $<5.0 \times 10^{-8}$) are shown in bold. p-values $<5.0 \times 10^{-2}$ are shown in blue.* the lead SNP of the MMP12 locus in AIS and LAS are in LD (r^2=0.54).

	Chr	Locus	Position of segment	No. of SNPs in segment	Posterior Probability			
					Model 1	Model 1	Model 3	Model 4
LAS/SVS	12q24	SH2B3	110,336,875-113,261,104	3,589	6.87E-04	6.02E-04	**0.969087**	0.00143664
LAS/CES	9q34	ABO	135,298,917-137,027,547	5,074	2.15E-04	1.97E-04	**0.995321**	0.00273861

Supplementary Table 10 Shared genetic influences of individual loci on ischemic stroke subtypes. Shown are overlapping signals for LAS/SVS and LAS/CES with a posterior probability > 0.9 for model 3, pointing to a shared genetic signal at the specified genomic segment. gwas-pw estimates the probability that a given genomic region contains a genetic variant that influences the first trait (model 1), contains a genetic variant that influences the second trait (model 2), contains a genetic variant that influences both traits (model 3), or contains both a genetic variant that influences the first trait and a separate genetic variant that influences the second trait (model 4).

Supplementary Table 11 Results of the conditional analysis (GCTA-COJO) in the European sample. Shown are the 2-SNP or 3-SNP solutions for each lead SNP after conditioning on the lead SNP in Europeans. P-values of SNP2 and SNP3 were considered significant at p<5E-8. SVS is omitted because there were no genome-wide significant signals to investigate.

Enclosed electronic excel file

Study	Trait	Main manuscript Reference	Sample size	Data publicly available
IGEN-BP	SBP, DBP, HTN, PPP, MAP	[24]	320,251	
ENGAGE	LDL, HDL, TG	[25]	62,166	x
DIAGRAM	T2D	[26]	34,840 / 114,981	x
CHARGE_cIMT	cIMT, PLQ	[27]	31,211	
CHARGE WMH	WMH	[28]	21,079	
AFGen	AF	[29]	6,707 / 52,426	
INVENT	VTE	[30]	7,507 / 52,632	
CARDIoGRAMplusC4D	CAD	[31]	60,081 / 123,504	x

Supplementary Table 12 Overview of studies with available summary statistics from related vascular traits used for the look-ups and LD score regression analyses. Data were obtained from the respective consortia or downloaded from the following URLs: for blood lipids: http://diagram-consortium.org/2015_ENGAGE_1KG/; for T2D: http://diagram-consortium.org/downloads.html; Data on coronary artery disease have been contributed by CARDIoGRAMplusC4D investigators and have been downloaded from www.CARDIOGRAMPLUSC4D.ORG.

Supplementary Table 13 Results from look-ups of the 32 genome-wide significant loci for stroke in published GWAS data from related phenotypes. Column D specifies the index SNPs of the non-stroke phenotype or SNPs in high LD with the index SNP (r2>0.9) with the lowest p-value in the respective non-stroke phenotype. Index SNPs or proxy SNPs reaching a p-value p<1.30 x 10-4 (0.05/32 loci/12 related vascular traits) in the respective related phenotype are shown. Index SNPs and proxy SNPs reaching genome-wide significance are marked by an asterisk in column G. Column F specifies the r2 between the index SNP and the lead SNP in stroke.

Enclosed electronic excel file

Phenotype 1	Phenotype 2	Number of SNPs	beta	SE	p-value
Venous Thrombo-embolism	AS	9	0.06	0.01	**3.10E-05**
	AIS	9	0.07	0.01	**1.46E-06**
	LAS	9	0.17	0.04	**2.37E-06**
	CES	9	0.16	0.03	**5.54E-08**
	SVS	9	-0.04	0.03	2.15E-01
Diastolic Blood Pressure	AS	41	0.05	0.00	**3.60E-26**
	AIS	41	0.06	0.01	**2.44E-27**
	LAS	41	0.07	0.01	**6.02E-07**
	CES	41	0.05	0.01	**2.31E-06**
	SVS	41	0.05	0.01	**1.50E-04**
Systolic Blood Pressure	AS	37	0.04	0.00	**2.38E-30**
	AIS	37	0.04	0.00	**1.31E-31**
	LAS	37	0.05	0.01	**5.11E-09**
	CES	37	0.03	0.01	**2.37E-06**
	SVS	37	0.04	0.01	**5.50E-07**
Mean Arterial Pressure	AS	30	0.06	0.01	**1.54E-22**
	AIS	30	0.06	0.01	**9.30E-23**
	LAS	30	0.10	0.02	**1.95E-10**
	CES	30	0.04	0.01	**4.84E-04**
	SVS	30	0.06	0.01	**1.59E-05**
Pulse Pressure	AS	17	0.06	0.01	**7.15E-12**
	AIS	17	0.06	0.01	**1.21E-10**
	LAS	17	0.12	0.02	**2.02E-08**
	CES	17	0.04	0.02	1.49E-02
	SVS	17	0.05	0.02	7.81E-03
Hypertension	AS	13	0.17	0.03	**1.71E-08**
	AIS	13	0.15	0.03	**2.18E-06**
	LAS	13	0.13	0.08	9.68E-02
	CES	13	0.17	0.06	5.79E-03
	SVS	13	0.08	0.07	2.60E-01
HDL levels	AS	71	-0.05	0.02	6.86E-02
	AIS	71	-0.05	0.03	4.56E-02
	LAS	71	-0.15	0.07	2.79E-02
	CES	71	-0.03	0.05	6.34E-01
	SVS	71	-0.19	0.06	**2.10E-03**
LDL levels	AS	53	0.05	0.02	5.90E-02
	AIS	53	0.04	0.03	1.52E-01
	LAS	53	0.19	0.07	5.69E-03
	CES	53	-0.06	0.05	2.27E-01
	SVS	53	0.04	0.06	5.07E-01
Triglyceride levels	AS	38	0.01	0.03	7.44E-01
	AIS	38	0.01	0.03	7.67E-01
	LAS	38	0.08	0.08	3.29E-01
	CES	38	-0.09	0.07	1.75E-01
	SVS	38	0.18	0.08	1.79E-02
T2 Diabetes	AS	38	0.08	0.02	**1.11E-06**
	AIS	38	0.09	0.02	**2.07E-07**
	LAS	38	0.22	0.04	**1.54E-07**
	CES	38	0.04	0.03	2.21E-01
	SVS	38	0.17	0.04	**2.09E-05**

Coronary Artery Disease	**AS**	58	0.16	0.02	**9.78E-20**
	AIS	58	0.17	0.02	**4.04E-19**
	LAS	58	0.37	0.05	**8.51E-16**
	CES	58	0.13	0.04	**6.22E-04**
	SVS	58	0.08	0.04	7.62E-02

Supplementary Table 14 Results of the weighted genetic risk score (wGRS) analysis in related vascular traits**.** For each of the related traits, a wGRS was constructed using the indicated number of SNPs and tested for association in the respective stroke phenotype. Given are the effect size beta, the standard error and the p-value. P-values below p < 5.6 x 10-3 correcting for 9 independent phenotypes are shown in bold.

Supplementary Table 15 MR-Egger regression and comparison with Inverse-Variance Weighted (IVW) estimates, for vascular wGRS showing a significant association with stroke risk. IVW estimates are derived from a fixed effects analysis using the GTX software (**Methods**); for the intercept of the MR-Egger analysis (Egger_intercept, **Methods**) we used a significance threshold of P<0.05. effect estimates are given per unit increase in the wGRS; CI: confidence interval; OR: odds ratio

*The MR-Egger intercept estimate was nominally significant (p=0.015) only for the association between the SBP wGRS and AS, and this was no longer the case after removing 6 of 37 SNPs that appeared as outliers on the leave-one-out plot (Methods), leading to causal estimates in broad agreement across regression techniques, with larger standard errors using the MR-Egger method as is typically the case (www.biorxiv.org/content/biorxiv/early/2017/07/05/159442.full.pdf and PMID: 26050253, 28527048). The causal estimates obtained by the weighted median approach (PMID: 27061298) are also in broad agreement with those from the IVW and the MR-Egger (beta ± standard error: 0.032 ± 0.005, OR [95%CI]: 1.03 [1.02-1.04], p=9.48x10-10)

Enclosed electronic excel file

Phenotype 1	Phenotype 2	European ancestry			East Asian ancestry		
		R(g)	(SE_R(g))	p-value	R(g)	(SE_R(g))	p-value
Venous Thrombo-embolism	AS	0.2815	0.1308	3.13E-02	NA	NA	NA
	AIS	0.2141	0.1253	8.77E-02	NA	NA	NA
	LAS	-0.0934	0.4442	8.34E-01	NA	NA	NA
	CES	0.1875	0.1615	2.46E-01	NA	NA	NA
	SVS	-0.1232	0.2479	6.19E-01	NA	NA	NA
Diastolic Blood Pressure	AS	0.3593	0.1051	**6.00E-04**	NA	NA	NA
	AIS	0.3114	0.1007	**2.00E-03**	0.4895	0.1036	**2.30E-06**
	LAS	0.3308	0.2255	1.42E-01	0.5971	0.2601	2.17E-02
	CES	0.1016	0.1162	3.82E-01	-0.2357	0.327	4.71E-01
	SVS	0.3112	0.1861	9.46E-02	0.3502	0.1352	9.60E-03
Systolic Blood Pressure	AS	0.3799	0.0895	**2.18E-05**	NA	NA	NA
	AIS	0.3387	0.0855	**6.74E-05**	0.5254	0.0946	**2.80E-08**
	LAS	0.6067	0.2345	9.70E-03	0.6864	0.2727	1.21E-02
	CES	0.1827	0.1161	1.16E-01	0.0227	0.2746	9.34E-01
	SVS	0.3533	0.1626	2.98E-02	0.3953	0.1269	**1.80E-03**
Mean Arterial Pressure	AS	0.3929	0.1001	**8.73E-05**	NA	NA	NA
	AIS	0.3404	0.0948	**3.00E-04**	0.5159	0.0979	**1.40E-07**
	LAS	0.4908	0.2264	3.02E-02	0.6494	0.2642	1.40E-02
	CES	0.1535	0.1145	1.80E-01	-0.1207	0.2871	6.74E-01
	SVS	0.3558	0.1817	5.02E-02	0.3702	0.1287	**4.00E-03**
Pulse Pressure	AS	0.3202	0.0884	**3.00E-04**	NA	NA	NA
	AIS	0.294	0.0868	**7.00E-04**	0.4081	0.1011	**5.40E-05**
	LAS	0.6341	0.2545	1.27E-02	0.5698	0.2681	3.36E-02
	CES	0.1974	0.1339	1.41E-01	0.2741	0.3385	4.18E-01
	SVS	0.2589	0.1479	8.01E-02	0.3162	0.1356	1.97E-02
Hypertension	AS	0.3138	0.1402	2.52E-02	NA	NA	NA
	AIS	0.2654	0.1325	4.58E-02	0.6235	0.1501	**3.26E-05**
	LAS	0.6587	0.3503	6.00E-02	0.5691	0.2963	5.48E-01
	CES	0.0984	0.2064	6.33E-01	-0.3895	0.479	4.61E-01
	SVS	0.4589	0.2542	7.11E-02	0.4170	0.1978	3.50E-02
HDL levels	AS	**-0.2347**	**0.0716**	**1.00E-03**	NA	NA	NA
	AIS	**-0.2337**	**0.0675**	**5.00E-03**	-0.0155	0.1262	9.02E-01
	LAS	-0.7982	0.4177	5.61E-02	-0.084	0.1492	5.74E-01
	CES	-0.0596	0.0991	5.47E-01	0.1041	0.2429	6.68E-01
	SVS	**-0.2629**	**0.1269**	3.80E-02	0.0373	0.1537	8.09E-01
LDL levels	AS	0.0484	0.0773	5.31E-01	NA	NA	NA
	AIS	0.0817	0.0818	3.18E-01	-0.0925	0.1099	4.00E-01
	LAS	0.2710	0.2619	3.01E-01	-0.0404	0.1986	8.39E-01
	CES	-0.0815	0.1126	4.50E-01	0.0255	0.2442	9.17E-01
	SVS	-0.0905	0.1732	6.01E-01	0.0572	0.138	6.79E-01
Triglyceride levels	AS	**0.1502**	**0.0545**	5.90E-03	NA	NA	NA
	AIS	**0.1612**	**0.0538**	**2.70E-03**	**0.1899**	**0.0749**	1.12E-02
	LAS	0.6480	0.3687	7.92E-02	**0.2503**	**0.1122**	2.57E-02
	CES	0.0265	0.0684	7.00E-01	0.2468	0.1773	1.64E-01
	SVS	0.0665	0.1064	5.33E-01	0.1956	0.11	7.53E-02
T2 Diabetes	AS	**0.2865**	**0.0663**	**1.50E-05**	NA	NA	NA
	AIS	**0.2721**	**0.0668**	**4.70E-05**	**0.6925**	**0.0505**	**7.64E-43**
	LAS	0.6356	0.3443	6.52E-02	**0.3638**	**0.1142**	**1.40E-03**
	CES	-0.0016	0.1050	9.88E-01	0.1627	0.1711	3.42E-01
	SVS	**0.3186**	**0.1526**	3.74E-02	**0.6855**	**0.1032**	**3.15E-11**
Coronary Artery Disease	AS	**0.5209**	**0.0522**	**1.82E-23**	NA	NA	NA
	AIS	**0.5132**	**0.0535**	**8.80E-22**	NA	NA	NA
	LAS	**1.112***	**0.4964**	2.51E-02	NA	NA	NA
	CES	**0.2925**	**0.0632**	**3.66E-06**	NA	NA	NA
	SVS	**0.4446**	**0.1123**	**7.47E-05**	NA	NA	NA

Supplementary Table 16 Shared genetic contribution between stroke and related vascular traits as determined by LD scores regression. Significant correlations are shown in bold. R(g), genetic correlation, SE, standard error. P-values below p < 5.6 x 10-3 correcting for 9 independent phenotypes are shown in bold.

Supplementary Table 17 Results of the epigwas analysis. Shown is the enrichment p-value of GWAS results in specific tissues. EpiGWAS was used to calculate enrichment p-values for H3K4me1 (enhancers), H3K4me3 (promoters) and H3K9ac (active promoters)

Enclosed electronic excel file

Supplementary Table 18 Results of DEPICT pathway analysis. For each stroke subtype, SNPs with BF>5 from the trans-ethnic meta-analysis were analysed. Gene sets with a FDR<0.05 were considered significant. Columns E-N show the Z-scores of the genes in the gene set.

Enclosed electronic excel file

Supplementary Table 19 Results from the Ingenuity Pathway Analysis. Shown are enrichment p-values for the corresponding Ingenuity canonical pathway and the proteins involved in the respective pathway. P-values are derived from Fisher's exact test. FDR < 0.05 was considered significant and are displayed in bold. For The IPA Diseases and Bio Functions and for the IPA Tox Functions, p-values are given for the enrichment of specific function annotations.

Enclosed electronic excel file

Supplementary Table 20 Results from the VEGAS2 pathway analysis. Shown are pathways for each stroke subtype, the ethnicity specific p-values and the meta-analysis p-value. Pathways with FDR<0.05 were considered significant and are displayed in bold (CES only)

Enclosed electronic excel file

Supplementary Table 21 Results of the 95% credible set analysis. Results were obtained separately in European, East Asian, and African American ancestry samples. Shown is the number of SNPs in the 95% credible set (numerator) and the total number of SNPs in the analysis (denominator, r2>0.1)

Enclosed electronic excel file

Supplementary Table 22 Detailed functional and biological information on SNPs at the 32 stroke risk loci. Shown are the lead SNPs and all proxy SNPs with r^2>0.8. We show information on nearby genes, the genomic consequence (intergenic, intronic, missense, regulatory), chromatin marks, eQTLs (GRASP_v2, GTEX_v6, BIOS, BLUEPRINT, STARNET, UCLA and HGVD), meQTLS (BLUEPRINT and ARIC) and pQTLs (KORA). We also give information whether this specific SNP is included in the 95% credible set analysis and the p-value of the Riviera-beta-analysis.

Enclosed electronic excel file

Supplementary Table 23 Relation of the lead and proxy SNPs (r^2>0.8) from 32 stroke risk loci with the best cis eQTL, meQTL and pQTL from various human bio-resources, grouped per tissue or cell type. Shown is the stroke subtype showing the most significant association; for meQTL CpG probe numbers are indicated in bracket after the gene name.

Enclosed electronic excel file

Supplementary Table 24 Biological candidate gene prioritization of 149 genes located in the 32 stroke associated risk loci. For each gene we first list the biological score derived from 14 biological criteria and the overall score by including other biological information. All colored boxes have a value of 1, values of 0 signify no information or not satisfied criteria. For the genomic context, filled red boxes indicate that the criteria are satisfied. Filled blue boxes indicate significant QTL association (eQTL: gene-expression; meQTL: methylation; pQTL: protein). Filled yellow boxes indicate overlap with H3K4me3, H3K9ac and H3K4me1 peaks in cells types that showed significant enrichment in Epigwas analysis. Filled green boxes indicate significantly enriched pathways. Filled purple boxes indicate overlap with drug target genes (ATC-C: Cardiovascular; ATC-B01: Antithrombotic).

Enclosed electronic excel file

Supplementary Table 25 Results of the drug class enrichment analysis. Shown is the number of genes falling into the respective Anatomical Therapeutic Chemical (ATC) drug class together with the respective statistics for genome-wide loci (BF>6) and suggestive loci (BF>5) both with and whithout the SH2B3 locus.

Enclosed electronic excel file

Study	No. of SNPs passing QC
CHARGE	9,478,234
METASTROKE	8,940,233
SIGN	9,256,608
DECODE	7,855,222
EPIC-CVD	7,398,053
Young Lacunar DNA	7,846,740
SIFAP	8,234,135
INTERSTROKE EUR	3,984,831
HVH1	7,598,761
Glasgow	2,110,148
CADISP	9,109,502
Barcelona	8,486,260
FINLAND	7,208,625
SAHLSIS	5,816,883
MDC	5,840,041
HVH2	6,367,660
ICH	7,669,007
Biobank Japan	7,567,123
HISAYAMA	7,444,658
RACE1	7,409,565
RACE2	8,430,980
SDS	5,111,778
COMPASS	15,639,475
INTERSTROKE ASN	3,789,783
INTERSTROKE LAT	5,904,129

Supplementary Table 26 Overview of SNPs passing quality control (QC). For each study, the number of SNPs passing centralized QC are given. Number are based on the any stroke (AS) phenotype.

Supplementary Table 27 Information on the SNPs selected for the wGRS analysis. Given are the related vascular traits from which the respectzive wGRS were derived, the marker name (rs_id), the risk/other allele and the beta used as weight for the wGRS approach

Enclosed electronic excel file

2. Supplementary Figures

Supplementary Figure 1 QQ-Plots and Manhattan plots for any stroke (AS) for the transethnic fixed-effects meta-analysis (QQ-plot), the transethnic MANTRA meta-analysis (Manhattan plot) and the Europeans-only fixed effects meta-analysis (QQ-plot and Manhattan plot). For the QQ-plots, shown in black are the observed versus expected –log(p-value) distributions from both fixed effect-analyses. The red line shows the expected (null) distribution of the statistic. For the Manhattan plots, shown are the $\log_{10}$(BF) for the transethnic MANTRA analysis and the –log(p-value) for the Europeans-only analysis for each variant studied. Genomic inflation values (lambda) were estimated to be 1.174 for the trans-ethnic analysis and 1.134 for the Europeans-only analysis. The LD score regression intercept was estimated to be 1.061 for the Europeans-only analysis.

Supplementary Figure 2 QQ-Plots and Manhattan plots for any ischemic stroke (AIS) for the transethnic fixed-effects meta-analysis (QQ-plot), the transethnic MANTRA meta-analysis (Manhattan plot) and the Europeans-only fixed effects meta-analysis (QQ-plot and Manhattan plot). For the QQ-plots, shown in black are the observed versus expected –log(p-value) distributions from both fixed effect-analyses. The red line shows the expected (null) distribution of the statistic. For the Manhattan plots, shown are the $\log_{10}$(BF) for the transethnic MANTRA analysis and the –log(p-value) for the Europeans-only analysis for each variant studied. Genomic inflation values (lambda) were estimated to be 1.166 for the trans-ethnic analysis and 1.122 for the Europeans-only analysis. The LD score regression intercept was estimated to be 1.049 for the Europeans-only analysis.

Supplementary Figure 3 QQ-Plots and Manhattan plots for large artery stroke (LAS) for the transethnic fixed-effects meta-analysis (QQ-plot), the transethnic MANTRA meta-analysis (Manhattan plot) and the Europeans-only fixed effects meta-analysis (QQ-plot and Manhattan plot). For the QQ-plots, shown in black are the observed versus expected –log(p-value) distributions from both fixed effect-analyses. The red line shows the expected (null) distribution of the statistic. For the Manhattan plots, shown are the $\log_{10}$(BF) for the transethnic MANTRA analysis and the –log(p-value) for the Europeans-only analysis for each variant studied. Genomic inflation values (lambda) were estimated to be 1.112 for the trans-ethnic analysis and 1.146 for the Europeans-only analysis. The LD score regression intercept was estimated to be 1.095 for the Europeans-only analysis.

Supplementary Figure 4 QQ-Plots and Manhattan plots for cardioembolic stroke (CES) for the transethnic fixed-effects meta-analysis (QQ-plot), the transethnic MANTRA meta-analysis (Manhattan plot) and the Europeans-only fixed effects meta-analysis (QQ-plot and Manhattan plot). For the QQ-plots, shown in black are the observed versus expected –log(p-value) distributions from both fixed effect-analyses. The red line shows the expected (null) distribution of the statistic. For the Manhattan plots, shown are the $\log_{10}$(BF) for the transethnic MANTRA analysis and the –log(p-value) for the Europeans-only analysis for each variant studied. Genomic inflation values (lambda) were estimated to be 1.123 for the trans-ethnic analysis and 1.141 for the Europeans-only analysis. The LD score regression intercept was estimated to be 1.070 for the Europeans-only analysis.

Supplementary Figure 5 QQ-Plots and Manhattan plots for small vessel stroke (SVS) for the transethnic fixed-effects meta-analysis (QQ-plot), the transethnic MANTRA meta-analysis (Manhattan plot) and the Europeans-only fixed effects meta-analysis (QQ-plot and Manhattan plot). For the QQ-plots, shown in black are the observed versus expected –log(p-value) distributions from both fixed effect-analyses. The red line shows the expected (null) distribution of the statistic. For the Manhattan plots, shown are the $\log_{10}$(BF) for the transethnic MANTRA analysis and the –log(p-value)

for the Europeans-only analysis for each variant studied. Genomic inflation values (lambda) were estimated to be 1.090 for the trans-ethnic analysis and 1.127 for the Europeans-only analysis. The LD score regression intercept was estimated to be 1.079 for the Europeans-only analysis.

Supplementary Figure 6 Regional Association Plots for lead variants. (A-A') Results from the transethnic meta-analysis and (B'-F') Europeans-only meta-analysis. Shown in purple is the lead variant for the respective stroke phenotype as specified in Table 1. Shown is the region for the top signal ± 500kb. The y-axis represents the $\log_{10}$(BF) or –log(p-value) from the transethnic MANTRA analysis or Europeans-only fixed-effects meta-analysis, respectively. Variants in LD with the lead variant are shown in red (r^2>0.8), orange (r^2>0.6), green (r^2>0.4) and blue (r^2>0.2). Grey peaks represent estimated recombination rates.

Supplementary Figure 7 Forest plots for lead variants at the 32 loci reaching genome-wide significance. Shown are study names, effect sizes and 95% confidence intervals for each study contributing summary statistics to the respective variant. Effect direction is the direction of the risk allele. Also shown are meta-analysis effect sizes and confidence intervals for each ethnicity separately, where appropriate. The transethnic meta-analysis value is from the transethnic fixed-effects meta-analysis; OR: Odds Ratio, CI: confidence interval.

Supplementary Figure 8 Comparison of allele frequencies and effect sizes in Europeans and East Asians. (A) Shown are the effect allele frequencies in Europeans and East Asians. Data were drawn from the any ischemic stroke (AIS) dataset. Each symbol represents one lead SNP. (B-E) Odds Ratios in Europeans and East Asians for AIS (B), LAS (C), CES (D) and SVS (E) with respect to the minor allele.

Supplementary Figure 9 Results of the gene-based tests. Shown are Manhattan plots for the VEGAS2 gene-based tests in AS (A), AIS (B), LAS (C), CES (D) and SVS (E). Each symbol represents one tested gene. The y-axis represents the –log(p-values) from the gene-based tests. The dashed grey line corresponds to the Bonferroni corrected significance threshold of $p< 2.14 \times 10^{-6}$ (23,350 genes). Due to space restrictions, gene names are only shown in (C-E).

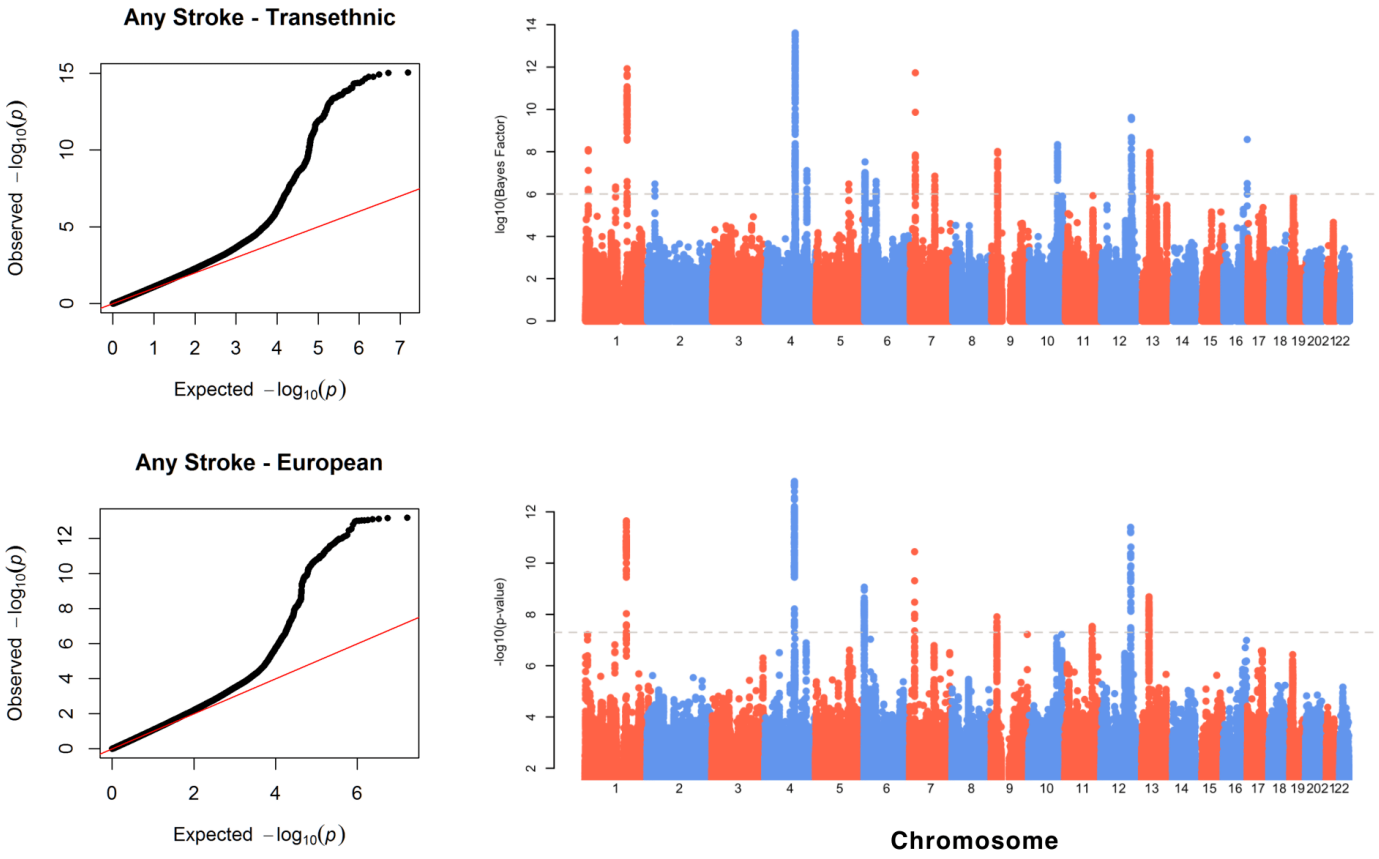
Supplementary Figure 10 Regional association plot of variants at the ICA1L-WDR12 locus. (A-C) The variant rs149163995 acts as an eQTL for multiple genes at this locus and the association is confined to the SVS phenotype (C). No clear signal is visible for LAS (A) or CES (B). Shown in purple is the lead variant rs149163995. Shown is the region for the top signal ± 500kb. The y-axis represents the $\log_{10}$(BF) from the transethnic MANTRA analysis. Variants in LD with the lead variant are shown in red (r^2>0.8), orange (r^2>0.6), green (r^2>0.4) and blue (r^2>0.2). Grey peaks represent estimated recombination rates.

Supplementary Figure 11 Results of the gwas-pw analysis. Shown are the SNP-wise results for the gwas-pw analysis for (A) the LAS-SVS analysis and (B) the LAS-CES analysis. The x-axis represents the genomic region found to be significant (PP_model 3>0.9). For each variant analysed, the posterior probability for model 3 is plotted on the y-axis. Shown are also the analysis results for each single trait in the Europeans-only analysis with p-values transformed to log10(Bayes Factors) using Wakefield's method for each SNP displayed on the y-axis. (C for the LAS-SVS analysis and D for the LAS-CES analysis). For all plots, the lead variant (purple) is the variant with the highest PP for model 3 in the SNP-wise results. Variants in LD with the lead variant are shown in red (r2>0.8), orange (r2>0.6), green (r2>0.4) and blue (r2>0.2). Grey peaks represent estimated recombination rates.

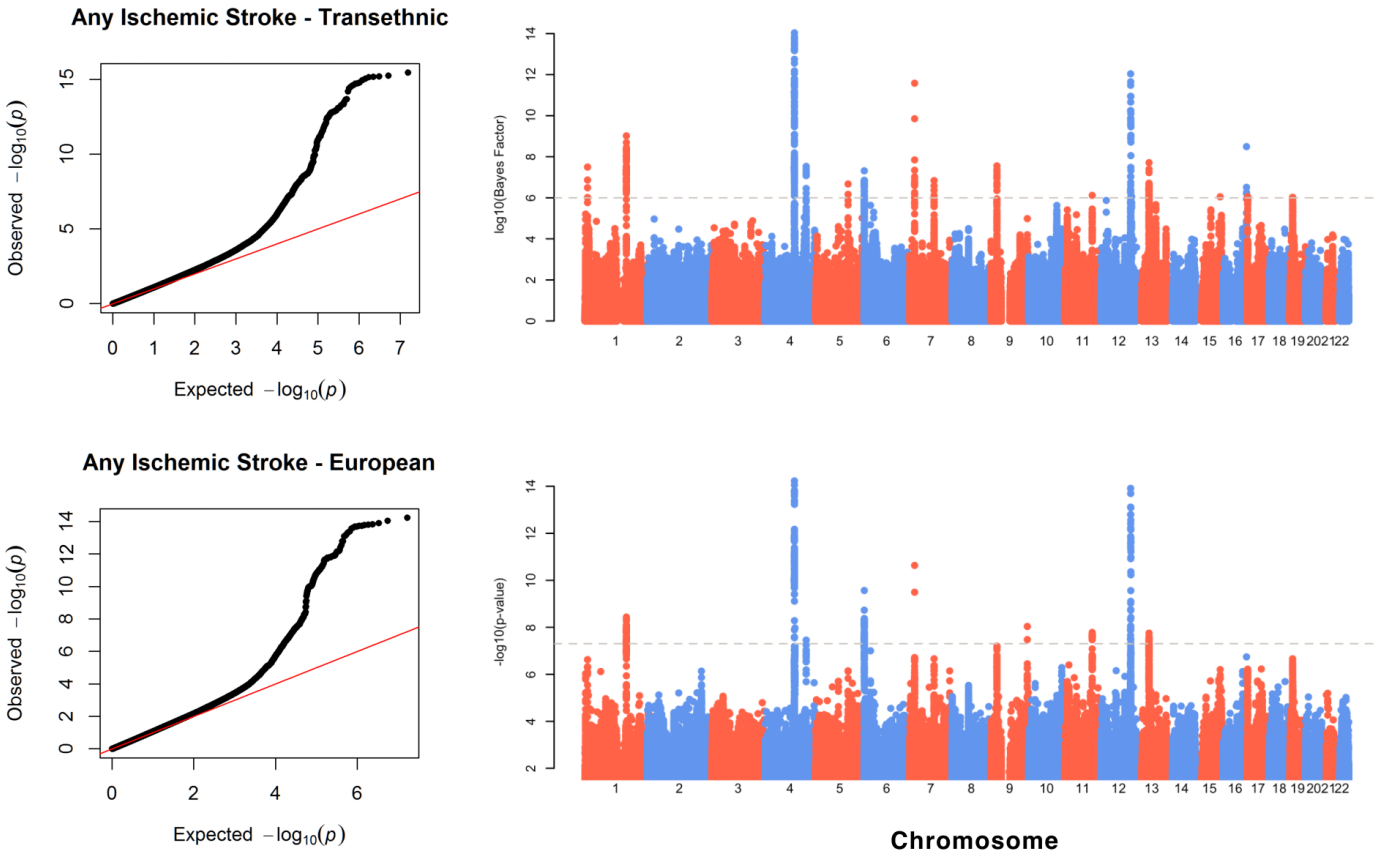
Supplementary Figure 12 Results of the conditional analysis at the PITX2 locus. Shown are the unconditioned analysis in the Europeans-only fixed-effects meta-analysis, the conditional analysis on rs2466455 and the conditional analysis on both rs2466455 and rs1906611. Shown is the region for the top signal ± 500kb. The y-axis represents the -log(p-value) from the Europeans-only fixed-effects meta-analysis. Variants in LD with the lead variant are shown in red (r^2>0.8), orange (r^2>0.6), green (r^2>0.4) and blue (r^2>0.2). Grey peaks represent estimated recombination rates.

Supplementary Figure 13 RiVIERA credible SNP set analysis. Shown are the GWAS association statistics for each locus studies, (A) PMF1-SEMA4A, (B) SH3PXD2A and (C) EDNRA, the final RiVIERA posterior probability (PPA), the weighted Epigenome information using the RoadMap epigenome data of 127 tissue types with information on 7 chromatin marks (H3K4me1, H3K4me3, H3K36me3, H3K27me3, H3K9me3, H3K27ac, H3K9ac) as well as DNA accessibility marks (DNaseI). Also shown are PolII binding sites and transcription factor (TF) binding sites in the region. Epigenetic enrichment over a fixed window size (50bp) per tissue group was generated by taking the cumulative sum of empirical prior weighted global epigenetic enrichment. Tissues were grouped into 19 groups as defined in the NIH RoadMap epigenome project.

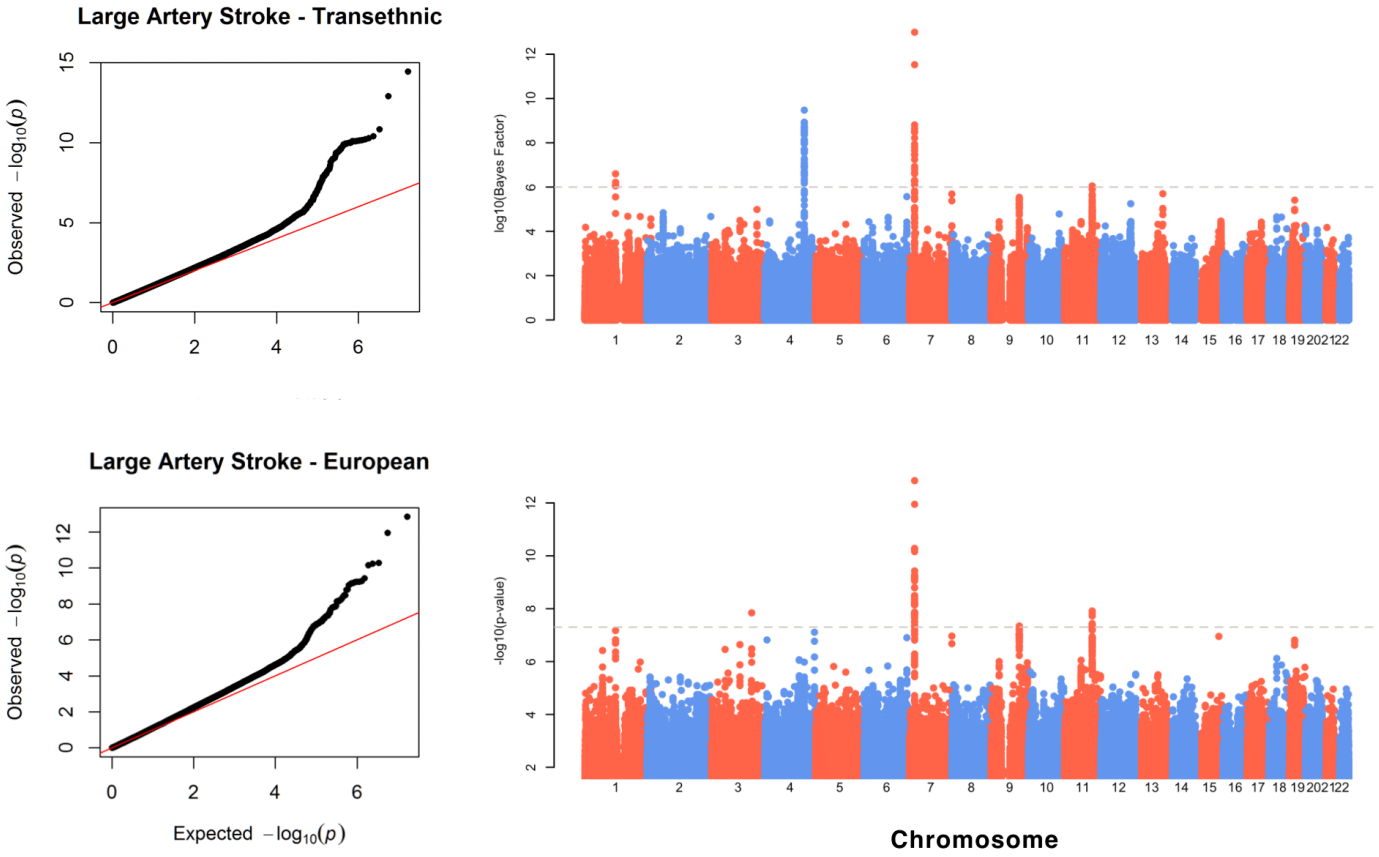
Supplementary Figure 1



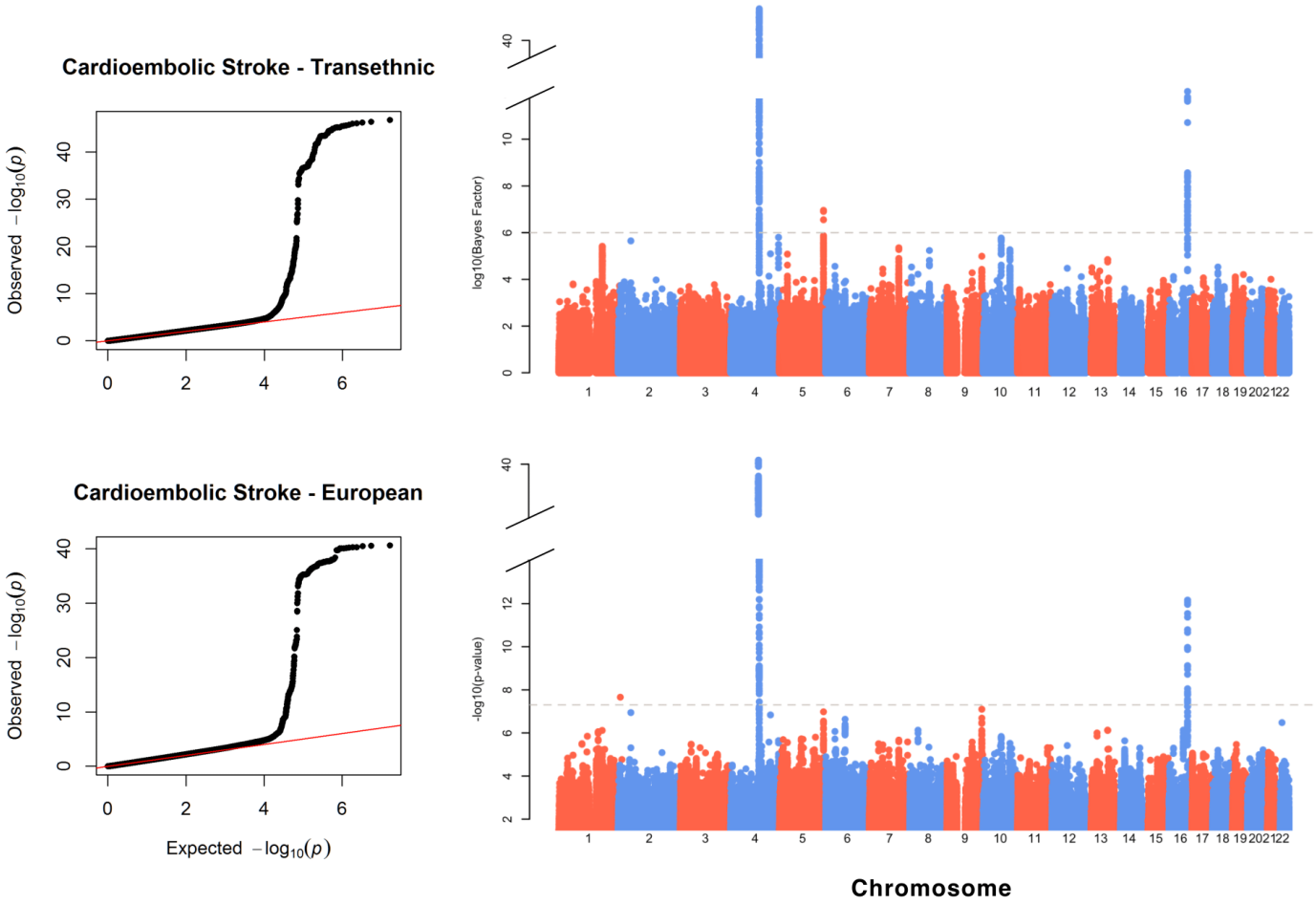
Supplementary Figure 2



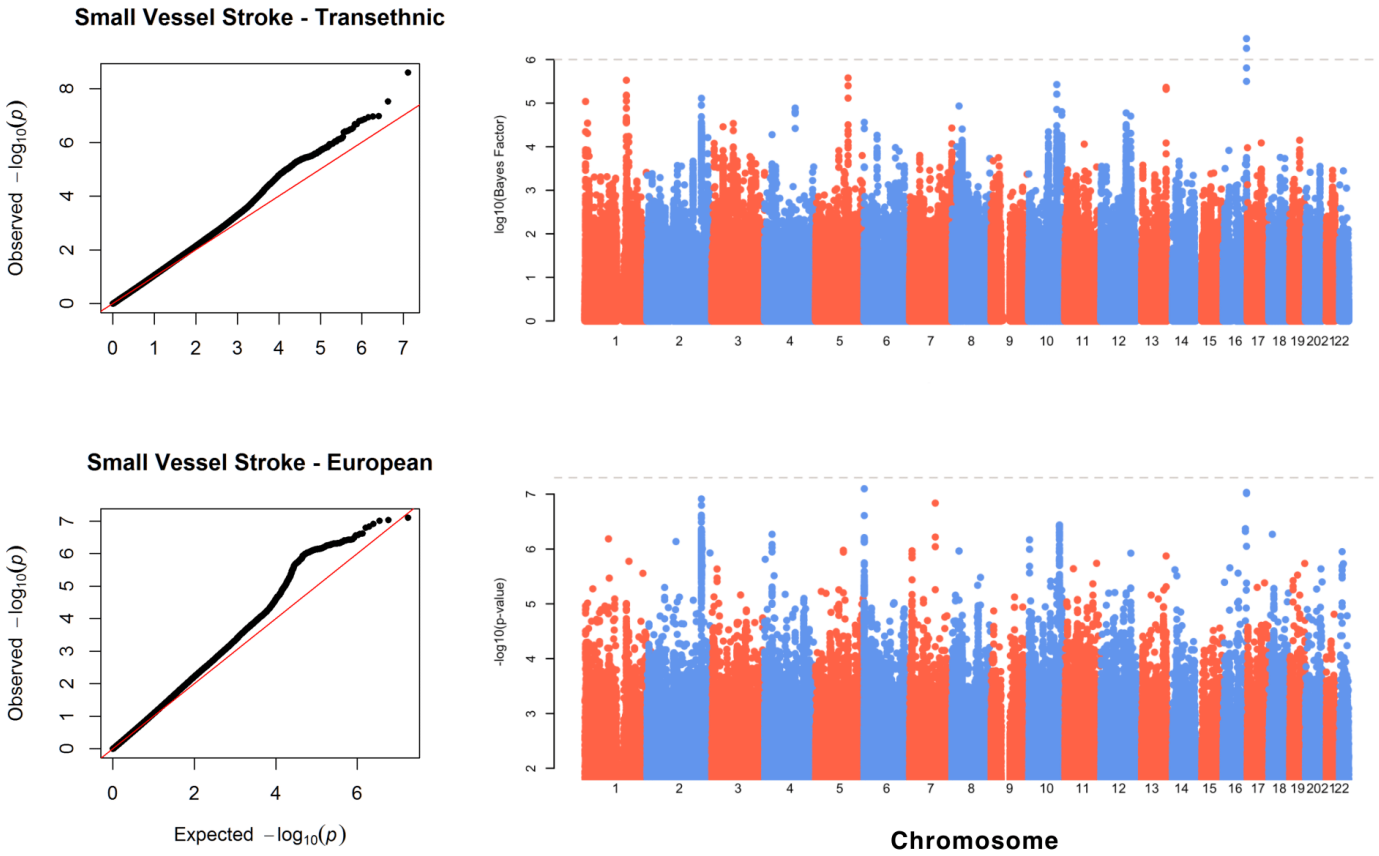
Supplementary Figure 3



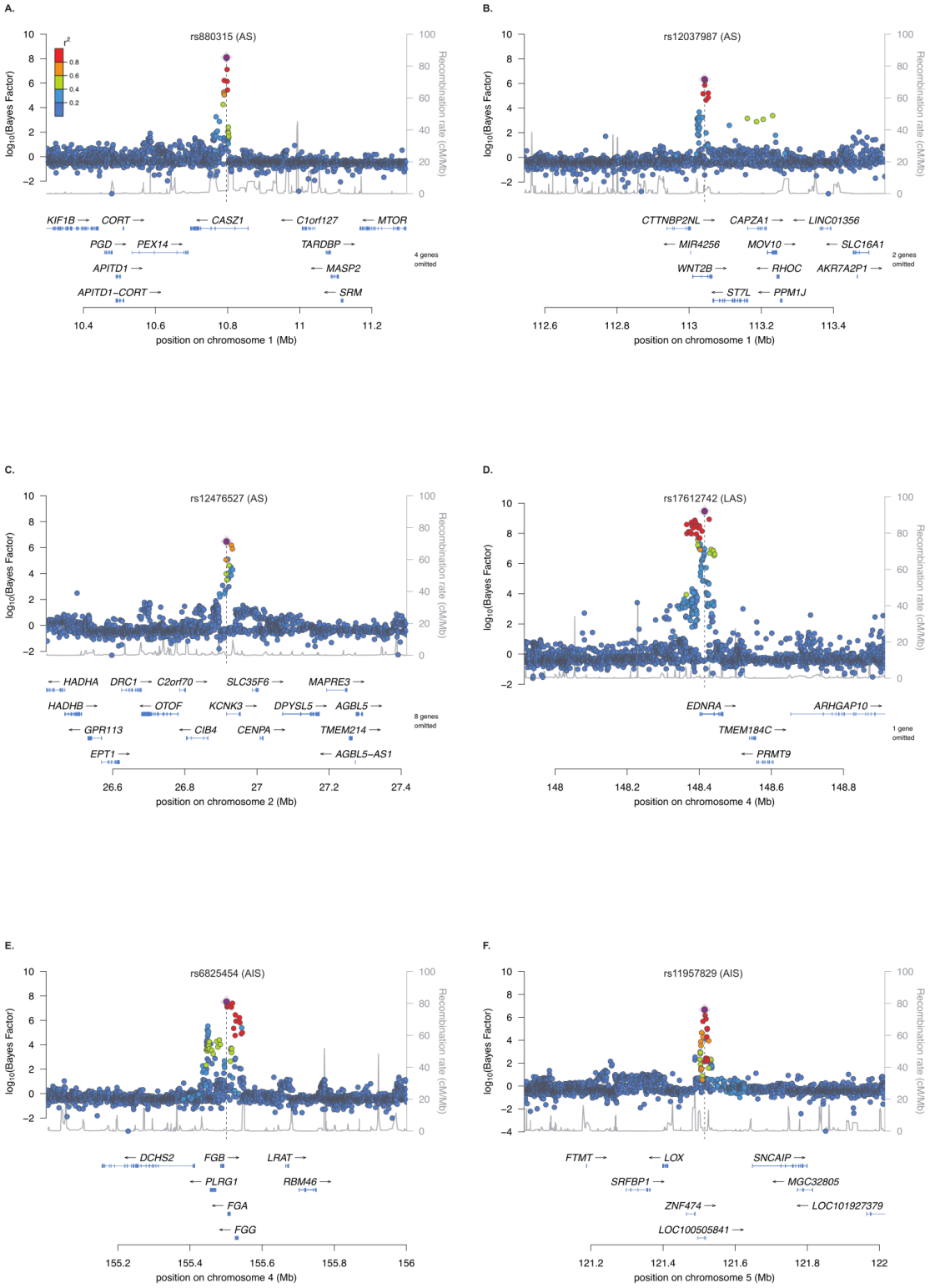
Supplementary Figure 4

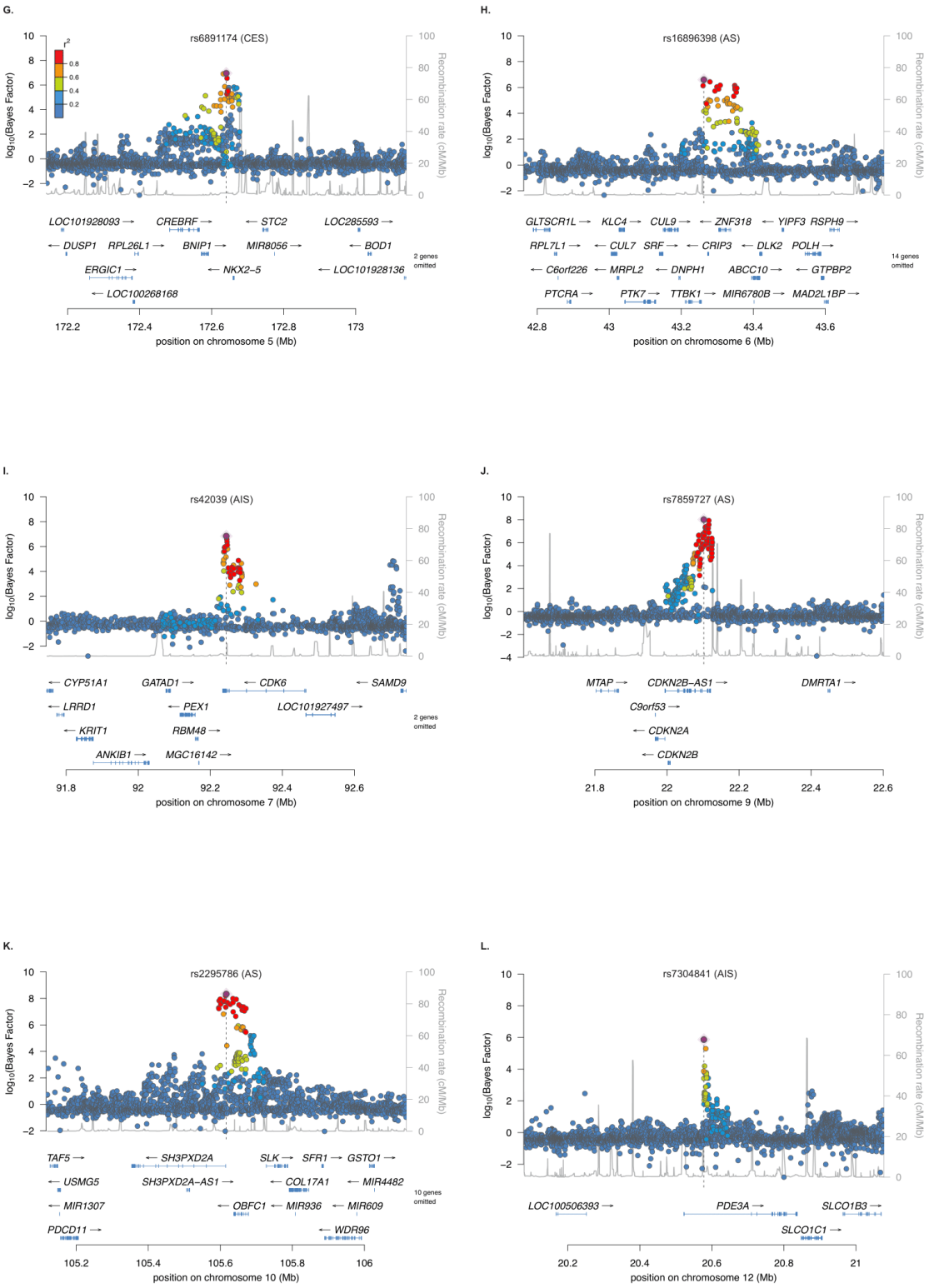


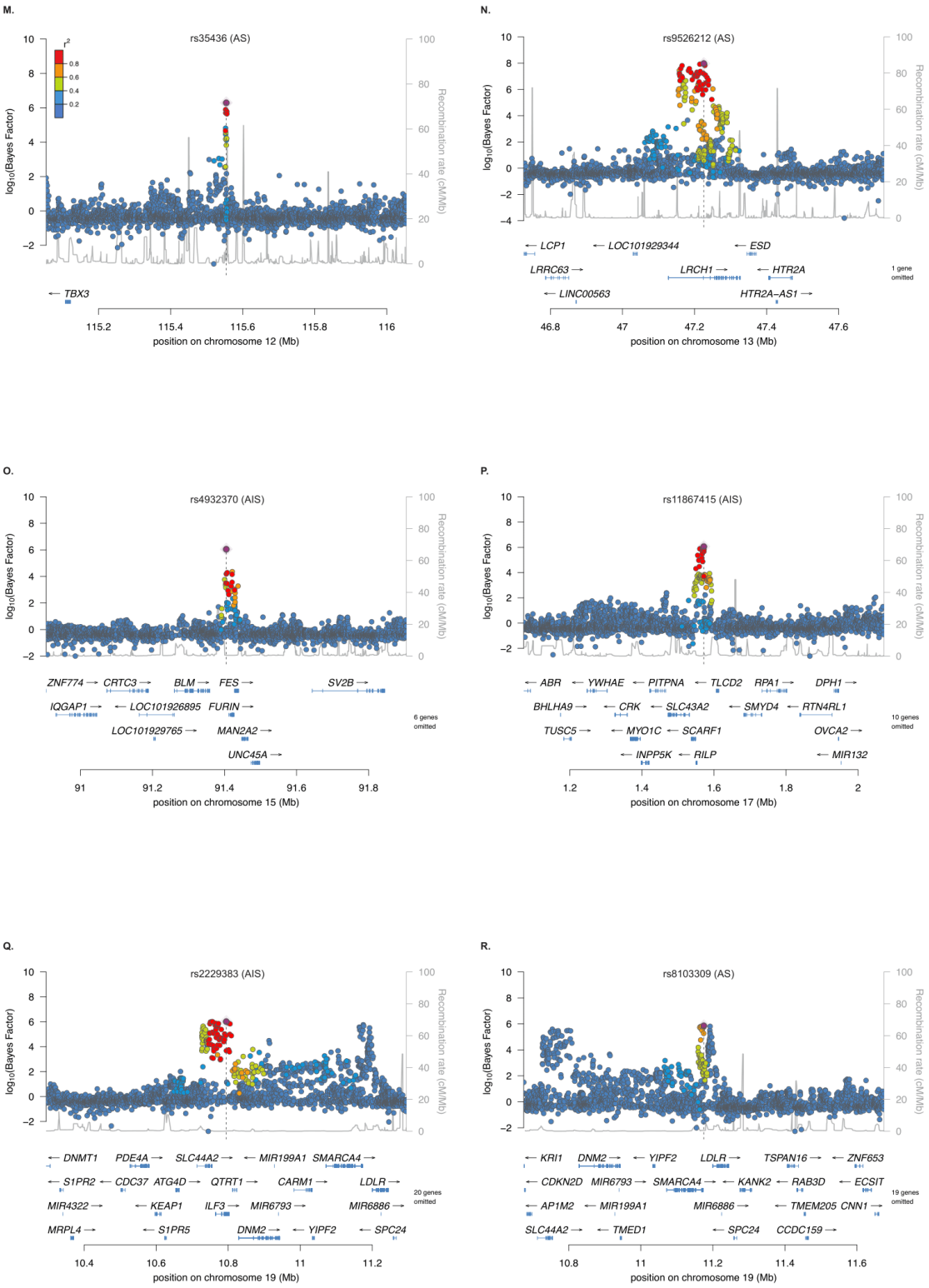
Supplementary Figure 5



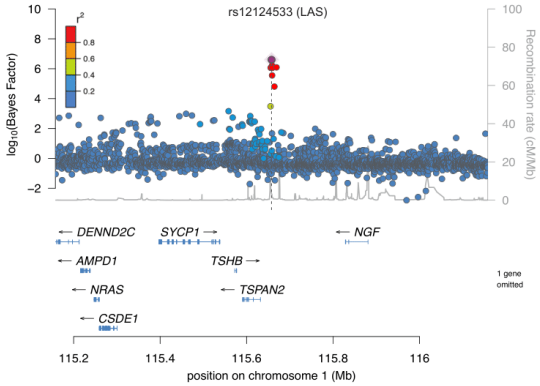
Supplementary Figure 6



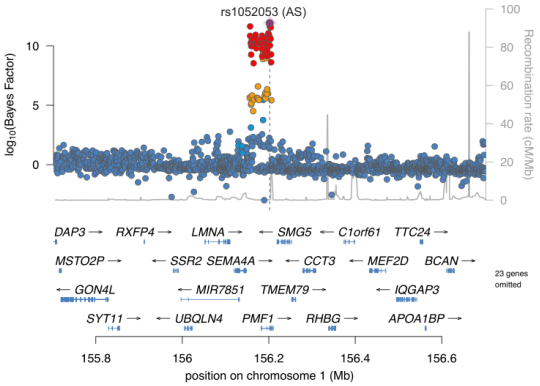

G.
rs6891174 (CES)
log10(Bayes Factor)
Recombination rate (cM/Mb)
r2
0.8
0.6
0.4
0.2
LOC101928093
CREBRF
STC2
LOC285593
DUSP1
RPL26L1
BNIP1
MIR8056
BOD1
2 genes omitted
ERGIC1
NKX2−5
LOC101928136
LOC100268168
172.2
172.4
172.6
172.8
173
position on chromosome 5 (Mb)
H.
rs16896398 (AS)
log10(Bayes Factor)
Recombination rate (cM/Mb)
GLTSCR1L
KLC4
CUL9
ZNF318
YIPF3
RSPH9
RPL7L1
CUL7
SRF
CRIP3
DLK2
POLH
14 genes omitted
C6orf226
MRPL2
DNPH1
ABCC10
GTPBP2
PTCRA
PTK7
TTBK1
MIR6780B
MAD2L1BP
42.8
43
43.2
43.4
43.6
position on chromosome 6 (Mb)
I.
rs42039 (AIS)
log10(Bayes Factor)
Recombination rate (cM/Mb)
CYP51A1
GATAD1
CDK6
SAMD9
LRRD1
PEX1
LOC101927497
2 genes omitted
KRIT1
RBM48
ANKIB1
MGC16142
91.8
92
92.2
92.4
92.6
position on chromosome 7 (Mb)
J.
rs7859727 (AS)
log10(Bayes Factor)
Recombination rate (cM/Mb)
MTAP
CDKN2B−AS1
DMRTA1
C9orf53
CDKN2A
CDKN2B
21.8
22
22.2
22.4
22.6
position on chromosome 9 (Mb)
K.
rs2295786 (AS)
log10(Bayes Factor)
Recombination rate (cM/Mb)
TAF5
SH3PXD2A
SLK
SFR1
GSTO1
USMG5
SH3PXD2A−AS1
COL17A1
MIR4482
10 genes omitted
MIR1307
OBFC1
MIR936
MIR609
PDCD11
WDR96
105.2
105.4
105.6
105.8
106
position on chromosome 10 (Mb)
L.
rs7304841 (AIS)
log10(Bayes Factor)
Recombination rate (cM/Mb)
LOC100506393
PDE3A
SLCO1B3
SLCO1C1
20.2
20.4
20.6
20.8
21
position on chromosome 12 (Mb)


M.
rs35436 (AS)
log10(Bayes Factor)
Recombination rate (cM/Mb)
r²
0.8
0.6
0.4
0.2
TBX3
position on chromosome 12 (Mb)
N.
rs9526212 (AS)
LCP1
LOC101929344
ESD
LRRC63
LRCH1
HTR2A
1 gene omitted
LINC00563
HTR2A-AS1
position on chromosome 13 (Mb)
O.
rs4932370 (AIS)
ZNF774
CRTC3
BLM
FES
SV2B
IQGAP1
LOC101926895
FURIN
6 genes omitted
LOC101929765
MAN2A2
UNC45A
position on chromosome 15 (Mb)
P.
rs11867415 (AIS)
ABR
YWHAE
PITPNA
TLCD2
RPA1
DPH1
BHLHA9
CRK
SLC43A2
SMYD4
RTN4RL1
10 genes omitted
TUSC5
MYO1C
SCARF1
OVCA2
INPP5K
RILP
MIR132
position on chromosome 17 (Mb)
Q.
rs2229383 (AIS)
DNMT1
PDE4A
SLC44A2
MIR199A1
SMARCA4
S1PR2
CDC37
ATG4D
QTRT1
CARM1
LDLR
20 genes omitted
MIR4322
KEAP1
ILF3
MIR6793
MIR6886
MRPL4
S1PR5
DNM2
YIPF2
SPC24
position on chromosome 19 (Mb)
R.
rs8103309 (AS)
KRI1
DNM2
YIPF2
LDLR
TSPAN16
ZNF653
CDKN2D
MIR6793
SMARCA4
KANK2
RAB3D
ECSIT
19 genes omitted
AP1M2
MIR199A1
MIR6886
TMEM205
CNN1
SLC44A2
TMED1
SPC24
CCDC159
position on chromosome 19 (Mb)

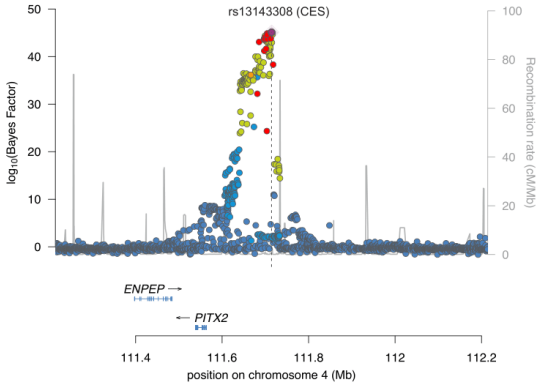
S.


rs12124533 (LAS)
log10(Bayes Factor)
Recombination rate (cM/Mb)
r2
0.8
0.6
0.4
0.2
DENND2C
SYCP1
NGF
AMPD1
TSHB
NRAS
TSPAN2
CSDE1
1 gene omitted
115.2
115.4
115.6
115.8
116
position on chromosome 1 (Mb)

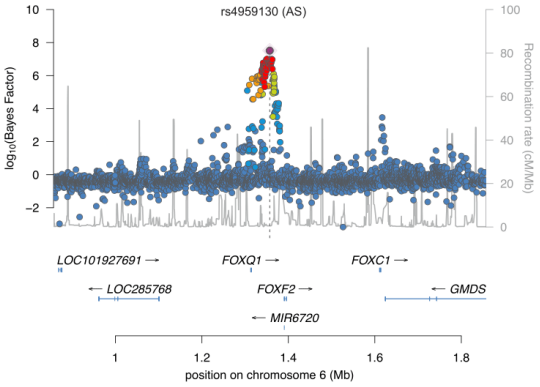
T.


rs1052053 (AS)
log10(Bayes Factor)
Recombination rate (cM/Mb)
DAP3
RXFP4
LMNA
SMG5
C1orf61
TTC24
MSTO2P
SSR2
SEMA4A
CCT3
MEF2D
BCAN
GON4L
MIR7851
TMEM79
IQGAP3
SYT11
UBQLN4
PMF1
RHBG
APOA1BP
23 genes omitted
155.8
156
156.2
156.4
156.6
position on chromosome 1 (Mb)

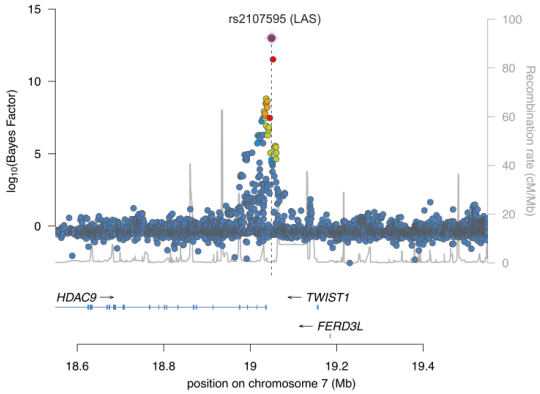
U.


rs13143308 (CES)
log10(Bayes Factor)
Recombination rate (cM/Mb)
ENPEP
PITX2
111.4
111.6
111.8
112
112.2
position on chromosome 4 (Mb)

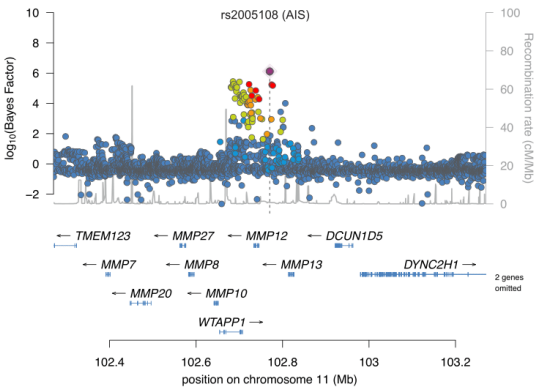
V.


rs4959130 (AS)
log10(Bayes Factor)
Recombination rate (cM/Mb)
LOC101927691
FOXQ1
FOXC1
LOC285768
FOXF2
GMDS
MIR6720
1
1.2
1.4
1.6
1.8
position on chromosome 6 (Mb)

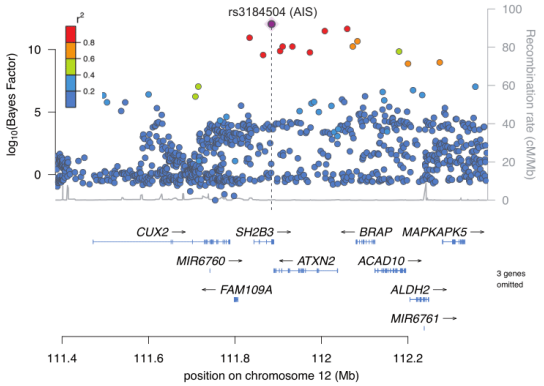
W.


rs2107595 (LAS)
log10(Bayes Factor)
Recombination rate (cM/Mb)
HDAC9
TWIST1
FERD3L
18.6
18.8
19
19.2
19.4
position on chromosome 7 (Mb)

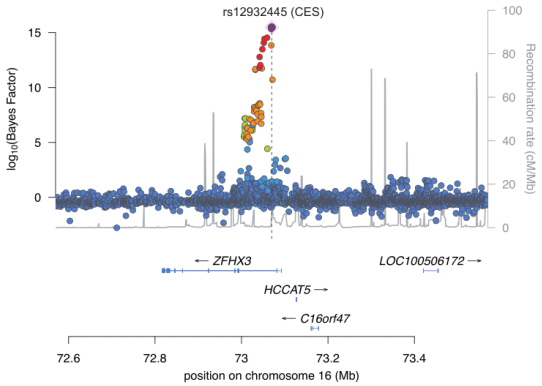
X.


rs2005108 (AIS)
log10(Bayes Factor)
Recombination rate (cM/Mb)
TMEM123
MMP27
MMP12
DCUN1D5
MMP7
MMP8
MMP13
DYNC2H1
MMP20
MMP10
WTAPP1
2 genes omitted
102.4
102.6
102.8
103
103.2
position on chromosome 11 (Mb)

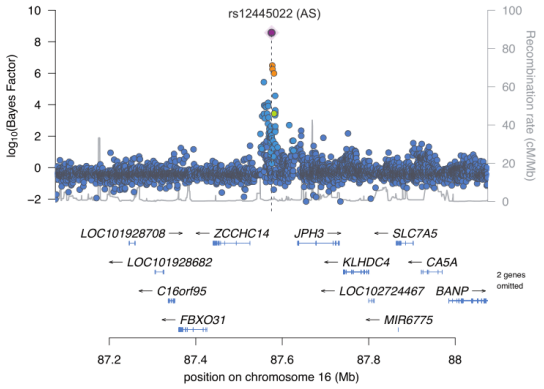
Y.


rs3184504 (AIS)
r²
0.8
0.6
0.4
0.2
log10(Bayes Factor)
Recombination rate (cM/Mb)
CUX2
SH2B3
BRAP
MAPKAPK5
MIR6760
ATXN2
ACAD10
3 genes omitted
FAM109A
ALDH2
MIR6761
111.4
111.6
111.8
112
112.2
position on chromosome 12 (Mb)

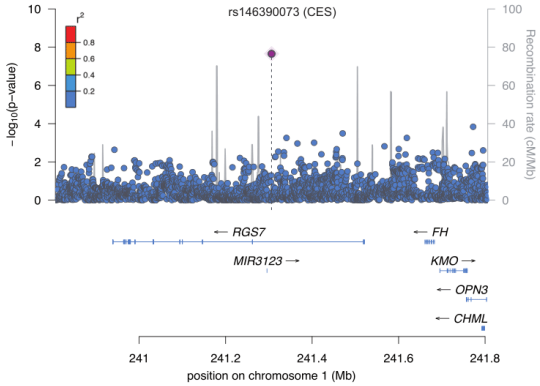
Z.


rs12932445 (CES)
log10(Bayes Factor)
Recombination rate (cM/Mb)
ZFHX3
LOC100506172
HCCAT5
C16orf47
72.6
72.8
73
73.2
73.4
position on chromosome 16 (Mb)

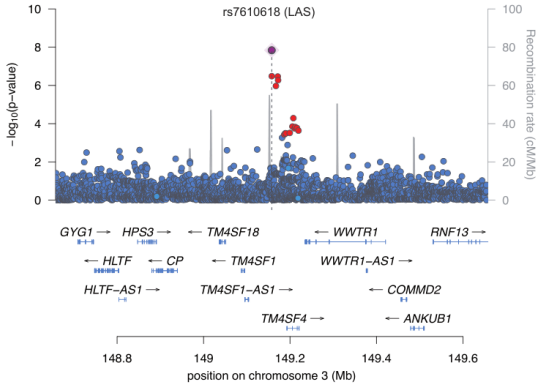
A'.


rs12445022 (AS)
log10(Bayes Factor)
Recombination rate (cM/Mb)
LOC101928708
ZCCHC14
JPH3
SLC7A5
LOC101928682
KLHDC4
CA5A
2 genes omitted
C16orf95
LOC102724467
BANP
FBXO31
MIR6775
87.2
87.4
87.6
87.8
88
position on chromosome 16 (Mb)

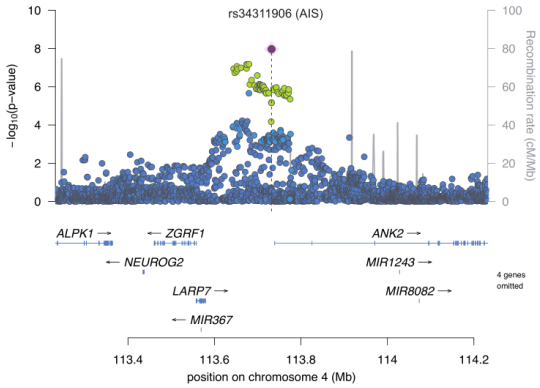
B'.


rs146390073 (CES)
r²
0.8
0.6
0.4
0.2
−log10(p-value)
Recombination rate (cM/Mb)
RGS7
FH
MIR3123
KMO
OPN3
CHML
241
241.2
241.4
241.6
241.8
position on chromosome 1 (Mb)

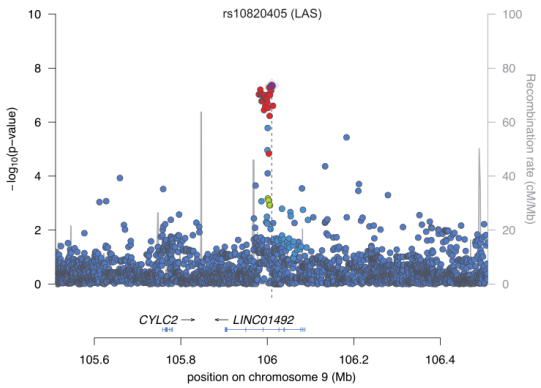
C'.


rs7610618 (LAS)
−log10(p-value)
Recombination rate (cM/Mb)
GYG1
HPS3
TM4SF18
WWTR1
RNF13
HLTF
CP
TM4SF1
WWTR1–AS1
HLTF–AS1
TM4SF1–AS1
COMMD2
TM4SF4
ANKUB1
148.8
149
149.2
149.4
149.6
position on chromosome 3 (Mb)

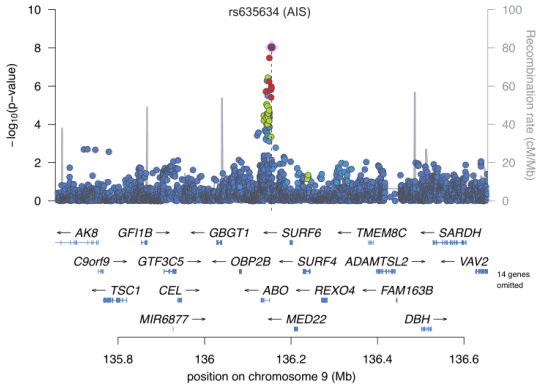
D'.


rs34311906 (AIS)
−log10(p-value)
Recombination rate (cM/Mb)
ALPK1
ZGRF1
ANK2
NEUROG2
MIR1243
4 genes omitted
LARP7
MIR8082
MIR367
113.4
113.6
113.8
114
114.2
position on chromosome 4 (Mb)

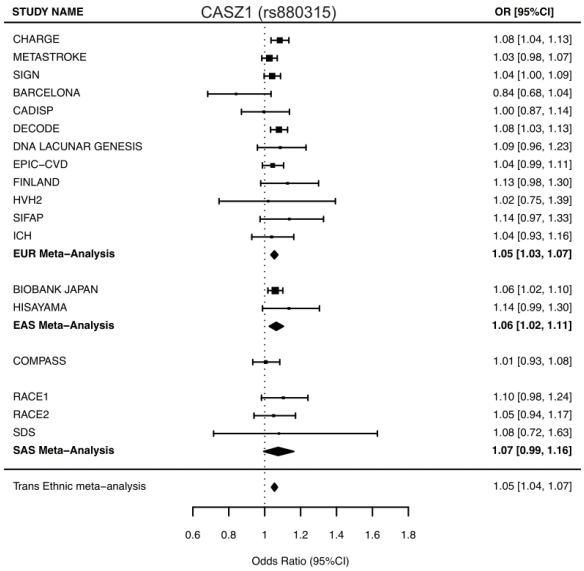
E'.

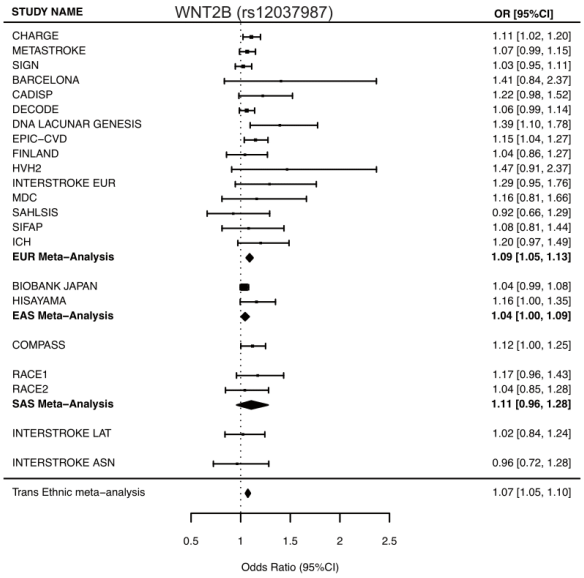

rs10820405 (LAS)
−log10(p-value)
Recombination rate (cM/Mb)
CYLC2
LINC01492
105.6
105.8
106
106.2
106.4
position on chromosome 9 (Mb)

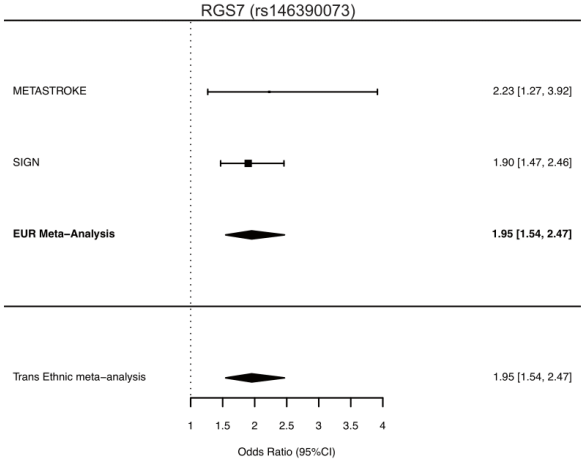
F'.

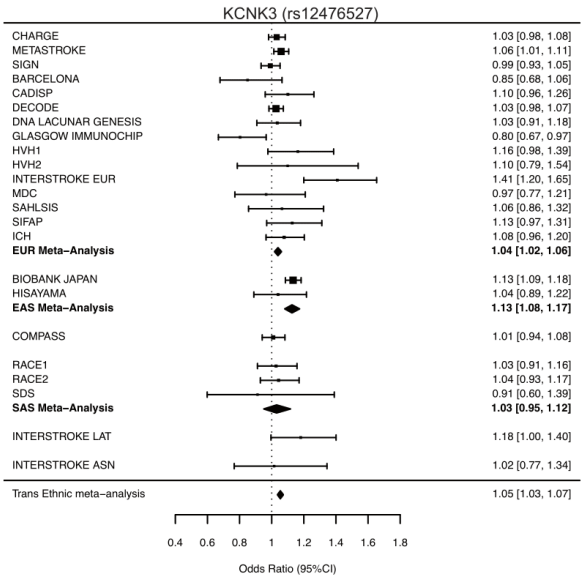

rs635634 (AIS)
−log10(p-value)
Recombination rate (cM/Mb)
AK8
GFI1B
GBGT1
SURF6
TMEM8C
SARDH
C9orf9
GTF3C5
OBP2B
SURF4
ADAMTSL2
VAV2
14 genes omitted
TSC1
CEL
ABO
REXO4
FAM163B
MIR6877
MED22
DBH
135.8
136
136.2
136.4
136.6
position on chromosome 9 (Mb)

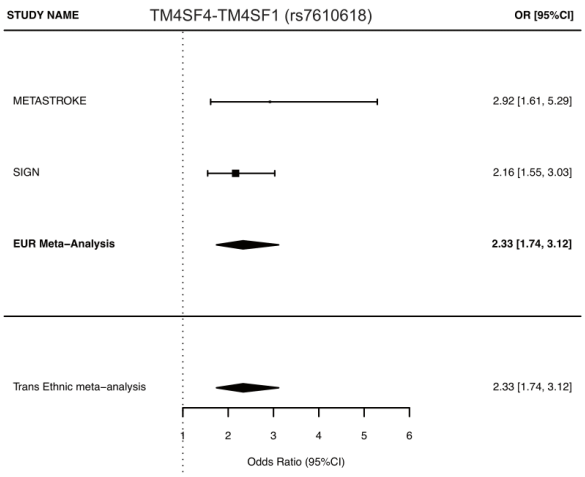
Supplementary Figure 7

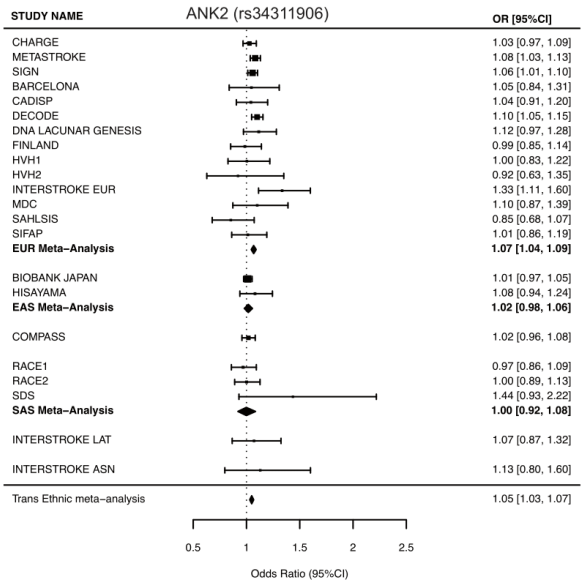


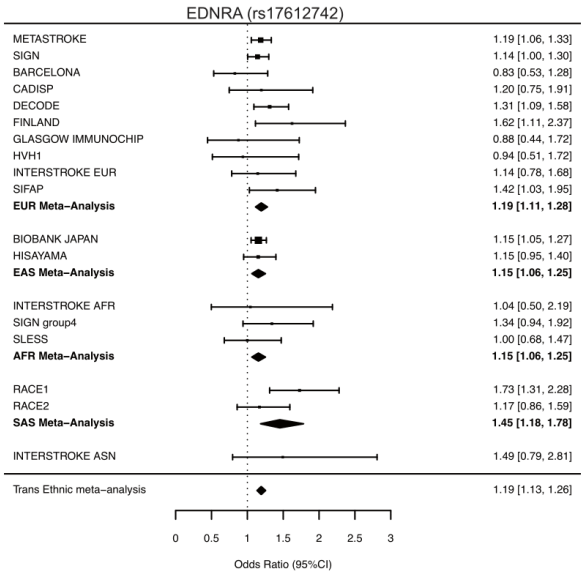


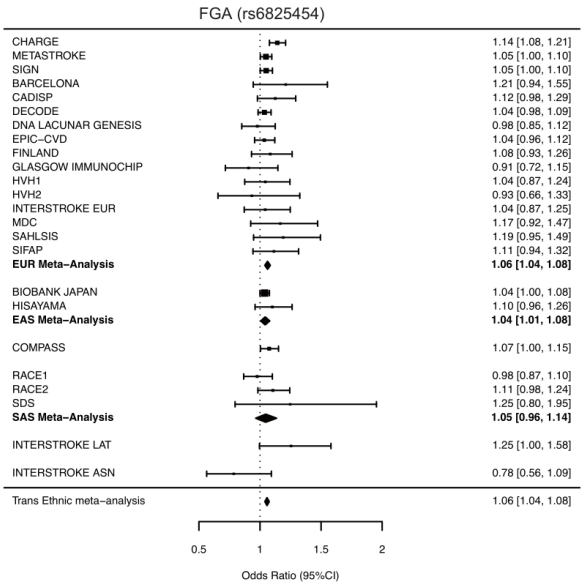


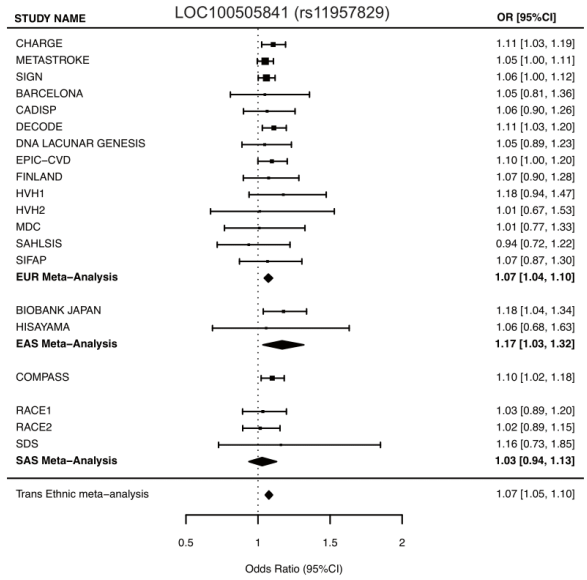


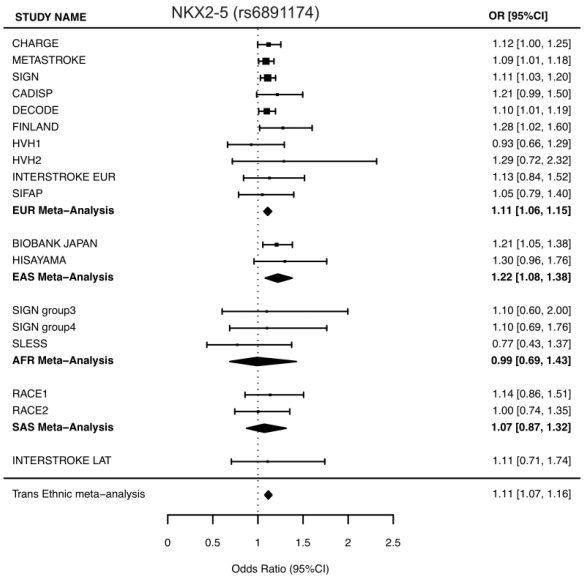

STUDY NAME
TM4SF4-TM4SF1 (rs7610618)
OR [95%CI]
METASTROKE
2.92 [1.61, 5.29]
SIGN
2.16 [1.55, 3.03]
EUR Meta−Analysis
2.33 [1.74, 3.12]
Trans Ethnic meta−analysis
2.33 [1.74, 3.12]
1
2
3
4
5
6
Odds Ratio (95%CI)

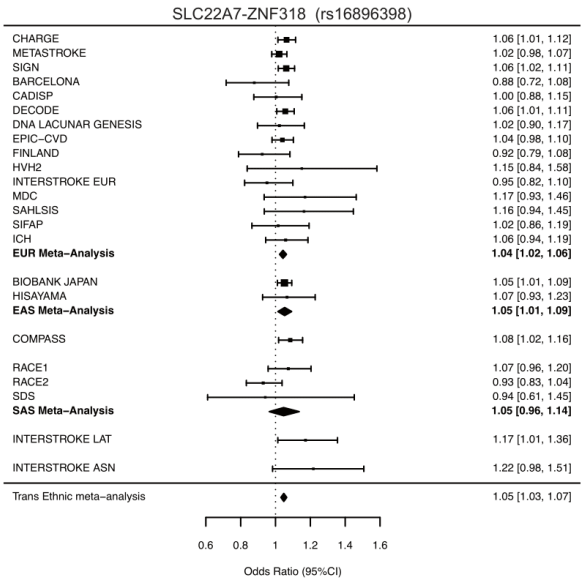

STUDY NAME
ANK2 (rs34311906)
OR [95%CI]
CHARGE
1.03 [0.97, 1.09]
METASTROKE
1.08 [1.03, 1.13]
SIGN
1.06 [1.01, 1.10]
BARCELONA
1.05 [0.84, 1.31]
CADISP
1.04 [0.91, 1.20]
DECODE
1.10 [1.05, 1.15]
DNA LACUNAR GENESIS
1.12 [0.97, 1.28]
FINLAND
0.99 [0.85, 1.14]
HVH1
1.00 [0.83, 1.22]
HVH2
0.92 [0.63, 1.35]
INTERSTROKE EUR
1.33 [1.11, 1.60]
MDC
1.10 [0.87, 1.39]
SAHLSIS
0.85 [0.68, 1.07]
SIFAP
1.01 [0.86, 1.19]
EUR Meta−Analysis
1.07 [1.04, 1.09]
BIOBANK JAPAN
1.01 [0.97, 1.05]
HISAYAMA
1.08 [0.94, 1.24]
EAS Meta−Analysis
1.02 [0.98, 1.06]
COMPASS
1.02 [0.96, 1.08]
RACE1
0.97 [0.86, 1.09]
RACE2
1.00 [0.89, 1.13]
SDS
1.44 [0.93, 2.22]
SAS Meta−Analysis
1.00 [0.92, 1.08]
INTERSTROKE LAT
1.07 [0.87, 1.32]
INTERSTROKE ASN
1.13 [0.80, 1.60]
Trans Ethnic meta−analysis
1.05 [1.03, 1.07]
0.5
1
1.5
2
2.5
Odds Ratio (95%CI)

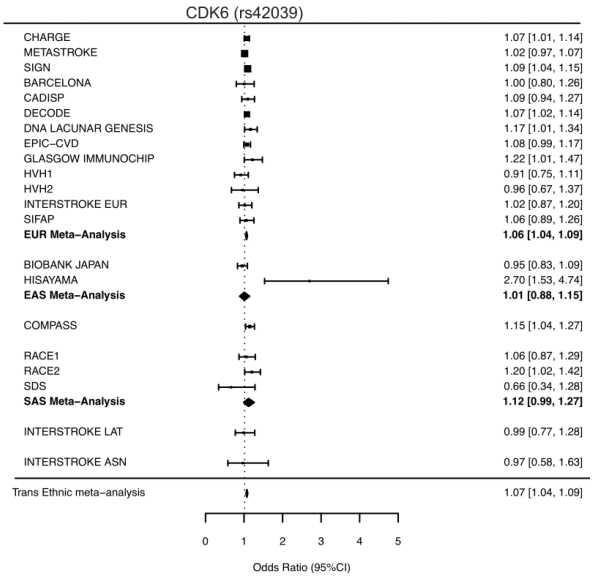

EDNRA (rs17612742)
METASTROKE
1.19 [1.06, 1.33]
SIGN
1.14 [1.00, 1.30]
BARCELONA
0.83 [0.53, 1.28]
CADISP
1.20 [0.75, 1.91]
DECODE
1.31 [1.09, 1.58]
FINLAND
1.62 [1.11, 2.37]
GLASGOW IMMUNOCHIP
0.88 [0.44, 1.72]
HVH1
0.94 [0.51, 1.72]
INTERSTROKE EUR
1.14 [0.78, 1.68]
SIFAP
1.42 [1.03, 1.95]
EUR Meta−Analysis
1.19 [1.11, 1.28]
BIOBANK JAPAN
1.15 [1.05, 1.27]
HISAYAMA
1.15 [0.95, 1.40]
EAS Meta−Analysis
1.15 [1.06, 1.25]
INTERSTROKE AFR
1.04 [0.50, 2.19]
SIGN group4
1.34 [0.94, 1.92]
SLESS
1.00 [0.68, 1.47]
AFR Meta−Analysis
1.15 [1.06, 1.25]
RACE1
1.73 [1.31, 2.28]
RACE2
1.17 [0.86, 1.59]
SAS Meta−Analysis
1.45 [1.18, 1.78]
INTERSTROKE ASN
1.49 [0.79, 2.81]
Trans Ethnic meta−analysis
1.19 [1.13, 1.26]
0
0.5
1
1.5
2
2.5
3
Odds Ratio (95%CI)

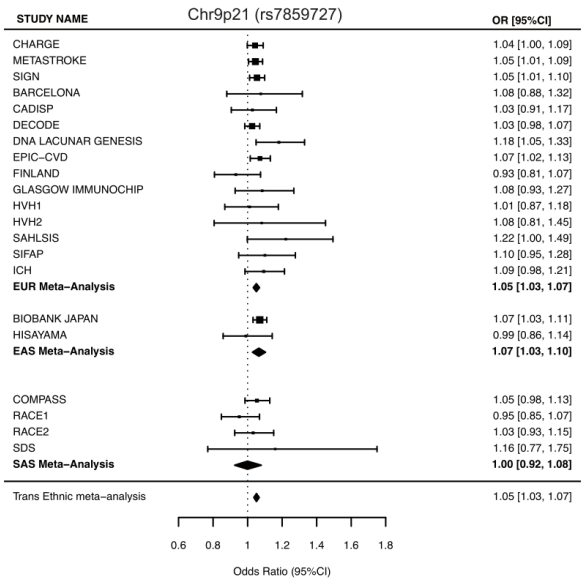

FGA (rs6825454)
CHARGE
1.14 [1.08, 1.21]
METASTROKE
1.05 [1.00, 1.10]
SIGN
1.05 [1.00, 1.10]
BARCELONA
1.21 [0.94, 1.55]
CADISP
1.12 [0.98, 1.29]
DECODE
1.04 [0.98, 1.09]
DNA LACUNAR GENESIS
0.98 [0.85, 1.12]
EPIC−CVD
1.04 [0.96, 1.12]
FINLAND
1.08 [0.93, 1.26]
GLASGOW IMMUNOCHIP
0.91 [0.72, 1.15]
HVH1
1.04 [0.87, 1.24]
HVH2
0.93 [0.66, 1.33]
INTERSTROKE EUR
1.04 [0.87, 1.25]
MDC
1.17 [0.92, 1.47]
SAHLSIS
1.19 [0.95, 1.49]
SIFAP
1.11 [0.94, 1.32]
EUR Meta−Analysis
1.06 [1.04, 1.08]
BIOBANK JAPAN
1.04 [1.00, 1.08]
HISAYAMA
1.10 [0.96, 1.26]
EAS Meta−Analysis
1.04 [1.01, 1.08]
COMPASS
1.07 [1.00, 1.15]
RACE1
0.98 [0.87, 1.10]
RACE2
1.11 [0.98, 1.24]
SDS
1.25 [0.80, 1.95]
SAS Meta−Analysis
1.05 [0.96, 1.14]
INTERSTROKE LAT
1.25 [1.00, 1.58]
INTERSTROKE ASN
0.78 [0.56, 1.09]
Trans Ethnic meta−analysis
1.06 [1.04, 1.08]
0.5
1
1.5
2
Odds Ratio (95%CI)

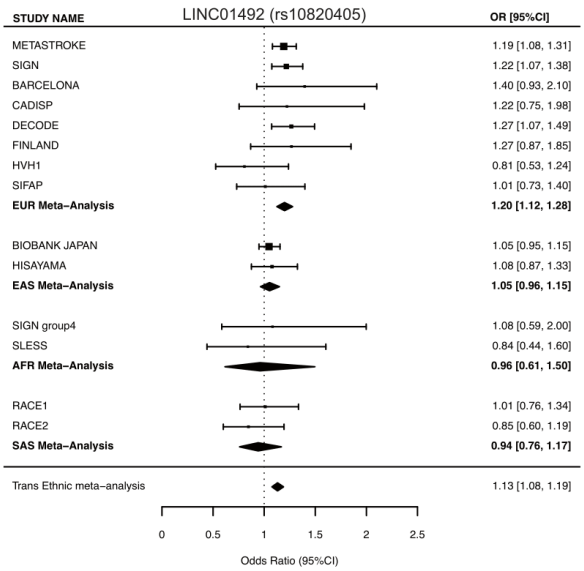

LOC100505841 (rs11957829)
STUDY NAME
OR [95%CI]
CHARGE 1.11 [1.03, 1.19]
METASTROKE 1.05 [1.00, 1.11]
SIGN 1.06 [1.00, 1.12]
BARCELONA 1.05 [0.81, 1.36]
CADISP 1.06 [0.90, 1.26]
DECODE 1.11 [1.03, 1.20]
DNA LACUNAR GENESIS 1.05 [0.89, 1.23]
EPIC–CVD 1.10 [1.00, 1.20]
FINLAND 1.07 [0.90, 1.28]
HVH1 1.18 [0.94, 1.47]
HVH2 1.01 [0.67, 1.53]
MDC 1.01 [0.77, 1.33]
SAHLSIS 0.94 [0.72, 1.22]
SIFAP 1.07 [0.87, 1.30]
EUR Meta–Analysis 1.07 [1.04, 1.10]
BIOBANK JAPAN 1.18 [1.04, 1.34]
HISAYAMA 1.06 [0.68, 1.63]
EAS Meta–Analysis 1.17 [1.03, 1.32]
COMPASS 1.10 [1.02, 1.18]
RACE1 1.03 [0.89, 1.20]
RACE2 1.02 [0.89, 1.15]
SDS 1.16 [0.73, 1.85]
SAS Meta–Analysis 1.03 [0.94, 1.13]
Trans Ethnic meta–analysis 1.07 [1.05, 1.10]
0.5
1
1.5
2
Odds Ratio (95%CI)

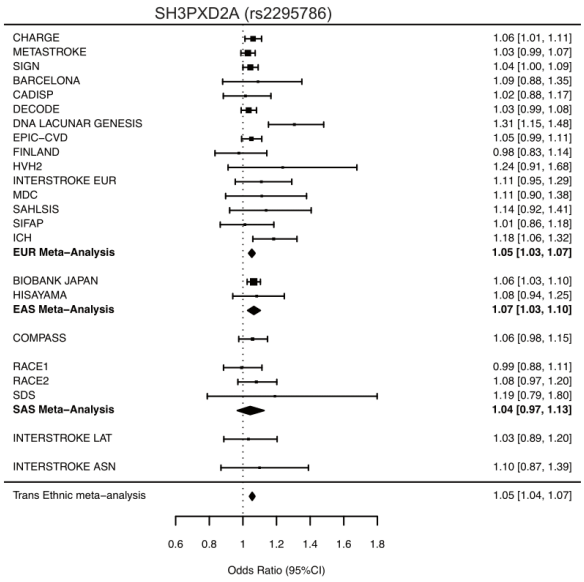

NKX2-5 (rs6891174)
STUDY NAME
OR [95%CI]
CHARGE 1.12 [1.00, 1.25]
METASTROKE 1.09 [1.01, 1.18]
SIGN 1.11 [1.03, 1.20]
CADISP 1.21 [0.99, 1.50]
DECODE 1.10 [1.01, 1.19]
FINLAND 1.28 [1.02, 1.60]
HVH1 0.93 [0.66, 1.29]
HVH2 1.29 [0.72, 2.32]
INTERSTROKE EUR 1.13 [0.84, 1.52]
SIFAP 1.05 [0.79, 1.40]
EUR Meta–Analysis 1.11 [1.06, 1.15]
BIOBANK JAPAN 1.21 [1.05, 1.38]
HISAYAMA 1.30 [0.96, 1.76]
EAS Meta–Analysis 1.22 [1.08, 1.38]
SIGN group3 1.10 [0.60, 2.00]
SIGN group4 1.10 [0.69, 1.76]
SLESS 0.77 [0.43, 1.37]
AFR Meta–Analysis 0.99 [0.69, 1.43]
RACE1 1.14 [0.86, 1.51]
RACE2 1.00 [0.74, 1.35]
SAS Meta–Analysis 1.07 [0.87, 1.32]
INTERSTROKE LAT 1.11 [0.71, 1.74]
Trans Ethnic meta–analysis 1.11 [1.07, 1.16]
0
0.5
1
1.5
2
2.5
Odds Ratio (95%CI)

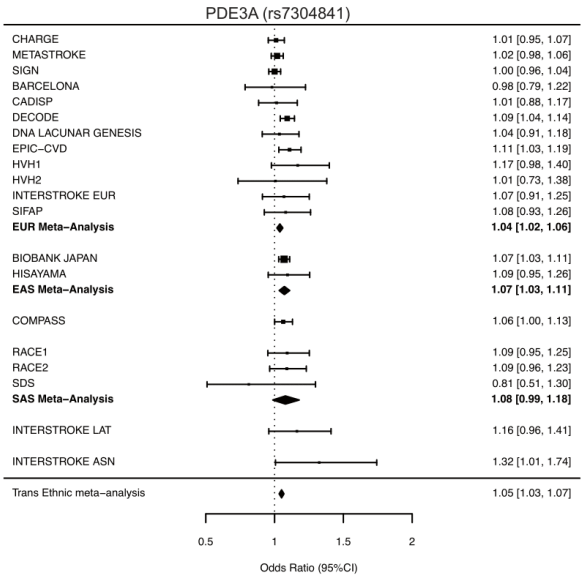

SLC22A7-ZNF318 (rs16896398)
CHARGE 1.06 [1.01, 1.12]
METASTROKE 1.02 [0.98, 1.07]
SIGN 1.06 [1.02, 1.11]
BARCELONA 0.88 [0.72, 1.08]
CADISP 1.00 [0.88, 1.15]
DECODE 1.06 [1.01, 1.11]
DNA LACUNAR GENESIS 1.02 [0.90, 1.17]
EPIC–CVD 1.04 [0.98, 1.10]
FINLAND 0.92 [0.79, 1.08]
HVH2 1.15 [0.84, 1.58]
INTERSTROKE EUR 0.95 [0.82, 1.10]
MDC 1.17 [0.93, 1.46]
SAHLSIS 1.16 [0.94, 1.45]
SIFAP 1.02 [0.86, 1.19]
ICH 1.06 [0.94, 1.19]
EUR Meta–Analysis 1.04 [1.02, 1.06]
BIOBANK JAPAN 1.05 [1.01, 1.09]
HISAYAMA 1.07 [0.93, 1.23]
EAS Meta–Analysis 1.05 [1.01, 1.09]
COMPASS 1.08 [1.02, 1.16]
RACE1 1.07 [0.96, 1.20]
RACE2 0.93 [0.83, 1.04]
SDS 0.94 [0.61, 1.45]
SAS Meta–Analysis 1.05 [0.96, 1.14]
INTERSTROKE LAT 1.17 [1.01, 1.36]
INTERSTROKE ASN 1.22 [0.98, 1.51]
Trans Ethnic meta–analysis 1.05 [1.03, 1.07]
0.6
0.8
1
1.2
1.4
1.6
Odds Ratio (95%CI)

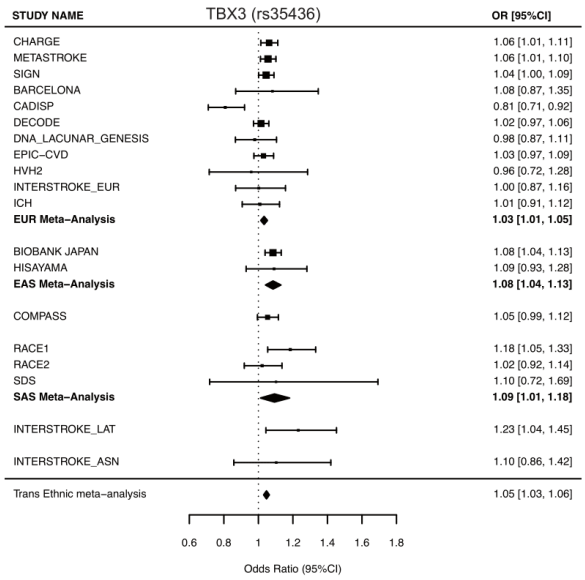

CDK6 (rs42039)
CHARGE 1.07 [1.01, 1.14]
METASTROKE 1.02 [0.97, 1.07]
SIGN 1.09 [1.04, 1.15]
BARCELONA 1.00 [0.80, 1.26]
CADISP 1.09 [0.94, 1.27]
DECODE 1.07 [1.02, 1.14]
DNA LACUNAR GENESIS 1.17 [1.01, 1.34]
EPIC–CVD 1.08 [0.99, 1.17]
GLASGOW IMMUNOCHIP 1.22 [1.01, 1.47]
HVH1 0.91 [0.75, 1.11]
HVH2 0.96 [0.67, 1.37]
INTERSTROKE EUR 1.02 [0.87, 1.20]
SIFAP 1.06 [0.89, 1.26]
EUR Meta–Analysis 1.06 [1.04, 1.09]
BIOBANK JAPAN 0.95 [0.83, 1.09]
HISAYAMA 2.70 [1.53, 4.74]
EAS Meta–Analysis 1.01 [0.88, 1.15]
COMPASS 1.15 [1.04, 1.27]
RACE1 1.06 [0.87, 1.29]
RACE2 1.20 [1.02, 1.42]
SDS 0.66 [0.34, 1.28]
SAS Meta–Analysis 1.12 [0.99, 1.27]
INTERSTROKE LAT 0.99 [0.77, 1.28]
INTERSTROKE ASN 0.97 [0.58, 1.63]
Trans Ethnic meta–analysis 1.07 [1.04, 1.09]
0
1
2
3
4
5
Odds Ratio (95%CI)

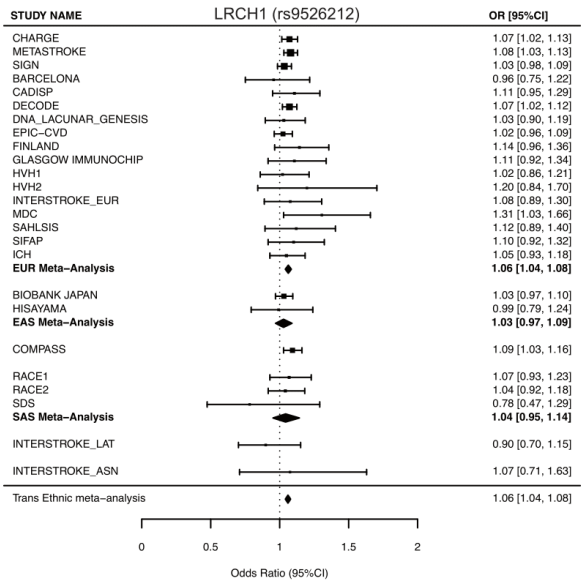

Chr9p21 (rs7859727)
STUDY NAME
OR [95%CI]
CHARGE 1.04 [1.00, 1.09]
METASTROKE 1.05 [1.01, 1.09]
SIGN 1.05 [1.01, 1.10]
BARCELONA 1.08 [0.88, 1.32]
CADISP 1.03 [0.91, 1.17]
DECODE 1.03 [0.98, 1.07]
DNA LACUNAR GENESIS 1.18 [1.05, 1.33]
EPIC–CVD 1.07 [1.02, 1.13]
FINLAND 0.93 [0.81, 1.07]
GLASGOW IMMUNOCHIP 1.08 [0.93, 1.27]
HVH1 1.01 [0.87, 1.18]
HVH2 1.08 [0.81, 1.45]
SAHLSIS 1.22 [1.00, 1.49]
SIFAP 1.10 [0.95, 1.28]
ICH 1.09 [0.98, 1.21]
EUR Meta–Analysis 1.05 [1.03, 1.07]
BIOBANK JAPAN 1.07 [1.03, 1.11]
HISAYAMA 0.99 [0.86, 1.14]
EAS Meta–Analysis 1.07 [1.03, 1.10]
COMPASS 1.05 [0.98, 1.13]
RACE1 0.95 [0.85, 1.07]
RACE2 1.03 [0.93, 1.15]
SDS 1.16 [0.77, 1.75]
SAS Meta–Analysis 1.00 [0.92, 1.08]
Trans Ethnic meta–analysis 1.05 [1.03, 1.07]
0.6 0.8 1 1.2 1.4 1.6 1.8
Odds Ratio (95%CI)

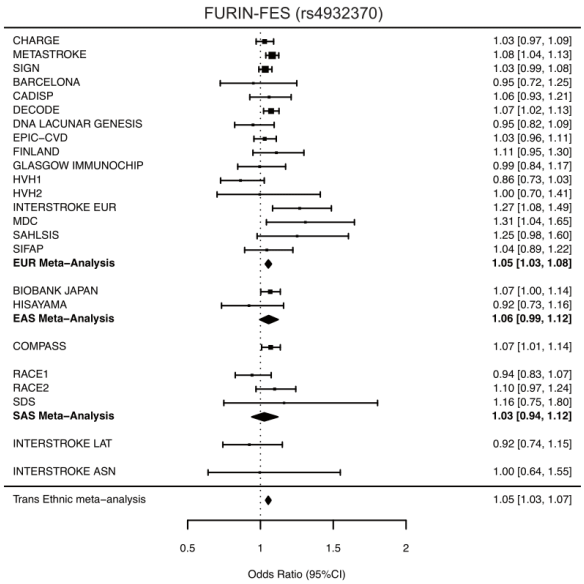

LINC01492 (rs10820405)
STUDY NAME
OR [95%CI]
METASTROKE 1.19 [1.08, 1.31]
SIGN 1.22 [1.07, 1.38]
BARCELONA 1.40 [0.93, 2.10]
CADISP 1.22 [0.75, 1.98]
DECODE 1.27 [1.07, 1.49]
FINLAND 1.27 [0.87, 1.85]
HVH1 0.81 [0.53, 1.24]
SIFAP 1.01 [0.73, 1.40]
EUR Meta–Analysis 1.20 [1.12, 1.28]
BIOBANK JAPAN 1.05 [0.95, 1.15]
HISAYAMA 1.08 [0.87, 1.33]
EAS Meta–Analysis 1.05 [0.96, 1.15]
SIGN group4 1.08 [0.59, 2.00]
SLESS 0.84 [0.44, 1.60]
AFR Meta–Analysis 0.96 [0.61, 1.50]
RACE1 1.01 [0.76, 1.34]
RACE2 0.85 [0.60, 1.19]
SAS Meta–Analysis 0.94 [0.76, 1.17]
Trans Ethnic meta–analysis 1.13 [1.08, 1.19]
0 0.5 1 1.5 2 2.5
Odds Ratio (95%CI)

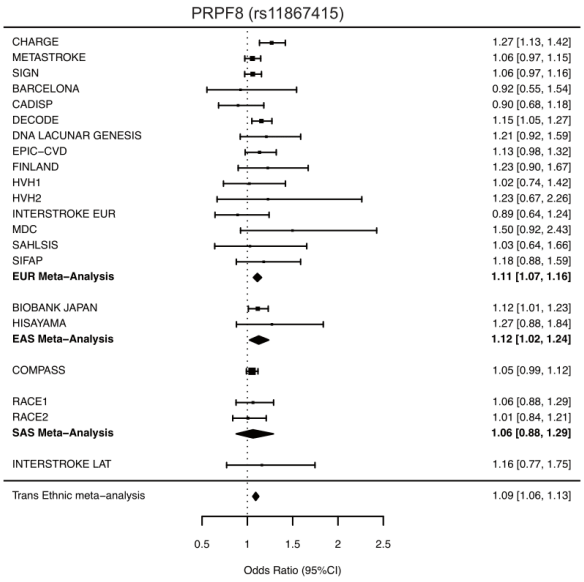

SH3PXD2A (rs2295786)
CHARGE 1.06 [1.01, 1.11]
METASTROKE 1.03 [0.99, 1.07]
SIGN 1.04 [1.00, 1.09]
BARCELONA 1.09 [0.88, 1.35]
CADISP 1.02 [0.88, 1.17]
DECODE 1.03 [0.99, 1.08]
DNA LACUNAR GENESIS 1.31 [1.15, 1.48]
EPIC–CVD 1.05 [0.99, 1.11]
FINLAND 0.98 [0.83, 1.14]
HVH2 1.24 [0.91, 1.68]
INTERSTROKE EUR 1.11 [0.95, 1.29]
MDC 1.11 [0.90, 1.38]
SAHLSIS 1.14 [0.92, 1.41]
SIFAP 1.01 [0.86, 1.18]
ICH 1.18 [1.06, 1.32]
EUR Meta–Analysis 1.05 [1.03, 1.07]
BIOBANK JAPAN 1.06 [1.03, 1.10]
HISAYAMA 1.08 [0.94, 1.25]
EAS Meta–Analysis 1.07 [1.03, 1.10]
COMPASS 1.06 [0.98, 1.15]
RACE1 0.99 [0.88, 1.11]
RACE2 1.08 [0.97, 1.20]
SDS 1.19 [0.79, 1.80]
SAS Meta–Analysis 1.04 [0.97, 1.13]
INTERSTROKE LAT 1.03 [0.89, 1.20]
INTERSTROKE ASN 1.10 [0.87, 1.39]
Trans Ethnic meta–analysis 1.05 [1.04, 1.07]
0.6 0.8 1 1.2 1.4 1.6 1.8
Odds Ratio (95%CI)

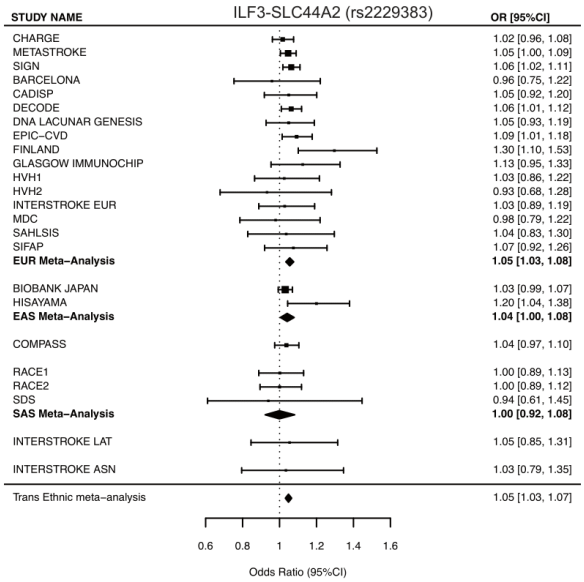

PDE3A (rs7304841)
CHARGE 1.01 [0.95, 1.07]
METASTROKE 1.02 [0.98, 1.06]
SIGN 1.00 [0.96, 1.04]
BARCELONA 0.98 [0.79, 1.22]
CADISP 1.01 [0.88, 1.17]
DECODE 1.09 [1.04, 1.14]
DNA LACUNAR GENESIS 1.04 [0.91, 1.18]
EPIC–CVD 1.11 [1.03, 1.19]
HVH1 1.17 [0.98, 1.40]
HVH2 1.01 [0.73, 1.38]
INTERSTROKE EUR 1.07 [0.91, 1.25]
SIFAP 1.08 [0.93, 1.26]
EUR Meta–Analysis 1.04 [1.02, 1.06]
BIOBANK JAPAN 1.07 [1.03, 1.11]
HISAYAMA 1.09 [0.95, 1.26]
EAS Meta–Analysis 1.07 [1.03, 1.11]
COMPASS 1.06 [1.00, 1.13]
RACE1 1.09 [0.95, 1.25]
RACE2 1.09 [0.96, 1.23]
SDS 0.81 [0.51, 1.30]
SAS Meta–Analysis 1.08 [0.99, 1.18]
INTERSTROKE LAT 1.16 [0.96, 1.41]
INTERSTROKE ASN 1.32 [1.01, 1.74]
Trans Ethnic meta–analysis 1.05 [1.03, 1.07]
0.5 1 1.5 2
Odds Ratio (95%CI)

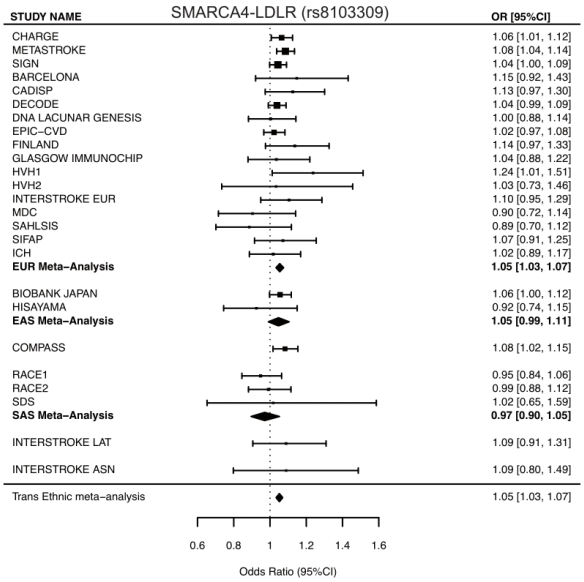

STUDY NAME
TBX3 (rs35436)
OR [95%CI]
CHARGE 1.06 [1.01, 1.11]
METASTROKE 1.06 [1.01, 1.10]
SIGN 1.04 [1.00, 1.09]
BARCELONA 1.08 [0.87, 1.35]
CADISP 0.81 [0.71, 0.92]
DECODE 1.02 [0.97, 1.06]
DNA_LACUNAR_GENESIS 0.98 [0.87, 1.11]
EPIC–CVD 1.03 [0.97, 1.09]
HVH2 0.96 [0.72, 1.28]
INTERSTROKE_EUR 1.00 [0.87, 1.16]
ICH 1.01 [0.91, 1.12]
EUR Meta–Analysis 1.03 [1.01, 1.05]
BIOBANK JAPAN 1.08 [1.04, 1.13]
HISAYAMA 1.09 [0.93, 1.28]
EAS Meta–Analysis 1.08 [1.04, 1.13]
COMPASS 1.05 [0.99, 1.12]
RACE1 1.18 [1.05, 1.33]
RACE2 1.02 [0.92, 1.14]
SDS 1.10 [0.72, 1.69]
SAS Meta–Analysis 1.09 [1.01, 1.18]
INTERSTROKE_LAT 1.23 [1.04, 1.45]
INTERSTROKE_ASN 1.10 [0.86, 1.42]
Trans Ethnic meta–analysis 1.05 [1.03, 1.06]
0.6 0.8 1 1.2 1.4 1.6 1.8
Odds Ratio (95%CI)

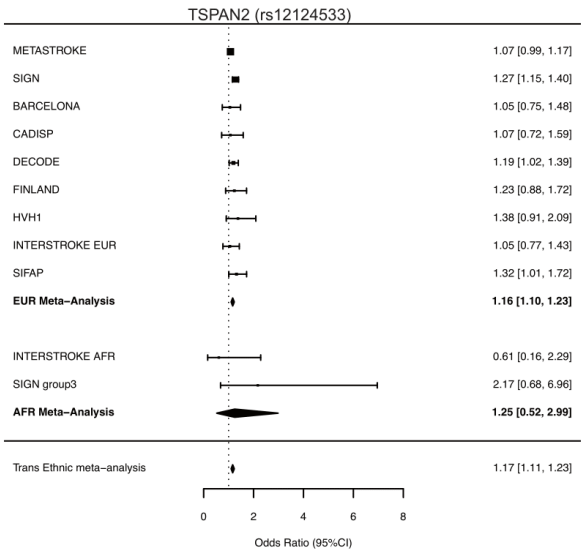

STUDY NAME
LRCH1 (rs9526212)
OR [95%CI]
CHARGE 1.07 [1.02, 1.13]
METASTROKE 1.08 [1.03, 1.13]
SIGN 1.03 [0.98, 1.09]
BARCELONA 0.96 [0.75, 1.22]
CADISP 1.11 [0.95, 1.29]
DECODE 1.07 [1.02, 1.12]
DNA_LACUNAR_GENESIS 1.03 [0.90, 1.19]
EPIC–CVD 1.02 [0.96, 1.09]
FINLAND 1.14 [0.96, 1.36]
GLASGOW IMMUNOCHIP 1.11 [0.92, 1.34]
HVH1 1.02 [0.86, 1.21]
HVH2 1.20 [0.84, 1.70]
INTERSTROKE_EUR 1.08 [0.89, 1.30]
MDC 1.31 [1.03, 1.66]
SAHLSIS 1.12 [0.89, 1.40]
SIFAP 1.10 [0.92, 1.32]
ICH 1.05 [0.93, 1.18]
EUR Meta–Analysis 1.06 [1.04, 1.08]
BIOBANK JAPAN 1.03 [0.97, 1.10]
HISAYAMA 0.99 [0.79, 1.24]
EAS Meta–Analysis 1.03 [0.97, 1.09]
COMPASS 1.09 [1.03, 1.16]
RACE1 1.07 [0.93, 1.23]
RACE2 1.04 [0.92, 1.18]
SDS 0.78 [0.47, 1.29]
SAS Meta–Analysis 1.04 [0.95, 1.14]
INTERSTROKE_LAT 0.90 [0.70, 1.15]
INTERSTROKE_ASN 1.07 [0.71, 1.63]
Trans Ethnic meta–analysis 1.06 [1.04, 1.08]
0 0.5 1 1.5 2
Odds Ratio (95%CI)

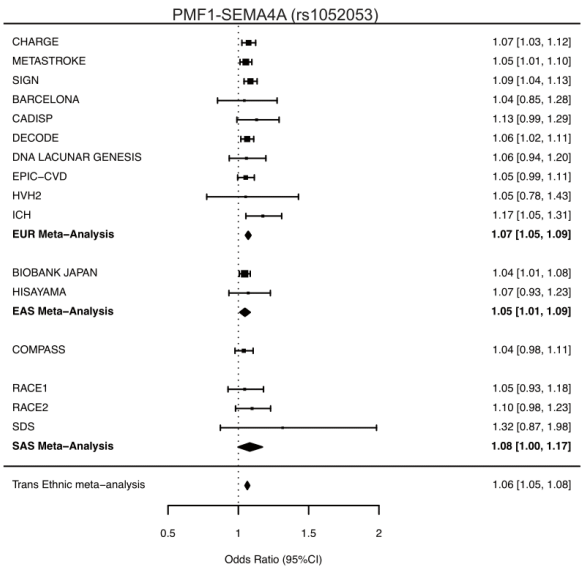

FURIN-FES (rs4932370)
CHARGE 1.03 [0.97, 1.09]
METASTROKE 1.08 [1.04, 1.13]
SIGN 1.03 [0.99, 1.08]
BARCELONA 0.95 [0.72, 1.25]
CADISP 1.06 [0.93, 1.21]
DECODE 1.07 [1.02, 1.13]
DNA LACUNAR GENESIS 0.95 [0.82, 1.09]
EPIC–CVD 1.03 [0.96, 1.11]
FINLAND 1.11 [0.95, 1.30]
GLASGOW IMMUNOCHIP 0.99 [0.84, 1.17]
HVH1 0.86 [0.73, 1.03]
HVH2 1.00 [0.70, 1.41]
INTERSTROKE EUR 1.27 [1.08, 1.49]
MDC 1.31 [1.04, 1.65]
SAHLSIS 1.25 [0.98, 1.60]
SIFAP 1.04 [0.89, 1.22]
EUR Meta–Analysis 1.05 [1.03, 1.08]
BIOBANK JAPAN 1.07 [1.00, 1.14]
HISAYAMA 0.92 [0.73, 1.16]
EAS Meta–Analysis 1.06 [0.99, 1.12]
COMPASS 1.07 [1.01, 1.14]
RACE1 0.94 [0.83, 1.07]
RACE2 1.10 [0.97, 1.24]
SDS 1.16 [0.75, 1.80]
SAS Meta–Analysis 1.03 [0.94, 1.12]
INTERSTROKE LAT 0.92 [0.74, 1.15]
INTERSTROKE ASN 1.00 [0.64, 1.55]
Trans Ethnic meta–analysis 1.05 [1.03, 1.07]
0.5 1 1.5 2
Odds Ratio (95%CI)

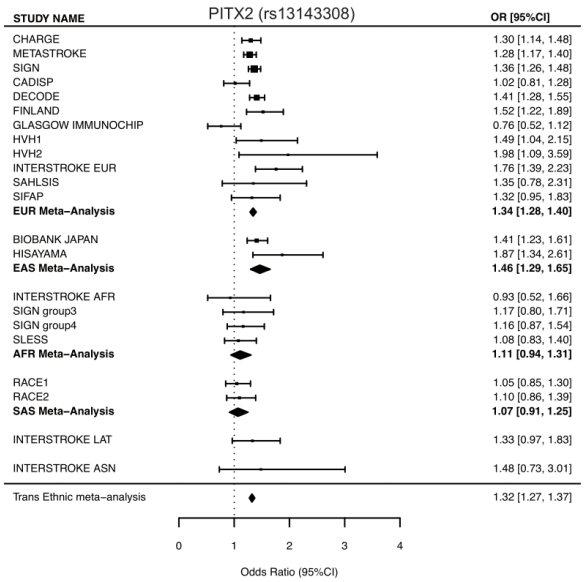

PRPF8 (rs11867415)
CHARGE 1.27 [1.13, 1.42]
METASTROKE 1.06 [0.97, 1.15]
SIGN 1.06 [0.97, 1.16]
BARCELONA 0.92 [0.55, 1.54]
CADISP 0.90 [0.68, 1.18]
DECODE 1.15 [1.05, 1.27]
DNA LACUNAR GENESIS 1.21 [0.92, 1.59]
EPIC–CVD 1.13 [0.98, 1.32]
FINLAND 1.23 [0.90, 1.67]
HVH1 1.02 [0.74, 1.42]
HVH2 1.23 [0.67, 2.26]
INTERSTROKE EUR 0.89 [0.64, 1.24]
MDC 1.50 [0.92, 2.43]
SAHLSIS 1.03 [0.64, 1.66]
SIFAP 1.18 [0.88, 1.59]
EUR Meta–Analysis 1.11 [1.07, 1.16]
BIOBANK JAPAN 1.12 [1.01, 1.23]
HISAYAMA 1.27 [0.88, 1.84]
EAS Meta–Analysis 1.12 [1.02, 1.24]
COMPASS 1.05 [0.99, 1.12]
RACE1 1.06 [0.88, 1.29]
RACE2 1.01 [0.84, 1.21]
SAS Meta–Analysis 1.06 [0.88, 1.29]
INTERSTROKE LAT 1.16 [0.77, 1.75]
Trans Ethnic meta–analysis 1.09 [1.06, 1.13]
0.5 1 1.5 2 2.5
Odds Ratio (95%CI)

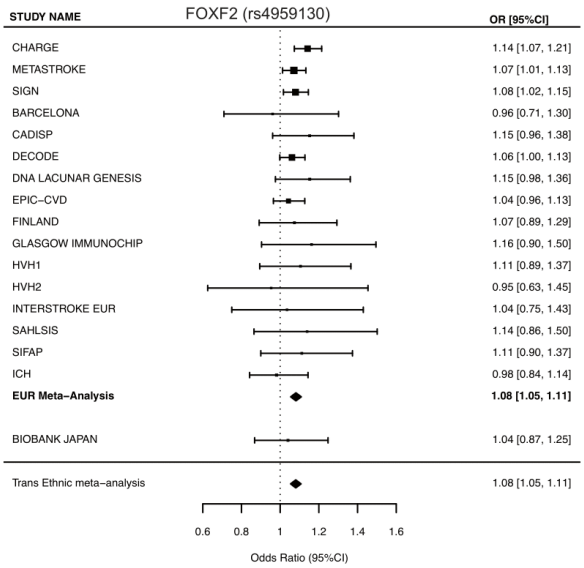

ILF3-SLC44A2 (rs2229383)
STUDY NAME
OR [95%CI]
CHARGE 1.02 [0.96, 1.08]
METASTROKE 1.05 [1.00, 1.09]
SIGN 1.06 [1.02, 1.11]
BARCELONA 0.96 [0.75, 1.22]
CADISP 1.05 [0.92, 1.20]
DECODE 1.06 [1.01, 1.12]
DNA LACUNAR GENESIS 1.05 [0.93, 1.19]
EPIC–CVD 1.09 [1.01, 1.18]
FINLAND 1.30 [1.10, 1.53]
GLASGOW IMMUNOCHIP 1.13 [0.95, 1.33]
HVH1 1.03 [0.86, 1.22]
HVH2 0.93 [0.68, 1.28]
INTERSTROKE EUR 1.03 [0.89, 1.19]
MDC 0.98 [0.79, 1.22]
SAHLSIS 1.04 [0.83, 1.30]
SIFAP 1.07 [0.92, 1.26]
EUR Meta–Analysis 1.05 [1.03, 1.08]
BIOBANK JAPAN 1.03 [0.99, 1.07]
HISAYAMA 1.20 [1.04, 1.38]
EAS Meta–Analysis 1.04 [1.00, 1.08]
COMPASS 1.04 [0.97, 1.10]
RACE1 1.00 [0.89, 1.13]
RACE2 1.00 [0.89, 1.12]
SDS 0.94 [0.61, 1.45]
SAS Meta–Analysis 1.00 [0.92, 1.08]
INTERSTROKE LAT 1.05 [0.85, 1.31]
INTERSTROKE ASN 1.03 [0.79, 1.35]
Trans Ethnic meta–analysis 1.05 [1.03, 1.07]
0.6 0.8 1 1.2 1.4 1.6
Odds Ratio (95%CI)

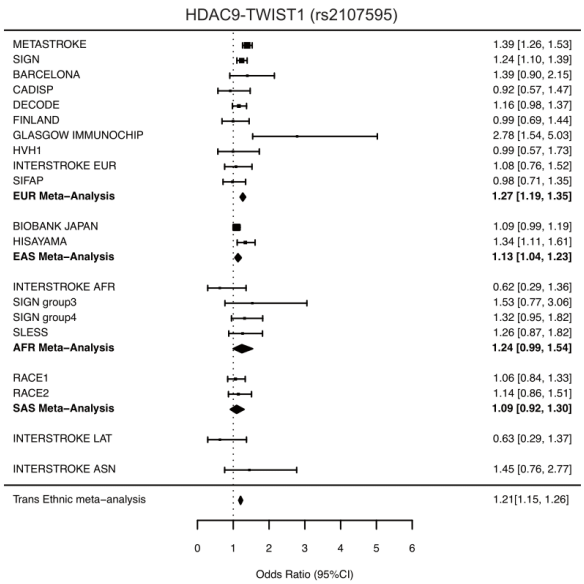

SMARCA4-LDLR (rs8103309)
STUDY NAME
OR [95%CI]
CHARGE 1.06 [1.01, 1.12]
METASTROKE 1.08 [1.04, 1.14]
SIGN 1.04 [1.00, 1.09]
BARCELONA 1.15 [0.92, 1.43]
CADISP 1.13 [0.97, 1.30]
DECODE 1.04 [0.99, 1.09]
DNA LACUNAR GENESIS 1.00 [0.88, 1.14]
EPIC–CVD 1.02 [0.97, 1.08]
FINLAND 1.14 [0.97, 1.33]
GLASGOW IMMUNOCHIP 1.04 [0.88, 1.22]
HVH1 1.24 [1.01, 1.51]
HVH2 1.03 [0.73, 1.46]
INTERSTROKE EUR 1.10 [0.95, 1.29]
MDC 0.90 [0.72, 1.14]
SAHLSIS 0.89 [0.70, 1.12]
SIFAP 1.07 [0.91, 1.25]
ICH 1.02 [0.89, 1.17]
EUR Meta–Analysis 1.05 [1.03, 1.07]
BIOBANK JAPAN 1.06 [1.00, 1.12]
HISAYAMA 0.92 [0.74, 1.15]
EAS Meta–Analysis 1.05 [0.99, 1.11]
COMPASS 1.08 [1.02, 1.15]
RACE1 0.95 [0.84, 1.06]
RACE2 0.99 [0.88, 1.12]
SDS 1.02 [0.65, 1.59]
SAS Meta–Analysis 0.97 [0.90, 1.05]
INTERSTROKE LAT 1.09 [0.91, 1.31]
INTERSTROKE ASN 1.09 [0.80, 1.49]
Trans Ethnic meta–analysis 1.05 [1.03, 1.07]
0.6 0.8 1 1.2 1.4 1.6
Odds Ratio (95%CI)

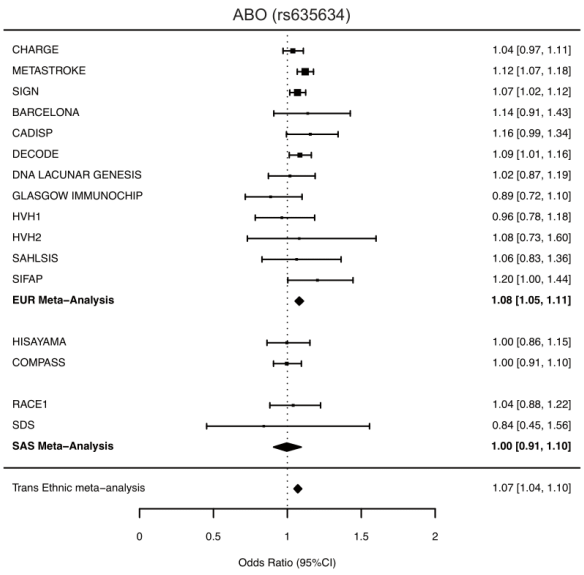

TSPAN2 (rs12124533)
METASTROKE 1.07 [0.99, 1.17]
SIGN 1.27 [1.15, 1.40]
BARCELONA 1.05 [0.75, 1.48]
CADISP 1.07 [0.72, 1.59]
DECODE 1.19 [1.02, 1.39]
FINLAND 1.23 [0.88, 1.72]
HVH1 1.38 [0.91, 2.09]
INTERSTROKE EUR 1.05 [0.77, 1.43]
SIFAP 1.32 [1.01, 1.72]
EUR Meta–Analysis 1.16 [1.10, 1.23]
INTERSTROKE AFR 0.61 [0.16, 2.29]
SIGN group3 2.17 [0.68, 6.96]
AFR Meta–Analysis 1.25 [0.52, 2.99]
Trans Ethnic meta–analysis 1.17 [1.11, 1.23]
0 2 4 6 8
Odds Ratio (95%CI)

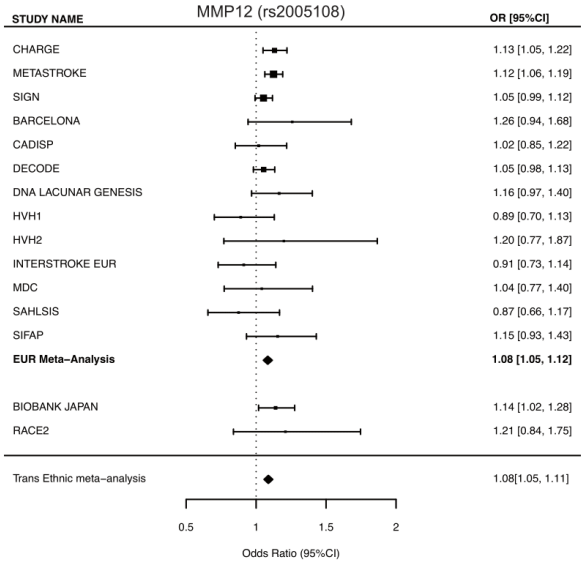

PMF1-SEMA4A (rs1052053)
CHARGE 1.07 [1.03, 1.12]
METASTROKE 1.05 [1.01, 1.10]
SIGN 1.09 [1.04, 1.13]
BARCELONA 1.04 [0.85, 1.28]
CADISP 1.13 [0.99, 1.29]
DECODE 1.06 [1.02, 1.11]
DNA LACUNAR GENESIS 1.06 [0.94, 1.20]
EPIC–CVD 1.05 [0.99, 1.11]
HVH2 1.05 [0.78, 1.43]
ICH 1.17 [1.05, 1.31]
EUR Meta–Analysis 1.07 [1.05, 1.09]
BIOBANK JAPAN 1.04 [1.01, 1.08]
HISAYAMA 1.07 [0.93, 1.23]
EAS Meta–Analysis 1.05 [1.01, 1.09]
COMPASS 1.04 [0.98, 1.11]
RACE1 1.05 [0.93, 1.18]
RACE2 1.10 [0.98, 1.23]
SDS 1.32 [0.87, 1.98]
SAS Meta–Analysis 1.08 [1.00, 1.17]
Trans Ethnic meta–analysis 1.06 [1.05, 1.08]
0.5 1 1.5 2
Odds Ratio (95%CI)

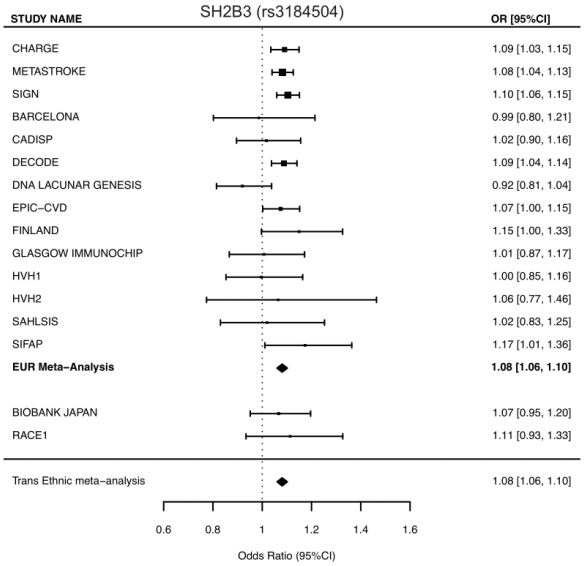

PITX2 (rs13143308)
STUDY NAME
OR [95%CI]
CHARGE 1.30 [1.14, 1.48]
METASTROKE 1.28 [1.17, 1.40]
SIGN 1.36 [1.26, 1.48]
CADISP 1.02 [0.81, 1.28]
DECODE 1.41 [1.28, 1.55]
FINLAND 1.52 [1.22, 1.89]
GLASGOW IMMUNOCHIP 0.76 [0.52, 1.12]
HVH1 1.49 [1.04, 2.15]
HVH2 1.98 [1.09, 3.59]
INTERSTROKE EUR 1.76 [1.39, 2.23]
SAHLSIS 1.35 [0.78, 2.31]
SIFAP 1.32 [0.95, 1.83]
EUR Meta−Analysis 1.34 [1.28, 1.40]
BIOBANK JAPAN 1.41 [1.23, 1.61]
HISAYAMA 1.87 [1.34, 2.61]
EAS Meta−Analysis 1.46 [1.29, 1.65]
INTERSTROKE AFR 0.93 [0.52, 1.66]
SIGN group3 1.17 [0.80, 1.71]
SIGN group4 1.16 [0.87, 1.54]
SLESS 1.08 [0.83, 1.40]
AFR Meta−Analysis 1.11 [0.94, 1.31]
RACE1 1.05 [0.85, 1.30]
RACE2 1.10 [0.86, 1.39]
SAS Meta−Analysis 1.07 [0.91, 1.25]
INTERSTROKE LAT 1.33 [0.97, 1.83]
INTERSTROKE ASN 1.48 [0.73, 3.01]
Trans Ethnic meta−analysis 1.32 [1.27, 1.37]
0 1 2 3 4
Odds Ratio (95%CI)

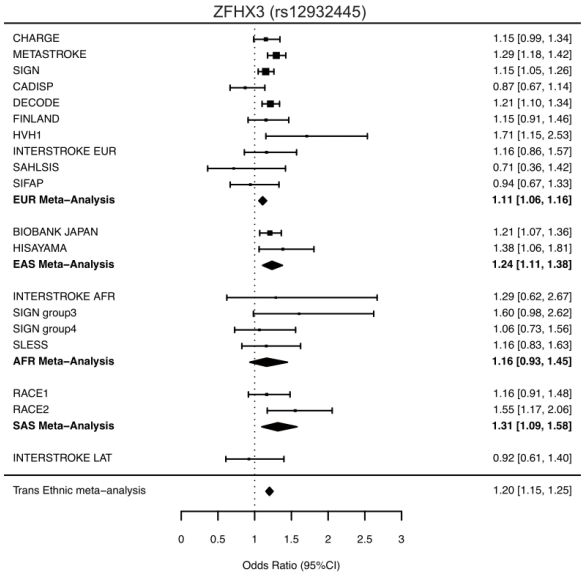

FOXF2 (rs4959130)
STUDY NAME
OR [95%CI]
CHARGE 1.14 [1.07, 1.21]
METASTROKE 1.07 [1.01, 1.13]
SIGN 1.08 [1.02, 1.15]
BARCELONA 0.96 [0.71, 1.30]
CADISP 1.15 [0.96, 1.38]
DECODE 1.06 [1.00, 1.13]
DNA LACUNAR GENESIS 1.15 [0.98, 1.36]
EPIC−CVD 1.04 [0.96, 1.13]
FINLAND 1.07 [0.89, 1.29]
GLASGOW IMMUNOCHIP 1.16 [0.90, 1.50]
HVH1 1.11 [0.89, 1.37]
HVH2 0.95 [0.63, 1.45]
INTERSTROKE EUR 1.04 [0.75, 1.43]
SAHLSIS 1.14 [0.86, 1.50]
SIFAP 1.11 [0.90, 1.37]
ICH 0.98 [0.84, 1.14]
EUR Meta−Analysis 1.08 [1.05, 1.11]
BIOBANK JAPAN 1.04 [0.87, 1.25]
Trans Ethnic meta−analysis 1.08 [1.05, 1.11]
0.6 0.8 1 1.2 1.4 1.6
Odds Ratio (95%CI)

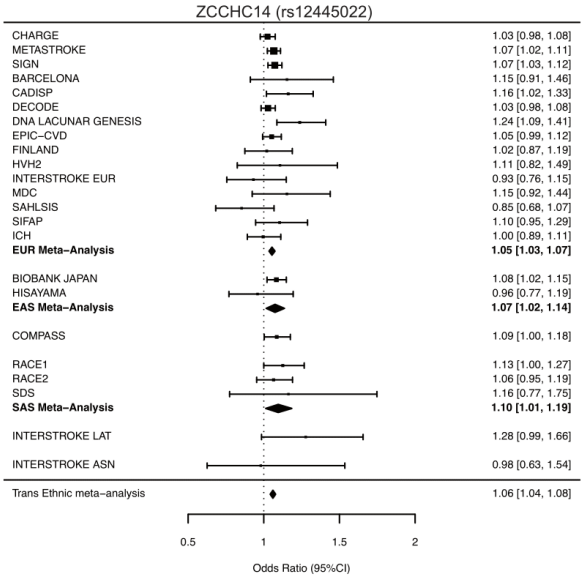

HDAC9-TWIST1 (rs2107595)
METASTROKE 1.39 [1.26, 1.53]
SIGN 1.24 [1.10, 1.39]
BARCELONA 1.39 [0.90, 2.15]
CADISP 0.92 [0.57, 1.47]
DECODE 1.16 [0.98, 1.37]
FINLAND 0.99 [0.69, 1.44]
GLASGOW IMMUNOCHIP 2.78 [1.54, 5.03]
HVH1 0.99 [0.57, 1.73]
INTERSTROKE EUR 1.08 [0.76, 1.52]
SIFAP 0.98 [0.71, 1.35]
EUR Meta−Analysis 1.27 [1.19, 1.35]
BIOBANK JAPAN 1.09 [0.99, 1.19]
HISAYAMA 1.34 [1.11, 1.61]
EAS Meta−Analysis 1.13 [1.04, 1.23]
INTERSTROKE AFR 0.62 [0.29, 1.36]
SIGN group3 1.53 [0.77, 3.06]
SIGN group4 1.32 [0.95, 1.82]
SLESS 1.26 [0.87, 1.82]
AFR Meta−Analysis 1.24 [0.99, 1.54]
RACE1 1.06 [0.84, 1.33]
RACE2 1.14 [0.86, 1.51]
SAS Meta−Analysis 1.09 [0.92, 1.30]
INTERSTROKE LAT 0.63 [0.29, 1.37]
INTERSTROKE ASN 1.45 [0.76, 2.77]
Trans Ethnic meta−analysis 1.21[1.15, 1.26]
0 1 2 3 4 5 6
Odds Ratio (95%CI)


ABO (rs635634)
CHARGE 1.04 [0.97, 1.11]
METASTROKE 1.12 [1.07, 1.18]
SIGN 1.07 [1.02, 1.12]
BARCELONA 1.14 [0.91, 1.43]
CADISP 1.16 [0.99, 1.34]
DECODE 1.09 [1.01, 1.16]
DNA LACUNAR GENESIS 1.02 [0.87, 1.19]
GLASGOW IMMUNOCHIP 0.89 [0.72, 1.10]
HVH1 0.96 [0.78, 1.18]
HVH2 1.08 [0.73, 1.60]
SAHLSIS 1.06 [0.83, 1.36]
SIFAP 1.20 [1.00, 1.44]
EUR Meta−Analysis 1.08 [1.05, 1.11]
HISAYAMA 1.00 [0.86, 1.15]
COMPASS 1.00 [0.91, 1.10]
RACE1 1.04 [0.88, 1.22]
SDS 0.84 [0.45, 1.56]
SAS Meta−Analysis 1.00 [0.91, 1.10]
Trans Ethnic meta−analysis 1.07 [1.04, 1.10]
0 0.5 1 1.5 2
Odds Ratio (95%CI)

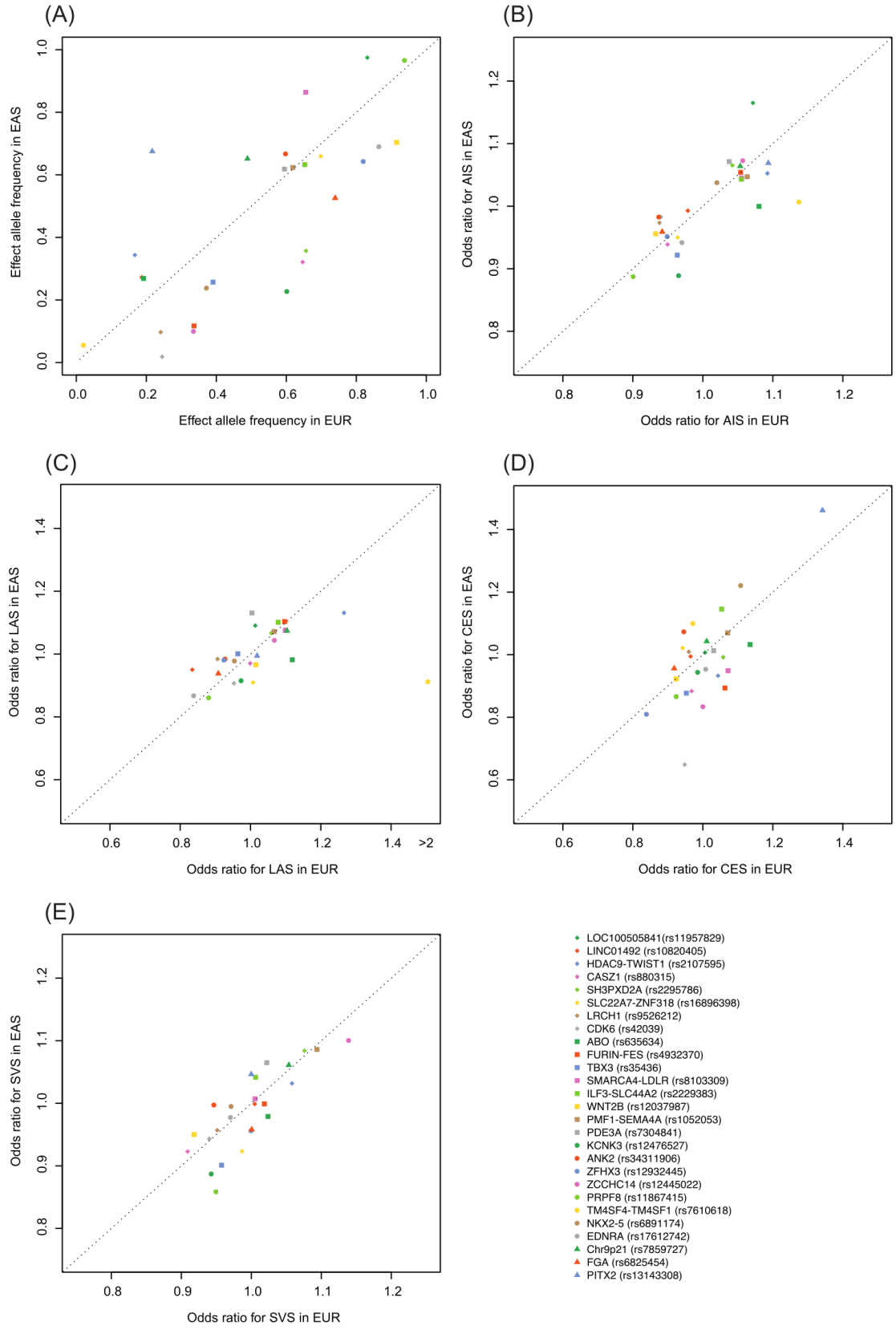

MMP12 (rs2005108)
STUDY NAME
OR [95%CI]
CHARGE
1.13 [1.05, 1.22]
METASTROKE
1.12 [1.06, 1.19]
SIGN
1.05 [0.99, 1.12]
BARCELONA
1.26 [0.94, 1.68]
CADISP
1.02 [0.85, 1.22]
DECODE
1.05 [0.98, 1.13]
DNA LACUNAR GENESIS
1.16 [0.97, 1.40]
HVH1
0.89 [0.70, 1.13]
HVH2
1.20 [0.77, 1.87]
INTERSTROKE EUR
0.91 [0.73, 1.14]
MDC
1.04 [0.77, 1.40]
SAHLSIS
0.87 [0.66, 1.17]
SIFAP
1.15 [0.93, 1.43]
EUR Meta−Analysis
1.08 [1.05, 1.12]
BIOBANK JAPAN
1.14 [1.02, 1.28]
RACE2
1.21 [0.84, 1.75]
Trans Ethnic meta−analysis
1.08[1.05, 1.11]
0.5
1
1.5
2
Odds Ratio (95%CI)


SH2B3 (rs3184504)
STUDY NAME
OR [95%CI]
CHARGE
1.09 [1.03, 1.15]
METASTROKE
1.08 [1.04, 1.13]
SIGN
1.10 [1.06, 1.15]
BARCELONA
0.99 [0.80, 1.21]
CADISP
1.02 [0.90, 1.16]
DECODE
1.09 [1.04, 1.14]
DNA LACUNAR GENESIS
0.92 [0.81, 1.04]
EPIC−CVD
1.07 [1.00, 1.15]
FINLAND
1.15 [1.00, 1.33]
GLASGOW IMMUNOCHIP
1.01 [0.87, 1.17]
HVH1
1.00 [0.85, 1.16]
HVH2
1.06 [0.77, 1.46]
SAHLSIS
1.02 [0.83, 1.25]
SIFAP
1.17 [1.01, 1.36]
EUR Meta−Analysis
1.08 [1.06, 1.10]
BIOBANK JAPAN
1.07 [0.95, 1.20]
RACE1
1.11 [0.93, 1.33]
Trans Ethnic meta−analysis
1.08 [1.06, 1.10]
0.6
0.8
1
1.2
1.4
1.6
Odds Ratio (95%CI)

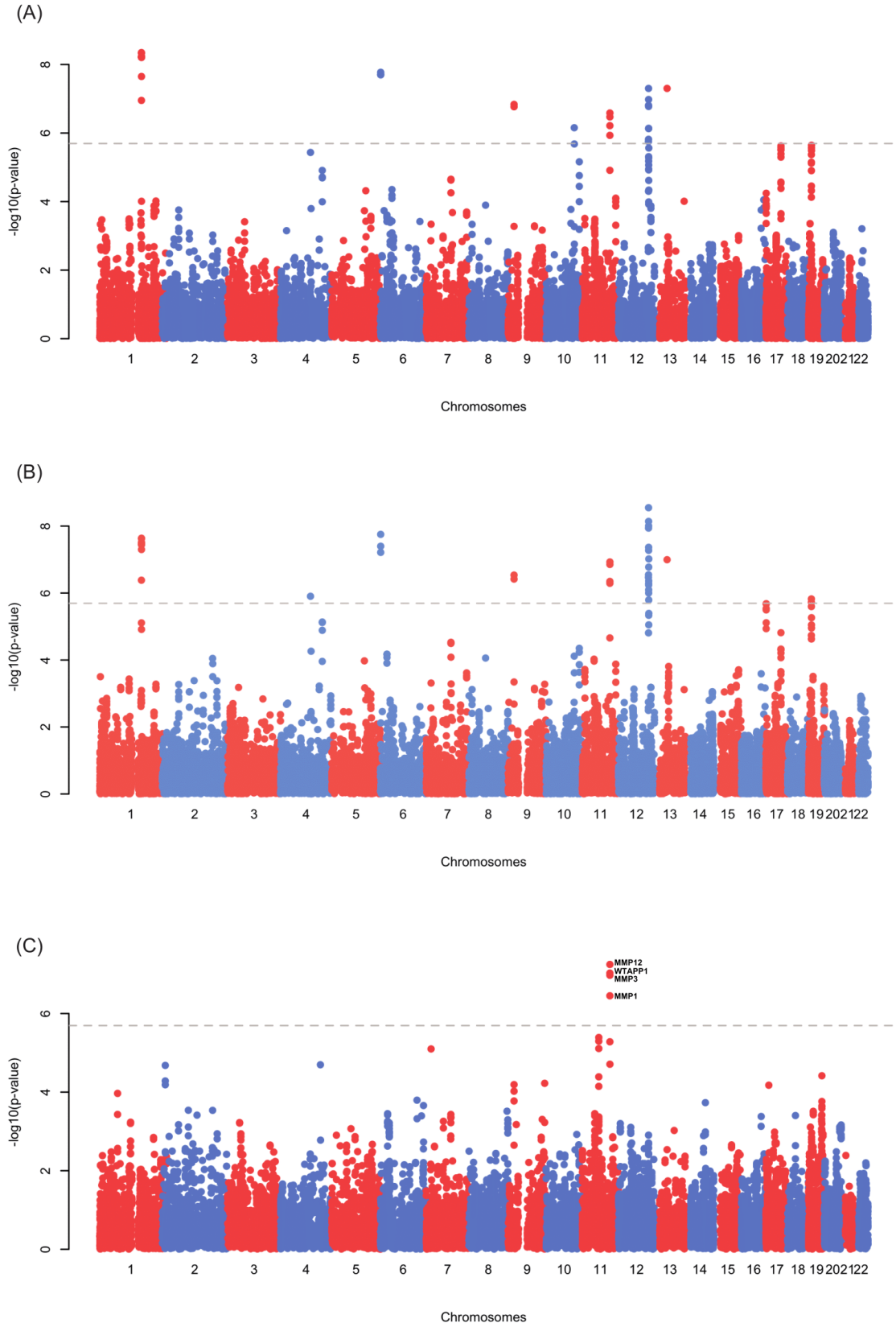

ZFHX3 (rs12932445)
CHARGE
1.15 [0.99, 1.34]
METASTROKE
1.29 [1.18, 1.42]
SIGN
1.15 [1.05, 1.26]
CADISP
0.87 [0.67, 1.14]
DECODE
1.21 [1.10, 1.34]
FINLAND
1.15 [0.91, 1.46]
HVH1
1.71 [1.15, 2.53]
INTERSTROKE EUR
1.16 [0.86, 1.57]
SAHLSIS
0.71 [0.36, 1.42]
SIFAP
0.94 [0.67, 1.33]
EUR Meta−Analysis
1.11 [1.06, 1.16]
BIOBANK JAPAN
1.21 [1.07, 1.36]
HISAYAMA
1.38 [1.06, 1.81]
EAS Meta−Analysis
1.24 [1.11, 1.38]
INTERSTROKE AFR
1.29 [0.62, 2.67]
SIGN group3
1.60 [0.98, 2.62]
SIGN group4
1.06 [0.73, 1.56]
SLESS
1.16 [0.83, 1.63]
AFR Meta−Analysis
1.16 [0.93, 1.45]
RACE1
1.16 [0.91, 1.48]
RACE2
1.55 [1.17, 2.06]
SAS Meta−Analysis
1.31 [1.09, 1.58]
INTERSTROKE LAT
0.92 [0.61, 1.40]
Trans Ethnic meta−analysis
1.20 [1.15, 1.25]
0
0.5
1
1.5
2
2.5
3
Odds Ratio (95%CI)


ZCCHC14 (rs12445022)
CHARGE
1.03 [0.98, 1.08]
METASTROKE
1.07 [1.02, 1.11]
SIGN
1.07 [1.03, 1.12]
BARCELONA
1.15 [0.91, 1.46]
CADISP
1.16 [1.02, 1.33]
DECODE
1.03 [0.98, 1.08]
DNA LACUNAR GENESIS
1.24 [1.09, 1.41]
EPIC−CVD
1.05 [0.99, 1.12]
FINLAND
1.02 [0.87, 1.19]
HVH2
1.11 [0.82, 1.49]
INTERSTROKE EUR
0.93 [0.76, 1.15]
MDC
1.15 [0.92, 1.44]
SAHLSIS
0.85 [0.68, 1.07]
SIFAP
1.10 [0.95, 1.29]
ICH
1.00 [0.89, 1.11]
EUR Meta−Analysis
1.05 [1.03, 1.07]
BIOBANK JAPAN
1.08 [1.02, 1.15]
HISAYAMA
0.96 [0.77, 1.19]
EAS Meta−Analysis
1.07 [1.02, 1.14]
COMPASS
1.09 [1.00, 1.18]
RACE1
1.13 [1.00, 1.27]
RACE2
1.06 [0.95, 1.19]
SDS
1.16 [0.77, 1.75]
SAS Meta−Analysis
1.10 [1.01, 1.19]
INTERSTROKE LAT
1.28 [0.99, 1.66]
INTERSTROKE ASN
0.98 [0.63, 1.54]
Trans Ethnic meta−analysis
1.06 [1.04, 1.08]
0.5
1
1.5
2
Odds Ratio (95%CI)

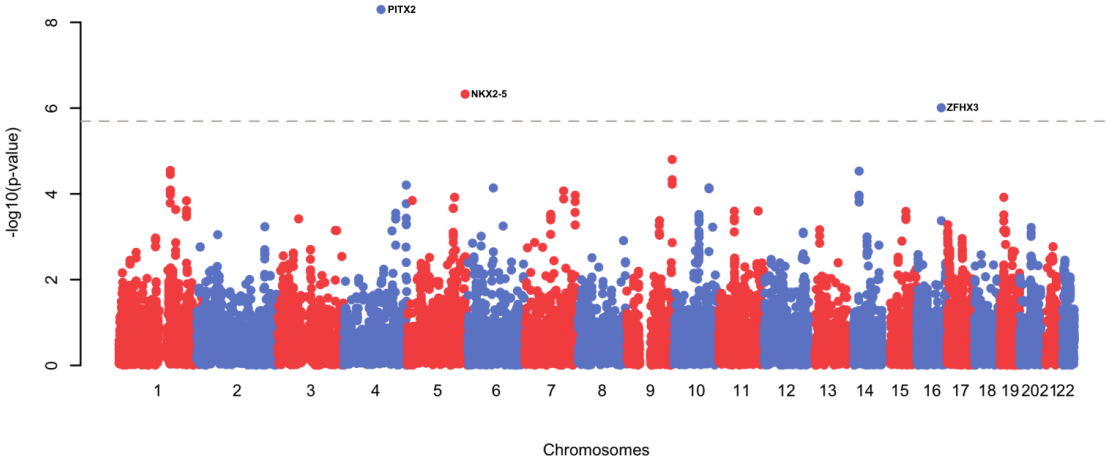
Supplementary Figure 8



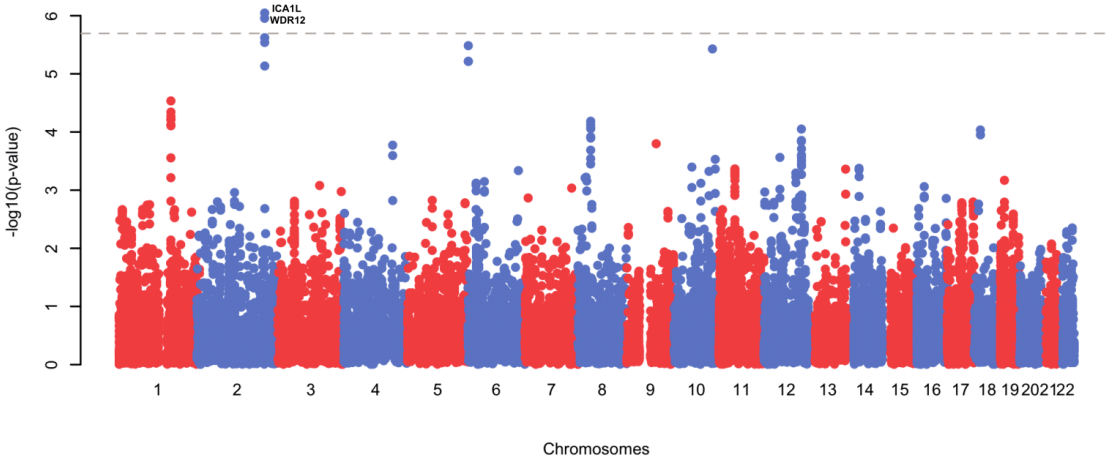
Supplementary Figure 9



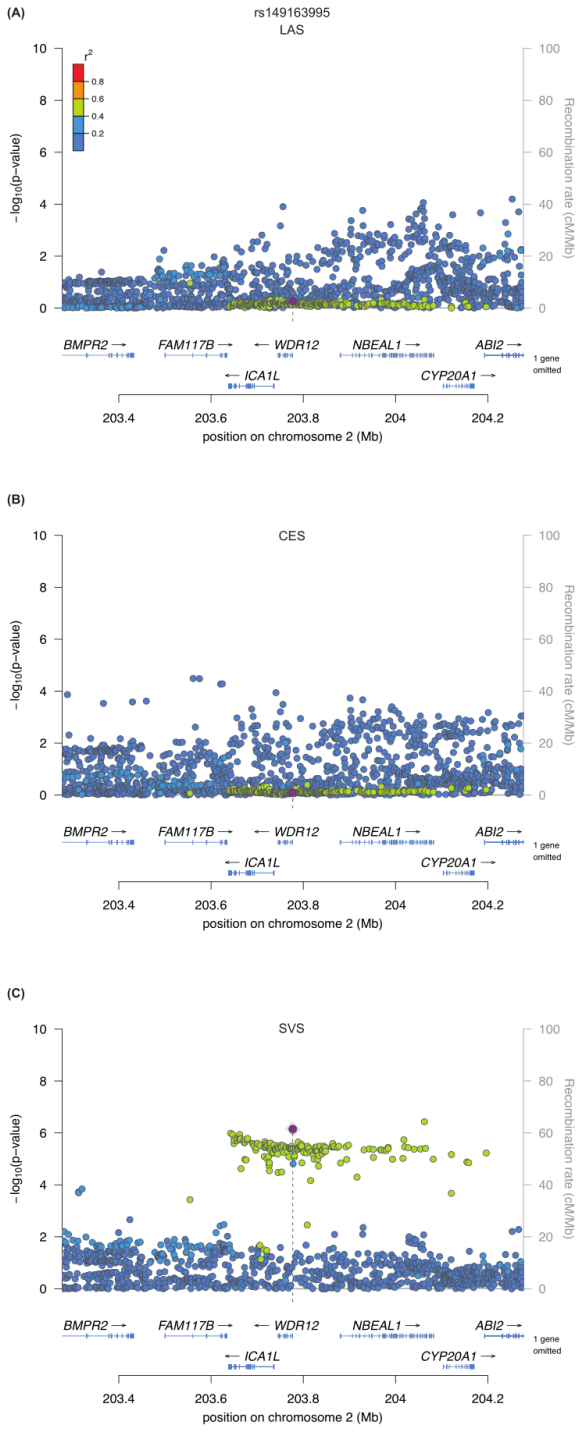
(D)


PITX2
NKX2-5
ZFHX3
-log10(p-value)
0
2
4
6
8
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
Chromosomes

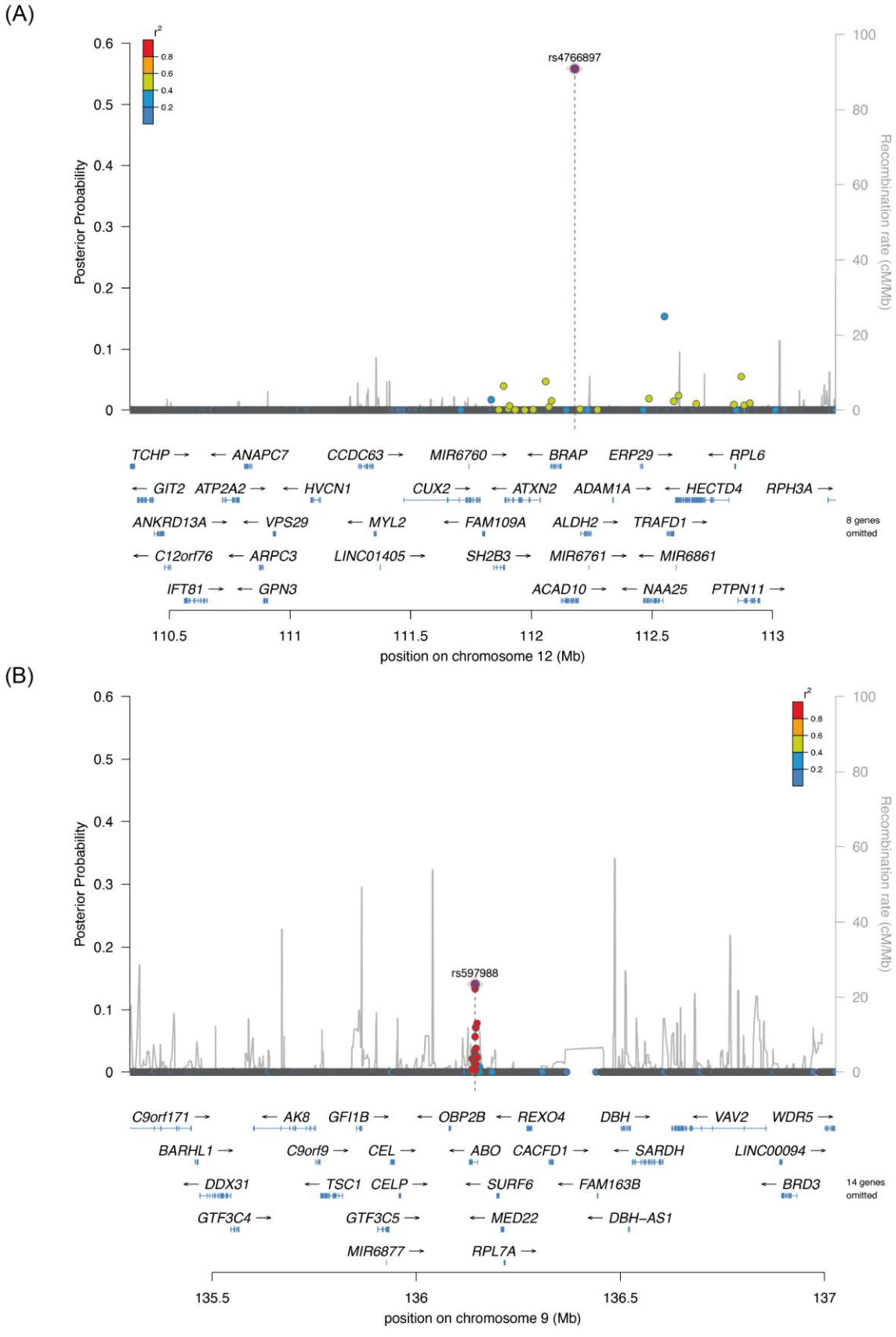
(E)


ICA1L
WDR12
-log10(p-value)
0
1
2
3
4
5
6
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
Chromosomes

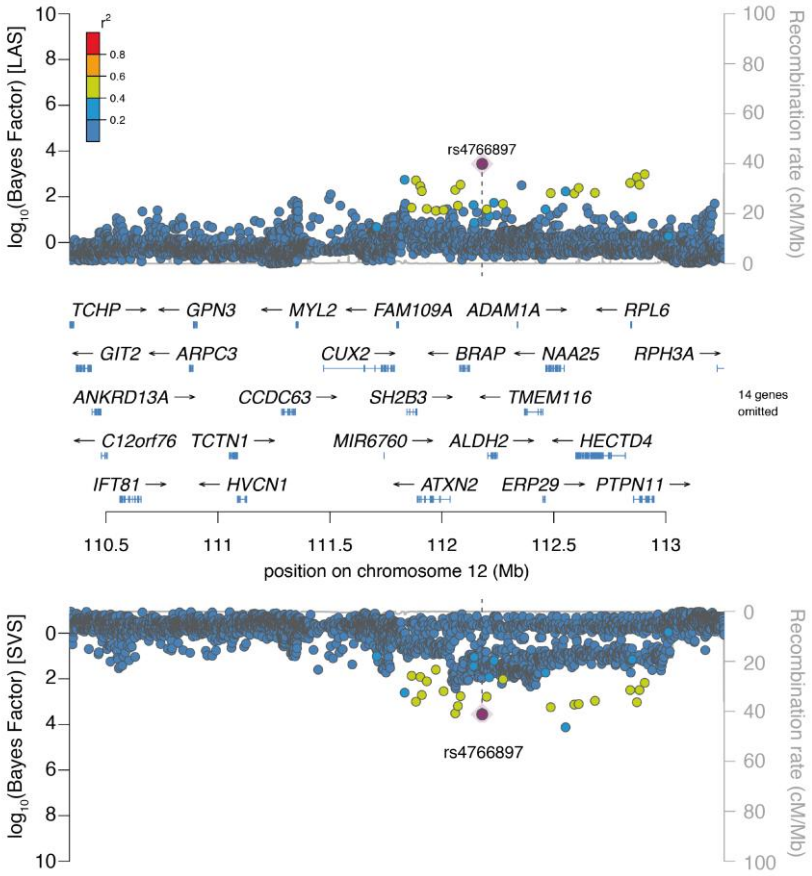
Supplementary Figure 10



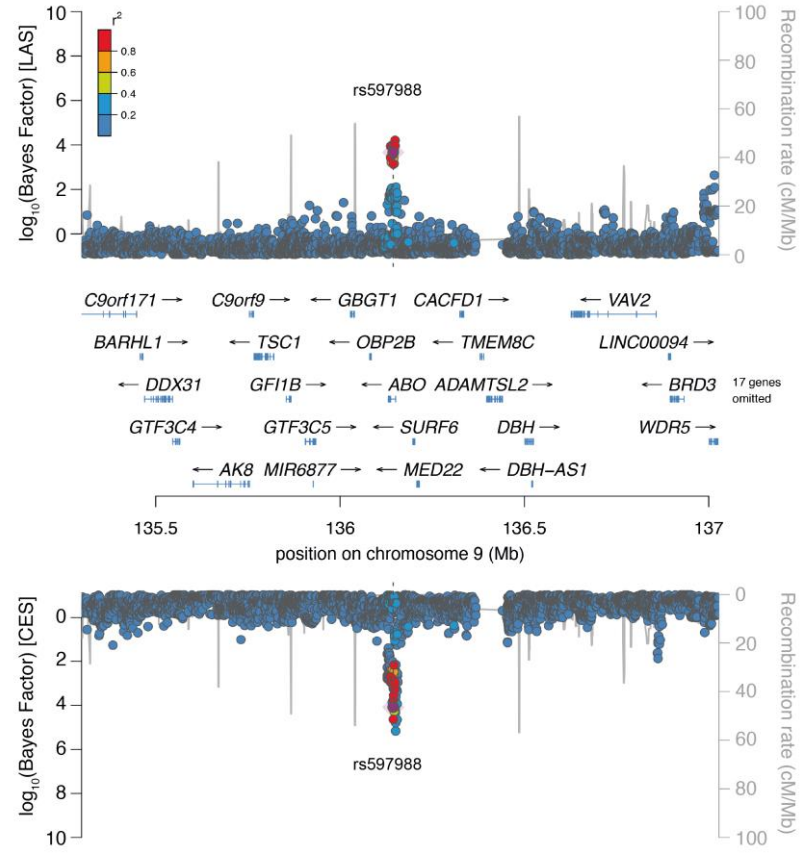
Supplementary Figure 11



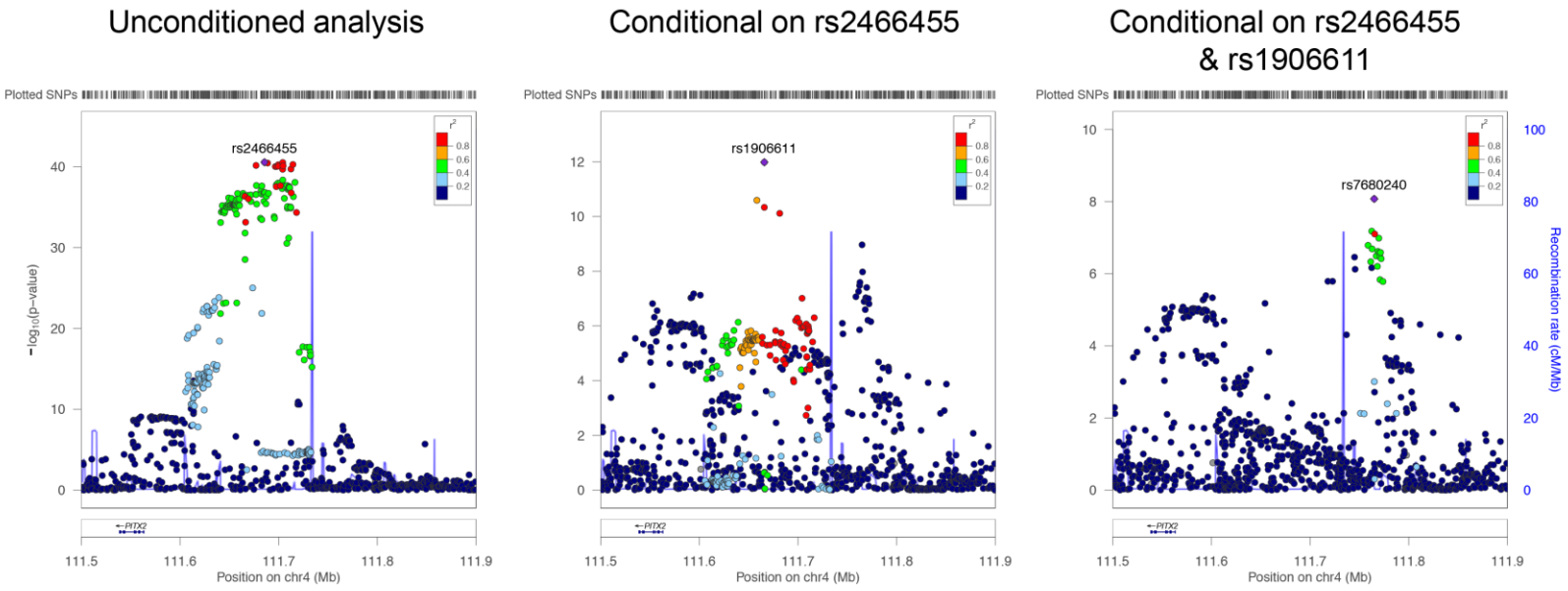
(C)


log10(Bayes Factor) [LAS]
r2
0.8
0.6
0.4
0.2
rs4766897
Recombination rate (cM/Mb)
TCHP GPN3 MYL2 FAM109A ADAM1A RPL6
GIT2 ARPC3 CUX2 BRAP NAA25 RPH3A
ANKRD13A CCDC63 SH2B3 TMEM116
14 genes omitted
C12orf76 TCTN1 MIR6760 ALDH2 HECTD4
IFT81 HVCN1 ATXN2 ERP29 PTPN11
110.5 111 111.5 112 112.5 113
position on chromosome 12 (Mb)
log10(Bayes Factor) [SVS]
rs4766897
Recombination rate (cM/Mb)

(D)

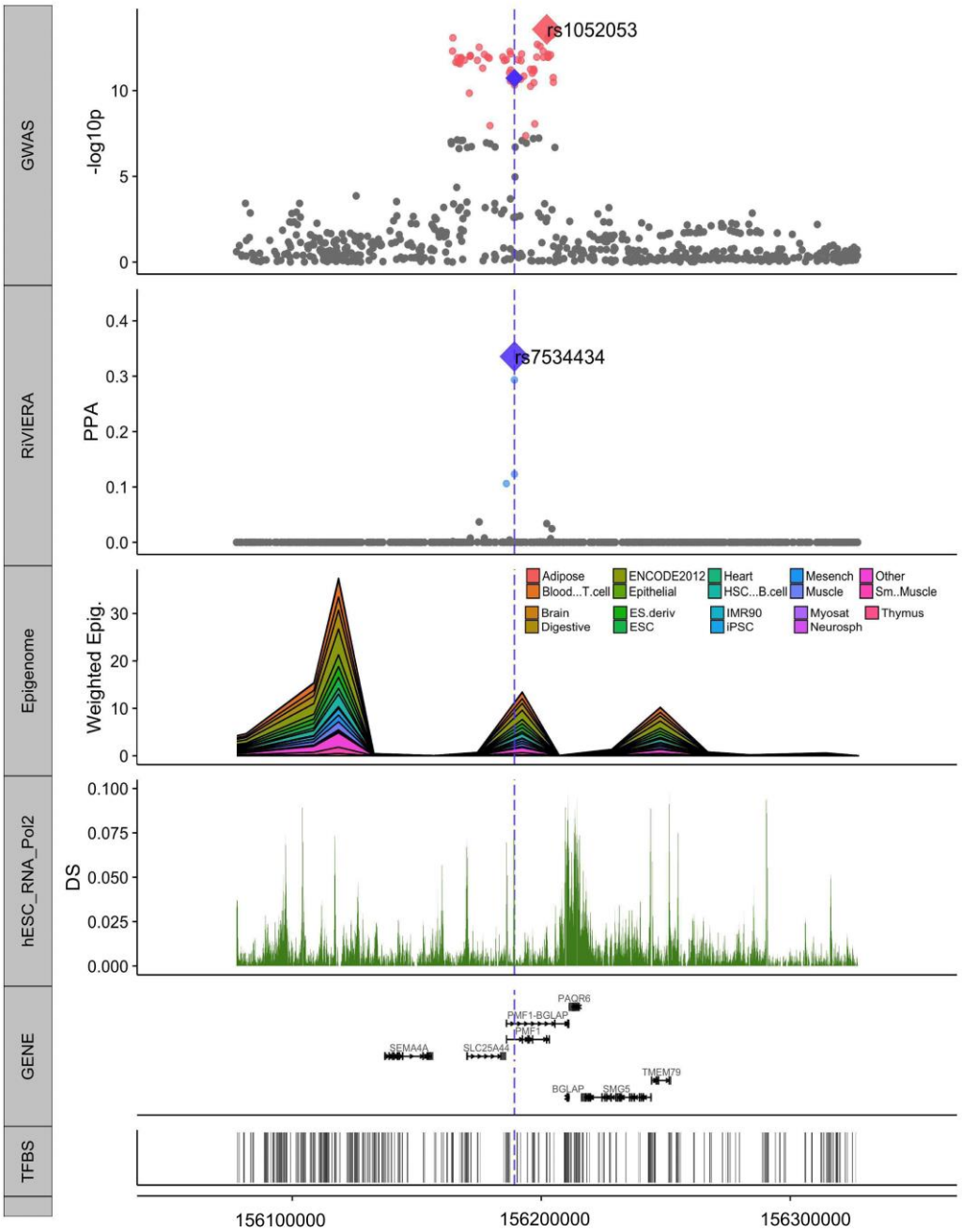

log10(Bayes Factor) [LAS]
r2
0.8
0.6
0.4
0.2
rs597988
Recombination rate (cM/Mb)
C9orf171 C9orf9 GBGT1 CACFD1 VAV2
BARHL1 TSC1 OBP2B TMEM8C LINC00094
DDX31 GFI1B ABO ADAMTSL2 BRD3
17 genes omitted
GTF3C4 GTF3C5 SURF6 DBH WDR5
AK8 MIR6877 MED22 DBH-AS1
135.5 136 136.5 137
position on chromosome 9 (Mb)
log10(Bayes Factor) [CES]
rs597988
Recombination rate (cM/Mb)

Supplementary Figure 12

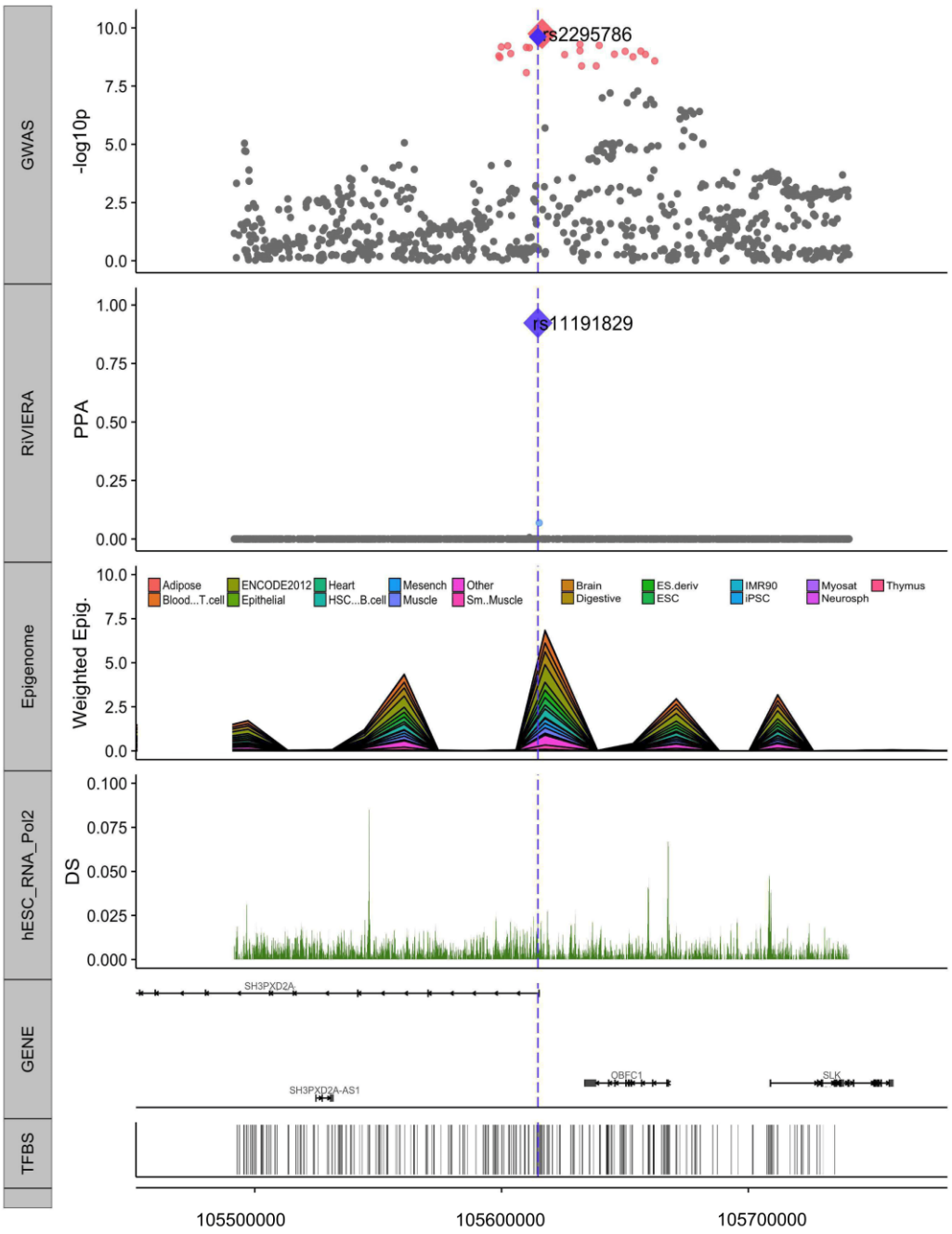


Supplementary Figure 13

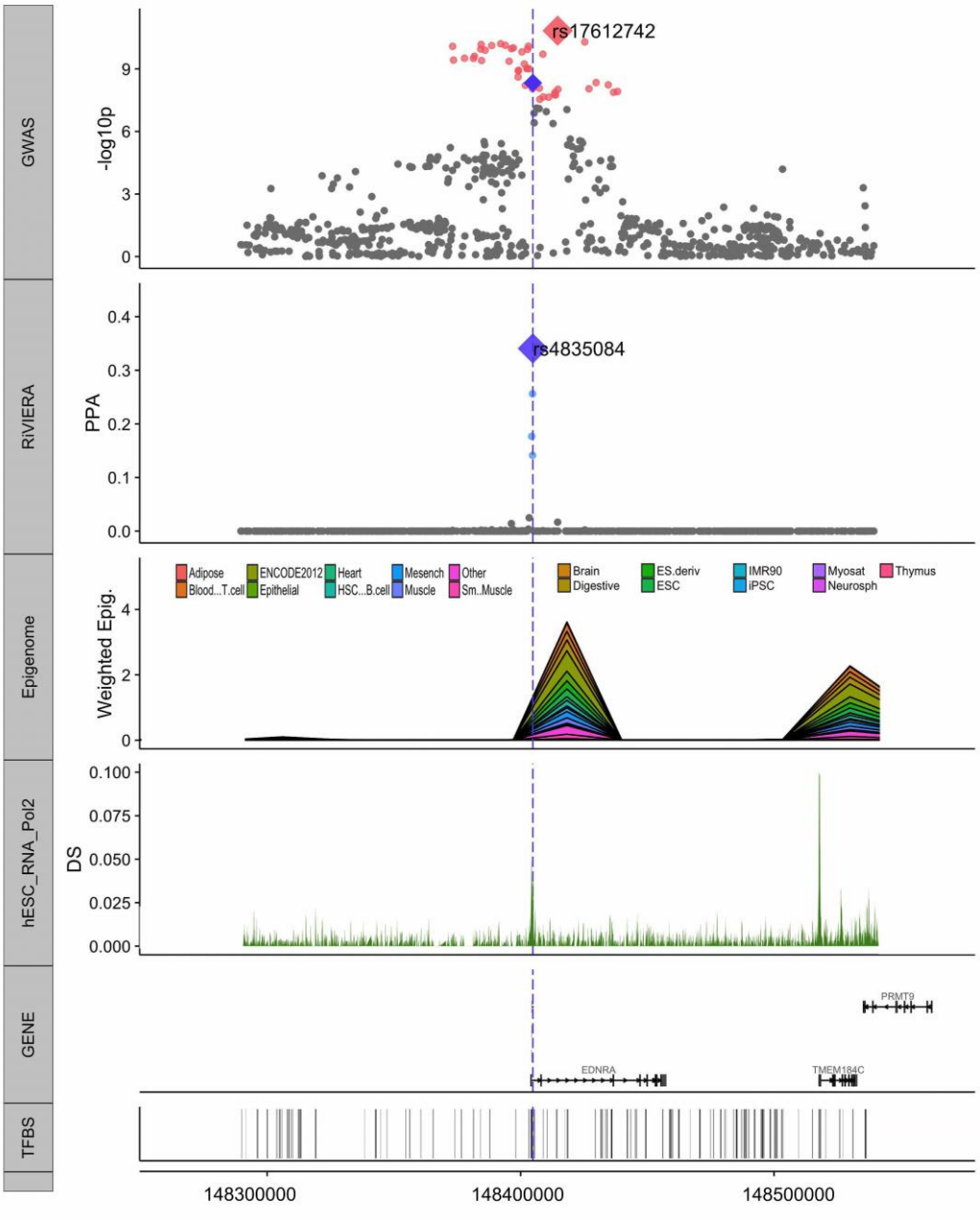
(A) PMF1-SEMA4A



(B) SH3PXD2A


GWAS
RiVIERA
Epigenome
hESC_RNA_Pol2
GENE
TFBS
-log10p
rs2295786
PPA
rs11191829
Weighted Epig.
Adipose
Blood...T.cell
ENCODE2012
Epithelial
Heart
HSC...B.cell
Mesench
Muscle
Other
Sm..Muscle
Brain
Digestive
ES.deriv
ESC
IMR90
iPSC
Myosat
Neurosph
Thymus
DS
SH3PXD2A
SH3PXD2A-AS1
OBFC1
SLK
105500000
105600000
105700000

(C) EDNRA


GWAS
RiVIERA
Epigenome
hESC_RNA_Pol2
GENE
TFBS
-log10p
rs17612742
PPA
rs4835084
Weighted Epig.
Adipose
Blood...T.cell
ENCODE2012
Epithelial
Heart
HSC...B.cell
Mesench
Muscle
Other
Sm..Muscle
Brain
Digestive
ES.deriv
ESC
IMR90
iPSC
Myosat
Neurosph
Thymus
DS
PRMT9
EDNRA
TMEM184C
148300000
148400000
148500000

3. Supplementary Note

3.1 Description of study populations in the MEGASTROKE consortium

Stroke was defined according to the World Health Organization (WHO), i.e. rapidly developing signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin. Strokes were defined as ischemic stroke (IS) or intracerebral hemorrhage (ICH) based on clinical and imaging criteria. IS was further subdivided into the following categories mostly using the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria): i) large vessel ischemic stroke (LV-IS); ii) cardioembolic ischemic stroke (CE-IS); iii) small vessel ischemic stroke (SV-IS). Subarachnoid hemorrhages were excluded from all analyses. Study-populations and study-specific stroke ascertainment and subtyping are described below.

METASTROKE consortium

Australian Stroke Genetics Collaborative (ASGC)

ASGC stroke cases comprised European-ancestry stroke patients admitted to four clinical centres across Australia (The Neurosciences Department at Gosford Hospital, Gosford, New South Wales (NSW); the Neurology Department at John Hunter Hospital, Newcastle, NSW; The Queen Elizabeth Hospital, Adelaide; and the Royal Perth Hospital, Perth) between 2003 and 2008. Stroke was defined by WHO criteria as a sudden focal neurologic deficit of vascular origin, lasting more than 24 hours and confirmed by imaging such as computerised tomography (CT) and/or magnetic resonance imaging (MRI) brain scan. Other investigative tests such as electrocardiogram, carotid doppler and transoesophageal echocardiogram were conducted to define IS mechanism as clinically appropriate. Cases were excluded from participation if aged <18 years, diagnosed with haemorrhagic stroke or transient ischemic attack rather than IS, or were unable to undergo baseline brain imaging. Based on these criteria, a total of 1230 IS cases were included in the current study. IS subtypes were assigned using TOAST criteria, based on clinical, imaging and risk factor data.

ASGC controls were participants in the Hunter Community Study (HCS), a population-based cohort of individuals aged 55-85 years, predominantly of European Caucasian ancestry and residing in the Hunter Region, NSW, Australia. Detailed recruitment methods for the HCS have been previously described.[1] Briefly, participants were randomly selected from the NSW State electoral roll and contacted by mail between 2004 and 2007. Consenting participants completed five detailed self-report questionnaires and attended the HCS data collection centre, at which time a series of clinical measures were obtained. A total of 1280 HCS participants were genotyped for the current study.

All study participants gave informed consent for participation in genetic studies. Approval for the individual studies was obtained from relevant institutional ethics committees.

Bio-Repository of DNA in Stroke (BRAINS)

The Bio-Repository of DNA in Stroke (BRAINS) is an international study recruiting highly phenotyped patients with stroke. For the purposes of the current work all patients were Caucasians.

Diagnosis of stroke was confirmed using positive imaging (MRI or CT) and ischemic stroke subtypes were assigned using TOAST criteria, based on clinical, imaging and risk factor data. Controls were European-Ancestry, stroke-free participants from the shared WTCCC controls, a prospectively

collected cohort of individuals born in 1958 (1958 Birth Cohort). The cohort has been described in detail elsewhere.[2]

Genetics of Early Onset Stroke (GEOS) Study

GEOS is a population-based case-control study designed to identify genes associated with early-onset stroke in patients with first-ever ischemic stroke aged 15-49 years from the greater Baltimore-Washington area between 1992 and 2008. Only patients of European descent are included in this meta-analysis.

Cases were identified through discharge surveillance from 59 participating hospitals and direct physician referral from a defined geographic region. Abstracted medical records were reviewed and adjudicated for ischemic stroke subtype by two neurologists, with discrepancies resolved by a third neurologist. Controls with no history of ischemic stroke were identified through random digit dialing and were frequency-matched to cases based on sex, age, geographic location and, during the later study periods, ethnicity.

Heart Protection Study (HPS)

The Heart Protection Study (HPS) was a large randomized trial involving individuals at increased risk of vascular events.[3] Between 1994-1997 20,536 men and women aged 40-80 years were recruited from 69 collaborating hospitals in the United Kingdom (with ethics committee approval). Participants were eligible for inclusion provided they had non-fasting blood total cholesterol concentrations of at least 135 mg/dL (3.5 mmol/L) and either a previous diagnosis of coronary disease, ischemic stroke, other occlusive disease of non-coronary arteries, diabetes mellitus, or (if were men 65 years or older) treated hypertension. None of them was on statin therapy. At the initial screening visit, all participants provided written consent and began a "run-in" phase involving 4 weeks of placebo followed by 4 to 6 weeks of 40 mg simvastatin daily, after which compliant and eligible individuals were randomly allocated 40 mg simvastatin daily or matching placebo for approximately 5 years. Individuals entering HPS with a clinical diagnosis of ischemic stroke were used as cases in the METASTROKE study. Individuals entering HPS with pre-existing diabetes but no history of cerebrovascular disease, coronary heart disease or peripheral vascular disease were used as controls.

Ischemic Stroke Genetics Study (ISGS)/ Siblings With Ischemic Stroke Study (SWISS)

SWISS is a prospective multicenter affected sibling pair study of first-ever or recurrent ischemic stroke. Subjects were recruited from 54 enrolling hospitals across the US and Canada. Samples were collected between 1999-2011. Ischemic stroke probands were enrolled at 66 US medical centers and 4 Canadian medical centers. All recruits were extensively clinically phenotyped and have imaging-confirmed ischemic stroke using either CT or MRI brain scans. Probands are adult men and women over the age of 18 years diagnosed with ischemic stroke confirmed by a study neurologist on the basis of history, physical examination and CT or MR imaging of the brain who also have a history of at least one living sibling with a history of stroke. Probands were excluded if 1) they had a mechanical aortic or mitral valve at the time of the index ischemic stroke, central nervous system vasculitis, or bacterial endocarditis or 2) were known to have cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), Fabry disease, homocystinuria, mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS), or sickle cell anemia. Siblings were enrolled using proband- initiated direct contact when permitted by Institutional Review Boards. Concordant siblings had their diagnosis of ischemic stroke confirmed by review of medical records by a central vascular neurology committee. Concordant siblings had the same eligibility criteria as probands. Subtype diagnoses were assigned to the index strokes of probands and concordant siblings according to TOAST criteria. Discordant siblings of the proband were confirmed to be stroke-free using the Questionnaire for Verifying Stroke-free Status. DNA samples were genotyped using the

Illumina 660 array and data analyses were supported by the high-performance computational capabilities of the Biowulf Linux cluster at the NIH (http://biowulf.nih.gov).

The Ischemic Stroke Genetic Study (ISGS) is a multicenter study where inpatient cases were recruited from five United States academic medical centers.[4] Cases are adult men and women over the age of 18 years diagnosed with first-ever ischemic stroke confirmed by a study neurologist on the basis of history, physical examination and CT or MR imaging of the brain who were enrolled within 30 days of onset of stroke symptoms. Cases exclusion criteria include: a mechanical aortic or mitral valve at the time of the index ischemic stroke, central nervous system vasculitis, bacterial endocarditis, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), Fabry disease, homocystinuria, mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS), or sickle cell anemia. Stroke severity at enrollment was assessed using the NIH Stroke Scale with the diagnostic evaluation including head CT (95%) or MRI (83%), electrocardiography (92%), cervical arterial imaging (86%), and echocardiography (74%). Medical records from all cases were centrally reviewed by a vascular neurology committee and assigned ischemic stroke subtype diagnoses according to criteria from the Trial of ORG10172 (TOAST), the Oxfordshire Community Stroke Project, and the Baltimore-Washington Young Stroke Study.

MGH Genes Affecting Stroke Risk and Outcome Study (MGH-GASROS)

Cases were all consecutive patients aged 18 years presenting with ischemic stroke and admitted to the Massachusetts General Hospital (MGH) Stroke Unit through the Emergency Department, or evaluated in the MGH Neurology outpatient clinics, as well as on the inpatient Medical and Vascular Surgical services from January 2003 to July 2008. Only patients of European ancestry (confirmed by principal component analysis using genome-wide SNP data) were included in the present analysis. Ischemic stroke was defined as either (1) a radiographically proven (head CT or MRI) infarct associated with the appropriate clinical stroke syndrome, or (2) a fixed neurological deficit persisting more than 24 hours, consistent with a vascular pattern of involvement and without radiographic evidence of demyelinating disease, or other non-vascular structural disease. Patients with specific vascular disorders (vasculitis, subacute bacterial endocarditis, fibromuscular dysplasia, vasospasm) were excluded from the study. All subjects were evaluated by a neurologist upon presentation and provided informed consent. Clinical and laboratory data were collected during the admission for qualifying ischemic stroke event. Diagnostic work-up included: head CT (100%), brain MRI (90%), cervical and intracranial vessel imaging using CTA or MRA (75%), carotid and/or transcranial ultrasound (24%), echocardiography (86%), and Holter monitoring (16%). Controls were recruited among the stroke-free adults presenting to the MGH outpatient clinics and matched with the stroke cases on the basis of age, sex and ancestry information obtained from principal component analysis of GWAS data.

Milano

This study includes consecutive Italian patients referred to Besta Institute from 2000 to 2009 with stroke and included in the Besta Cerebrovascular Diseases Registry (CEDIR). Ischemic stroke cases, first ever or recurrent, confirmed on brain imaging, were selected for this study. All cases were of self-reported Caucasian ancestry and had clinically relevant diagnostic workup performed. All cases were phenotyped by an experienced stroke neurologist according to TOAST criteria, based on relevant clinical imaging and available information on cardiovascular risk factors. Controls are Italian individuals enrolled within the PROCARDIS Study, with no personal or sibling history of coronary heart disease before age 66 years.

Wellcome Trust Case-Control Consortium 2 (WTCCC2)

The WTCCC2 samples were genotyped as part of the WTCCC 2 ischemic stroke study.[5] Stroke cases included samples recruited by investigators at St. George's University London (SGUL), University of

Oxford, University of Edinburgh and the Department of Neurology, Klinikum Großhadern, Ludwig-Maximilians- University, Munich.
The SGUL collection comprised 1224 ischemic stroke samples from a hospital based setting. All cases were of self reported Caucasian ancestry. Ischemic stroke subtypes were determined according to TOAST criteria based on relevant clinical imaging and available information on cardiovascular risk factors. The University of Oxford collection comprised 896 ischemic stroke cases, consecutively collected as part of the Oxford vascular study (OXVASC). Cases were of self reported Caucasian ancestry, and ischemic stroke subtypes were determined according to TOAST criteria based on relevant clinical imaging. The University of Edinburgh collection comprised 727 ischaemic stroke cases, consecutively collected as part of the Edinburgh Stroke Study. Cases were of self-reported Caucasian ancestry, with ischaemic stroke subtypes determined according to TOAST criteria based on relevant clinical and imaging data. The Munich samples included 1383 ischemic stroke cases. Cases were consecutive European Caucasians recruited from a single dedicated Stroke Unit at the Department of Neurology, Klinikum Großhadern, Ludwig-Maximilians-University, Munich. Ischemic stroke subtypes were determined according to TOAST criteria based on relevant clinical and imaging data. Controls for the UK samples were drawn from shared WTCCC controls obtained from the 1958 Birth Cohort. This is a prospectively collected cohort of individuals born in 1958, and ascertained as part of the national child development study.[6] Data from this cohort are available as a common control set for a number of genetic and epidemiological studies. For the German samples controls were Caucasians of German origin participating into the population KORAgen study.[7] This survey represents a gender- and age stratified random sample of all German residents of the Augsburg area and consists of individuals 25 to 74 years of age, with about 300 subjects for each 10-year increment. All controls were free of a history of stroke or transient ischemic attack.

VISP
Population. VISP was a multi-center, double-blind, randomized, controlled clinical trial that enrolled patients aged 35 or older with homocysteine levels above the 25th percentile at screening and a non-disabling cerebral infarction (NDCI) within 120 days of randomization. The trial was designed to determine if daily intake of a multivitamin tablet with high dose folic acid, vitamin B6 and vitamin B12 reduced recurrent cerebral infarction (1° endpoint), and nonfatal myocardial infarction (MI) or mortality (2° endpoints). Subjects were randomly assigned to receive daily doses of the high-dose formulation (n=1,827), containing 25mg pyridoxine (B6), 0.4mg cobalamin (B12), and 2.5mg folic acid; or the low-dose formulation (n=1,853), containing 200µg pyridoxine, 6µg cobalamin and 20µg folic acid. Enrollment in VISP began in August 1997, and was completed in December 2001, with 3,680 participants enrolled, from 55 clinic sites across the US and Canada and one site in Scotland. A subset of VISP participants gave consent and were included in the GWAS component of VISP, supported by the National Human Genome Research Institute (NHGRI), Grant U01 HG005160, as part of the Genomics and Randomized Trials Network (GARNET)
Stroke Ascertainment. NDCI was defined as an ischemic brain infarction not due to embolism from a cardiac source, characterized by the sudden onset of a neurological deficit. The deficit must have persisted for at least 24 hours, or if not, an infarction in the part of the brain corresponding to the symptoms must have been demonstrated by CT or MRI imaging.
Genotyping. Samples were genotyped at the Center for Inherited Disease Research using the Illumina HumanOmni1-Quad_v1-0_B BeadChip (Illumina, San Diego, CA, USA). Genotype data from the VISP study, through GARNET, is available via dbGAP, Study Accession: phs000343.v1.p1; http://www.ncbi.nlm.nih.gov/projects/gap/cgi-bin/study.cgi?study_id=phs000343.v3.p1)

WHI

The Women's Health Initiative Hormone Trial HT (WHI-HT) consisted of two separate clinical trials in postmenopausal women ages 50 to 79 years at baseline—a trial of combined estrogen and progestin (Estrogen plus Progestin or E+P) in women who had an intact uterus at baseline (n=16,608)[8] and a trial of estrogen (Estrogen Alone or E-Alone) in women who had a prior hysterectomy at baseline (n=10,739).[9] Postmenopausal women who gave written informed consent were enrolled in the WHI at 40 clinical centers in the United States. Exclusions for safety reasons included prior diagnosis of breast cancer or other cancers within the past 10 years (except nonmelanoma skin cancer). Women with systolic blood pressure (SBP) of 200 mm Hg or higher or diastolic blood pressure (DBP) of 105 mm Hg or higher were advised to see their physician within a specified period depending on blood pressure level and were temporarily excluded from the clinical trials until their blood pressure was determined to be under control. Stroke diagnosis requiring and/or occurring during hospitalization was based on rapid onset of a neurological deficit attributable to an obstruction or rupture of an arterial vessel system. Hospitalized incident stroke events were identified by semiannual questionnaires and adjudicated following medical record review, which occurred both locally and centrally. Ischemic strokes were further classified by the central neurologist adjudicators according to the Oxfordshire and Trial of Org 10172 Acute Stroke Trial (TOAST) criteria to examine stroke subtypes. The TOAST classification focuses on the presumed underlying stroke mechanism and requires detailed investigations (such as brain computed tomography, magnetic resonance imaging, angiography, carotid ultrasound, and echocardiography).

NINDS-SIGN consortium

BASEede datos de ICtus del hospital del MAR (BASICMAR)

BASICMAR is an ongoing prospective study of all acute strokes assessed since 2005 at the IMIM-Hospital Universitari del Mar (Barcelona, Spain). It includes both first-ever and recurrent strokes. There were no exclusion criteria regarding age or race-ethnicity of the individuals. All patients had an electrocardiogram (ECG), a blood analysis, and neuroimaging at the acute stage. Additional diagnostic procedures were s performed when clinically indicated. A follow-up of three months after stroke was completed for all survivors.

Ischemic stroke etiologic subtypes were classified according to TOAST criteria.[10] For this study, only individuals of European origin with ischemic stroke were selected from BASICMAR, with eligible events defined as a clinical syndrome of any duration associated with a radiographically proven acute infarct, without radiographic evidence of a demyelinating or neoplastic disease or other structural disease including primary intracerebral hemorrhage.

GCNKSS

The GCNKSS is a population-based epidemiologic study of stroke in blacks and whites that is designed to measure temporal trends and racial differences in incidence of stroke. The catchment area includes two southwestern Ohio, U.S.A., counties (Hamilton, which includes the city of Cincinnati, and Clermont to the east) and three Northern Kentucky, U.S.A., counties (Boone, Kenton, and Campbell) to the south of Cincinnati across the Ohio River. As part of the GCNKSS, for calendar years 1999 and 2005, prospective cohorts of first-ever and recurrent ischemic stroke cases were assembled using "hot pursuit" methodology at all local hospitals in the region (18 in 1999, and 17 in 2005), except for one hospital that is solely devoted to treating pediatric cases. Participants remained eligible if they were in a treatment trial, but participation in a treatment trial was not required for enrollment. Subjects with all degrees of severity of stroke were eligible, and no particular racial group was intentionally oversampled (about 80% were white participants and 20% black). Study research nurses prospectively screened inpatient admission and emergency department logs to identify acute

ischemic stroke patients. When a case was identified and the treating physician had given permission to approach the patient, a study nurse asked the subject or a proxy (the most closely related competent individual, preferably a person living with the subject prior to the stroke) to consent to participate in the cohort. After consent was granted, a study nurse performed an extensive interview, and a blood sample was obtained for genetic analysis. In addition, a study nurse abstracted information about the individual, the subject's medical history, the stroke event, and imaging studies from the hospital chart. A study physician reviewed every abstract, along with the imaging studies, to verify that an acute stroke had occurred, and to classify the event according to TOAST[10] and CCS criteria.[11]

GRAZ

Between 1994 and 2003, subjects with first-ever and recurrent ischemic strokes admitted to the stroke unit of the Department of Neurology, Medical University of Graz (Graz, Austria) were included. All race-ethnic groups were eligible and there was no intentional oversampling. All age groups were allowed, though only subjects above the age of 18 were admitted to our department. Ischemic stroke was defined as an episode of focal neurological deficits with acute onset and lasting > 24 hours. There were no selection criteria based on stroke severity. Those individuals in treatment trials were excluded. 685 subjects were eligible to participate in this study (278 women, 407 men). All cases were Caucasian. Mean age was 68.9 ± 13.8 years with an age range from 19 – 101 years. In addition to a standardized protocol including a laboratory examination and carotid ultrasound or magnetic resonance angiography and ECG, 304 subjects underwent neuroimaging by CT and 381 by MRI. More extensive cardiac examination, including transesophageal echocardiography or transthoracic echocardiography and Holter, was performed in subjects with suspected cardiac embolism. Stroke subtypes were assessed according to modified TOAST criteria1 and were conducted by trained stroke neurologists.

KRAKOW

All consecutive subjects with ischemic stroke (fulfilling WHO criteria[12](3)) who were admitted to the Stroke Unit at the Jagiellonian University (Krakow, Poland) and who provided informed consent were included in the study. The Stroke Unit serves as a stroke emergency center for one district of Krakow, Poland (200,000 inhabitants) and as a referral center for South East Poland (up to 15% of all admissions). For this on-going, prospective single-center, hospital-based study participants with first ever or recurrent strokes were recruited from January 22, 2002 to September 9, 2010. The local research ethics committee approved the study. Participants in treatment trials were excluded. All subjects were of European origin. Stroke severity was not a criterion for inclusion or exclusion. All cases had performed clinically relevant diagnostic workup, including brain imaging with CT (100%) and/or MRI (up to 20%) as well as ancillary diagnostic investigations including duplex ultrasonography of the carotid and vertebral arteries (approximately 90%), and transthoracic echocardiography (approximately 70%). Magnetic resonance angiography (MRA), computed tomographic angiography (CTA), and ambulatory ECG monitoring, transesophageal echocardiography and blood tests for hypercoagulability were performed. Stroke cases were classified into etiologic subtypes according to TOAST.[10] All cases were phenotyped independently by two experienced stroke neurologists with review of original imaging. Cases were subsequently classified additionally using the CCS system[11].

Leuven Stroke Genetics Study (LSGS)

Cases of European descent with cerebral ischemia, defined as a clinical stroke with imaging confirmation or a TIA with a new ischemic lesion on diffusion-weighted imaging, who were admitted to the Stroke Unit of the University Hospitals (Leuven, Belgium) were enrolled in the LSGS between 2005 and 2009. All participants from the LSGS study underwent brain imaging (MRI in 91% of

patients, CT in the remainder) and a standardized protocol including lab examination, carotid ultrasound or CTA and cardiac examination (echocardiography and ambulatory ECG monitoring) in all patients. Based on clinical presentation and results from the diagnostic work-up, cases were classified into ischemic stroke etiologic subtypes according to modified TOAST criteria[10] by a single reviewer. The reviewer had access to all information and imaging. Large-vessel disease was defined as either occlusive or significant stenosis (corresponding to > 50% luminal diameter reduction according to North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria[13] of a clinically relevant pre-cerebral or cerebral artery, presumably due to atherosclerosis. Carotid ultrasound was used as a screening tool, and in principle, additional imaging with CTA or MRA was performed when a high-grade stenosis was identified. In case CTA was used as the primary imaging modality, stenosis was confirmed by carotid ultrasound. In case of posterior circulation infarcts on imaging, CTA or MRA was used as the primary imaging modality to determine the degree of stenosis. Probable causes of cardiac embolism were excluded. The presence of a patent foramen ovale was not considered a cardiac source in this context. Intracranial atherosclerosis was considered present only if repeat imaging after at least one week revealed a similar degree of stenosis or persistent occlusion. If not, the findings were interpreted as an embolism from a proximal source. Small-vessel disease was defined as a symptomatic infarct of < 20 mm on DWI in areas supplied by single, small penetrating branches from middle cerebral artery, posterior cerebral artery or basilar artery in the absence of both a cardioembolic source and significant stenosis/occlusion due to atherosclerosis of an appropriate major brain artery. Cardioembolic stroke was defined as ischemic stroke in the presence of atrial fibrillation, sick sinus syndrome, myocardial infarction in the past four weeks, cardiac thrombus, infective endocarditis, atrial myxoma, prosthetic mitral or aortic valve, valvular vegetations, left ventricular akinetic segment, dilated cardiomyopathy, or patent foramen ovale or atrial septal aneurysm. Significant stenosis/occlusion due to atherosclerosis of an appropriate pre-cerebral or cerebral artery should be excluded. Other determined cause of stroke included those with arterial dissection, vasculitis, hematologic disorders, monogenic syndromes and complications of cardiovascular procedures. Dissection was diagnosed by typical findings on contrast-enhanced MRA and T1-fat suppressed MRI. Cryptogenic stroke was defined when no cause was identified despite an extensive evaluation. Strokes associated with significant aortic arch atheroma with plaques of ≥ 4 mm were also considered cryptogenic strokes. In addition to this primary classification, cases were reclassified using CCS.[11]

Lund Stroke Register (LSR)

The LSR is an ongoing study including consecutive subjects with first-ever stroke since March 1, 2001 from the local uptake area of Skåne University Hospital, Lund (Sweden). Stroke was defined using the WHO criteria.[12] Subjects aged 18 years or older with stroke caused by cerebral infarct, intracerebral hemorrhage or subarachnoid hemorrhage are included. Cases are included regardless of stroke severity, race-ethnic group belonging, or participation in any treatment trial. Those with iatrogenic or traumatic stroke are excluded.

In the discovery phase of the SiGN study, subjects from LSR with first-ever ischemic stroke between March 1, 2001 and February 28, 2010 were included if they or their next of kin provided informed consent. Age over 90 years was set to 90 years to maintain anonymity. Every participant underwent CT, MRI, or autopsy of the brain; and ECG. Echocardiography, ultrasound, CTA or MRA of cerebral arteries was performed when judged clinically relevant. The subtype of ischemic stroke was determined using CCS.[11]

For the secondary phase of SiGN, LSR individuals not included in the SiGN discovery phase participated after genotyping in the South Swedish genome-wide association study as follows: first ever ischemic stroke cases recruited in 2006 and 2010 to 2012, and age- and sex-matched LSR control

subjects without stroke recruited in 2001 to 2002 and 2006 to 2007 from the same geographical area with use of the official Swedish population register.

Middlesex County Ischemic Stroke Study (MCISS)

The MCISS was initiated as a prospective hospital based stroke registry at the New Jersey Neuroscience Institute (Edison, NJ, U.S.A.). All cases over age 18 years were included, and no specific ethnic/racial group was targeted or excluded. From 2000 to 2009, 1,139 subjects with ischemic strokes were enrolled in this registry. There was no selection criterion based upon stroke severity, and both first-ever and recurrent strokes were included. Cases that were participants in treatment trials were not excluded. The major race/ethnic groups are Whites (67.2%), African Americans (14.3%), Asian Indians (8.2%), Hispanic (5.5%) and others (4.8%, Chinese and other Asians). All subjects with clinical suspicion of a stroke were admitted through the emergency room to a dedicated stroke unit supervised by a vascular neurologist. After a history and neurological examination, a standardized series of investigations were performed: complete blood count and differential, comprehensive metabolic panel, electrolytes, blood urea nitrogen, creatinine, lipid panel (total cholesterol, low-density lipoprotein, high-density lipoprotein, triglyceride levels, homocysteine levels, a cerebral MRI/MRA (if the MRI could not be performed, a head CT scan was done), carotid duplex ultrasound, ECG and an echocardiogram. The diagnosis of cerebral infarct was confirmed by the imaging studies. The epidemiological and clinical data on these participants was collected prospectively. Two independent investigators (one of which was a board-certified neurologist with expertise in vascular neurology) reviewed the data, and all strokes were classified into etiological subtypes using TOAST criteria[10]. In addition, the Oxfordshire stroke classification[14] was applied, and the vascular distribution of stroke was tabulated. All procedures, including the generation of the databases and recruitment of the stroke subjects, were conducted following Institutional Review Board policies and procedures at the New Jersey Neuroscience Institute/JFK Hospital.

Miami Stroke Registry and Biorepository (MIAMISR)

The MIAMISR at the University of Miami/Jackson Memorial Hospital (Miami, FL, U.S.A.) is an ongoing prospective hospital registry of consecutive patients subjects with prevalent stroke (ischemic and hemorrhagic) and TIA with available neuroimaging (CT or MRI) who provide informed consent. There are no specific exclusion criteria with the respect to age, stroke severity, disability or participation in treatment trials. It was established in November of 2008 in order to investigate stroke type, ischemic stroke subtypes, stroke genetics and stroke outcomes in diverse ethnic population of Miami. The stroke population is predominately Hispanic (63%), with Cuba (32%), Nicaragua (4.8%), Colombia (4.8%), and Puerto Rico (4.1%) contributing the most subjects. Jackson Memorial Hospital is a 1,550-bed county hospital affiliated with the University of Miami with approximately 900 stroke and TIA admissions per year. Demographic and clinical data along with blood samples for genetic and other research have been collected prospectively during the hospitalizations. Follow-up information was obtained at 90 days by telephone interview or in person. Trained research staff obtained written informed consent from the stroke patients or the health care proxy when available for participation in MIAMISR.[15]

Nurses' Healthy Study (NHS)

The NHS cohort consists of 121,700 female registered nurses aged 30 – 55 years who were residing in 11 U.S. states and who were enrolled in 1976 through responding to a mailed questionnaire on their medical history and lifestyle practices. They have been followed with biennial mailed questionnaires collecting information on disease risk factors and health status. From 1989 – 1990, blood samples were collected from 32,826 participants. Among these participants, we prospectively identified incident strokes and confirmed ischemic stroke cases by medical record review. Clinical symptoms

consistent with stroke and exclusion of alternate etiologies were required for classification of stroke. Virtually all cases had imaging, but confirmation on CT or MRI was not required. No participants were excluded based on race/ethnicity. Neither stroke severity nor enrollment in a treatment trial was part of the eligibility criteria.

Northern Manhattan Study (NOMAS)

NOMAS is an ongoing population-based study designed to determine stroke incidence, risk factors and outcome in an urban multiethnic population.[16] NOMAS started in 1993 as a case-control study of index ischemic stroke cases admitted to the Columbia University Presbyterian Medical Center (New York, NY, U.S.A.) and affiliated hospitals and matching community controls (Northern Manhattan Stroke Study, NOMASS) and continued as a prospective stroke incidence study by following up controls in 1997 (NOMAS). Demographic and clinical data were collected prospectively during the hospitalizations and annually by phone or in person. Genetic samples were derived from two sources: (a) the population-based case-control study conducted from 1993-98 (NOMASS) and (b) the ongoing prospective cohort study (NOMAS). First-ever ischemic stroke cases were identified for the case-control study by screening of patient admissions, discharge codes, and referrals for neuroimaging at 15 acute care hospitals in the defined study area and multiple approaches to monitor for non-hospitalized cases. Incident ischemic stroke cases were identified from the prospective cohort study through follow-up visits and scheduled telephone contacts. Ischemic stroke cases from both sources were followed at 6 months by telephone and then annually afterwards in order to assess functional status and other outcomes. The administrative coordinating center of NOMAS moved from New York to Miami in 2007. The Institutional Review Boards of both institutions, Columbia University and the University of Miami (Miami, FL, U.S.A.), approved the study.

Reasons for Geographic and Racial Differences in Stroke (REGARDS)

The REGARDS study is a U.S. national, population-based, longitudinal cohort of 30,239 African American and white adults aged ≥ 45 years, recruited January 2003 to October 2007 with ongoing follow-up. Suspected stroke is queried every six months and triggered by participant self-report of stroke, stroke symptom(s), hospitalization, or proxy report of death. Stroke severity and participation in a treatment trial did not limit inclusion in this study. Medical records for these reported events are retrieved and reviewed by at least two members of a committee of stroke experts with disagreements resolved by a third adjudicator. A symptom-based approach, independent of neuroimaging outcome, is used to confirm events using the WHO definition of stroke.[12] An infarct did not need to be seen on brain imaging to be included in this study. Ischemic stroke subtype classification is conducted using the TOAST system.[10, 17]

Secondary Prevention of Small Subcortical Strokes (SPS3)

The SPS3 trial (NCT00059306) is a randomized, multicenter, Phase 3 trial of antiplatelet therapy and antihypertensive therapy. Participants are randomized to aspirin alone or the combination of aspirin and clopidogrel. Participants are also randomized to two groups of blood pressure control: either to a target systolic blood pressure of 130 – 149 mm Hg or < 130 mm Hg. Principal eligibility criteria include man or woman at least 30 years of age with clinical evidence of small subcortical stroke and brain MRI evidence of small subcortical infarct. Subjects were required to not have evidence of ipsilateral symptomatic cervical carotid stenosis or high-risk cardioembolic sources for embolism. Further details of eligibility criteria have been published.[18] Primary outcomes include ischemic and hemorrhagic stroke. DNA samples were collected from 38% (1,139/3,020) of participants in the trial. These samples were obtained from 46% (37/81) participating centers across the U.S., Canada, Spain, Mexico, Chile, Ecuador and Peru. No additional eligibility criteria were necessary beyond informed

consent for participating in the DNA sub-study. A total of 0.9% (10/1,139) of DNA donors gave sample at time of randomization, with the remainder donating at a later time point in follow-up.

Washington University St. Louis (WUSTL) Study

The WUSTL patient collection included ischemic stroke cases admitted to Barnes-Jewish Hospital/Washington University Medical Center (St. Louis, MO, U.S.A.) for genetic studies starting from August 1, 2008. Participants were identified for the genetic studies by screening admissions at our tertiary care hospital (both in the Emergency Department and on the Inpatient Stroke Service) without regard to age, race or ethnicity, including both first-ever and recurrent strokes. Subjects were retained in the study if their discharge diagnosis was ischemic stroke (without requirement for the stroke to be visualized on CT or MRI). Demographic and clinical data were collected prospectively during the hospitalization and at 90 days, by phone or in person. Genetic samples were derived from subjects enrolled in 3 different studies: (a) Acute tPA pharmacogenomics study (Ischemic stroke cases who received tPA and were admitted to BJH/Washington University; serial NIHSS scores,[19] and data on hemorrhagic transformation was collected) (b) Recovery Genomics after Ischemic Stroke Study (ReGenesIS, Ischemic stroke cases with NIHSS > 3 points without underlying chronic neurological disease, and expected survival up to 3 months after stroke), and (c) the Cognitive Recovery and Rehabilitation Group (CRRG) Registry (all ischemic stroke cases admitted to BJH/Washington University who consent to entering their clinical data into a stroke registry, and the collection of blood for genetic analysis). Cases that were part of a treatment trial were excluded from the tissue plasminogen activator pharmacogenomics and ReGenesIS study, but not the CRRG registry.

Controls for discovery analysis

Attention-deficit Hyperactivity Disorder (ADHD)

The Vall d'Hebron Research Institute (VHIR) cohort included 435 blood donors of Caucasian origin recruited from 2004 to 2008 at the Hospital Universitari Vall d'Hebron (Barcelona, Spain) to identify loci conferring susceptibility to Attention-Deficit Hyperactivity Disorder. Seventy-six percent of participants were male (N = 330) and the average age at assessment was 43.8 years (s.d. = 14.3). Genome-wide genotyping was performed with the Illumina HumanOmni1-Quad BeadChip platform. The study was approved by the ethics committee of the institution and informed consent was obtained from all participants in accordance with the Declaration of Helsinki.

Health ABC (HABC)

The Health Aging and Body Composition (Health ABC) Study is a National Institute on Aging (NIA)-sponsored cohort study of the factors that contribute to incident disability and the decline in function of healthier older persons, with a particular emphasis on changes in body composition in old age. Between April 15, 1997 and June 5, 1998, the Health ABC study recruited 3,075 70 – 79 year old community-dwelling adults (41% African American), who initially had no indications of disability related to mobility and activities of daily living. The key components of Health ABC include a baseline exam, annual follow-up clinical exams, and phone contacts every six months to identify major health events and document functional status between clinic visits.

The core yearly examination for Health ABC includes measurement of body composition by dual energy x-ray absorptiometry (DXA), walking ability, strength, an interview that includes self-report of limitations and weight, and a medication survey. At baseline, visceral adiposity was measured by computerized tomography (CT). Provision has been made for banking of blood specimens and

extracted DNA (HealthABC repository). The overall goal of this project is to identify genetic determinants of visceral adiposity.

Hispanic Community Health Study/Study of Latinos (HCHS/SOL)

The Hispanic Community Health Study/Study of Latinos (HCHS/SOL) was initiated in 2006 to investigate the prevalence and risk factors affecting several health conditions, including heart, lung and blood disorders, kidney and liver function, diabetes, cognitive function, dental conditions and hearing disorders.24,25 Participants aged 18 – 74 self-identified as Hispanic or Latino, with substantial representation of Mexican, Puerto Rican, Dominican, Cuban, Central and South American groups. They were recruited from four field centers in the United States: San Diego, CA; the Bronx, NY; Chicago, IL; and Miami, FL. 12,803 study participants consented to genetic studies and will be included in the HCHS/SOL dbGaP posting.

Genotyping of the HCHS/SOL participants was performed at Illumina Microarray Services using the SOL HCHS Custom 15041502 array (annotation version "B3", genome build 37), which includes 2,575,443 variants (of which 2,427,090 are in common with the Illumina HumanOmni2.5 and 148,353 are custom content).

Health and Retirement Study (HRS)

The University of Michigan Health and Retirement Study (HRS) is a longitudinal panel study that surveys a representative sample of more than 20,000 Americans over the age of 50 every two years. Supported by the National Institute on Aging (NIA U01AG009740) and the Social Security Administration, the HRS explores the changes in labor force participation and the health transitions that individuals undergo toward the end of their work lives and in the years that follow.

Since its launch in 1992, the study has collected information about income, work, assets, pension plans, health insurance, disability, physical health and functioning, cognitive functioning, and health care expenditures.

HRS is intended to be a nationally representative sample with 2:1 oversampling of minority groups including African-American and Hispanic/Latino populations.26 In Phases I – II, 12,507 study participants were included in the dbGaP posting.

Genotyping of the HRS Phase I – II participants was performed at CIDR using the Illumina HumanOmni2.5-4v1 array (annotation version "D", genome build 37) and released a total of 2,443,179 variants.

INfancia y Medio Ambiente (INMA)

The INfancia y Medio Ambiente (Environment and Childhood) project is a research project comprising a Spanish population-based birth cohort created to study the role of the environmental pollutants during pregnancy and first stages of life and their effects on childhood growth and development. The cohort was established between 2003 and 2008 from mothers enrolled in four regions within Spain and included their infants.

MONICA/KORA Augsburg Study

For the German MUNICH discovery samples and the Stroke in Young Fabry Patients (SIFAP) samples, independent control groups were selected from Caucasians of German origin participating into the population KORAgen study. .This survey represents a sex- and age stratified random sample of all German residents of the Augsburg area and consists of individuals 25 – 74 years of age, with about 300 subjects for each 10-year increment. All controls were free of a history of stroke or transient ischemic attack.

KORA samples were genotyped on the Illumina Human 550k platform. QC was identical for all WTCCC cohorts.

KRAKOW

The control group included unrelated subjects taken from the population of southern Poland. Control subjects had no apparent neurological disease based on the findings in a structured questionnaire and a neurological examination. Local research ethics committees approved the study and informed consent was obtained from all participants.

Leuven Stroke Genetics Study (LSGS)

Control individuals were recruited in the same population amongst healthy individuals, spouses of patients suffering from neurological diseases (amyotrophic lateral sclerosis, ischemic stroke or multiple sclerosis), and from the Leuven University Gerontology Database as previously described.27

Osteoarthritis Initiative (OAI)

The OAI is a publicly and privately funded prospective longitudinal cohort with a primary objective of identifying risk factors for incidence and progression of tibiofemoral knee OA. The OAI utilized a focused population-based recruitment to enroll 4,674 men and women between the ages of 45 – 79 years who either had radiographic symptomatic knee OA or who were without radiographic symptomatic OA in both knees but were considered high risk for OA because they had two or more known risk factors for knee OA. Subjects were recruited into the baseline phase of the OAI at multiple sites throughout the US between 2004 and 2006. All subjects were invited back for follow-up examinations to assess incidence or progression of OA annually, for up to 5 years.

Phenotype data from the baseline and follow-up examinations are available for public access from the Osteoarthritis Initiative (OAI) database.

The Genetic Components of Knee Osteoarthritis (GeCKO) Study was initiated in 2009 as a genetic ancillary study to perform a genome-wide association study to identify genetic variants associated with radiographic osteoarthritis. This study included 4,482 individuals participating in the parent OAI study genotyped on the Illumina HumanOmni2.5M

CHARGE consortium

We combined data from white participants in eighteen large, prospective community-based cohort studies, participating in the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) consortium.[20]

All participating studies approved guidelines for collaboration, and a neurology working-group arrived at a consensus on phenotype harmonization, covariate selection and analytic plans for within-study analyses and meta-analysis of results. Each study has an Institutional Review Board that approved the consent procedures, examination and surveillance components, data security processes, genotyping protocols and current study design.

The structure of each participating cohort study is summarized below.

Age, Gene/Environment Susceptibility (AGES) -Reykjavik Study

The AGES-Reykjavik Study is a single center prospective cohort study based on the Reykjavik Study. The Reykjavik Study was initiated in 1967 by the Icelandic Heart Association to study cardiovascular disease and risk factors.[21] The cohort included men and women born between 1907 and 1935 who lived in Reykjavik at the 1967 baseline examination. Re-examination of surviving members of the cohort was initiated in 2002 as part of the AGES-Reykjavik Study. The AGES-Reykjavik Study is designed to investigate aging using a multifaceted comprehensive approach that includes detailed measures of brain function and structure. All cohort members were European Caucasians. Briefly, as part of a comprehensive examination, all participants answered a questionnaire, underwent a clinical examination and had blood drawn.Among AGES participants with GWAS data (N=3,219), after exclusion of participants with prevalent stroke (N=224), and those without follow-up for incident stroke events (N=114), N=2,996 participants were available for analyses.

Stroke ascertainment in AGES: Incident stroke cases were ascertained from multiple sources including hospital, general practice, nursing home records and death certificates. All possible cases were adjudicated with standard TOAST criteria by two Neurologists and a Neuroradiologist with expertise in evaluating stroke cases for epidemiologic studies.

Cardiovascular Health Study (CHS) – European Ancestry

The Cardiovascular Health Study (CHS) is a population-based cohort study of risk factors for coronary heart disease and stroke in adults ≥65 years conducted across four field centers.29 The original predominantly European ancestry cohort of 5,201 persons was recruited in 1989-1990 from random samples of the Medicare eligibility lists; subsequently, an additional predominantly African-American cohort of 687 persons was enrolled for a total sample of 5,888. Blood samples were drawn from all participants at their baseline examination and DNA was subsequently extracted from available samples. Because the other cohorts in the CHARGE analysis were predominantly European ancestry, the African American participants were excluded from this analysis to reduce the possibility of confounding by population structure. European ancestry participants were excluded from this GWAS study sample due to the presence at study baseline of coronary heart disease, congestive heart failure, peripheral vascular disease, valvular heart disease, stroke or transient ischemic attack, or lack of available DNA. Beyond laboratory genotyping failures, participants were excluded if they had a call rate<=95% or if their genotype was discordant with known sex or prior genotyping. After quality control, genotyping was successful for 3,268 European ancestry participants. CHS was approved by institutional review committees at each field center and individuals in the present analysis had available DNA and gave informed consent including consent to use of genetic information for the study of cardiovascular disease.

Stroke ascertainment in CHS: Participants were examined annually from enrollment to 1999 and continued to be under surveillance for stroke following 1999.[22, 23] Since baseline, participants have

also been contacted twice a year to identify potential cardiovascular events, including stroke. In addition, all hospitalizations were screened for potential stroke events. For suspected fatal and non-fatal events occurring with or without hospitalization, information was collected from the participant or next of kin, from medical records, and, if needed, from the participant's physician. When available, scans or reports of CT, MRI or both were reviewed centrally. Final at a consensus conference using all available information vascular neurologists adjudicated the occurrence of fatal and non-fatal stroke, stroke types, and subtypes. Stroke definitions were derived from the criteria used for the Systolic Hypertension in the Elderly Program (SHEP).[24] Stroke types were ischemic, hemorrhagic and other based on brain imaging. Hemorrhagic stroke subtypes were intra-parenchymal, subarachnoid, and other. Ischemic stroke subtypes were 1) small vessel, 2) large vessel, 3) cardioembolic, and 4) other that included mostly uncertain subtypes. The approach used in CHS was developed before the TOAST criteria were published in 1993.[10] Nonetheless, the two approaches are quite similar.

FHS

The Framingham Heart Study (FHS) is a three-generation, single-site, community-based, ongoing cohort study that was initiated in 1948 to investigate prospectively the risk factors for CVD including stroke. It now comprises 3 generations of participants (N=10,333): the Original cohort followed since 1948;[25] their Offspring and spouses of the Offspring, followed since 1971;[26] and children from the largest Offspring families enrolled in 2000 (Gen 3).[27] Gen 3 participants were not included in this analysis since they are young (mean age 40±9 years) and few have suffered strokes. The Original cohort enrolled 5209 men and women who comprised two-thirds of the adult population then residing in Framingham, MA. Survivors continue to receive biennial examinations. The Offspring cohort comprises 5124 persons (including 3514 biological offspring) who have been examined approximately once every 4 years. The population of Framingham was virtually entirely white (Europeans of English, Scots, Irish and Italian descent) in 1948 when the Original cohort was recruited. At the initial examination participants were asked for country of birth and whether or not they had any Italian ancestry. At a later examination (the 8th) the Offspring cohort participants were asked to identify their race from the following choices: Caucasian or white, African-American or black, Asian, Native Hawaiian or other Pacific Islander, American Indian or Alaska native or 'prefer not to answer'. They were either asked to identify their ethnicity as either 'Hispanic or Latino' or not. Almost all the FHS Original and Offspring participants are white/Caucasian and none were excluded from the discovery cohort. FHS participants had DNA extracted and provided consent for genotyping in the 1990s. All available eligible participants underwent genome-wide genotyping. In 272 persons (31 with stroke), small amounts of DNA were extracted from stored whole blood and required whole genome amplification prior to genotyping. Cell lines were available for most of the remaining participants.

Among FHS participants with GWAS data (N=4,535), after exclusion of participants with prevalent stroke (N=138), and those without follow-up for incident stroke events (N=12), N=4,385 participants were available for analyses.

Stroke ascertainment in FHS: At each clinic exam, participants receive questionnaires, physical examinations and laboratory testing; between examinations they remain under surveillance (regardless of whether or not they live in the vicinity) via physician referrals, record linkage and annual telephone health history updates. Incident strokes have been identified since 1948 through this ongoing system of FHS clinic and local hospital surveillance and methods used have been detailed previously;[28-30] they include review of medical records and collaboration with local general practitioners, emergency rooms and imaging facilities. If a participant saw a physician or was admitted to the hospital, visited an emergency room or obtained any brain imaging between biennial examinations for symptoms suggestive of TIA or stroke, a stroke neurologist from the Heart Study attempted to visit the person within 48 hours and recorded a complete history and neurological examination; this was repeated at 1,

3 and 6 months. All medical records from practitioners, hospitals, imaging centers, rehabilitation centers and nursing homes were procured for review. A panel of 3 investigators (at least 2 neurologists) adjudicated the diagnosis of stroke and determined stroke subtype in each case based on the Framingham evaluations and external records. The recruitment of Original and Offspring cohort participants at FHS had occurred long before the DNA collection with the result that the majority of stroke events in the FHS (although ascertained prospectively) were prevalent at the time of DNA collection and were excluded from these analyses. While this reduced the sample size from FHS, the meta-analyses presented here focused on incident events.

FINRISK

FINRISK surveys are cross-sectional, population-based studies conducted every 5 years since 1972 to monitor the risk of chronic diseases. For each survey, a representative random sample was selected from 25- to 74-year-old inhabitants of different regions in Finland. The survey included a questionnaire and a clinical examination, at which a blood sample was drawn, with linkage to national registers of cardiovascular and other health outcomes. The study protocol has been described elsewhere.[31] The current study included eligible individuals from FINRISK surveys conducted in 1992, 1997, 2002, and 2007. The GWAS genotyping has been done earlier in several phases for different substudies: PredictCVD, Corogene and CoreExome.

PredictCVD is a case-cohort sample from FINRISK 1992, 1997, 2002 and 2007 studies, consisting of all CVD (either CHD or stroke) cases, plus so-called sub-cohort, representative of the general study cohort. Such sample must be analyzed taking into account the sampling weights (inverse inclusion probabilities). Information on case-cohort sampling and analyses were described elsewhere.[32] Among PredictCVD participants with GWAS data (N=1,877), after exclusion of participants with prevalent stroke (N=22), or incident or prevalent CHD (but who were not in the sub-cohort, N=552), N=1,303 participants were available for analyses. Among Corogene controls with GWAS data (N=1,893), after exclusion of participants with prevalent stroke (N=6), N=1,887 participants were available for analyses. The CoreExome participants were participants from FINRISK 1997 and 2002 cohorts for whom a GWAS was not done earlier (as part of PredictCVD or Corogene studies). Among CoreExome participants with GWAS data (N=5,288), after exclusion of participants with prevalent stroke (N=86), N=5,202 participants were available for analyses.

Stroke ascertainment in FINRISK: During follow-up, participants were monitored for stroke through linkage of the study database with the National Hospital Discharge Register and the National Causes-of-Death Register. The clinical outcomes were linked to study subjects using their unique national social security ID, which is assigned to every permanent resident of Finland. The registers are countrywide covering all cardiovascular events that have led either to hospitalization or death in Finland. Their stroke diagnoses have been validated.[33] With both registers the diagnostic classification was done using the Finnish adaptation of ICD-codes: I63; not I63.6, I64 (ICD-10) / 4330A, 4331A, 4339A, 4340A, 4341A, 4349A, 436 (ICD-9) / 433, 434, 436 (ICD-8) for Ischemic stroke excluding any hemorrhagic strokes, and I60-I61,I63-I64 (not I63.6) (ICD-10) / 430, 431, 4330A, 4331A, 4339A, 4340A, 4341A, 4349A, 436 (ICD-9) / 430, 431 (except 431.01, 431.91), 433, 434, 436 (ICD-8) for all-stroke including SAH. ICD-8 codes 430, 431 (excluding codes 431.01, 431.91 of the Finnish adaptation of ICD-8*), 432, 433, 434 or with ICD-9 codes 430, 431, 433 (excluding codes 4330X, 4331X, 4339X of the Finnish adaptation of ICD-9*), 434 (excluding code 4349X of the Finnish adaptation of ICD-9*), 436, 437, 438 or with ICD-10 codes I60, I61, I63 (excluding I63.6), I64 or I69.[34] The stroke was classified as a first-ever event if there was no evidence of a previous stroke event in the patient's history. An event found in either register was sufficient for diagnosis.

Health, Aging, and Body Composition (Health ABC) Study

The Health ABC study is a prospective cohort study designed to examine the associations between body composition, weight-related health conditions, and functional limitations in older adults aged 70-79 years at inception.[35] In 1997-1998, 3,075 participants were recruited from a random sample of white and all African-American Medicare eligible residents in the Pittsburgh, PA and Memphis, TN metropolitan areas. Genome-wide genotyping was performed in 1732 white participants and 1663 met all QC criteria. All participants provided informed consent and protocols were approved by the institutional review boards at both study sites.

Among Health ABC participants with GWAS data (N=1663), after exclusion of participants without follow-up for incident stroke events (N=2), N=1,661 participants were available for analyses.

Stroke ascertainment in Health, Aging, and Body Composition (Health ABC) Study: Participants were screened for stroke events every 6 months alternating between semi-annual phone interviews and annual clinical visits. Any self-reported hospitalization for stroke led to medical record abstraction and verification by a Health ABC Disease Adjudicator at each site. Date and causes of death were obtained from the death certificate. Causes of death were adjudicated based on the review of medical records, proxy information and autopsy report (when performed).[36, 37] Stroke subtyping was done from medical records review. If the medical record indicated the event was hemorrhagic or ischemic in nature, this was recorded in the Health ABC data.

Rotterdam Study

The Rotterdam Study is a population-based cohort study among inhabitants of a district of Rotterdam (Ommoord), The Netherlands, and aims to examine the determinants of disease and health in the elderly with a focus on neurogeriatric, cardiovascular, bone, and eye disease.[38-40] All inhabitants aged ≥55 years (N=10,275) were invited and the participation rate was 78%, yielding a total of 7983 subjects. All participants gave written informed consent to retrieve information from treating physicians. Baseline measurements were obtained from 1990 to 1993 and consisted of an interview at home and two visits to the research center for physical examination. At this baseline examination ancestry was determined by self-report. Participants were asked to identify with one of the following categories that best described their ancestry: Dutch, Caucasian, Asian, Indian, Indonesian, Mediterranean, Negroid. Less than 1% of participants chose an ancestry other than Dutch or Caucasian. Survivors have been re-examined three times: in 1993-1995, 1997-1999, and 2002-2004. All persons attending the baseline examination in 1990-93 consented to genotyping and had DNA extracted. Genome-wide genotyping was attempted in persons with high-quality extracted DNA.

In 1990-1993, 7 983 persons 55 years of age or over participated and were re-examined every 3 to 4 years. In 1999, 3 011 individuals who had become 55 years of age or moved into the study district since the start of the study were added to the cohort (Rotterdam Study-II).[41] All participants had DNA extracted at their first visit. Genotyping was attempted in participants with high-quality extracted DNA.

Among Rotterdam Study-I participants with GWAS data (N=6,291), after exclusion of participants with prevalent stroke (N=179), and those without follow-up for incident stroke events (N=46), N=6,066 participants were available for analyses.

Among Rotterdam Study-II participants with GWAS data (N=2,157), after exclusion of participants with prevalent stroke (N=76), and those without follow-up for incident stroke events (N=1), N=2,080 participants were available for analyses.

Stroke ascertainment in Rotterdam: All participants have been continuously monitored for major events (including stroke) through automated linkage of the study database with files from general practitioners and the municipality. In addition physician files from nursing homes and general practitioner records of participants who moved out of the Ommoord district were reviewed twice a

year. For suspected stroke and TIA events, both fatal and non-fatal, additional information (including neuroimaging) was obtained from general practitioner' and hospital records and research physicians discussed available information with an experienced stroke neurologist to verify all diagnoses and to subclassify the strokes. Strokes were subclassified into ischemic or hemorrhagic based on neuroimaging (CT or MRI within 3 weeks) mentioned in medical records. If a hemorrhage was shown the stroke was subclassified as hemorrhagic, if there were no signs of hemorrhage, the stroke was subclassified as ischemic. Furthermore, strokes were subclassified according to TOAST criteria based on the diagnostic workup mentioned in medical records.[42, 43]

Study of Health in Pomerania (SHIP)

The "Study of Health in Pomerania" is a population-based epidemiological study in the region of Western Pomerania, Germany.[44] In brief, from the total population of West Pomerania comprising 213 057 inhabitants in 1996, a two-stage stratified cluster sample of adults aged 20–79 years was drawn. The net sample (without migrated or deceased persons) comprised 6 265 eligible subjects, out of which 4 308 completed their baseline examinations. From July 2007 to October 2010 the 'Life-Events and Gene-Environment Interaction in Depression' (LEGENDE) study was carried out in the SHIP cohort. After exclusion of SHIP- 1 participants without GWAS data and a positive lifetime prevalence of stroke before the SHIP-1 examination (N=188), N=3,112 participants were available for analyses.

Stroke ascertainment in SHIP: SHIP participants were followed-up after a median (range) of 5.0 (4.3–8.5) years on average. New stroke events were identified based on the following sources: Self-report by participants during the follow-up visit at the clinic center, with specific questions asking for a physician diagnosis (self-reported physician's diagnosis of stroke);[45] ICD codes based on the statutory health insurance, a survey among family doctors, inpatient visits at the Greifswald University Hospital, and Death Certificates. We included cases with fatal and non-fatal strokes. For in- and outpatient data we defined any stroke as cases with a coded ICD I61, I63, I64, I69.1, I69.3, I69.4 diagnosis. For ischemic stroke we included all cases with I63.x codes based on in- and outpatient data. Data from participants with self-reported events lacking an external validation were right censored at the estimated date of event. All participants with any stroke event from any source before the baseline examination were excluded from analyses.

Women's Genome Health Study (WGHS)

The WGHS (Women's Genome Health Study) is a large cohort for genome-wide genetic analysis of a wide range of clinical phenotypes among >25 000 women, 45 years or older at baseline and with ongoing follow-up observation, now for approximately 18 years.[46] The population is derived from participants in the Women's Health Study (WHS) who provided a blood sample at baseline. By design, participants included in the WGHS were free from dementia and stroke at baseline. Similarly, follow-up for incident stroke events was complete in the WGHS. Therefore, the total number of WGHS participants with whole genome genetic data for analysis was N=23,294.

*Stroke ascertainment in WGHS:*Since enrollment WGHS participants were followed-up annually for the occurrence of relevant clinical endpoints including stroke. The end-point ascertainment was continued in a blinded fashion through the scheduled end of the trial (March 31, 2004), when the cohort was converted to observational mode. Follow-up and validation of reported end points continues through the ongoing observational period. When a stroke endpoint was reported to occur, full medical reports were obtained and reviewed by an endpoints committee of physicians unaware of randomized treatment assignment. A confirmed stroke was defined as a new neurologic deficit of sudden onset that persisted for >24 h. Clinical information as well as computed tomographic scans or

MRI were used to distinguish hemorrhagic from ischemic events.[46] Stroke subtyping definition distinguishes ischemic versus hemorrhagic events according to TOAST criteria.[10]

Multi-Ethnic Study of Atherosclerosis (MESA)

The Multi-Ethnic Study of Atherosclerosis (MESA) is a study of the characteristics of subclinical cardiovascular disease (disease detected non-invasively before it has produced clinical signs and symptoms) and the risk factors that predict progression to clinically overt cardiovascular disease or progression of the subclinical disease.[47] MESA researchers study a diverse, population-based sample of 6,814 asymptomatic men and women aged 45-84. Thirty-eight percent of the recruited participants are white, 28 percent African-American, 22 percent Hispanic, and 12 percent Asian, predominantly of Chinese descent. Only white participants were used for the present analysis.

Participants were recruited from six field centers across the United States: Wake Forest University, Columbia University, Johns Hopkins University, University of Minnesota, Northwestern University and University of California - Los Angeles. The first examination took place over two years, from July 2000 - July 2002. It was followed by four examination periods that were 17-20 months in length. Participants have been contacted every 9 to 12 months throughout the study to assess clinical morbidity and mortality.[47]

Prevalent stroke was an exclusion criterion for MESA at baseline. Among MESA white participants with GWAS data (N=2,685), we excluded those with unexpected ancestry as inferred by principal components (N=124), those with unexpected relatedness (N=35), and those without follow-up for incident stroke events (N=162), N=2,364 participants were available for analyses.

Stroke ascertainment in MESA: New occurrences of stroke were recorded over 9-years of follow-up. In brief, a telephone interviewer contacted each participant every 9–12 months. Information about all new cardiovascular conditions, hospital admissions, cardiovascular outpatient diagnoses, treatments, and deaths were obtained. To verify self-reported diagnoses, information was collected from death certificates and medical records for all hospitalizations and outpatient cardiovascular diagnoses, using ICD-9 and ICD-10 codes. In the case of out-of-hospital deaths, next-of-kin interviews or questionnaires were administered to physicians, relatives or friends. Two physicians from the MESA study events committee independently reviewed all medical records for end point classification and assignment of incidence dates. The reviewers were blinded to the study data. If the reviewing physicians disagreed on the event classification, they adjudicated differences. Neurologists reviewed and classified stroke as present if there was a focal neurologic deficit lasting 24 hours or until death, or if <24h, there was a clinically relevant lesion on brain imaging and no nonvascular cause. Patients with focal neurological deficits secondary to brain trauma, tumor, infections, or other non-vascular cause were excluded.[48] Ischemic strokes were distinguished from hemorrhagic stroke using findings on imaging, surgery, autopsy, or some combination of these. Ischemic stroke subtypes were assigned based on an extension of the Trial of Org 10172 in Acute Stroke Treatment (TOAST) scheme to try to reduce the number classified as undetermined.

PROspective Study of Pravastatin in the Elderly at Risk (PROSPER)

PROSPER was a prospective multicenter randomized placebo-controlled trial to assess whether treatment with pravastatin diminishes the risk of major vascular events in elderly. Between December 1997 and May 1999, we screened and enrolled subjects in Scotland (Glasgow), Ireland (Cork), and the Netherlands (Leiden). Men and women aged 70-82 years were recruited if they had pre-existing vascular disease or increased risk of such disease because of smoking, hypertension, or diabetes. A total number of 5804 subjects were randomly assigned to pravastatin or placebo. A large number of prospective tests were performed including Biobank tests and cognitive function measurements. A detailed description of the study has been published elsewhere.[49, 50]

Among PROSPER participants with GWAS data (N=5,244), after exclusion of participants with prevalent stroke (N=586), and those without follow-up for incident stroke events (N=0), N=4,658 participants were available for analyses.

Stroke ascertainment in PROSPER: Stroke was defined as any event that meets the criteria listed below:

(a) Ischemic stroke (1 of the following conditions must be met): (1) Rapid onset of focal neurologic deficit lasting ≥24 hours or leading to death plus evidence from neuroimaging (computed tomography or magnetic resonance imaging) showing cerebral/cerebellar infarction or no abnormality, or postmortem examination showing cerebral and/or cerebellar infarction. (2) Rapid onset of global neurologic deficit (e.g., coma) lasting ≥24 hours or leading to death plus evidence from neuroimaging showing infarction, or postmortem examination showing infarction. (3) Focal neurologic deficit (mode of onset uncertain) lasting ≥24 hours or leading to death plus evidence from neuroimaging showing infarction, or postmortem examination showing infarction.

(b) Primary intracerebral and/or cerebellar hemorrhage (1 of the following conditions must be met): (1) Rapid onset of focal neurologic deficit lasting ≥24 hours or leading to death, plus neuroimaging or postmortem examination showing primary intracerebral and/or cerebellar hemorrhage. (2) Rapid onset of global neurologic deficit (e.g., coma) lasting ≥24 hours or leading to death, plus evidence from neuroimaging or postmortem examination showing primary intracerebral and cerebellar hemorrhage. (3) Focal neurologic deficit (mode of onset uncertain) lasting ≥24 hours or leading to death, plus evidence from neuroimaging or postmortem examination showing primary intracerebral and/or cerebellar hemorrhage.

(c) Not known (1 of the following conditions must be met): (1) Rapid onset of focal neurologic deficit lasting ≥24 hours or leading to death, without neuroimaging or postmortem data available. (2) Rapid onset of global neurologic deficit (e.g., coma) lasting ≥24 hours or leading to death, without neuroimaging or postmortem data available. (3) Focal neurologic deficit (mode of onset uncertain) lasting ≥24 hours or leading to death, without neuroimaging or postmortem data available.

The PROSPER Endpoints Committee was responsible for the classification of all possible study end points. The Committee received all annual study electrocardiograms showing serial changes, information regarding domiciliary visits or hospitalizations associated with possible myocardial infarction, and information on all deaths (including postmortem reports, death certificates, hospital records, general practitioners' records, and/or interviews of family members or witnesses).

TWINGENE

The TwinGene study originates from the Swedish Twin Registry (STR).[51] The STR conducted mailed questionnaires in 1961, 1963, 1967 and 1970 for all like-sexed twins born between 1886 and 1925, and in 1973 for all like-sexed pairs born in 1926–1958. A more recent STR wave contacted adult twins via the Screening Across the Lifespan Twin (SALT) study (1998–2002), which targeted all twins born in 1958 or earlier. For TwinGene, which took place between 2004 and 2008, 12 614 twins who had previously taken part in the SALT study donated a blood sample during in-person testing.

Among TWINGENE participants with GWAS data (N=9,617), after random exclusion of one twin from each pair and exclusion of participants with prevalent stroke, N=6,702 participants were available for analyses.

Stroke ascertainment in TWINGENE: Data on stroke were extracted from the Swedish National Patient Register and the Cause of Death Register using the twins' personal identification numbers; the information was based on the International Classification of Disease (ICD). Only main diagnoses were considered for cardiovascular outcomes. For stroke, the following ICD codes were used: ICD-8 codes 430–436, ICD-9 codes 430–436 and ICD-10 codes I60-I64 and G45.[52] Further classification into stroke subtypes was done using ICD-8 codes 432-434, ICD-9 codes 433-434, and ICD-10 code I63 for

ischemic stroke, and ICD-8 codes 430-431, ICD-9 codes 430-432, and ICD-10 codes I60-I62 for hemorrhagic stroke.[53] One twin was randomly selected per pair if data were available for both twins.

Uppsala Longitudinal Study of Adult Men (ULSAM)

ULSAM is a unique, ongoing, longitudinal, epidemiologic study based on all available men, born between 1920 and 1924, in Uppsala County, Sweden. The men were investigated at the ages of 50, 60, 70, 77, 82 and 88 years. The ULSAM cohort focuses on identification of metabolic risk factors for cardiovascular disease, to which all 50-year-old men living in Uppsala, Sweden, in 1970-974 were invited. The ULSAM originally comprised 2322 participants (82% of the invited). A re-investigation was performed around 20 years later between 1991 and 1995.[54]

Among ULSAM participants with GWAS data (N=1,179), after exclusion of participants with prevalent stroke, N=1,139 participants were available for analyses.

Stroke ascertainment in ULSAM: Information on the occurrence of stroke was extracted from the Swedish Hospital Discharge Record and Cause of Death Registries and validated by examination of all the medical records by one physician. They cover hospitalization and mortality from strokes using ICD-8 codes 430-431 and 433-434, ICD-9 codes 430-432, 434 or ICD-10 codes I60-I64. Further classification into stroke subtypes was done using ICD-8 codes 433-434, ICD-9 code 434, and ICD-10 code I63 for ischemic stroke, and ICD-8 codes 430-431, ICD-9 codes 430-432 and ICD-10 codes I60-I62 for hemorrhagic stroke.[54, 55]

3C-Study

The Three-City study is a prospective study aiming to assess the association between vascular diseases and risk of dementia. The detailed protocol of the study has been previously described.[56] The Three-City cohort is composed of non-institutionalized individuals aged 65 years and over, randomly selected from electoral rolls of three cities of France (Bordeaux, Dijon, and Montpellier), and agreeing to participate in the study. Between March 1999 and March 2001, 9,294 persons were enrolled (4,931 in Dijon, 2,104 in Bordeaux and 2,259 in Montpellier).

Up to five face-to-face examinations were performed during follow-up. Trained nurses and psychologists performed interviews and physical and cognitive measurements at the participant's home and at the study centre. As imputation was performed separately in the 3C-Dijon sample on the one hand and the Bordeaux and Montpellier samples on the other hand, analyses were run separately in these datasets (3C-Dijon and 3C-Bordeaux-Montpellier).

In the 3C-Dijon study, among participants with GWAS data (N=4,077), after exclusion of participants with prevalent stroke (N=204), and those without follow-up for incident stroke events (N=111), N=3,762 participants were available for analyses.

In the 3C-Bordeaux-Montpellier study, after exclusion of participants without GWAS data and with prevalent stroke and those without follow-up for incident stroke events N=2,153 participants were available for analyses.

Stroke ascertainment in 3C-Study: At each follow-up visit, participants or informants for deceased participants were systematically questioned about the occurrence of any severe medical event or hospitalization since the last contact. For those reporting a possible stroke event, all available clinical information was collected from hospital records, and interviews with the participant's physician, nursing home staff (for participants admitted in a nursing home during follow-up) or family. Expert panels including at least one physician specialized in vascular medicine reviewed all available clinical information and classified each event according to the International Classification of Diseases – 10th Edition. Stroke was confirmed if the participant had a new focal neurological deficit of sudden onset attributable to a cerebrovascular event that persisted for more than 24 hours. Stroke was classified by

the panel as ischemic stroke, intracerebral hemorrhage or of unspecified type and ischemic stroke (IS) was classified by the panel according to the TOAST classification into cardioembolic IS, large-artery IS, small vessel disease IS, IS of other etiologies, and IS of undetermined etiology.[10]

EPIC

EPIC is a multi-centre prospective cohort study of 519,978 participants (366,521 women and 153,457 men, mostly aged 35–70 years) recruited between 1992 and 2000 in 23 centres located in 10 European countries.[57] Participants were invited mainly from population-based registers (Denmark, Germany, certain Italian centres, the Netherlands, Norway, Sweden, UK. Other sampling frameworks included: blood donors (Spain and Turin and Ragusa in Italy); screening clinic attendees (Florence in Italy and Utrecht in the Netherlands); people in health insurance programmes (France); and health conscious individuals (Oxford, UK). About 97% of the participants were of white European ancestry. Prevalent CVD was ascertained through self-reported history of MI or angina, or registry-ascertained CVD event prior to baseline. EPIC-CVD employs a nested case-cohort design,[58] analogous to the EPIC-InterAct study for type-2 diabetes which established a common set of referents through selection of a random sample of the entire cohort ("subcohort").[59]

Stroke ascertainment in EPIC: Centres were asked to ascertain suspected stroke cases from registries, hospital records or self-report (i.e. follow-up questionnaires). Stroke events were defined by ICD10 codes as follows: Ischemic I63, Haemorrhagic I61, SAH I60, Unclassified I64, Other CRBV I62, I65-I69, F01. Incident stroke cases have been defined as fatal and non-fatal. All centres have recorded cause-specific mortality through mortality registries and/or active follow-up, and have ascertained and validated incident fatal and non-fatal stroke through a combination of methods.

Ascertained non-fatal stroke events were validated by clinical symptoms and imaging evidence (CT/MRI) or confirmed through hospital/GP records (with assessment of notes) or confirmed through hospital records (without assessment of notes). Individuals were excluded if they had clinical symptoms but no validation was possible e.g. there was no imaging evidence, nor GP/primary care records (without assessment of notes) or registry information. Fatal stroke events were validated either by autopsy or hospital records and death certificate or by death certificate if they died in hospital. Individuals where validation was not possible were excluded. Participants with a history of stroke or MI at baseline were excluded. No further stroke subtyping was performed.

AIDHS/SDS

Asian Indian Diabetic Heart Study/Sikh Diabetes Study (AIDHS/SDS) is a case-control study designed to investigate the association between genetic and environmental factors and their risk on type 2 diabetes (T2D) and cardiovascular disease in a population of Punjabi ancestry from India.[60, 61] All AIDHS/SDS participants were recruited from the northern part of India between 2003 to 2006. Information regarding stroke was obtained from patient records. Stroke was defined on the basis of an event requiring hospitalization. Diagnosis of ischemic stroke was established based on either evidence of an infarction in neuroimaging (CT/MRI scan) or symptom duration >24 hours. A total of 52 (3.3%) participants had a stroke. A total of 1,566 subjects included in this investigation were available with genome-wide genotyping data (Illumina's 660W-Quad BeadChip). Imputation was performed using IMPUTE2 with the reference panel of 1092 worldwide subjects from 1000 Genomes Project Phase I integrated variant set (March 2012 release) in NCBI Build 37 (hg19) coordinates as described previously.[62] Both men and women aged 20-90 years participated. Inclusion was based on those with Sikh surnames of North Indian origin, and speaking the Punjabi language. Excluded were individuals of South, East and Central Indian origin. All blood samples were obtained at the baseline visits. All participants signed a written informed consent for the investigations. The study was reviewed and approved by the University of Oklahoma Health Sciences Center's Institutional Review Board, as well as the Human Subject Protection Committees at the participating hospitals and institutes in India.

VHIR-FMT-Barcelona

The Barcelona cohort is a subset of Caucasian Ischemic stroke subjects that were enrolled as a part of the Genetic contribution to functional Outcome and Disability after Stroke (GODs) project. Cases were selected through demonstration of acute ischemic stroke in a neuroimaging study during the first 7 days after stroke. We included cases with a first-ever and with a recurrent stroke. We did not include lacunar strokes due to the study was focused only on disability after stroke of non-lacunar cases. We did not use age or stroke severity as exclusion criteria. Participants were not part of a treatment trial. Etiologic subgroups were classified following TOAST criteria. Controls were healthy subjects older than 40 years old without history of ischemic stroke. The control cohort was collected in primary care centers from Barcelona city and some hospital in the Spanish Network as a part of the Investigating Silent Stroke in hYpertensives: A magnetic resonance imaging Study (ISSYS) and Genotyping RECurrence Risk Of Stroke (GRECOS) study. All the samples (cases and controls) were genotyped using the Infinium Human Core Exome Chip (Illumina). Written informed consent was obtained from all subjects with approval from the ethics committee of all participating institutions.

Biobank Japan

BioBank Japan Project was started in 2003 and collected DNA and clinical information from a total of 200,000 patients suffering from at least one of 47 common diseases. Eligibility of cases was determined by physicians from a collaborative network of 66 hospitals. Overall, 16,256 ischemic stroke cases were registered at the biobank, named as BBJ. Of all ischemic stroke cases, 1,256 were classified as large artery strokes, 710 as cardioembolic and 4,613 as small vessel stroke. Clinical information was collecrted by standdardized questionnaire though medical records survey. As for the controls, we used genotyping information of 27,294 individuals aged over 40 years from three population based controls: Japan Multi-Institutional Collaborative Cohort Study(J-MICC), Japan Public Health Center-based Prospective Study (JPHC), and the Tohoku Medical Megabank Project (TMM).

Stroke ascertainment in Biobank Japan: Stroke patients > 40 years old were selected from BioBank Japan. Ischemic stroke was diagnosed by physicians at collaborating hospitals and its subtypes were determined by medical record survey according to the TOAST criteria.

CADISP

The Cervical Artery Dissections and Ischemic Stroke Patients (CADISP) study was designed to identify genetic risk variants for cervical artery dissections (CeAD), a major cause of ischemic stroke in young adults.[63] As part of a secondary analysis, patients with an ischemic stroke without cervical artery dissection (non-CeAD ischemic stroke) were also recruited, in the same centers as CeAD patients. These were patients with a diagnosis of ischemic stroke, in whom CeAD had been formally ruled out according to CADISP inclusion criteria (see attachment). Non-CeAD ischemic stroke patients were frequency-matched on age (by 5-year intervals) and gender on CeAD patients. A total of 658 non-CeAD ischemic stroke patients were included in Belgium, Finland, France, Germany, Italy, and Switzerland. We excluded 19 patients due to unavailability of geographically matched healthy controls, or due to non-European origin; of the remaining 639 non-CeAD IS patients, 613 individuals had good quality DNA available and were genotyped at the CNG. Of these, a total of 555 non-CeAD IS patients aged < 60 years, who were successfully genotyped and met genotyping quality control criteria, were used for the present analysis.

The abstracted hospital records of cases were reviewed and adjudicated for IS subtype by a neurologist in each participating center. Each item required for the subtype classification was also recorded in a standardized fashion. Based on this, IS subtypes were then centrally re-adjudicated by a panel of

neurologists, in agreement with the TOAST system,[10] using a more detailed subtype description from an early version of the Causative Classification System (CCS).[64]
The majority of controls (N=9,046, of which 74 Finns and 8,972 non-Finnish Europeans) were selected from an anonymized control genotype database at the Centre National de Génotypage [CNG], in order to match cases for ethnic background, based on principal component analysis. European reference samples from the genotype repository at the CNG were also analyzed simultaneously to provide improved geographical resolution. Additional Finnish controls were recruited within the CADISP study, both from the general population and among spouses and unrelated friends of CADISP patients, within the Helsinki area. A total of 234 individuals were eligible for genotyping at the CNG. Of these, 213 individuals who were genotyped successfully and met quality control criteria were available for the present analysis.[63] All participants were of European ancestry.

COMPASS

COMPASS contains African American participants from several cohort studies. Diagnosis of stroke was adjudicated by a physician. The study has been described previously,[65] details on the individual cohorts are as follows.

Atherosclerosis Risk in Communities (ARIC) Study

The ARIC study is a prospective population-based study of atherosclerosis and clinical atherosclerotic diseases in 15,792 men and women, including 11,478 non-Hispanic white participants, drawn from 4 U.S. communities (Suburban Minneapolis, Minnesota; Washington County, Maryland; Forsyth County, North Carolina, and Jackson, Mississippi). In the first three communities, the sample reflects the demographic composition of the community. In Jackson, only black residents were enrolled. Ancestry was self-reported during an interview. Participants were handed a card and asked to tell the interviewer which best described his or her race. Choices offered were: White, Black, American Indian/Alaskan Native, Asian/Pacific Islander, Other: specify. Over 99% identified as either white or black. Only self-identified blacks were included in for COMPASS. Participants were between age 45 and 64 years at their baseline examination in 1987-1989 when blood was drawn for DNA extraction and participants consented to genetic testing. Only individuals free of stroke or TIA at baseline were included in the analysis. Single-nucleotide polymorphisms (SNPs) were genotyped on the Affymetrix 6.0 chip and were imputed to ≈2.5 million SNPs based on a panel of cosmopolitan reference haplotypes from HapMap CEU and YRI (HapMap II CEU and YRI (build 35, release 21)). MACH v1.0.16 was used to perform genotype imputations and allele dosage information was summarized in the imputation results.

Stroke ascertainment in ARIC: Hospitalized strokes that occurred by December 31, 2012 were included in the present study. During annual telephone contacts, trained interviewers asked each ARIC participant to list all hospitalizations during the past year. Hospital records for any hospitalizations identified were then obtained. In addition, all local hospitals annually provided lists of stroke discharges (International Classification of Diseases, Ninth Revision, Clinical Modification codes 430 to 438), which were scrutinized for ARIC participant discharges. Details on quality assurance for ascertainment and classification of stroke are described elsewhere. Briefly, the stroke diagnosis was assigned according to criteria adapted from the National Survey of Stroke. Strokes secondary to trauma, neoplasm, hematologic abnormality, infection, or vasculitis were excluded, and a focal deficit lasting <24 hours was not considered to be a stroke. Out-of-hospital stroke was not ascertained and validated; thus, these potential stroke events were not included. Strokes were classified into hemorrhagic stroke (subarachnoid and intracerebral hemorrhage) and ischemic stroke (thrombotic and embolic brain infarction). A stroke was classified as ischemic when a brain CT or MRI revealed acute infarction and showed no evidence of hemorrhage. All definite ischemic strokes were further classified as lacunar, nonlacunar thrombotic, or cardioembolic on the basis of the recorded neuroimaging results. For this analysis, the hemorrhagic strokes identified by ARIC were censored at the time of their occurrence.

Cardiovascular Health Study (CHS) – African-Americans

The Cardiovascular Health Study (CHS) is a population-based cohort study of risk factors for coronary heart disease and stroke in adults ≥65 years conducted across four field centers [PMID: 1669507]. The original predominantly European ancestry cohort of 5,201 persons was recruited in 1989-1990 from random samples of the Medicare eligibility lists; subsequently, an additional predominantly African-American cohort of 687 persons were enrolled for a total sample of 5,888. Because the COMPASS consortium focused on non-European samples, only self-described African-Americans contributed to the COMPASS analyses.

Blood samples were drawn from all participants at their baseline examination and DNA was subsequently extracted from available samples. Genotyping was performed at the General Clinical Research Center's Phenotyping/Genotyping Laboratory at Cedars-Sinai among CHS African-American participants who consented to genetic testing and had DNA available using Illumina HumanOmni1-Quad_v1 BeadChip system.

Beyond laboratory genotyping failures, participants were excluded if they had a call rate<=95% or if their genotype was discordant with known sex or prior genotyping (to identify possible sample swaps). After quality control, genotyping was successful for 823 African-American participants.

CHS was approved by institutional review committees at each field center and individuals in the present analysis had available DNA and gave informed consent including consent to use of genetic information for the study of cardiovascular disease.

The Healthy Aging in Neighborhoods of Diversity across the Life Span Study (HANDLS) – African Americans

In the absence of non-stroke control samples from the VISP, ISGS, and SWISS studies, controls from the Healthy Aging in Neighborhoods of Diversity across the Life Span study (HANDLS) study were used for the VISP and SWISS-ISGS case-control analyses (with no overlap across studies). Controls were sex and race/ethnicity-matched and randomly selected from all HANDLS participants not reporting history of stroke at baseline or reporting adjudicated stroke during follow-up.

HANDLS is an interdisciplinary, community-based, prospective longitudinal epidemiologic study examining the influences of race and socioeconomic status (SES) on the development of age-related health disparities among socioeconomically diverse African Americans and whites in Baltimore, MD, USA. This study assesses physical parameters over a 20-year period while evaluating genetic, biologic, demographic, and psychosocial influences. HANDLS recruited 3,722 participants (2200 African Americans (59%) and 1522 whites (41%)) from Baltimore, MD.

Stroke Ascertainment. Stroke status at baseline was determined through self-report while incident strokes, other vascular events, and deaths were determined using medical records and clinic visits during follow-up.

Genotyping was focused on a subset of participants self-reporting as African American and was performed at the Laboratory of Neurogenetics, National Institute on Aging, National Institutes of Health. Genotype data (for up to 907,763 SNPs) were generated for 1,024 participants using either Illumina 1M and 1M duo arrays (n=709) ,or a combination of 550K, 370K, 510S and 240S to equate the million SNP level of coverage. Inclusion criteria for genetic data in HANDLS includes concordance between self-reported sex and sex estimated from X chromosome heterogeneity, > 95% call rate per participant (across all equivalent arrays), concordance between self-reported African ancestry and ancestry confirmed by analyses of genotyped SNPs, and no cryptic relatedness to any other samples at a level of proportional sharing of genotypes > 15% (effectively excluding 1st cousins

and closer relatives from the set of probands used in analyses). In addition, SNPs included in the analysis were filtered for HWE p-value > 1e-7, missing by haplotype p-values > 1e-7, minor allele frequency > 0.01, and call rate > 95%. Data analyses utilized the high-performance computational capabilities of the Biowulf Linux cluster at the NIH, Bethesda, Md. (http://biowulf.nih.gov).

INTERSTROKE-African Americans

INTERSTROKE is an international, multi-centered, case-control study of stroke investigating the global burden of risk factors across 32 countries and 18 different ethnic groups around the world. A detailed report of the study design has been published (Neuroepidemiology. 2010; 35:36-44). Briefly, cases were patients with acute first stroke (within 5 days of symptoms onset and 72 hours of hospital admission) in whom neuroimaging (CT or MRI) was performed. The TOAST classification system was used to define ischemic stroke subtypes. Cases were excluded if 1) they were unable to communicate due to severe stroke without a valid surrogate respondent (e.g. first-degree relative or spouse), 2) they were hospitalized for acute coronary syndrome/myocardial infarction, or 3) stroke was attributed to non-vascular causes (e.g. tumor). Controls were selected from the community and had no history of stroke.

A subset of INTERSTROKE participants consenting to genetic analysis with sufficient DNA quantities were genotyped on the Illumina Infinium Cardiometabo BeadChip. All samples were genotyped at a central site (the Genetic Molecular Epidemiology Laboratory in Hamilton, Ontario, Canada). Samples were excluded if they had 1) a high proportion of missing variants (missingness > 0.05), 2) inconsistencies between reported and genetically determined sex or ethnicity or 3) exhibited cryptic relatedness. Genotyped variants were excluded if they were rare (MAF < 0.01), exhibited high missingness across samples (missingness > 0.01), or deviated from hardy-weinberg equilibrium ($P<5x10^{-6}$). Pre-phasing and imputation were perforrmed with SHAPEIT2 and IMPUTE, respectively, using the 1000Genomes Phase 1 Version 3 (November 23, 2010 subversion) reference panel. Imputed variants were removed if they were rare (MAF < 0.01) or of poor quality (INFO SCORE < 0.30).

Ischemic Stroke Genetic Study (ISGS)-African Americans

ISGS is a multicenter inception cohort study. Cases were recruited from inpatient stroke services at five United States academic medical centers. Cases are adult men and women over the age of 18 years diagnosed with first-ever ischemic stroke confirmed by a study neurologist on the basis of history, physical examination and CT or MR imaging of the brain. Cases had to be enrolled within 30 days of onset of stroke symptoms. Cases were excluded if they had: a mechanical aortic or mitral valve at the time of the index ischemic stroke, central nervous system vasculitis, or bacterial endocarditis. They were also excluded if they were known to have: cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), Fabry disease, homocystinuria, mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS), or sickle cell anemia. Diagnostic evaluation included: head CT (95%) or MRI (83%), electrocardiography (92%), cervical arterial imaging (86%), and echocardiography (74%). Medical records from all cases were centrally reviewed by a vascular neurology committee and assigned ischemic stroke subtype diagnoses according to TOAST criteria, Oxfordshire Community Stroke the Baltimore-Washington Young Stroke Stud. DNA was donated to the NINDS DNA Repository (Coriell Institute, Camden, NJ) for eligible samples with appropriate written informed consent. DNA samples were genotyped using the Illumina 610 array and data analyses were supported by the high-performance computational capabilities of the Biowulf Linux cluster at the NIH (http://biowulf.nih.gov).

Jackson Heart Study (JHS)

The JHS is a single-site, prospective, population-based study designed to explore the environmental, behavioral, and genetic factors that influence the development of CVD among African Americans. A total of 5,301 women and men between the ages of 21 and 94 were recruited between 2000 and 2004 from a tri-county area of Mississippi: Hinds, Madison, and Rankin Counties. Participants were

recruited from four sources, including (1) randomly sampled households from a commercial listing; (2) ARIC participants; (3) a structured volunteer sample that was designed to mirror the eligible population; and (4) a nested family cohort. Overviews of the JHS including the sampling and recruitment, sociocultural, and laboratory methods have been described and published previously.[66-69] The institutional review boards of the following participating institutions approved the study: the University of Mississippi Medical Center, Jackson State University, and Tougaloo College. All of the participants provided written informed consent. Unrelated participants were between 35 and 84 years old, and members of the family cohort were ≥ 21 years old when consent for genetic testing was obtained and blood was drawn for DNA extraction.
The baseline examination consisted of a home interview, self-administered questionnaires, and a clinic visit. Medications taken in the prior 2 weeks were brought to clinic and transcribed verbatim with subsequent coding by a pharmacist. After an overnight fast, anthropometric and seated blood pressure measurements were obtained and venipuncture/urine collection was performed in accordance with the National Committee for Clinical Laboratory Standards. Blood pressure was measured by trained technicians using a Hawksley random zero manometer and determined by the arithmetic average of two readings taken 1 minute apart after a five-minute rest.[70]

Stroke Assessment in the JHS: In addition to the standard JHS examinations, participants were contacted by telephone annually beginning in 2005 to obtain interim information about cardiovascular events. (ICD-9 code 428 for hospitalizations). During the annual follow up phone call, participants or designated representative provide self-reported information of hospitalization or death. Identification and abstraction of CVD illness and death data are performed by a certified medical record abstractor. Incident stroke is defined as stroke that occurred while the participants was enrolled the study, i.e. stroke event occurred after the baseline visit. Strokes are classified as either definite or probable stroke. The definition of stroke was based on the World Health Organization (WHO) criteria for definition of stroke or clinical criteria in which case the WHO criteria might not have been satisfied, but there is clinical evidence sufficient for a diagnosis of stroke to be made. More details on identification and classification of stroke events in the JHS have already been published.[71, 72] Although not directly relevant in this study, ischemic stroke subtyping in the JHS was done the TOAST classification criteria.

The Sea Islands Genetics Network (SIGNET) & REasons for Geographic And Racial Differences in Stroke (REGARDS) – African Americans

The Sea Islands Genetics Network (SIGNET) study consists of the REasons for Geographic And Racial Differences in Stroke (REGARDS), the Sea Islands Genetic African American Registry (Project SuGAR), a COBRE for Oral Health study (COBRE), and the Systemic Lupus Erythematosus in Gullah Health study (SLEIGH). All subjects are African Americans (AA), and all provided written informed consent.

All SIGNET samples (n= 4,298) were genotyped using the Affymetrix Genome-Wide Human SNP Array 6.0. Imputation was performed using MACH (version 1.0.16) to impute all autosomal SNPs using the CEU+YRI reference panel (as supplied by Goncalo Abecasis) from build 36 (2,318,207 SNPs in total).

REGARDS is an observational cohort of 30,239 AA and white men and women enrolled in their homes after a telephone interview in 2003-7 (Howard VJ et al., 2005). Participants were a national sample oversampled from the southeastern stroke belt (56%) and were 58% female and 42% black by design. Participants were followed every 6 months by telephone to ascertain health outcomes, with validation of stroke, coronary heart disease, death and other ancillary study endpoints. For SIGNET, we selected all AA REGARDS type 2 diabetes (T2D) cases recruited from SC, GA, NC, and AL, and an equivalent number of race, sex, and age-strata matched diabetes-free controls. We also included all participants not already included that were current residents of the 15-county "Low Country" region of SC and GA (SC counties Beaufort, Berkeley, Charleston, Colleton, Dorchester, Georgetown, Hampton, Horry, Jasper; GA counties Bryan, Camden, Chatham, Glynn, Liberty, McIntosh). The subset of REGARDS participants genotyped under SIGNET are referred to as SIGNET-REGARDS.

GWAS genotyping was completed among 2398 SIGNET-REGARDS AA participants, including 1149 with diabetes and 1249 without diabetes.

Siblings with Ischemic Stroke Study (SWISS) – African Americans

SWISS is a prospective multicenter affected sibling pair study of first-ever or recurrent ischemic stroke. Subjects were recruited from 54 enrolling hospitals across the US and Canada. Samples were collected between 1999-2011. Ischemic stroke probands were enrolled at 66 US medical centers and 4 Canadian medical centers. All recruits were extensively clinically phenotyped and have imaging-confirmed ischemic stroke using either CT or MRI brain scans. Probands are adult men and women over the age of 18 years diagnosed with ischemic stroke confirmed by a study neurologist on the basis of history, physical examination and CT or MR imaging of the brain who also have a history of at least one living sibling with a history of stroke. Probands were excluded if 1) they had a mechanical aortic or mitral valve at the time of the index ischemic stroke, central nervous system vasculitis, or bacterial endocarditis or 2) were known to have cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), Fabry disease, homocystinuria, mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS), or sickle cell anemia. Siblings were enrolled using proband- initiated direct contact when permitted by Institutional Review Boards. Concordant siblings had their diagnosis of ischemic stroke confirmed by review of medical records by a central vascular neurology committee. Concordant siblings had the same eligibility criteria as probands. Subtype diagnoses were assigned to the index strokes of probands and concordant siblings according to TOAST criteria. Discordant siblings of the proband were confirmed to be stroke-free using the Questionnaire for Verifying Stroke-free Status. DNA samples were genotyped using the Illumina 660 array and data analyses were supported by the high-performance computational capabilities of the Biowulf Linux cluster at the NIH (http://biowulf.nih.gov).

Women's Health Initiative (WHI) – African Americans

The goal of the WHI was to investigate the etiology and prevention of chronic disease in post-menopausal women . Approximately 161,000 postmenopausal women 50–79 years of age from 40 clinical centers in the US were recruited between 1993 and 1998. WHI consists of an observational study (OS), and clinical trials (CT) of postmenopausal hormone therapy (estrogen alone or estrogen plus progestin), a calcium and vitamin D supplement trial, and a dietary modification trial. A subset of 8,515 African American women who provided consent for DNA analysis were randomly selected for genome-wide genotyping as part of the SNP Health Association Resource (SHARe). .

Genetic data were obtained from genome-wide scans using the Genome-wide Human SNP Array 6.0 (Affymetrix, Santa Clara, CA, www.affymetrix.com) of 909,622 single nucleotide polymorphisms (SNPs). Genotyping quality control included examination of concordance rates for blinded and un-blinded duplicates. Approximately 1% of SNPs failed genotyping and SNPs with call rates < 95% or concordance rates <98%, or minor allele frequency <1% were excluded. In addition to the genotyping, SNPs were imputed using 1000 Genomes Project phase 1 integrated variant set (Aug 2012). Principal components were calculated for each individual and evaluated for their contribution to ancestral variation. Because most of the ancestral variation was explained by the first 4 PCs, only these were included as covariates in the analyses.

Stroke ascertainment in WHI: All incident strokes, other vascular events, and deaths were identified through self-report at annual (OS) and semi-annual (CT) participant contacts, and through third- party reports by family members and proxies. Medical records were obtained for potential strokes, and adjudication was performed by trained physician adjudicators who assigned a diagnosis. Stroke diagnosis requiring and/or occurring during hospitalization was based on rapid onset of a neurological deficit attributable to an obstruction or rupture of an arterial vessel system. The deficit was not known to be secondary to brain trauma, tumor, infection or other cause and must have lasted more than 24 hours unless death supervened or a lesion compatible with acute stroke was evident on computed tomography or magnetic resonance imaging were classified as ischemic, hemorrhagic or

unknown/missing. Ischemic stroke subtypes were further classified using Trial of Org 10172 in Acute Stroke Treatment (TOAST) analyses, strokes subtypes judged as 'probable' or 'possible' were combined. African American women passing the above genotyping quality control criteria, with follow-up data, and without a history of stroke at baseline were included in the WHI analyses. All participants provided written, informed consent.

deCODE study

Icelandic ischemic stroke cases (5,520), were identified from a registry of individuals diagnosed with ischemic stroke or TIA at Landspitali University Hospital in Reykjavik, the only tertiary referral centre in Iceland, during the years 1993 to 2013. The ischemic stroke or TIA diagnoses were based on standard WHO criteria and imaging evidence (either CT or MRI), and were clinically confirmed by neurologists. Eligible patients who survived the stroke were invited to participate the genetic study, either by attending a recruitment centre for deCODE's genetic studies, or they were visited at their home by a study nurse. Patients were classified into causative subtypes according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST).

The study is based on whole-genome sequencing of 8,453 Icelanders and Illumina SNP chip genotyping of 151,677 Icelanders. Genotypes for the chip-typed individuals are phased using the method of long-rage phasing (Kong et al. Detection of sharing by descent, long-range phasing and haplotype imputation Nat Genet 40, 1068-75, 2008). and genotype probabilities for un-typed variants are imputed into the chip-typed individuals, and their close relatives, using phased genotypes for the 8.453 WGS individuals as reference. Association testing for case–control analysis was performed using logistic regression, adjusting for age and county and assuming a multiplicative model of risk. About 25 million variants, all with imputation info over 0.8, were tested for association. To account for inflation in the test statistics due to cryptic relatedness and stratification within the case and control sample sets, we applied the method of LD score regression (Bulik-Sullivan B. K. et al. LD Score regression distinguishes confounding from polygenicity in genome-wide association studies. Nat. Genet. 47, 291–295, 2015).

Control comprised 254,176 individuals recruited through different genetic projects at at deCODE. Individuals with confirmed stroke (identified by cross-matching with hospital lists) were excluded as controls.

The study was approved by the Data Protection Commission of Iceland and the National Bioethics Committee of Iceland. All participants gave informed consent.

Glasgow Stroke Sample

Cases with ischemic stroke attending the cerebrovascular service of the Western Infirmary, Glasgow, were recruited between 1990 and 2004 as part of an ongoing study of genetic and circulating biomarkers in stroke. All patients underwent brain imaging and extracranial carotid ultrasound in accordance with a standard clinical protocol. The study was approved by the West Ethics Committee.

Controls were drawn from shared WTCCC controls obtained from the 1958 Birth Cohort. This is a prospectively collected cohort of individuals born in 1958, and ascertained as part of the national child development study.[6] Data from this cohort are available as a common control set for a number of genetic and epidemiological studies.

Helsinki 2000 Ischemic Stroke Genetics Study

Helsinki 2000 Ischemic Stroke Genetics Study was designed for investigating genetic factors underlying ischemic stroke in a Finnish population and in the long-term to be incorporated to multicenter multinational similar datasets. The study aims at recruiting 2000 eligible patients and the

study is still recruiting patients. This study received approval from local ethics committee (October 27, 2010; §266 and Amended June 27, 2016; §142). All ischemic stroke cases in this study were recruited from the Helsinki University Central Hospital, which is the only neurological emergency unit for a population of 1.5 million inhabitants[73]. Only patients with positive neuroimaging findings for a new-onset brain infarction were recruited following written informed consent. Stroke subtyping was performed using the TOAST definition, utilizing electrocardiogram-Holter, carotid Doppler, carotid angiography, and transesophageal echocardiogram. Cardiologist was consulted when considered necessary. Detailed phenotype data were collected and recorded along with venous blood samples stored at -80° C freezer. The controls were obtained from the FINRISK 1992, 1997, and 2002 study[74] participants residing in the same geographic area (Greater Helsinki region). They were frequency-matched to cases by age and sex, and were free of major adverse cardiovascular events. All included patients and control subjects are of Finnish, Caucasian, origin and were followed-up based on nationwide register data. The FINRISK surveys have been approved by the Coordinating Ethical Committee of the Helsinki and Uusimaa Hospital District and the participants have signed an informed consent. Cases and controls were genotyped on the Illumina HumanExomeCore array.

Hisayama-FSR study

A detailed study description was described previously[75]. The individuals with ischemic stroke were recruited from seven hospitals in Fukuoka Prefecture, Japan (Kyushu University Hospital, Hakujyuji Hospital, Fukuoka Red Cross Hospital, Kyushu Medical Center, Imazu Red Cross Hospital, Fukuoka Higashi Medical Center, and Seiai Rehabilitation Hospital) in 2004 (The Fukuoka Stroke Registry [FSR]) . In the genome-wide association study, 1113 cases with ischemic stroke (370 large artery stroke, 137 cardioembolic stroke, 483 small vessel occlusion, 123 undetermined subtype) were included. Control subjects were enrolled from the participants in the Hisayama Study, an ongoing population-based epidemiological study of cardiovascular disease in the town of Hisayama, Fukuoka Prefecture, Japan. A total of 3,328 individuals aged 40 years or older participated in the screening survey and underwent a comprehensive assessment in 2002-2003. After excluding subjects with a history of stroke or coronary heart disease, 901 control subjects were included in the genome-wide association study.

Stroke ascertainment in the Hisayama-FSR study: Ischemic stroke was defined as a sudden non-convulsive, focal neurologic deficit lasting longer than 24 hours due to brain ischemia. The diagnoses of ischemic stroke and its subtypes for all cases were made by stroke neurologists of the hospitals, referring to detailed clinical features and ancillary laboratory examinations: namely, cerebral angiography, brain imaging (including computed tomography and magnetic resonance imaging), echocardiography, and carotid duplex imaging. Subtypes of ischemic stroke were determined on the basis of the Classification of Cerebrovascular Disease III proposed by the National Institute of Neurological Disorders and Stroke and the TOAST classification.

Heart and Vascular Health Study (HVH 1 & 2)

The setting for this study was Group Health (GH), a large integrated health care system in western Washington State (Kaiser Permanente Washington, as of February 2017).

Data were utilized from an ongoing case-control study of incident myocardial infarction (MI) and stroke cases with a shared common control group. Methods for the study have been described previously and are briefly summarized below.[76-78] The study was approved by the human subjects committee at GH, and written informed consent was provided by all study participants.

All study participants were GH members and aged 30-79 years. MI and stroke cases were identified from hospital discharge diagnosis codes and were validated by medical record review. Controls were a

random sample of GH members frequency matched to MI cases on age (within decade), sex, treated hypertension, and calendar year of identification. The index date for controls was a computer-generated random date within the calendar year for which they had been selected. For stroke cases, the index date was the date of admission for the first acute stroke. Participants were excluded if they were recent enrollees at GH, had a history of prior stroke, or if the incident event was a complication of a procedure or surgery.

Trained medical record abstractors collected eligibility and risk factor information from a review of the GH medical record using only data available prior to the index date and through a telephone interview. Medication use was ascertained using computerized GH pharmacy records. A venous blood sample was collected from all consenting subjects, and DNA was extracted from white blood cells using standard procedures.

Diagnostic criteria for ischemic stroke were adopted from the Cardiovascular Health Study.[23] These criteria included (1) rapid onset of neurologic deficit or subarachnoid hemorrhage, (2) deficit persisting for longer than 24 hours unless computed tomography or magnetic resonance imaging show evidence of permanent damage, and (3) no underlying brain trauma, tumor, or infection to cause symptoms.

Ischemic stroke cases satisfied one or more of the following criteria: (a) Focal deficit, without evidence of blood on CT or MRI, (b) Focal deficit, with mottled appearance in the appropriate location on CT, or (c) surgery or autopsy evidence of infarction.

Among ischemic strokes, the subtypes were defined as follows:

Small artery IS required either: (a) CT/MRI demonstrates a deep area of infarction (decreased density) less than 2 cm. across, or (b) A normal CT, but the clinical syndrome is typical of a lacunar infarction, that is: a pure motor stroke, a pure sensory stroke, hemiparesis plus ataxia, or dysarthria plus a clumsy hand. Cardioembolic IS required either (a) a recognized source of emboli such as atrial fibrillation, endocarditis, mitral stenosis, thrombus in heart, recent MI or cardiac surgery, or (b) a mottled appearance consistent with infarction on the CT. Large artery IS was defined by the absence of apparent source of emboli or evidence of lacunar infarction and evidence of large vessel atherosclerosis by carotid ultrasound or angiography.

All participants were of European ancestry.

INTERSTROKE (integrated European, Asian, and Latin americans)

INTERSTROKE is an international, multi-centered, case-control study of stroke investigating the global burden of risk factors across various regions and ethnic groups around the world. A detailed report of the study design has been published.[79] Briefly, cases were stroke patients with acute first stroke (within 5 days of symptoms onset and 72 hours of hospital admission) in whom neuroimaging (CT or MRI) was performed. Stroke was defined with the WHO clinical criteria for stroke. The TOAST classification system was used to define ischemic stroke subtypes. Cases were excluded if 1) they were unable to communicate due to severe stroke without a valid surrogate respondent (e.g. first-degree relative or spouse), 2) they were hospitalized for acute coronary syndrome/myocardial infarction, or 3) stroke was attributed to non-vascular causes (e.g. tumor). Controls were selected from the community and had no history of stroke. The study was approved by the ethics committees in all participating centres. All participants, or their proxy, provided written informed consent before taking part in the study.

MDC

MDC is a prospective, population-based cohort study that included 28 449 randomly selected men (born between 1923 and 1945) and women (born between 1923 and 1950) at baseline examinations between 1991 and 1996.[80]

Controls were drawn from the same cohort matched for gender, age, and time of baseline investigation. All participants provided written informed consent, and the study was approved by the ethical committee at Lund University, Lund, Sweden.

Stroke ascertainment in MDC: Subjects with ischemic stroke after the baseline examination were identified in the Stroke Register of Malmö until December 31, 2005. A specialized nurse from the stroke register systematically searched for and registered patients with stroke who lived in the city of Malmö. The research nurse, with a senior physician, validated the diagnosis by reviewing medical records. Criteria for stroke was rapidly developing clinical signs of local or global loss of cerebral function lasting for >24 hours or leading to death before then, with no apparent cause other than cerebral ischemia or hemorrhage. Stroke was classified as subarachnoid hemorrhage (International Classification of Diseases, Ninth Revision [ICD-9] code 430), intracerebral hemorrhage (ICD 431), cerebral infarction (ICD 434), and undetermined stroke. Subjects with stroke before the baseline examination were excluded.

RACE

The Risk Assessment of Cerebrovascular Events (RACE) Study, Pakistan is a retrospective case-control study designed to identify and evaluate genetic, lifestyle and biomarker determinants of stroke and its subtype in Pakistan. Samples were recruited from six hospital centres in Pakistan. Cases were eligible for inclusion in the study if they: (1) are aged at least 18 years; (2) presented with a sudden onset of neurological deficit affecting a vascular territory with sustained deficit at 24 hours verified by medical attention within 72 hours after onset (onset is defined by when the patient was last seen normal and not when found with deficit); (3) the diagnosis was supported by CT/MRI; and (4) presented with a Modified Rankin Score of < 2 prior to the stroke. TOAST and Oxfordshire classification systems were used to sub-phenotype all stroke cases. Control participants were individuals enrolled in the Pakistan Risk of Myocardial Infarction Study (PROMIS), a case/control study of acute MI based in Pakistan.[81] Controls in PROMIS were recruited following procedures and inclusion criteria as adopted for RACE cases. In order to minimize any potential selection biases, PROMIS controls selected for this stroke study were frequency matched to RACE cases based on age and gender and were recruited in the following order of priority: (1) non-blood related or blood related visitors of patients of the out-patient department; (2) non-blood related visitors of stroke patients; (3) patients of the out-patient department presenting with minor complaints.

SAHLSIS

SAHLSIS is a case-control study of ischemic stroke based in Gothenburg, Sweden. Adult subjects who presented with first-ever or recurrent acute ischemic stroke before 70 years of age were recruited consecutively at stroke units in western Sweden from 1998 to 2012. All participants were of European origin. Patients were not excluded based on stroke severity or whether they were enrolled in a treatment trial. All participants underwent ECG and neuroimaging at the acute stage (all by CT and 58% also by MRI). Additional diagnostic work-up was performed when clinically indicated. Inclusion criteria was ischemic stroke which was defined as an episode of focal neurological deficits with acute onset and lasting > 24 hours or until death, with no apparent non-vascular cause, and no signs of primary hemorrhage on brain imaging. Subjects were excluded if they had a diagnosis of cancer at advanced stage, infectious hepatitis or human immunodeficiency virus. Ischemic stroke was assigned according to modified TOAST criteria.

SIFAP

The SIFAP study is a multicenter study carried out to determine the frequency of Fabry disease in an unselected group of young adult patients with acute cerebrovascular events defined as having had an acute ischemic stroke or transient ischemic attack less than three months before enrollment into the

study. The study is briefly summarized here. First-ever (80.5%) and recurrent ischemic strokes were included. MRI was a mandatory procedure but, in the case of negative or missing MRI, a qualified stroke neurologist could confirm the clinical diagnosis. For this project, ischemic stroke cases recruited from 15 sites throughout Germany and determined not to have Fabry Disease were included in the analysis. All were of European ancestry and had age of first stroke of 18 – 55 years. The diagnosis of Fabry disease was based in males as well as in females in the first level on the sequencing data of the entire exon structure including promoter of the α-galactosidase gene. In cases where a mutation was detected, biochemical analysis was done. Stroke cases from SIFAP were genotyped at CIDR (Baltimore, MD) using the Illumina Human Omni 2.5MQuad array. Only those cases without Fabry disease were selected for genotyping. Controls free of cardiovascular diseases were selected from the KORA Study previously genotyped at CIDR in the same platform. The Cooperative Health Research in the Region of Augsburg (KORA) study is a population-based study of cardiovascular and metabolic traits carried out in the region of Augsburg, Southern Germany. A subset of control subjects (N = 28) was re-genotyped together with cases to provide cross-set duplicates. This joint clustering was used to minimize possible artifactual differences in allelic frequency between cases and controls due to genotyping at different times, and the cross-set duplicates were used to detect such artifacts that may have occurred.

SLESS

The South London Ethnicity and Stroke Study (SLESS) is a prospective study begun in 1999 that has recruited consecutive black patients with stroke from a contiguous catchment area covered by 3 hospitals in South London (Guy's and St Thomas' Hospitals, King's College Hospital, and St George's Hospital).[82] Ethnicity was defined according to the UK Census 2001 definition and classified as Black African or Black Caribbean. Recruitment of black controls was done by random selection from General Practice lists in the catchment areas of St George's, Guys and St Thomas, and King's College Hospital between 1999 and 2012. Potential controls were selected from age and gender strata matched to stroke cases. Furthermore controls were identified within St George's University of London and St George's Hospital staff and contacted via email. Additionally, posters inviting healthy Black African and Black Caribbean individuals were displayed in local leisure centres, General Practice surgeries, churches and communities centres within the same catchment area as the that of the cases. The study was reviewed and approved by the Wandsworth Local Research Ethics Committee, and informed consent was obtained from all participants. One consultant neurologist performed stroke subtyping using data collected on a standard proforma with additional review of all original brain imaging in all patients, as well as review of original notes when necessary. The pathophysiological Trial of Org 10172 in Acute Stroke Treatment (TOAST) subtyping classification was used for subtyping of ischemic stroke.

Stroke ascertainment in SLESS: One consultant neurologist performed stroke subtyping using data collected on a standard proforma with additional review of all original brain imaging in all patients, as well as review of original notes when necessary. The pathophysiological Trial of Org 10172 in Acute Stroke Treatment (TOAST) subtyping classification was used for subtyping of ischemic stroke.

UK - young lacunar stroke DNA resource

A total of 1,029 Caucasian patients with lacunar stroke, aged ≤70 years, were recruited from 72 specialist's stroke centres throughout the UK between 2002 and 2012, as part of the Young Lacunar Stroke DNA Resource. DNA samples were available in 930 patients. An additional 82 Caucasian patients of all ages with lacunar stroke were recruited from St. George's Hospital, London as part of the GENESIS study.[83] Lacunar stroke was defined as a clinical lacunar syndrome, with an anatomically compatible lesion on MRI (subcortical infarct ≤15 mm in diameter). All patients

underwent full stroke investigation including brain MRI, imaging of the carotid arteries and ECG. Echocardiography was performed when appropriate. All MRIs and clinical histories were reviewed centrally by one physician. Exclusion criteria were: stenosis >50% in the extra- or intracranial cerebral vessels, or previous carotid endarterectomy; cardioembolic source of stroke, defined according to the TOAST (Trial of Org 10172 in Acute Stroke Treatment) criteria as high or moderate probability; cortical infarct on MRI; subcortical infarct > 15mm in diameter, as these can be caused by embolic mechanisms (striatocapsular infarcts); any other specific cause of stroke (e.g. lupus anticoagulant, cerebral vasculitis, dissection, monogenic cause of stroke). All cases were screened for *NOTCH3* CADASIL and Fabry disease mutations and positive cases excluded.
Unrelated Caucasian controls, free of clinical cerebrovascular disease, were obtained by random sampling, stratified for age and sex, from general practice lists from the same geographical location as the patients. All patients and controls underwent a standardized clinical assessment and completed a standardized study questionnaire. MRI was not performed in controls.
The study was approved by the Multi-Centre Research Ethics Committee (04/MRE00/36) and informed consent was obtained from all participants.

ICH

Case and control subjects included in the discovery phase were subjects of European ancestry aged >55 years in the Genetics of Cerebral Hemorrhage with Anticoagulation13 (GOCHA) study (multicenter study in the US) and aged >18 years in the Genetic and Environmental Risk Factors for Hemorrhagic Stroke (GERFHS) studies I and II in Cincinnati, OH; Hospital del Mar Intracerebral Hemorrhage study and Vall d'Hebron Hospita lCH study in Barcelona, Spain; Jagiellonian University Hemorrhagic Stroke Study in Krakow, Poland; and the Lund Stroke Register study in Lund, Sweden. Because of their limited sample sizes, data from the four European studies (ESs) were analyzed together for the purposes of quality control, imputation, and association testing.

Cases were ascertained across participating studies according to predefined standardized criteria. Spontaneous ICH was defined as a new and acute neurological deficit with compatible brain imaging (computed tomography or magnetic resonance imaging) showing the presence of intraparenchymal bleeding. According to standard research and clinical practice in the field, ICH location was assigned based on admission images by neurologists who were blinded to genotype data. ICH originating at the cerebral cortex or cortical-subcortical junction (with or without involvement of subcortical white matter) was defined as lobar, and ICH originating at the thalamus, internal capsule, basal ganglia, deep periventricular white matter, cerebellum, or brain stem was defined as nonlobar. Exclusion criteria included trauma, brain tumor, hemorrhagic transformation of ischemic stroke, vascular malformation, and any other cause of secondary ICH.

Control subjects were ICH-free individuals enrolled from the same population that gave rise to the case subjects at each participating study site, aged >55 years (GOCHA) and >18 years (GERFHS and ESs). Control subjects were sampled by random digit dialing in GERFHS and from ambulatory clinics in the remainder of the studies.

All studies were approved by the Institutional Review Board or ethics committee at each participating site. Participants provided informed consent; when subjects were not able to communicate, consent was obtained from their legal proxies.

The Stockholm-Tartu Atherosclerosis Reverse Network Engineering Task (STARNET) study – the worlds largest genetics of gene expression study.

PI: JOHAN LM BJÖRKEGREN and ARNO RUUSALEPP

Coronary artery disease (CAD) patients eligible for coronary artery by-pass grafting CABG and non-CAD patients (controls) eligible for other open-thorax surgery at the Tartu University Hospitals were asked to participate. All patients were informed about the study by the attending doctor and in writing and gave written consent (Ethical Approvals Dnr 154/7 and 188/M-1, 2007). Patients with other severe, active systemic disease (e.g., active systemic inflammatory disease and cancer) were excluded. Pre-operative blood samples were collected for biochemical screens and isolation of primary blood monocytes. The primary end point was the extent of coronary atherosclerosis (CAD score), assessed by pre-operative angiography; controls had no significant CAD requiring angioplasty or CABG. Each participant completed a questionnaire to assess disease history, current drug regimens, and lifestyle factors (e.g., daily activity, alcohol consumption, and smoking habits). In total, up to 114 continuous and noncontinuous variables were assessed in each participant. All participants are of Caucasian ethnicity (10% Swedish, 10% Russian, and 80% Estonian\). Of the 600 cases, 31% are females; 32% have diabetes, 75% hypertension, and 67% hyperlipidaemia, and 33% had a heart attack before the age of 60 years. According to the New York Heart Association (NYHA) criteria, 45% are class I (CAD, but no symptoms and no limitation in ordinary physical activity, stable angina), 42% are class II (mild shortness of breath and/or angina with slight limitation during ordinary activity), 9% are class IIII (marked limitation in activity due to symptoms, even during less-than-ordinary activity, such as walking 20–100 m, and comfortable only at rest) and 1% are class IV (severe limitations, symptoms while at rest, mostly bedbound patients). The 5-year follow-up of mortality and morbidity (CAD and other diseases) after the primary open thorax surgery is ongoing.

A total of 7 RNA samples/patient from this cohort (atherosclerotic and non-atherosclerotic arterial wall (Uppsala/CGN), liver, skeletal muscle, subcutaneous and abdominal visceral fat were sequenced using the HighSeq2000 platform. DNA for all 600 patients was genotyped with OmniExpressExome arrays (Illumina, ~900k SNPs). Now completed, this dataset covering DNA variants of exomes and non-exome variants down to 5% major allele frequency together with RNA sequence at 25 million read-depths for > 3500 RNA samples (from 7 tissues) obtained from the same 600 patients.

For studies appearing multiple times in the description of sample collection, great care was taken to remove sample overlap.

3.2 Study-specific acknowledgements

METASTROKE

ASGC: Australian population control data were derived from the Hunter Community Study. We also thank the University of Newcastle for funding and the men and women of the Hunter region who participated in this study. This research was funded by grants from the Australian National and Medical Health Research Council (NHMRC Project Grant ID: 569257), the Australian National Heart Foundation (NHF Project Grant ID: G 04S 1623), the University of Newcastle, the Gladys M Brawn Fellowship scheme, and the Vincent Fairfax Family Foundation in Australia. Elizabeth G Holliday was supported by a Fellowship from the National Heart Foundation and National Stroke Foundation of Australia (ID: 100071).

BRAINS: Bio-Repository of DNA in Stroke (BRAINS) is partly funded by a Senior Fellowship from the Department of Health (UK) to P Sharma, the Henry Smith Charity and the UK-India Education Research Institutive (UKIERI) from the British Council.

GEOS: Genetics of Early Onset Stroke (GEOS) Study, Baltimore, USA was supported by the NIH Genes, Environment and Health Initiative (GEI) Grant U01 HG004436, as part of the GENEVA consortium under GEI, with additional support provided by the Mid-Atlantic Nutrition and Obesity Research Center (P30 DK072488), and the Office of Research and Development, Medical Research Service, and the Baltimore Geriatrics Research, Education, and Clinical Center of the Department of Veterans Affairs. Genotyping services were provided by the Johns Hopkins University Center for Inherited Disease Research (CIDR), which is fully funded through a federal contract from the NIH to the Johns Hopkins University (contract number HHSN268200782096C). Assistance with data cleaning was provided by the GENEVA Coordinating Center (U01 HG 004446; PI Bruce S Weir). Study recruitment and assembly of datasets were supported by a Cooperative Agreement with the Division of Adult and Community Health, Centers for Disease Control and Prevention and by grants from NINDS and the NIH Office of Research on Women's Health (R01 NS45012, U01 NS069208-01).

HPS: Heart Protection Study (HPS) (ISRCTN48489393) was supported by the UK Medical Research Council (MRC), British Heart Foundation, Merck and Co (manufacturers of simvastatin), and Roche Vitamins Ltd (manufacturers of vitamins). Genotyping was supported by a grant to Oxford University and CNG from Merck and Co. Jemma C Hopewell acknowledges support from the British Heart Foundation (FS/14/55/30806).

ISGS and SWISS: The Ischemic Stroke Genetics Study (ISGS) was supported by the NINDS (R01 NS42733; PI Dr Meschia). The Sibling with Ischemic Stroke Study (SWISS) was supported by the NINDS (R01 NS39987; PI Dr Meschia). Both SWISS and ISGS received additional support, in part, from the Intramural Research Program of the National Institute on Aging (Z01 AG000954-06; PI Andrew Singleton). SWISS and ISGS used samples and clinical data from the NIH-NINDS Human Genetics Resource Center DNA and Cell Line Repository (http://ccr.coriell.org/ninds), human subject protocol Nos. 2003-081 and 2004-147. SWISS and ISGS used stroke-free participants from the Baltimore Longitudinal Study of Aging (BLSA) as controls with the permission of Dr Luigi Ferrucci. The inclusion of BLSA samples was supported, in part, by the Intramural Research Program of the National Institute on Aging (Z01 AG000015-50), human subject protocol No. 2003-078. This study used the high-performance computational capabilities of the Biowulf Linux cluster at the NIH (http://biowulf.nih.gov). For SWISS and ISGS cases of African ancestry, a subset of the Healthy

Aging in Neighborhoods of Diversity across the Life Span study (HANDLS) were used as stroke-free controls. HANDLS is funded by the National Institute of Aging (1Z01AG000513; PI Michele K. Evans).

*MGH-GASROS***:** MGH Genes Affecting Stroke Risk and Outcome Study (MGH-GASROS) was supported by NINDS (U01 NS069208), the American Heart Association/Bugher Foundation Centers for Stroke Prevention Research 0775010N, the NIH and NHLBI's STAMPEED genomics research program (R01 HL087676), and a grant from the National Center for Research Resources. The Broad Institute Center for Genotyping and Analysis is supported by grant U54 RR020278 from the National Center for Research resources.

*MILANO***:** MILANO: Milano - Besta Stroke Register Collection and genotyping of the Milan cases within CEDIR were supported by the Italian Ministry of Health (Grant Numbers: RC 2007/LR6, RC 2008/LR6; RC 2009/LR8; RC 2010/LR8; GR-2011-02347041). FP6 LSHM-CT-2007-037273 for the PROCARDIS control samples.

*WTCCC2-UK***:** Wellcome Trust Case-Control Consortium 2 (WTCCC2) was principally funded by the Wellcome Trust, as part of the Wellcome Trust Case Control Consortium 2 project (085475/B/08/Z and 085475/Z/08/Z and WT084724MA). The Stroke Association provided additional support for collection of some of the St George's, London cases. The Oxford cases were collected as part of the Oxford Vascular Study which is funded by the MRC, Stroke Association, Dunhill Medical Trust, National Institute of Health Research (NIHR) and the NIHR Biomedical Research Centre, Oxford. The Edinburgh Stroke Study was supported by the Wellcome Trust (clinician scientist award to C Sudlow), and the Binks Trust. Sample processing occurred in the Genetics Core Laboratory of the Wellcome Trust Clinical Research Facility, Western General Hospital, Edinburgh. Much of the neuroimaging occurred in the Scottish Funding Council Brain Imaging Research Centre (www.sbirc.ed.ac.uk), Division of Clinical Neurosciences, University of Edinburgh, a core area of the Wellcome Trust Clinical Research Facility and part of the SINAPSE (Scottish Imaging Network—A Platform for Scientific Excellence) collaboration (www.sinapse.ac.uk), funded by the Scottish Funding Council and the Chief Scientist Office. Collection of the Munich cases and data analysis was supported by the Vascular Dementia Research Foundation. M Farrall and A Helgadottir acknowledge support from the BHF Centre of Research Excellence in Oxford and the Wellcome Trust core award (090532/Z/09/Z).

WTCCC2-D: This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreements No 666881, SVDs@target (to M Dichgans) and No 667375, CoSTREAM (to M Dichgans); the DFG as part of the Munich Cluster for Systems Neurology (EXC 1010 SyNergy) and the CRC 1123 (B3)(to M Dichgans); the Corona Foundation (to M Dichgans); the Fondation Leducq (Transatlantic Network of Excellence on the Pathogenesis of Small Vessel Disease of the Brain)(to M Dichgans); the e:Med program (e:AtheroSysMed) (to M Dichgans) and the FP7/2007-2103 European Union project CVgenes@target (grant agreement number Health-F2-2013-601456) (to M Dichgans).

*VISP***:** The GWAS component of the VISP study was supported by the United States National Human Genome Research Institute (NHGRI), Grant U01 HG005160 (PI Michèle Sale & Bradford Worrall), as part of the Genomics and Randomized Trials Network (GARNET). Genotyping services were provided by the Johns Hopkins University Center for Inherited Disease Research (CIDR), which is fully funded through a federal contract from the NIH to the Johns Hopkins University. Assistance with data cleaning was provided by the GARNET Coordinating Center (U01 HG005157; PI Bruce S Weir).

Study recruitment and collection of datasets for the VISP clinical trial were supported by an investigator-initiated research grant (R01 NS34447; PI James Toole) from the United States Public Health Service, NINDS, Bethesda, Maryland. Control data for comparison with European ancestry VISP stroke cases were obtained through the database of genotypes and phenotypes (dbGAP) High Density SNP Association Analysis of Melanoma: Case-Control and Outcomes Investigation (phs000187.v1.p1; R01CA100264, 3P50CA093459, 5P50CA097007, 5R01ES011740, 5R01CA133996, HHSN268200782096C; PIs Christopher Amos, Qingyi Wei, Jeffrey E. Lee). For VISP stroke cases of African ancestry, a subset of the Healthy Aging in Neighborhoods of Diversity across the Life Span study (HANDLS) were used as stroke free controls. HANDLS is funded by the National Institute of Aging (1Z01AG000513; PI Michele K. Evans).

WHI: Funding support for WHI-GARNET was provided through the NHGRI GARNET (Grant Number U01 HG005152). Assistance with phenotype harmonisation and genotype cleaning, as well as with general study coordination, was provided by the GARNET Coordinating Center (U01 HG005157). Funding support for genotyping, which was performed at the Broad Institute of MIT and Harvard, was provided by the NIH Genes, Environment, and Health Initiative (GEI; U01 HG004424).

SiGN

The SiGN study was funded by a cooperative agreement grant from the US National Institute of Neurological Disorders and Stroke, National Institutes of Health (U01 NS069208). The information about funding for each collection is reported below.

Discovery Case-only & Case and Control Cohorts:

BASICMAR: The Base de Datos de Ictus del Hospital del Mar (BASICMAR) Genetic Study was supported by the Ministerio de Sanidad y Consumo de España, Instituto de Salud Carlos III (ISC III) with the grants: Registro BASICMAR Funding for Research in Health (PI051737); GWA Study of Leukoaraiosis (GWALA) project from Fondos de Investigación Sanitaria ISC III (PI10/02064) and (PI12/01238); Agència de Gestió Ajuts Universitaris de Recerca (2014 SGR 1213) and Fondos European Regional Development Funding (FEDER/EDRF) Red INVICTUS-PLUS (RD16/0019/0002). Additional support was provided by the Fundació la Marató TV3 with the grant GODS project. Genestroke Consortium (76/C/2011) Recercaixa'13 (JJ086116). Assistance with data cleaning was provided by the Research in Cardiovascular and Inflammatory Diseases Program of Institute Hospital del Mar of Medical Investigations, Hospital del Mar, and the Barcelona Biomedical Research Park.

EDINBURGH: The Edinburgh Stroke Study was supported by the Wellcome Trust and the Binks Trust. Sample processing occurred in the Genetics Core Laboratory of the Wellcome Trust Clinical Research Facility, Western General Hospital, Edinburgh, UK. Much of the neuroimaging occurred in the Scottish Funding Council Brain Imaging Research Centre (www.sbirc.ed.ac.uk), University of Edinburgh, a core area of the Wellcome Trust Clinical Research Facility and part of the Scottish Imaging Network–A Platform for Scientific Excellence (SINAPSE) collaboration (www.sinapse.ac.uk), funded by the Scottish Funding Council and the Chief Scientist Office. Genotyping was performed at the Wellcome Trust Sanger Institute in the United Kingdom and funded by the Wellcome Trust as part of the Wellcome Trust Case Control Consortium 2 project (085475/B/08/Z and 085475/Z/08/Z and WT084724MA).

GCNKSS: The Greater Cincinnati/Northern Kentucky Stroke Study (GCNKSS) was supported by the NIH (NS030678).

GRAZ: The Austrian Stroke Prevention Study was supported by the Austrian Science Fund (FWF) grant Nos. P20545-P05 and P13180 and I904-B13 (Era-Net). The Medical University of Graz supports the databases of the Graz Stroke Study and the Austrian Stroke Prevention Study.

KRAKOW: Phenotypic data and genetic specimens collection were funded by the grant from the Polish Ministry of Science and Higher Education for Leading National Research Centers (KNOW) and by the grants from the Jagiellonian University Medical College in Krakow, Poland: K/ZDS/002848, K/ZDS/003844.

LEUVEN: The Leuven Stroke genetics study was supported by personal research funds from the Department of Neurology of the University Hospitals Leuven. Dr Lemmens is a Senior Clinical Investigator of FWO Flanders (FWO 1841913N).

LUND: The Lund Stroke Register was supported by the Swedish Research Council (K2010-61X-20378-04-3), The Swedish Heart-Lung Foundation, Region Skåne, Skåne University Hospital, the Freemasons Lodge of Instruction EOS in Lund, King Gustaf V's and Queen Victoria's Foundation, Lund University, and the Swedish Stroke Association. Biobank services were provided by Region Skåne Competence Centre (RSKC Malmö), Skåne University Hospital, Malmö, Sweden, and Biobank, Labmedicin Skåne, University and Regional Laboratories Region Skåne, Sweden.

MALMÖ: The Malmö Diet and Cancer Study was supported by the Swedish Research Council (Vetenskapsrådet), Heart and Lung Foundation (Hjärt och Lungfonden), and Swedish Stroke Foundation (Strokeförbundet).

MCISS: The Middlesex County Ischemic Stroke Study (MCISS) was supported by intramural funding from the New Jersey Neuroscience Institute/JFK Medical Center, Edison, NJ, and The Neurogenetics Foundation, Cranbury, NJ. We acknowledge Dr Souvik Sen for his advice and encouragement in the initiation and design of this study.

MIAMISR and NOMAS: The Northern Manhattan Study (NOMAS) was supported by grants from the NINDS (R37 NS029993, R01 NS27517). The Cerebrovascular Biorepository at University of Miami/Jackson Memorial Hospital (The Miami Stroke Registry, Institutional Review Board No. 20070386) was supported by the Department of Neurology at University of Miami Miller School of Medicine and Evelyn McKnight Brain Institute. Biorepository and DNA extraction services were provided by the Hussmann Institute for Human Genomics at the Miller School of Medicine.

MGH-GASROS: The Massachusetts General Hospital Stroke Genetics Group was supported by the NIH Genes Affecting Stroke Risks and Outcomes Study (GASROS) grant K23 NS042720, the American Heart Association/Bugher Foundation Centers for Stroke Prevention Research 0775010N, and NINDS K23NS042695, K23 NS064052, the Deane Institute for Integrative Research in Atrial Fibrillation and Stroke, and by the Keane Stroke Genetics Fund. Genotyping services were provided by the Broad Institute Center for Genotyping and Analysis, supported by grant U54 RR020278 from the National Center for Research Resources.

NHS: The Nurses' Health Study work on stroke is supported by grants from the NIH, including HL088521 and HL34594 from the National Heart, Lung, and Blood Institute, as well as grants from the National Cancer Institute funding the questionnaire follow-up and blood collection: CA87969 and CA49449.

OXVASC: The Oxford Vascular Study was supported by the Wellcome Trust, Wolfson Foundation, Stroke Association, Medical Research Council, Dunhill Medical Trust, NIH Research (NIHR), and NIHR Oxford Biomedical Research Centre based at Oxford University Hospitals NHS Trust and University of Oxford. Dr Rothwell is in receipt of Senior Investigator Awards from the Wellcome Trust and the NIHR.

REGARDS: The Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study was supported by a cooperative agreement U01 NS041588 from the NINDS, NIH, and Department of Health and Human Service. A full list of participating REGARDS investigators and institutions can be found at http://www.regardsstudy.org.

SPS3: The Secondary Prevention of Small Subcortical Strokes trial was funded by the US National Institute of Health and Neurological Disorders and Stroke grant No. U01NS38529-04A1 (principal investigator, Oscar R. Benavente; coprincipal investigator, Robert G. Hart). The SPS3 Genetic Substudy (SPS3-GENES) was funded by R01 NS073346 (coprincipal investigators, Julie A. Johnson, Oscar R. Benavente, and Alan R. Shuldiner) and U01 GM074492-05S109 (principal investigator, Julie A. Johnson).

ST. GEORGE'S: The principal funding for this study was provided by the Wellcome Trust, as part of the Wellcome Trust Case Control Consortium 2 project (085475/B/08/Z and 085475/Z/08/Z and WT084724MA). Collection of some of the St George's stroke cohort was supported by project grant support from the Stroke Association. Hugh Markus is supported by an NIHR Investigator award. Matthew Traylor was supported by project grant funding from the Stroke Association.(TSA 2013/01)

VISP: The GWAS component of the VISP study was supported by the United States National Human Genome Research Institute (NHGRI), Grant U01 HG005160 (PI Michèle Sale & Bradford Worrall), as part of the Genomics and Randomized Trials Network (GARNET). Genotyping services were provided by the Johns Hopkins University Center for Inherited Disease Research (CIDR), which is fully funded through a federal contract from the NIH to the Johns Hopkins University. Assistance with data cleaning was provided by the GARNET Coordinating Center (U01 HG005157; PI Bruce S Weir). Study recruitment and collection of datasets for the VISP clinical trial were supported by an investigator-initiated research grant (R01 NS34447; PI James Toole) from the United States Public Health Service, NINDS, Bethesda, Maryland. Control data for comparison with European ancestry VISP stroke cases were obtained through the database of genotypes and phenotypes (dbGAP) High Density SNP Association Analysis of Melanoma: Case-Control and Outcomes Investigation (phs000187.v1.p1; R01CA100264, 3P50CA093459, 5P50CA097007, 5R01ES011740, 5R01CA133996, HHSN268200782096C; PIs Christopher Amos, Qingyi Wei, Jeffrey E. Lee). For VISP stroke cases of African ancestry, a subset of the Healthy Aging in Neighborhoods of Diversity across the Life Span study (HANDLS) were used as stroke free controls. HANDLS is funded by the National Institute of Aging (1Z01AG000513; PI Michele K. Evans).

WHI-OS: The Women's Health Initiatives (WHI) program was funded by the National Heart, Lung, and Blood Institute, NIH, US Department of Health and Human Services through contracts N01WH22110, 24152, 32100-2, 32105-6, 32108-9, 32111-13, 32115, 32118 to 32119, 32122, 42107-26, 42129-32, and 44221. The Hormones and Biomarkers Predicting Stroke (HaBPS) was supported by a grant from the National Institutes of Neurological Disorders and Stroke (R01NS042618).

WUSTL: Washington University St. Louis Stroke Study (WUSTL): The collection, extraction of DNA from blood, and storage of specimens were supported by 2 NINDS NIH grants (P50 NS055977 and R01 NS8541901). Basic demographic and clinical characterization of stroke phenotype was prospectively collected in the Cognitive Rehabilitation and Recovery Group (CRRG) registry. The Recovery Genomics after Ischemic Stroke (ReGenesIS) study was supported by a grant from the Barnes-Jewish Hospital Foundation.

Control-only Cohorts:

ADHD: The ADHD-VHIR study from Barcelona was supported by Fundació Marató de TV3 (ref. 092330/31), the Miguel Servet Programme, Instituto de Salud Carlos III (CP09/00119 and CPII15/00023) and the European Regional Development Fund (ERDF).

Health ABC: The Health Aging and Body Composition Study was supported by NIA contracts N01AG62101, N01AG62103, and N01AG62106 and, in part, by the NIA Intramural Research Program. The genome-wide association study was funded by NIA grant 1R01AG032098-01A1 to Wake Forest University Health Sciences and genotyping services were provided by the Center for Inherited Disease Research (CIDR). CIDR is fully funded through a federal contract from the National Institutes of Health to The Johns Hopkins University, contract number HHSN268200782096C. This study utilized the high-performance computational capabilities of the Biowulf Linux cluster at the National Institutes of Health, Bethesda, Md. (http://biowulf.nih.gov). Mike A. Nalls' participation is supported by a consulting contract between Data Tecnica International (Dr. Nalls is the founder and primary consultant) and the National Institute on Aging, NIH, Bethesda, MD, USA, as a possible conflict of interest Dr. Nalls also consults for Illumina Inc, the Michael J. Fox Foundation and University of California Healthcare.

HCHS/SOL: The Hispanic Community Health Study/Study of Latinos was carried out as a collaborative study supported by contracts from the National Heart, Lung, and Blood Institute (NHLBI) to the University of North Carolina (N01-HC65233), University of Miami (N01-HC65234), Albert Einstein College of Medicine (N01-HC65235), Northwestern University (N01-HC65236), San Diego State University (N01-HC65237), and University of Washington (HHSN268201300005C). The following Institutes/Centers/Offices contribute to the HCHS/SOL through a transfer of funds to the NHLBI: National Center on Minority Health and Health Disparities, the National Institute of Deafness and Other Communications Disorders, the National Institute of Dental and Craniofacial Research, the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institute of Neurological Disorders and Stroke, and the Office of Dietary Supplements.

The authors thank the staff and participants of HCHS/SOL for their important contributions. A complete list of staff and investigators has been provided by Sorlie P., et al. in Ann Epidemiol. 2010 Aug;20: 642-649 and is also available on the study website http://www.cscc.unc.edu/hchs/.

HRS: HRS is supported by the National Institute on Aging (NIA U01AG009740). The genotyping was funded as a separate award from the National Institute on Aging (RC2 AG036495). Genotyping was conducted by the NIH Center for Inherited Disease Research (CIDR) at Johns Hopkins University. Genotyping quality control and final preparation of the data were performed by the Genetics Coordinating Center at the University of Washington. HRS genotype data have been deposited in the NIH GWAS repository (dbGaP). Researchers wishing to use the HRS genetic data must first apply to dbGaP for access. The process to request access to any dbGaP study is done via the dbGaP authorized access system. Researchers who wish to obtain HRS phenotype measures that are not in dbGaP must submit a data access use agreement to HRS. For further information, contact hrsquestions@umich.edu. Relevant websites describing HRS genotype and phenotype data are: www.ncbi.nlm.nih.gov/projects/gap/cgi-bin/study.cgi?study_id=phs000428.v1.p1 and http://hrsonline.isr.umich.edu.

INMA: This study was funded by grants from Instituto de Salud Carlos III (CB06/02/0041, G03/176, FIS PI041436, PI081151, PI041705, PI061756, PI091958, and PS09/00432, FIS-FEDER 03/1615, 04/1509, 04/1112, 04/1931 , 05/1079, 05/1052, 06/1213, 07/0314, 09/02647, 11/01007, 11/02591, 11/02038, 13/1944, 13/2032 and CP11/0178), Spanish Ministry of Science and Innovation (SAF2008-00357), European Commission (ENGAGE project and grant agreement HEALTH-F4-2007-201413, HEALTH.2010.2.4.5-1, FP7-ENV-2011 cod 282957), Fundació La Marató de TV3, Generalitat de Catalunya-CIRIT 1999SGR 00241 and Conselleria de Sanitat Generalitat Valenciana. Part of the DNA extractions and genotyping was performed at the Spanish National Genotyping Centre (CEGEN-Barcelona). The authors are grateful to Silvia Fochs, Anna Sànchez, Maribel López, Nuria Pey, Muriel Ferrer, Amparo Quiles, Sandra Pérez, Gemma León, Elena Romero, Maria Andreu, Nati Galiana, Maria Dolores Climent, Amparo Cases and Cristina Capo for their assistance in contacting the families and administering the questionnaires. The authors would particularly like to thank all the participants for their generous collaboration. A full roster of the INMA Project Investigators can be found at http://www.proyectoinma.org/presentacion-inma/listado-investigadores/en_listado-investigadores.html.

KORA: The KORA research platform (KORA, Cooperative Research in the Region of Augsburg) was initiated and financed by the Helmholtz Zentrum München - German Research Center for Environmental Health, which is funded by the German Federal Ministry of Education and Research and by the State of Bavaria. Furthermore, KORA research was supported within the Munich Center of Health Sciences (MC Health), Ludwig-Maximilians-Universität, as part of LMUinnovativ.

OAI: The OAI is a public–private partnership comprised of five contracts (N01-AR-2-2258; N01-AR-2-2259; N01-AR-2-2260; N01-AR-2-2261; N01-AR-2-2262) funded by the National Institutes of Health, a branch of the Department of Health and Human Services, and conducted by the OAI Study Investigators. Genotyping support was provided by grant RC2-AR-058950 from NIAMS/NIH. Private funding partners include Merck Research Laboratories; Novartis Pharmaceuticals Corporation, GlaxoSmithKline; and Pfizer, Inc. Private sector funding for the OAI is managed by the Foundation for the National Institutes of Health.

WTCCC2: Wellcome Trust Case-Control Consortium 2 (WTCCC2) was principally funded by the Wellcome Trust, as part of the Wellcome Trust Case Control Consortium 2 project (085475/B/08/Z and 085475/Z/08/Z and WT084724MA). The Stroke Association provided additional support for collection of some of the St George's, London cases. The Oxford cases were collected as part of the Oxford Vascular Study which is funded by the MRC, Stroke Association, Dunhill Medical Trust, National Institute of Health Research (NIHR) and the NIHR Biomedical Research Centre, Oxford.

The Edinburgh Stroke Study was supported by the Wellcome Trust (clinician scientist award to C Sudlow), and the Binks Trust. Sample processing occurred in the Genetics Core Laboratory of the Wellcome Trust Clinical Research Facility, Western General Hospital, Edinburgh. Much of the neuroimaging occurred in the Scottish Funding Council Brain Imaging Research Centre (www.sbirc.ed.ac.uk), Division of Clinical Neurosciences, University of Edinburgh, a core area of the Wellcome Trust Clinical Research Facility and part of the SINAPSE (Scottish Imaging Network—A Platform for Scientific Excellence) collaboration (www.sinapse.ac.uk), funded by the Scottish Funding Council and the Chief Scientist Office. Collection of the Munich cases and data analysis was supported by the Vascular Dementia Research Foundation. M Farrall and A Helgadottir acknowledge support from the BHF Centre of Research Excellence in Oxford and the Wellcome Trust core award (090532/Z/09/Z).
Barcelona The Neurovascular Research Laboratory takes part in the International Stroke Genetics Consortium (ISGC), the Spanish Stroke Genetics Consortium (www.genestroke.com), and the Cooperative Neurovascular Research RENEVAS (RD06/0026/0010). This study was funded by a grant of the Spanish government (PI10/01212.). The research leading to these results has received funding from the European Union's Seventh Framework Programme (FP7/2007-2013) under grant agreements #201024 and #202213 (European Stroke Network). Belgium Stroke Study (BSS) was supported by Erasme Funds. Edinburgh Stroke Study (ESS) (which contributed discovery cases as part of WTCCC2 and additional replication cases) was supported as described above. Lothian Birth Cohort 1936 was supported in part by Research into Aging, Help the Aged (Sidney De Haan Award and The Disconnected Mind Major Gift Campaign), MRC, and UK Biotechnology and Biological Sciences Research Council (BBSRC). Lothian Birth Cohort 1936 was also supported by a programme grant from Research Into Ageing and continues with programme grants from Help the Aged/Research Into Ageing (Disconnected Mind). The work was undertaken by The University of Edinburgh Centre for Cognitive Ageing and Cognitive Epidemiology, part of the cross council Lifelong Health and Wellbeing Initiative (G0700704/84698). Funding from the BBSRC, Engineering and Physical Sciences Research Council (EPSRC), Economic and Social Research Council (ESRC), and MRC is gratefully acknowledged. Genotyping of the LBC1936 was funded by the BBSRC.

Secondary Cohorts:

INTERSTROKE: We would like to acknowledge the Canadian Institutes of Health Research, Heart and Stroke Foundation of Canada, Canadian Stroke Network, Pfizer Cardiovascular Award, Merck, AstraZeneca, and Boehringer Ingelheim.

MILANO: Milano- Besta Stroke Register Collection and genotyping of the Milan cases within CEDIR were supported by Annual Research Funding of the Italian Ministry of Health (Grant Numbers: RC 2007/LR6, RC 2008/LR6; RC 2009/LR8; RC 2010/LR8). FP6 LSHM-CT-2007-037273 for the PROCARDIS control samples.

PROSPER: The Prospective Study on Pravastatin in the Elderly at Risk (PROSPER) was supported by an investigator initiated grant obtained from Bristol-Myers Squibb. Prof. Dr. J. W. Jukema is an Established Clinical Investigator of the Netherlands Heart Foundation (grant 2001 D 032). Support for genotyping was provided by the seventh framework program of the European commission (grant 223004) and by the Netherlands Genomics Initiative (Netherlands Consortium for Healthy Aging grant 050-060-810).

RACE: We are thankful to the RACE study participants. Fieldwork in RACE was funded by the R-21 grant provided by the NINDS and the Fogarty International Center (1R21NS064908-01) and educational grants available to Dr. Saleheen at the Center for Non-Communicable Diseases, Pakistan. We would also like to acknowledge the contributions made by Professor John Danesh, Dr. Ayeesha Kamal and Professor Panos Deloukas.

SIGNET: The Sea Islands Genetics Network (SIGNET) was supported by R01 DK084350 (MM Sale) from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and consists of data from the REasons for Geographic And Racial Differences in Stroke (REGARDS) cohort, (U01 NS041588; G Howard), Project SuGAR (Sea Islands Genetic African American Registry) (W.M. Keck Foundation; WT Garvey), a South Carolina Center of Biomedical Research Excellence (COBRE) in Oral Health Project P20 RR017696 (PI: Kirkwood; Sub-award: JK Fernandes), and the Systemic Lupus Erythematosus in Gullah Health (SLEIGH) study (PI: GS Gilkeson; K23 AR052364, DL Kamen; UL1 RR029882, KT Brady). Only data from the SIGNET-REGARDS sub-study were included in the current analyses. REGARDS is supported by a cooperative agreement U01 NS041588 from the National Institute of Neurological Disorders and Stroke (NINDS), National Institutes of Health (NIH), Department of Health and Human Service. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIDDK, NINDS or the NIH. Representatives of the funding agencies have been involved in the review of the manuscript but not directly involved in the collection, management, analysis or interpretation of the data. The authors thank the other investigators, the staff, and the participants of the REGARDS study for their valuable contributions. A full list of participating REGARDS investigators and institutions can be found at http://www.regardsstudy.org

Utrecht ImmunoChip/PROMISe: S.Achterberg was supported by in part by a grant from the Netherlands Heart Foundation, (grant no 2005B031) and a grant from the Dutch Brain Foundation (project 2008(1).10).

VHIR-FMT-Barcelona: The Barcelona GWAs Study was supported by the Genetic contribution to functional Outcome and Disability after Stroke (GODS) project, Fundació la Marató de TV3, GENERACION Project (Instituto de Salud Carlos III: PI15/01978), Pre-Test Stroke Project (Instituto de Salud Carlos III: PMP15/00022) and by the Miguel Servet grant (Pharmastroke project: CP12/03298). Neurovascular research Laboratory and the Stroke Pharmacogenomics and Genetics lab take part in the INVICTUS+ network. I. F-C. is supported by the Miguel Servet programme (CP12/03298), Instituto de Salud Carlos III.

WGHS: The WGHS is supported by the National Heart, Lung, and Blood Institute (HL043851, HL080467, and HL099355) and the National Cancer Institute (CA047988 and UM1CA182913), with collaborative scientific support and funding for genotyping provided by Amgen.

WHI-HT: WHI Funding support for WHI-GARNET was provided through the NHGRI GARNET (Grant Number U01 HG005152). Assistance with phenotype harmonisation and genotype cleaning, as well as with general study coordination, was provided by the GARNET Coordinating Center (U01 HG005157). Funding support for genotyping, which was performed at the Broad Institute of MIT and Harvard, was provided by the NIH Genes, Environment, and Health Initiative (GEI; U01 HG004424).

CHARGE

*AGES***:** Age, Gene/Environment Susceptibility (AGES) -Reykjavik The study was funded by the National Institute on Aging (NIA)(N01-AG-12100), Hjartavernd (the Icelandic Heart Association), and the Althingi (the Icelandic Parliament), with contributions from the Intramural Research Programs at the NIA, the National Heart, Lung, and Blood Institute, and the National Institute of Neurological Disorders and Stroke (Z01 HL004607-08 CE).
*ARIC***:** The Atherosclerosis Risk in Communities study was performed as a collaborative study supported by National Heart, Lung, and Blood Institute (NHLBI) contracts (HHSN268201100005C, HSN268201100006C, HSN268201100007C, HHSN268201100008C, HHSN268201100009C, HHSN268201100010C, HHSN268201100011C, and HHSN268201100012C), R01HL70825, R01HL087641, R01HL59367, and R01HL086694; National Human Genome Research Institute contract U01HG004402; and National Institutes of Health (NIH) contract HHSN268200625226C. Infrastructure was partly supported by grant No. UL1RR025005, a component of the NIH and NIH Roadmap for Medical Research. This project was also supported by NIH R01 grant NS087541 to MF.
*CHS***:** This CHS research was supported by NHLBI contracts HHSN268201200036C, HHSN268200800007C, N01HC55222, N01HC85079, N01HC85080, N01HC85081, N01HC85082, N01HC85083, N01HC85086, and HHSN268200960009C; and NHLBI grants U01HL080295, R01HL087652, R01HL105756, R01HL103612, R01HL120393, and R01HL130114 with additional contribution from the National Institute of Neurological Disorders and Stroke (NINDS). Additional support was provided through R01AG023629 from the National Institute on Aging (NIA). A full list of principal CHS investigators and institutions can be found at CHS-NHLBI.org. The provision of genotyping data was supported in part by the National Center for Advancing Translational Sciences, CTSI grant UL1TR000124, and the National Institute of Diabetes and Digestive and Kidney Disease Diabetes Research Center (DRC) grant DK063491 to the Southern California Diabetes Endocrinology Research Center. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.
FHS: This work was supported by the National Heart, Lung and Blood Institute's Framingham Heart Study (Contract No. N01-HC-25195 and No. HHSN268201500001I) and its contract with Affymetrix, Inc. for genotyping services (Contract No. N02-HL-6-4278). A portion of this research utilized the Linux Cluster for Genetic Analysis (LinGA-II) funded by the Robert Dawson Evans Endowment of the Department of Medicine at Boston University School of Medicine and Boston Medical Center. This study was also supported by grants from the National Institute of Neurological Disorders and Stroke (R01 NS017950), the National Heart, Lung and Blood Institute (R01 HL093029) and the National Institute of Aging (R01s AG033193, AG008122, AG016495, U01 AG049505).
FINRISK: V.S. was supported by the Academy of Finland (grant #139635) and the Finnish Foundation for Cardiovascular Research
HEALTH ABC: The Health ABC Study was supported by NIA contracts N01AG62101, N01AG62103, and N01AG62106 and, in part, by the NIA Intramural Research Program. The genome-wide association study was funded by NIA grant 1R01AG032098-01A1 to Wake Forest University Health Sciences and genotyping services were provided by the Center for Inherited Disease Research (CIDR). CIDR is fully funded through a federal contract from the National Institutes of Health to The Johns Hopkins University, contract number HHSN268200782096C. This study utilized the high-performance computational capabilities of the Biowulf Linux cluster at the National Institutes of Health, Bethesda, Md. (http://biowulf.nih.gov).
Rotterdam Study: The generation and management of GWAS genotype data for the Rotterdam Study is supported by the Netherlands Organisation of Scientific Research NWO Investments (nr. 175.010.2005.011, 911-03-012). This study is funded by the Research Institute for Diseases in the Elderly (014-93-015; RIDE2), the Netherlands Genomics Initiative (NGI)/Netherlands Organisation for Scientific Research (NWO) project nr. 050-060-810. The Rotterdam Study is funded by Erasmus Medical Center and Erasmus University, Rotterdam, Netherlands Organization for the Health

Research and Development (ZonMw), the Research Institute for Diseases in the Elderly (RIDE), the Ministry of Education, Culture and Science, the Ministry for Health, Welfare and Sports, the European Commission (DG XII), and the Municipality of Rotterdam. MAI is supported by an NWO Veni grant (916.13.054).
SHIP: SHIP is part of the Community Medicine Research net of the University of Greifswald, Germany, which is funded by the Federal State of Mecklenburg-West Pomerania. The data collections underlying this work have been funded by the Federal Ministry of Education and Research (grants no. 01ZZ9603, 01ZZ0103, and 01ZZ0403), the Ministry of Cultural Affairs as well as the Social Ministry of the Federal State of Mecklenburg-West Pomerania, and the German Research Foundation (SCHM 2744/1-1). Genome-wide data have been supported by the Federal Ministry of Education and Research (grant no. 03ZIK012) and a joint grant from Siemens Healthcare, Erlangen, Germany and the Federal State of Mecklenburg- West Pomerania.
WGHS: The WGHS is supported by HL043851, HL080467, and HL099355. from the National Heart, Lung, and Blood Institute and CA047988 from the National Cancer Institute with collaborative scientific support and funding for genotyping provided by Amgen.
MESA: MESA and the MESA SHARe project are conducted and supported by the National Heart, Lung, and Blood Institute (NHLBI) in collaboration with MESA investigators. Support for MESA is provided by contracts HHSN268201500003I, N01-HC-95159, N01-HC-95160, N01-HC-95161, N01-HC-95162, N01-HC-95163, N01-HC-95164, N01-HC-95165, N01-HC-95166, N01-HC-95167, N01-HC-95168, N01-HC-95169, UL1-TR-000040, UL1-TR-001079, UL1-TR-001420, UL1-TR-001881, and DK063491. Funding for SHARe genotyping was provided by NHLBI Contract N02-HL-64278. Genotyping was performed at Affymetrix (Santa Clara, California, USA) and the Broad Institute of Harvard and MIT (Boston, Massachusetts, USA) using the Affymetrix Genome-Wide Human SNP Array 6.0.
PROSPER: The PROSPER study was supported by an investigator initiated grant obtained from Bristol-Myers Squibb. Prof. Dr. J. W. Jukema is an Established Clinical Investigator of the Netherlands Heart Foundation (grant 2001 D 032). Support for genotyping was provided by the seventh framework program of the European commission (grant 223004) and by the Netherlands Genomics Initiative (Netherlands Consortium for Healthy Aging grant 050-060-810).
TWINGENE: This work was supported by grants from the Ministry for Higher Education, the Swedish Research Council (M-2005-1112 and 2009-2298), GenomEUtwin (EU/QLRT-2001-01254; QLG2-CT-2002-01254), NIH grant DK U01-066134, The Swedish Foundation for Strategic Research (SSF; ICA08-0047).
ULSAM: This work was supported by grants from Uppsala University, Swedish Research Council (2012-1397), Swedish Heart-Lung Foundation (20140422), Knut och Alice Wallenberg Foundation, European Research Council, Swedish Diabetes Foundation (2013-024). Andrew P Morris is a Wellcome Trust Senior Fellow in Basic Biomedical Science (grant numbers WT064890, WT090532 and WT098017)
3C: The 3-City Study is conducted under a partnership agreement among the Institut National de la Santé et de la Recherche Médicale (INSERM), the University of Bordeaux, and Sanofi-Aventis. The Fondation pour la Recherche Médicale funded the preparation and initiation of the study. The 3C Study is also supported by the Caisse Nationale Maladie des Travailleurs Salariés, Direction Générale de la Santé, Mutuelle Générale de l'Education Nationale (MGEN), Institut de la Longévité, Conseils Régionaux of Aquitaine and Bourgogne, Fondation de France, and Ministry of Research–INSERM Programme "Cohortes et collections de données biologiques." This work was supported by the National Foundation for Alzheimer's Disease and Related Disorders, the Institut Pasteur de Lille, the Centre National de Génotypage and the LABEX (Laboratory of Excellence program investment for the future) DISTALZ - Development of Innovative Strategies for a Transdisciplinary approach to ALZheimer's disease. Stéphanie Debette is supported by a grant from the Fondation Leducq, a starting

grant from the European Research Council, a grant from the Joint Programme of Neurodegenerative Disease research, and the Initiative of Excellence of Bordeaux University.

EPIC: EPIC was funded by the UK Medical Research Council (G0800270), British Heart Foundation (SP/09/002), UK National Institute for Health Research Cambridge Biomedical Research Centre, European Research Council (268834), European Commission Framework Programme 7 (HEALTH-F2-2012-279233).

AIDHS/SDS: This work was supported by NIH grants -R01DK082766 funded by the National Institute of Health (NIDDK) and NOT-HG-11-009 funded by NHGRI, VPR Bridge Grant and Harold Hamm Enrichment Grants from University of Oklahoma Health Sciences Center. Authors thank all the participants of AIDHS/SDS and are grateful for their contribution in this study.

VHIR-FMT-Barcelona: The Barcelona GWAs Study was supported by the Genetic contribution to functional Outcome and Disability after Stroke (GODS) project, Fundació la Marató de TV3 and by the Miguel Servet grant (Pharmastroke project: CP12/03298). Neurovascular research Laboratory takes part in the INVICTUS network. I. F-C. is supported by the Miguel Servet programme (CP12/03298), Instituto de Salud Carlos III.

Biobank Japan:
We would like to express our greatfulness to all the members of J-MICC, JPHC, and TMM. We extend our appreciation to staffs of BBJ for their outstanding assistance. This study was funded by the BioBank Japan project, which is supported by the Ministry of Education, Culture, Sports, Sciences and Technology (MEXT) of Japanese government and the Japan Agency for Medical Research and Development (AMED).

CADISP: The Cervical Artery Dissections and Ischemic Stroke Patients (CADISP) study has been supported by Inserm, Lille 2 University, Institut Pasteur de Lille and Lille University Hospital and received funding from the ERDF (FEDER funds) and Région Nord-Pas de Calais in the frame of Contrat de Projets Etat-Region 2007-2013 Région Nord-Pas-de-Calais - Grant N°09120030, Centre National de Genotypage, Emil Aaltonen Foundation, Paavo Ilmari Ahvenainen Foundation, Helsinki University Central Hospital Research Fund, Helsinki University Medical Foundation, Päivikki and Sakari Sohlberg Foundation, Aarne Koskelo Foundation, Maire Taponen Foundation, Aarne and Aili Turunen Foundation, Lilly Foundation, Alfred Kordelin Foundation, Finnish Medical Foundation, Orion Farmos Research Foundation, Maud Kuistila Foundation, the Finnish Brain Foundation, Biomedicum Helsinki Foundation, Projet Hospitalier de Recherche Clinique Régional, Fondation de France, Génopôle de Lille, Adrinord, Basel Stroke-Funds, Käthe-Zingg-Schwichtenberg-Fonds of the Swiss Academy of Medical Sciences, Swiss Heart Foundation.

COMPASS:

CHS: The CHS study was supported by National Heart, Lung, and Blood Institute contracts HHSN268201200036C, HHSN268200800007C, N01HC55222, N01HC85079, N01HC85080, N01HC85081, N01HC85082, N01HC85083, N01HC85086; and NHLBI grants U01HL080295, R01HL087652, R01HL105756, R01HL103612, R01HL120393, R01HL130114, and R01HL085251 with contributions from the National Institute of Neurological Disorders and Stroke. Additional support was provided through R01AG023629 from the National Institute on Aging. A full list of principal CHS investigators and institutions can be found at CHS-NHLBI.org. The provision of

genotyping data were supported, in part, by the National Center for Advancing Translational Sciences, grant UL1TR000124, and the National Institute of Diabetes and Digestive and Kidney Disease Research Center grant DK063491 to the Southern California Diabetes Endocrinology Research Center. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

HANDLS: Healthy Aging in Neighborhoods of Diversity across the Life Span was supported by the Intramural Research Program of the NIH, National Institute of Aging and the National Center on Minority Health and Health Disparities (project no. Z01-AG000513 and human subjects protocol no. 2009-149).

INTERSTROKE: The INTERSTROKE study was supported by the Canadian Institutes of Health Research, Heart and Stroke Foundation of Canada, Canadian Stroke Network, Health Research Board Ireland, Swedish Research Council, Swedish Heart and Lung Foundation, The Health & Medical Care Committee of the Regional Executive Board, Region Västra Götaland (Sweden), AstraZeneca, Boehringer Ingelheim (Canada), Pfizer (Canada), MSD, Chest, Heart and Stroke Scotland, and The Stroke Association, with support from The UK Stroke Research Network. Microarray genotyping for a subset of INTERSTROKE participants was funded by the Heart and Stroke Foundation of Canada Grant NA-6872 (PI: Drs Pare, Anand, O'Donnell, Xie, Yusuf).

ISGS and SWISS: Ischemic Stroke Genetics Study (ISGS) and Siblings with Ischemic Stroke Study (SWISS) were supported by the National Institute of Neurological Disorders and Stroke grants (R01 NS42733; PI Meschia) and (R01NS39987; PI Meschia), respectively with additional support, in part, from the Intramural Research Program of the National Institute of Aging (Z01 AG000954-06; PI Singleton). Both studies used samples and clinical data from the NIH-NINDS Human Genetics Resource Center DNA and Cell Line Repository, human subjects protocol no. 2003-081 and 2004-147.

SIGNET-REGARDS: We would like to thank all of the participants of the REGARDS Study for their valuable contributions, as well as REGARDS investigators and staff. The Sea Islands Genetics Network (SIGNET) was supported by R01 DK084350 (MM Sale), and SIGNET-REGARDS consists of data from the REasons for Geographic And Racial Differences in Stroke (REGARDS) cohort, supported by a cooperative agreement U01 NS041588 (G Howard).

VISP: Vitamin Intervention for Stroke Prevention (VISP) was funded by the National Institute of Neurological Disorders and Stroke (R01-NS34447). Genome-wide association study data for a subset of VISP participants supported by the National Human Genome Research Institute (U01-HG005160), as part of the Genomics and Randomized Trials Network (PI: Drs Sale and Worrall).

JHS: The Jackson Heart Study is supported by contracts HHSN268201300046C, HHSN268201300047C, HHSN268201300048C, HHSN268201300049C, HSN268201300050C from the National Heart, Lung, and Blood Institute and the National Institute on Minority Health and Health Disparities. The authors also wish to thank the staffs and participants of the JHS. A full list of the participating institution and investigators can be found at https://www.jacksonheartstudy.org/jhsinfo/Home/tabid/36/Default.aspx.

WHI: The WHI program is funded by the National Heart, Lung, and Blood Institute, National Institutes of Health, U.S. Department of Health and Human Services through contracts HHSN268201600018C, HHSN268201600001C, HHSN268201600002C, HHSN268201600003C, and HHSN268201600004C.
The authors thank the WHI investigators and staff for their dedication and the study participants for making the program possible. A full listing of WHI investigators can be found at: http://www.whi.org/researchers/Documents%20%20Write%20a%20Paper/WHI%20Investigator%20Long%20List.pdf.

Glasgow Stroke Sample: The work was supported by NHS Greater Glasgow Endowment funds.

Helsinki 2000 Ischemic Stroke Genetics Study: The study was supported by the Finnish Medical Foundation and the Helsinki University Central Hospital governmental subsidiary funds for clinical research. The investigators would like to thank Marja Metso, RN for her support of the study.

Hisayama-FSR study:
We thank Prof. Takanari Kitazono and Prof. Masahiro Kamouchi (Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan) for collecting clinical samples.

HVH 1 & 2:
The Heart and Vascular Health Study was supported by NHLBI grants R01HL085251, R01HL073410, and R01HL068986.

INTERSTROKE: We would like to acknowledge the Canadian Institutes of Health Research, Heart and Stroke Foundation of Canada, Canadian Stroke Network, Pfizer Cardiovascular Award, Merck, AstraZeneca, and Boehringer Ingelheim.

MDC: The Malmö Diet and Cancer Study was supported by the Swedish Research Council (Vetenskapsrådet), Heart and Lung Foundation (Hjärt och Lungfonden), and Swedish Stroke Foundation (Strokeförbundet).

RACE: Fieldwork in RACE was funded by the R-21 grant provided by the NINDS and the Fogarty International Center (1R21NS064908-01) and educational grants available to Dr. Saleheen at the Center for Non-Communicable Diseases, Pakistan. We would also like to acknowledge the contributions made by Professor John Danesh, Dr. Ayeesha Kamal and Professor Panos Deloukas.

SAHLSIS: The Sahlgrenska Academy Study of Ischemic Stroke was supported by the Swedish Research Council (K2014-64X-14605-12-5), the Swedish Heart and Lung Foundation, the Swedish state/Sahlgrenska University Hospital (ALFGBG-429981), the Swedish Stroke Association, the Swedish Society of Medicine, and the Rune and Ulla Amlöv Foundation.

SIFAP: The sifap study (Stroke In Young Fabry Patients, http://www.sifap.eu; ClinicalTrials.gov: NCT00414583) has been supported partially by an unrestricted scientific grant from Shire Human Genetic Therapies. Funding for genotyping and analysis of samples were supported by the National Institutes of Health Genes, Environment and Health Initiative (GEI) Grant U01 HG004436, as part of the GENEVA consortium.

SLESS: This work was supported by a Stroke Association (UK) Programme Grant (PROG 3), the National Institute for Health Research Biomedical Research Centre (NIHR BRC) at South London and

Maudsley NHS Foundation Trust and the National Institute for Health Research (NIHR) Biomedical Research Centre based at Guy's and St Thomas' NHS Foundation Trust and King's College London. Dr Rutten-Jacobs is supported by a British Heart Foundation Fellowship (FS/15/61/31626). Dr Markus is supported by the National Institute for Health Research Cambridge University Hospitals Comprehensive Biomedical Research Centre and a National Institute for Health Research Senior Investigator award.

UK - young lacunar stroke DNA resource: Collection of the UK Young Lacunar Stroke DNA Study (DNA Lacunar) was primarily supported by the Wellcome Trust (WT072952) with additional support from the Stroke Association (TSA 2010/01). Genotyping of the samples, and Dr Traylor, were supported by a Stroke Association Grant (TSA 2013/01). Dr Markus is supported by the National Institute for Health Research Cambridge University Hospitals Comprehensive Biomedical Research Centre and a National Institute for Health Research Senior Investigator award. Matthew Traylor is funded by a BHF programme grant RG/16/4/32218. Loes Rutten-Jacobs is supported by a BHF Early career fellowship BHF /15/61/31626.

ICH

Funding provided as follows: GERFHS, NIH grants NS36695 and NS30678; GOCHA, NIH grant R01NS059727, the Keane Stroke Genetics Research Fund, the Edward and Maybeth Sonn Research Fund, and the University of Michigan General Clinical Research Center M01 RR000042; ERICH, NIH grant NS069763; HM-ICH, Instituto de Salud Carlos III with the grants "Registro BASICMAR" Funding for Research in Health (PI051737), "GWALA project" from Fondos de Investigación Sanitaria ISC III (PI10/02064), and Fondos FEDER/EDRF Red de Investigación Cardiovascular (RD12/0042); JUHSS, Polish Ministry of Education grant N402 083934; LSR, Lund University, Region Skåne, the Swedish Research Council (K2010-61X-20378-04-3), the Swedish Stroke Association, the Freemasons Lodge of Instruction EOS in Lund, and the King Gustaf V and Queen Victoria's foundations; G.J.F. and H.B.B., NIH SPOTRIAS fellowship P50NS061343; C.D.A., fellowship from the American Brain Foundation; J.N.G., NIH grant 5K23NS059774; P.M.R., awards from the NIHR and the Wellcome Trust; M.S., NIH grant U01 NS074425; and D.L.B., NIH grants R01 NS062675, R01 HL098065, R01 NS070941, and R18 HS017690, the Blue Cross Blue Shield of Michigan Foundation, Michigan Department of Community Health, and the University of Michigan.

DAT and VC were financially supported by the Transatlantic Networks of Excellence Award (12CVD02) from Foundation Leducq

Statistical analyses were performed using the C2BIG computing cluster, funded by the Région Ile de France, Pierre and Marie Curie University, and the Institute for Cardiometabolism and Nutrition (ANR-10-IAHU-05).

AFGen

This work was supported by grants from the National Institutes of Health to Dr. Ellinor (1RO1HL092577, R01HL128914, K24HL105780). Dr. Ellinor is also supported by an Established Investigator Award from the American Heart Association (13EIA14220013) and by the Fondation Leducq (14CVD01). Dr. Lubitz is supported by NIH grants K23HL114724 and a Doris Duke Charitable Foundation Clinical Scientist Development Award 2014105. Dr. Christophersen is supported by a mobility grant from the Research Council of Norway [240149/F20].

3.3 BIOBANK JAPAN TRAIT ANALYSIS

The BioBank Japan Project (http://biobankjp.org)1 started at the Institute of Medical Science, the University of Tokyo in 2003 and has so far collected up to 300,000 cases consisting of 47 diseases. Subjects were recruited from 12 medical institutes in Japan including Osaka Medical Center for Cancer and Cardiovascular Diseases, the Cancer Institute Hospital of Japanese Foundation for Cancer Research, Juntendo University, Tokyo Metropolitan Geriatric Hospital, Nippon Medical School, Nihon University School of Medicine, Iwate Medical University, Tokushukai Hospitals, Shiga University of Medical Science, Fukujuji Hospital, National Hospital Organization Osaka National Hospital, and Iizuka Hospital.

We selected type 2 diabetes (T2) cases from individuals registered in BioBank Japan as having a diagnosis of T2D in their medical records (n = 36,832). As Genotype data from population-based control individuals (n = 28,870 individuals) were accessed through the Tohoku Medical Megabank organization, Japan Public Health Center-based Prospective study, and the Japan Multi-institutional Collaborative Cohort Study.

For lipid traits, we selected subjects enrolled in the BioBank Japan Project with data available for HDL (n = 70,657), LDL (n = 72,866) and TG (n = 105,597). Clinical information and medical measurements of subjects were retrieved from either self-report questionnaires (for age, height, weight, and smoking and drinking habits) or medical records (for other data including HDL, LDL, and TG). Subjects aged < 18 or > 85, or whose measured values were outside three times of interquartile range (IQR) of upper/lower quartile were excluded. For subjects taking a statin, we applied the following correction for LDL values: i) Measured LDL was adjusted as LDL / 0.7; ii) Derived LDL from the Friedewald equation was re-derived as (TC / 0.8) − HDL − (TG / 5). For TG values, we applied a common log transformation to achieve normality. The resulting values of each trait were adjusted for age, sex, top 10 principal components, 47 disease affection status in a linear regression model, and the residuals were normalized by Z-score.

We genotyped all of the samples described above by Illumina HumanOmniExpressExome or in combination of HumanOmniExpress and HumanExome BeadChips, and imputed their genotype dosages using mach and minimac softwares with 1000 Genomes Project Phase 1 (version 3) as reference haplotypes. For type 2 diabetes, we performed logistic regression analysis with age, sex and 20 principal components as covariates using mach2dat. For lipid traits, we conducted linear regression analyses using mach2qtl. All of the analyses assumed additive genetic effects of the SNP dosages. Summary statistics of high-quality common SNPs existed in the HapMap 3 East Asian reference panel were used for LD score regression analysis following the standard procedure. We used the East Asian LD Score retrieved from the authors' website (https://data.broadinstitute.org/alkesgroup/LDSCORE/).

3.4 Expression quantitative trait loci (eQTL) analysis other than GTEx-V6, HGVD, BIOS, Blueprint, STARNET, and HAEC

We queried the stroke index SNPs in over 100 separate eQTL datasets in a wide range of tissues. We considered SNPs to have evidence for influencing expression if they were the lead SNP, or in high LD (r^2>0.8)[1,2] with the lead eQTL SNPs reported for a particular gene and showed an association of at least P<$5x10^{-6}$ with expression of a transcript in the original study. A general overview of a subset of >50 eQTL studies has been published (PMID 24973796), with specific citations for >100 datasets included in the current query following here.

Blood cell related eQTL studies included fresh lymphocytes (PMID 17873875), fresh leukocytes (PMID 19966804), leukocyte samples in individuals with Celiac disease (PMID 19128478), whole blood samples (PMIDs 18344981, 21829388, 22692066, 23818875, 23359819, 23880221, 24013639, 23157493, 23715323, 24092820, 24314549, 24956270, 24592274, 24728292, 24740359, 25609184, 22563384, 25474530, 25816334, 25578447), lymphoblastoid cell lines (LCL) derived from asthmatic children (PMIDs 17873877, 23345460), HapMap LCL from 3 populations (PMID 17873874), a separate study on HapMap CEU LCL (PMID 18193047), additional LCL population samples (PMIDs 19644074, 22286170, 22941192, 23755361, 23995691, 25010687, 25951796), neutrophils (PMIDs 26151758, 26259071), CD19+ B cells (PMID 22446964), primary PHA-stimulated T cells (PMIDs 19644074, 23755361), CD4+ T cells (20833654), peripheral blood monocytes (PMIDs 19222302,20502693,22446964, 23300628, 25951796, 26019233), long non-coding RNAs in monocytes (PMID 25025429) and CD14+ monocytes before and after stimulation with LPS or interferon-gamma (PMID 24604202), CD11+ dendritic cells before and after *Mycobacterium tuberculosis* infection (PMID 22233810) and a separate study of dendritic cells before or after stimulation with LPS, influenza or interferon-beta (PMID 24604203). Micro-RNA QTLs (PMIDs 21691150, 26020509), DNase-I QTLs (PMID 22307276), histone acetylation QTLs (PMID 25799442), and ribosomal occupancy QTLs (PMID 25657249) were also queried for LCL. Splicing QTLs (PMID 25685889) and micro-RNA QTLs (PMID 25791433) were queried in whole blood.

Non-blood cell tissue eQTLs searched included omental and subcutaneous adipose (PMIDs 18344981, 21602305, 22941192, 23715323, 25578447), visceral fat (PMID 25578447) stomach (PMID 21602305), endometrial carcinomas (PMID 21226949), ER+ and ER- breast cancer tumor cells (PMID 23374354), liver (PMIDs 18462017,21602305,21637794, 22006096, 24665059, 25578447), osteoblasts (PMID 19654370), intestine (PMID 23474282) and normal and cancerous colon (PMIDs 25079323, 25766683), skeletal muscle (PMIDs 24306210, 25578447), breast tissue (normal and cancer)(PMIDs 24388359, 22522925), lung (PMIDs 23209423, 23715323, 24307700, 23936167, 26102239), skin (PMIDs 21129726, 22941192, 23715323, 25951796), primary fibroblasts (PMIDs 19644074, 23755361, 24555846), sputum (PMID 21949713), pancreatic islet cells (PMID 25201977), prostate (PMID 25983244), rectal mucosa (PMID 25569741), arterial wall (PMID 25578447) and heart tissue from left ventricles (PMIDs 23715323, 24846176) and left and right atria (PMID 24177373). Micro-RNA QTLs were also queried for gluteal and abdominal adipose (PMID 22102887) and liver (PMID 23758991). Methylation QTLs were queried in pancreatic islet cells (PMID 25375650). Further mRNA and micro-RNA QTLs were queried from ER+ invasive breast cancer samples, colon-, kidney renal clear-, lung- and prostate-adenocarcinoma samples (PMID 24907074).

Brain eQTL studies included brain cortex (PMIDs 19222302, 19361613, 22685416, 25609184, 25290266), cerebellar cortex (PMID 25174004), cerebellum (PMIDs 20485568, 22685416, 22212596, 22832957, 23622250), frontal cortex (PMIDs 20485568, 22832957, 25174004), gliomas (PMID 24607568), hippocampus (PMIDs 22832957, 25174004), inferior olivary nucleus (from medulla) (PMID 25174004), intralobular white matter (PMID 25174004), occiptal cortex (PMID 25174004), parietal lobe (PMID 22212596), pons (PMID 20485568), pre-frontal cortex (PMIDs 22031444, 20351726, 22832957, 23622250), putamen (at the level of anterior commussure) (PMID 25174004), substantia nigra (PMID 25174004), temporal cortex (PMIDs 20485568, 22685416, 22832957, 25174004), thalamus (PMID 22832957) and visual cortex (PMID 23622250).

Additional eQTL data was integrated from online sources including ScanDB and the Pritchard Lab (eqtl.uchicago.edu). Cerebellum, parietal lobe and liver eQTL data was downloaded from ScanDB and cis-eQTLs were limited to those with $P<1.0E-6$ and trans-eQTLs with $P<5.0E-8$.

3.5 REFERENCES

1. Krug T, Manso H, Gouveia L, Sobral J, Xavier JM, Albergaria I, et al. Kalirin: A novel genetic risk factor for ischemic stroke. *Hum Genet*. 2010;127:513-523
2. Yadav S, Schanz R, Maheshwari A, Khan MS, Slark J, de Silva R, et al. Bio-repository of DNA in stroke (brains): A study protocol. *BMC Med Genet*. 2011;12:34
3. Heart Protection Study Collaborative G. Mrc/bhf heart protection study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: A randomised placebo-controlled trial. *Lancet*. 2002;360:7-22
4. Meschia JF, Brott TG, Brown RD, Jr., Crook RJ, Frankel M, Hardy J, et al. The ischemic stroke genetics study (isgs) protocol. *BMC Neurol*. 2003;3:4
5. International Stroke Genetics C, Wellcome Trust Case Control C, Bellenguez C, Bevan S, Gschwendtner A, Spencer CC, et al. Genome-wide association study identifies a variant in hdac9 associated with large vessel ischemic stroke. *Nat Genet*. 2012;44:328-333
6. Power C, Elliott J. Cohort profile: 1958 british birth cohort (national child development study). *Int J Epidemiol*. 2006;35:34-41
7. Wichmann HE, Gieger C, Illig T, Group MKS. Kora-gen--resource for population genetics, controls and a broad spectrum of disease phenotypes. *Gesundheitswesen*. 2005;67 Suppl 1:S26-30
8. Wassertheil-Smoller S, Hendrix SL, Limacher M, Heiss G, Kooperberg C, Baird A, et al. Effect of estrogen plus progestin on stroke in postmenopausal women: The women's health initiative: A randomized trial. *JAMA*. 2003;289:2673-2684
9. Anderson GL, Limacher M, Assaf AR, Bassford T, Beresford SA, Black H, et al. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: The women's health initiative randomized controlled trial. *JAMA*. 2004;291:1701-1712
10. Adams HP, Jr., Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. Toast. Trial of org 10172 in acute stroke treatment. *Stroke*. 1993;24:35-41
11. Ay H, Furie KL, Singhal A, Smith WS, Sorensen AG, Koroshetz WJ. An evidence-based causative classification system for acute ischemic stroke. *Annals of neurology*. 2005;58:688-697
12. Hatano S. Experience from a multicentre stroke register: A preliminary report. *Bulletin of the World Health Organization*. 1976;54:541-553
13. Eliasziw M, Smith RF, Singh N, Holdsworth DW, Fox AJ, Barnett HJ. Further comments on the measurement of carotid stenosis from angiograms. North american symptomatic carotid endarterectomy trial (nascet) group. *Stroke*. 1994;25:2445-2449
14. Bamford J, Sandercock P, Dennis M, Burn J, Warlow C. Classification and natural history of clinically identifiable subtypes of cerebral infarction. *Lancet*. 1991;337:1521-1526
15. Romano JG, Arauz A, Koch S, Dong C, Marquez JM, Artigas C, et al. Disparities in stroke type and vascular risk factors between 2 hispanic populations in miami and mexico city. *Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association*. 2013;22:828-833
16. White H, Boden-Albala B, Wang C, Elkind MS, Rundek T, Wright CB, et al. Ischemic stroke subtype incidence among whites, blacks, and hispanics: The northern manhattan study. *Circulation*. 2005;111:1327-1331
17. Howard VJ, Kleindorfer DO, Judd SE, McClure LA, Safford MM, Rhodes JD, et al. Disparities in stroke incidence contributing to disparities in stroke mortality. *Annals of neurology*. 2011;69:619-627

18. Benavente OR, White CL, Pearce L, Pergola P, Roldan A, Benavente MF, et al. The secondary prevention of small subcortical strokes (sps3) study. *International journal of stroke : official journal of the International Stroke Society*. 2011;6:164-175
19. Kasner SE. Clinical interpretation and use of stroke scales. *The Lancet. Neurology*. 2006;5:603-612
20. Psaty BM, O'Donnell CJ, Gudnason V, Lunetta KL, Folsom AR, Rotter JI, et al. Cohorts for heart and aging research in genomic epidemiology (charge) consortium: Design of prospective meta-analyses of genome-wide association studies from 5 cohorts. . *Circ Cardiovasc Genet*. 2009;2:273-280
21. Harris TB, Launer LJ, Eiriksdottir G, Kjartansson O, Jonsson PV, Sigurdsson G, et al. Age, gene/environment susceptibility-reykjavik study: Multidisciplinary applied phenomics. *Am J Epidemiol*. 2007;165:1076-1087
22. Longstreth WT, Jr., Bernick C, Fitzpatrick A, Cushman M, Knepper L, Lima J, et al. Frequency and predictors of stroke death in 5,888 participants in the cardiovascular health study. *Neurology*. 2001;56:368-375
23. Price TR, Psaty B, O'Leary D, Burke G, Gardin J. Assessment of cerebrovascular disease in the cardiovascular health study. *Ann Epidemiol*. 1993;3:504-507
24. SHEP_Cooperative_Research_Group. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the systolic hypertension in the elderly program (shep). Shep cooperative research group. *Jama*. 1991;265:3255-3264
25. Dawber TR, Kannel WB. The framingham study. An epidemiological approach to coronary heart disease. *Circulation*. 1966;34:553-555
26. Feinleib M, Kannel WB, Garrison RJ, McNamara PM, Castelli WP. The framingham offspring study. Design and preliminary data. *Prev Med*. 1975;4:518-525
27. Splansky GL, Corey D, Yang Q, Atwood LD, Cupples LA, Benjamin EJ, et al. The third generation cohort of the national heart, lung, and blood institute's framingham heart study: Design, recruitment, and initial examination. *Am J Epidemiol*. 2007;165:1328-1335
28. Carandang R, Seshadri S, Beiser A, Kelly-Hayes M, Kase CS, Kannel WB, et al. Trends in incidence, lifetime risk, severity, and 30-day mortality of stroke over the past 50 years. *Jama*. 2006;296:2939-2946
29. Seshadri S, Beiser A, Kelly-Hayes M, Kase CS, Au R, Kannel WB, et al. The lifetime risk of stroke: Estimates from the framingham study. *Stroke*. 2006;37:345-350
30. Wolf PA, Kannel WB, Dawber TR. Prospective investigations: The framingham study and the epidemiology of stroke. *Adv Neurol*. 1978;19:107-120
31. Vartiainen E, Laatikainen T, Peltonen M, Juolevi A, Mannisto S, Sundvall J, et al. Thirty-five-year trends in cardiovascular risk factors in finland. *Int J Epidemiol*. 2010;39:504-518
32. Kulathinal S, Karvanen J, Saarela O, Kuulasmaa K. Case-cohort design in practice - experiences from the morgam project. *Epidemiol Perspect Innov*. 2007;4:15
33. Tolonen H, Salomaa V, Torppa J, Sivenius J, Immonen-Raiha P, Lehtonen A. The validation of the finnish hospital discharge register and causes of death register data on stroke diagnoses. *Eur J Cardiovasc Prev Rehabil*. 2007;14:380-385
34. Wakefield J. A bayesian measure of the probability of false discovery in genetic epidemiology studies. *American journal of human genetics*. 2007;81:208-227
35. Pahor M, Kritchevsky S. Research hypotheses on muscle wasting, aging, loss of function and disability. *J Nutr Health Aging*. 1998;2:97-100
36. Cesari M, Penninx BW, Newman AB, Kritchevsky SB, Nicklas BJ, Sutton-Tyrrell K, et al. Inflammatory markers and onset of cardiovascular events: Results from the health abc study. *Circulation*. 2003;108:2317-2322
37. Houston DK, Ding J, Lee JS, Garcia M, Kanaya AM, Tylavsky FA, et al. Dietary fat and cholesterol and risk of cardiovascular disease in older adults: The health abc study. *Nutr Metab Cardiovasc Dis*. 2011;21:430-437

38. Hofman A, Breteler MM, van Duijn CM, Krestin GP, Pols HA, Stricker BH, et al. The rotterdam study: Objectives and design update. *Eur J Epidemiol*. 2007;22:819-829
39. Hofman A, Breteler MM, van Duijn CM, Janssen HL, Krestin GP, Kuipers EJ, et al. The rotterdam study: 2010 objectives and design update. *Eur J Epidemiol*. 2009;24:553-572
40. Hofman A, Grobbee DE, de Jong PT, van den Ouweland FA. Determinants of disease and disability in the elderly: The rotterdam elderly study. *Eur J Epidemiol*. 1991;7:403-422
41. Hofman A. Recent trends in cardiovascular epidemiology. *Eur J Epidemiol*. 2009;24:721-723
42. Bots ML, Looman SJ, Koudstaal PJ, Hofman A, Hoes AW, Grobbee DE. Prevalence of stroke in the general population. The rotterdam study. *Stroke*. 1996;27:1499-1501
43. Hollander M, Koudstaal PJ, Bots ML, Grobbee DE, Hofman A, Breteler MM. Incidence, risk, and case fatality of first ever stroke in the elderly population. The rotterdam study. *J Neurol Neurosurg Psychiatry*. 2003;74:317-321
44. Volzke H, Alte D, Schmidt CO, Radke D, Lorbeer R, Friedrich N, et al. Cohort profile: The study of health in pomerania. *Int J Epidemiol*.40:294-307
45. Szentkiralyi A, Volzke H, Hoffmann W, Happe S, Berger K. A time sequence analysis of the relationship between cardiovascular risk factors, vascular diseases and restless legs syndrome in the general population. *J Sleep Res*. 2013;22:434-442
46. Ridker PM, Chasman DI, Zee RY, Parker A, Rose L, Cook NR, et al. Rationale, design, and methodology of the women's genome health study: A genome-wide association study of more than 25,000 initially healthy american women. *Clin Chem*. 2008;54:249-255
47. Bild DE, Bluemke DA, Burke GL, Detrano R, Diez Roux AV, Folsom AR, et al. Multi-ethnic study of atherosclerosis: Objectives and design. *Am J Epidemiol*. 2002;156:871-881
48. Kawasaki R, Xie J, Cheung N, Lamoureux E, Klein R, Klein BE, et al. Retinal microvascular signs and risk of stroke: The multi-ethnic study of atherosclerosis (mesa). *Stroke*. 2012;43:3245-3251
49. Shepherd J, Blauw GJ, Murphy MB, Bollen EL, Buckley BM, Cobbe SM, et al. Pravastatin in elderly individuals at risk of vascular disease (prosper): A randomised controlled trial. *Lancet*. 2002;360:1623-1630
50. Shepherd J, Blauw GJ, Murphy MB, Cobbe SM, Bollen EL, Buckley BM, et al. The design of a prospective study of pravastatin in the elderly at risk (prosper). Prosper study group. Prospective study of pravastatin in the elderly at risk. *Am J Cardiol*. 1999;84:1192-1197
51. Magnusson PK, Almqvist C, Rahman I, Ganna A, Viktorin A, Walum H, et al. The swedish twin registry: Establishment of a biobank and other recent developments. *Twin Res Hum Genet*. 2013;16:317-329
52. Dahl AK, Reynolds CA, Fall T, Magnusson PK, Pedersen NL. Multifactorial analysis of changes in body mass index across the adult life course: A study with 65 years of follow-up. *Int J Obes (Lond)*. 2014;38:1133-1141
53. Fall T, Hagg S, Magi R, Ploner A, Fischer K, Horikoshi M, et al. The role of adiposity in cardiometabolic traits: A mendelian randomization analysis. *PLoS Med*. 2013;10:e1001474
54. Wiberg B, Kilander L, Sundstrom J, Byberg L, Lind L. The relationship between executive dysfunction and post-stroke mortality: A population-based cohort study. *BMJ Open*. 2012;2
55. Liu JZ, McRae AF, Nyholt DR, Medland SE, Wray NR, Brown KM, et al. A versatile gene-based test for genome-wide association studies. *American journal of human genetics*. 2010;87:139-145
56. 3C-Study-Group. Vascular factors and risk of dementia: Design of the three-city study and baseline characteristics of the study population. *Neuroepidemiology*. 2003;22:316-325
57. Riboli E, Hunt KJ, Slimani N, Ferrari P, Norat T, Fahey M, et al. European prospective investigation into cancer and nutrition (epic): Study populations and data collection. *Public Health Nutr*. 2002;5:1113-1124
58. Danesh J, Saracci R, Berglund G, Feskens E, Overvad K, Panico S, et al. Epic-heart: The cardiovascular component of a prospective study of nutritional, lifestyle and biological factors in 520,000 middle-aged participants from 10 european countries. *Eur J Epidemiol*. 2007;22:129-141

59. InterAct C, Langenberg C, Sharp S, Forouhi NG, Franks PW, Schulze MB, et al. Design and cohort description of the interact project: An examination of the interaction of genetic and lifestyle factors on the incidence of type 2 diabetes in the epic study. *Diabetologia*. 2011;54:2272-2282
60. Sanghera DK, Ortega L, Han S, Singh J, Ralhan SK, Wander GS, et al. Impact of nine common type 2 diabetes risk polymorphisms in asian indian sikhs: Pparg2 (pro12ala), igf2bp2, tcf7l2 and fto variants confer a significant risk. *BMC Med Genet*. 2008;9:59
61. Saxena R, Saleheen D, Been LF, Garavito ML, Braun T, Bjonnes A, et al. Genome-wide association study identifies a novel locus contributing to type 2 diabetes susceptibility in sikhs of punjabi origin from india. *Diabetes*. 2013;62:1746-1755
62. Saxena R, Bjonnes A, Prescott J, Dib P, Natt P, Lane J, et al. Genome-wide association study identifies variants in casein kinase ii (csnk2a2) to be associated with leukocyte telomere length in a punjabi sikh diabetic cohort. *Circ Cardiovasc Genet*. 2014;7:287-295
63. Debette S, Kamatani Y, Metso TM, Kloss M, Chauhan G, Engelter ST, et al. Common variation in phactr1 is associated with susceptibility to cervical artery dissection. *Nat Genet*. 2015;47:78-83
64. Ay H, Benner T, Arsava EM, Furie KL, Singhal AB, Jensen MB, et al. A computerized algorithm for etiologic classification of ischemic stroke: The causative classification of stroke system. *Stroke*. 2007;38:2979-2984
65. Carty CL, Keene KL, Cheng YC, Meschia JF, Chen WM, Nalls M, et al. Meta-analysis of genome-wide association studies identifies genetic risk factors for stroke in african americans. *Stroke*. 2015;46:2063-2068
66. Taylor HA, Jr. The jackson heart study: An overview. *Ethnicity & disease*. 2005;15:S6-1-3
67. Carpenter MA, Crow R, Steffes M, Rock W, Heilbraun J, Evans G, et al. Laboratory, reading center, and coordinating center data management methods in the jackson heart study. *The American journal of the medical sciences*. 2004;328:131-144
68. Fuqua SR, Wyatt SB, Andrew ME, Sarpong DF, Henderson FR, Cunningham MF, et al. Recruiting african-american research participation in the jackson heart study: Methods, response rates, and sample description. *Ethnicity & disease*. 2005;15:S6-18-29
69. Payne TJ, Wyatt SB, Mosley TH, Dubbert PM, Guiterrez-Mohammed ML, Calvin RL, et al. Sociocultural methods in the jackson heart study: Conceptual and descriptive overview. *Ethnicity & disease*. 2005;15:S6-38-48
70. Wyatt SB, Akylbekova EL, Wofford MR, Coady SA, Walker ER, Andrew ME, et al. Prevalence, awareness, treatment, and control of hypertension in the jackson heart study. *Hypertension*. 2008;51:650-656
71. Keku E, Rosamond W, Taylor HA, Jr., Garrison R, Wyatt SB, Richard M, et al. Cardiovascular disease event classification in the jackson heart study: Methods and procedures. *Ethnicity & disease*. 2005;15:S6-62-70
72. Rosamond WD, Folsom AR, Chambless LE, Wang CH, McGovern PG, Howard G, et al. Stroke incidence and survival among middle-aged adults - 9-year follow-up of the atherosclerosis risk in communities (aric) cohort. *Stroke*. 1999;30:736-743
73. Putaala J, Metso AJ, Metso TM, Konkola N, Kraemer Y, Haapaniemi E, et al. Analysis of 1008 consecutive patients aged 15 to 49 with first-ever ischemic stroke: The helsinki young stroke registry. *Stroke*. 2009;40:1195-1203
74. Salomaa V. Genetic and environmental contributions to cardiovascular risk: Lessons from north karelia and finrisk. *Global heart*. 2016;11:229-233
75. Kubo M, Hata J, Ninomiya T, Matsuda K, Yonemoto K, Nakano T, et al. A nonsynonymous snp in prkch (protein kinase c eta) increases the risk of cerebral infarction. *Nat Genet*. 2007;39:212-217
76. Psaty BM, Heckbert SR, Atkins D, Lemaitre R, Koepsell TD, Wahl PW, et al. The risk of myocardial infarction associated with the combined use of estrogens and progestins in postmenopausal women. *Arch Intern Med*. 1994;154:1333-1339

77. Klungel OH, Heckbert SR, Longstreth WT, Jr., Furberg CD, Kaplan RC, Smith NL, et al. Antihypertensive drug therapies and the risk of ischemic stroke. *Arch Intern Med*. 2001;161:37-43
78. Psaty BM, Heckbert SR, Koepsell TD, Siscovick DS, Raghunathan TE, Weiss NS, et al. The risk of myocardial infarction associated with antihypertensive drug therapies. *Jama*. 1995;274:620-625
79. O'Donnell M, Xavier D, Diener C, Sacco R, Lisheng L, Zhang H, et al. Rationale and design of interstroke: A global case-control study of risk factors for stroke. *Neuroepidemiology*. 2010;35:36-44
80. Melander O, Newton-Cheh C, Almgren P, Hedblad B, Berglund G, Engstrom G, et al. Novel and conventional biomarkers for prediction of incident cardiovascular events in the community. *JAMA*. 2009;302:49-57
81. Saleheen D, Zaidi M, Rasheed A, Ahmad U, Hakeem A, Murtaza M, et al. The pakistan risk of myocardial infarction study: A resource for the study of genetic, lifestyle and other determinants of myocardial infarction in south asia. *Eur J Epidemiol*. 2009;24:329-338
82. Gulli G, Rutten-Jacobs LC, Kalra L, Rudd AG, Wolfe CD, Markus HS. Differences in the distribution of stroke subtypes in a uk black stroke population - final results from the south london ethnicity and stroke study. *BMC Med*. 2016;14:77
83. Traylor M, Bevan S, Baron JC, Hassan A, Lewis CM, Markus HS. Genetic architecture of lacunar stroke. *Stroke*. 2015;46:2407-2412

3.6 CONSORTIUM MEMBERSHIP

AFGen Consortium

Please note that the AFGen Consortium participants evolve over time. This is a list of contributors from the manuscript Christophersen et al. *Nature Genetics* 2017. Further information on the AFGen Consortium can be found at www.afgen.org and results are located at www.broadcvdi.org.

Ingrid E. Christophersen, MD, PhD,[1–3] Michiel Rienstra, MD, PhD,[4] Carolina Roselli, MSc,[1,5,6] Xiaoyan Yin, PhD,[7,8] Bastiaan Geelhoed, PhD,[4] John Barnard, PhD,[9] Honghuang Lin, PhD,[7,8] Dan E. Arking, PhD,[10], Albert V. Smith, PhD,[11,12] Christine M. Albert, MD, MPH,[13] Mark Chaffin, MSc[1], Nathan R. Tucker, PhD,[1,2] Molong Li, MD,[2] Derek Klarin, MD,[1] Nathan A Bihlmeyer, BS,[14] Siew-Kee Low, PhD,[15] Peter E. Weeke, MD, PhD,[16,17] Martina Müller-Nurasyid, PhD,[5,18,19] J. Gustav Smith, MD, PhD,[1,20] Jennifer A. Brody, BA,[21] Maartje N. Niemeijer MD,[22] Marcus Dörr, MD,[23,24] Stella Trompet, PhD,[25] Jennifer Huffman, PhD,[26] Stefan Gustafsson, PhD,[27] Claudia Schurmann, PhD,[28,29] Marcus E. Kleber, PhD,[30] Leo-Pekka Lyytikäinen, MD,[31] Ilkka Seppälä, MD,[31] Rainer Malik, PhD,[32] Andrea R. V. R. Horimoto, PhD,[33] Marco Perez, MD,[34] Juha Sinisalo, MD, PhD,[35] Stefanie Aeschbacher, MSc,[36,37] Sébastien Thériault, MD, MSc,[38,39] Jie Yao, MS,[40] Farid Radmanesh, MD, MPH,[1,41] Stefan Weiss, PhD,[24,42] Alexander Teumer, PhD,[24,43] Seung Hoan Choi, PhD,[1] Lu-Chen Weng, PhD[1,2] Sebastian Clauss, MD,[2,18] Rajat Deo, MD, MTR,[44] Daniel J. Rader, MD,[44] Svati Shah, MD, MHS,[45] Albert Sun, MD,[45] Jemma C. Hopewell, PhD,[46] Stephanie Debette, MD, PhD,[47–50] Ganesh Chauhan, PhD,[47,48] Qiong Yang, PhD,[51] Bradford B. Worrall, MD, MSc,[52], Guillaume Paré, MD, MSc,[38,39] Yoichiro Kamatani, MD, PhD,[15] Yanick P. Hagemeijer, MSc,[4] Niek Verweij, PhD,[4] Joylene E. Siland, BSc,[4] Michiaki Kubo, MD, PhD,[53] Jonathan D. Smith, PhD,[9] David R. Van Wagoner, PhD,[9] Joshua C. Bis, PhD,[21] Siegfried Perz, MSc,[54] Bruce M. Psaty, MD, PhD,[21,55–57] Paul M. Ridker, MD, MPH,[13] Jared W. Magnani, MD, MSc,[7,58] Tamara B. Harris, MD, MS,[59] Lenore J. Launer, PhD,[59] M. Benjamin Shoemaker, MD, MSCI,[16] Sandosh Padmanabhan, MD,[60] Jeffrey Haessler, MS,[61] Traci M. Bartz, MS,[62] Melanie Waldenberger, PhD,[19,54,63] Peter Lichtner, PhD,[64] Marina Arendt, MSc,[65] Jose E. Krieger, MD, PhD,[33] Mika Kähönen, MD, PhD,[66] Lorenz Risch, MD, MPH,[67] Alfredo J. Mansur, MD, PhD,[68] Annette Peters, PhD,[19,54,69] Blair H. Smith, MD,[70] Lars Lind, MD, PhD,[71] Stuart A. Scott, PhD,[72] Yingchang Lu, MD, PHD,[28,29] Erwin B. Bottinger, MD,[28,73] Jussi Hernesniemi, MD, PhD,[31,74] Cecilia M. Lindgren, PhD,[75] Jorge A Wong, MD,[76] Jie Huang, MD, MPH,[77] Markku Eskola, MD, PhD,[74] Andrew P. Morris, PhD,[75,78] Ian Ford, PhD,[79] Alex P. Reiner, MD, MSc,[61,80] Graciela Delgado, Msc,[30] Lin Y. Chen, MD, MS,[81] Yii-Der Ida Chen, PhD,[40] Roopinder K. Sandhu, MD, MPH,[82] Man Li, PhD,[83,84] Eric Boerwinkle, PhD,[85] Lewin Eisele, MD,[65] Lars Lannfelt, MD, PhD,[86] Natalia Rost, MD, MPH, FAAN,[1,87] Christopher D. Anderson, MD, MMSc,[1,41] Kent D. Taylor, PhD,[40] Archie Campbell, MA,[88] Patrik K. Magnusson, PhD,[89] David Porteous, PhD,[88] Lynne J. Hocking, PhD,[90] Efthymia Vlachopoulou, PhD,[91] Nancy L. Pedersen, MA, PhD,[89] Kjell Nikus, MD, PhD,[74] Marju Orho-Melander, PhD,[92] Anders Hamsten, MD, PhD,[93] Jan Heeringa, MD, PhD,[22] Joshua C. Denny, MD,[16] Jennifer Kriebel, PhD,[54,63,69] Dawood Darbar, MD,[94] Christopher Newton-Cheh, MD, MPH,[1,2] Christian Shaffer, BS,[16] Peter W. Macfarlane, PhD, DSc,[95] Stefanie Heilmann, PhD,[96,97] Peter Almgren, MSc,[92] Paul L. Huang, MD, PhD,[2] Nona Sotoodehnia, MD, MPH,[98] Elsayed Z. Soliman, MD, MSc, MS,[99] Andre G. Uitterlinden, PhD,[100] PhD, Albert Hofman, MD, PhD,[22] Oscar H. Franco, MD, PhD,[22] Uwe Völker, PhD,[24,42] Karl-Heinz Jöckel, PhD,[65] Moritz F. Sinner, MD, MPH,[18,19] Henry J. Lin, MD,[40] Xiuqing Guo, PhD,[40] Martin Dichgans, MD,[32,101,102], Erik Ingelsson, MD, PhD,[27,103] Charles Kooperberg, PhD,[61] Olle Melander, MD, PhD,[104] Ruth J. F. Loos, PhD,[28,29,105] Jari Laurikka, MD, PhD,[106] David Conen, MD, MPH,[36–38] Jonathan Rosand, MD, MSc,[1,41] Pim van der Harst, MD, PhD,[4] Marja-Liisa Lokki, PhD,[91] Sekar Kathiresan, MD,[1] Alexandre Pereira, MD, PhD,[107] J. Wouter Jukema, MD, PhD,[25,108,109] Caroline Hayward, PhD,[26] Jerome I. Rotter, MD,[110] Winfried März, MD,[111] Terho Lehtimäki, MD, PhD,[31] Bruno H. Stricker, MD, PhD,[112] Mina K. Chung, MD,[9] Stephan B. Felix, MD,[23,24] Vilmundur Gudnason, MD, PhD,[11,12] Alvaro Alonso, MD,

PhD,[113] Dan M. Roden, MD,[16] Stefan Kääb, MD, PhD,[18,19] Daniel I. Chasman, PhD,[1,114] Susan R. Heckbert, MD, PhD,[55,56] Emelia J. Benjamin, MD, ScM,[7,58,115] Toshihiro Tanaka, MD, PhD,[116,117] Kathryn L. Lunetta, PhD,[7,8] Steven A. Lubitz, MD, MPH,[1,2,118] Patrick T. Ellinor, MD, PhD,[1,2,118]

Affiliations
1. Program in Medical and Population Genetics, The Broad Institute of MIT and Harvard, Cambridge, MA, USA.
2. Cardiovascular Research Center, Massachusetts General Hospital, Boston, MA, USA.
3. Department of Medical Research, Bærum Hospital, Vestre Viken Hospital Trust, Norway.
4. Department of Cardiology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands.
5. Institute of Genetic Epidemiology, Helmholtz Zentrum München - German Research Center for Environmental Health, Neuherberg, Germany.
6. Institute of Medical Informatics, Biometry and Epidemiology, Chair of Genetic Epidemiology, Ludwig-Maximilians-Universität, Munich, Germany.
7. NHLBI and Boston University's Framingham Heart Study, Framingham, MA, USA.
8. Department of Biostatistics, Boston University School of Public Health, Boston, MA, USA.
9. Departments of Cardiovascular Medicine, Cellular and Molecular Medicine, Molecular Cardiology, and Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH, USA.
10. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA.
11. Icelandic Heart Association, Kopavogur, Iceland.
12. Faculty of Medicine, University of Iceland, Reykavik, Iceland.
13. Divisions of Preventive and Cardiovascular Medicine, Brigham and Women's Hospital & Harvard Medical School, Boston, MA, USA.
14. Predoctoral Training Program in Human Genetics, McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA.
15. Laboratory for Statistical Analysis, RIKEN Center for Integrative Medical Sciences, Yokohama, Japan.
16. Department of Medicine, Vanderbilt University Medical Center, Nashville, TN, USA.
17. The Heart Centre, Department of Cardiology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark.
18. Department of Medicine I, University Hospital Munich, Ludwig-Maximilians-University, Munich, Germany.
19. DZHK (German Centre for Cardiovascular Research), partner site: Munich Heart Alliance, Munich, Germany.
20. Molecular Epidemiology and Cardiology, Clinical Sciences, Lund University, Lund, Sweden.
21. Cardiovascular Health Research Unit, Department of Medicine, University of Washington, Seattle, WA, USA.
22. Department of Epidemiology, Erasmus University Medical Center Rotterdam, Rotterdam, the Netherlands.
23. Department of Internal Medicine B, University Medicine Greifswald, Greifswald, Germany.
24. DZHK (German Centre for Cardiovascular Research), partner site: Greifswald, Germany.
25. Department of Cardiology, Leiden University Medical Center, The Netherlands.
26. MRC Human Genetics Unit, Institute of Genetics and Molecular Medicine, University of Edinburgh, UK.
27. Department of Medical Sciences, Molecular Epidemiology and Science for Life Laboratory, Uppsala University, Uppsala, Sweden.
28. The Charles Bronfman Institute for Personalized Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, USA.
29. The Genetics of Obesity and Related Metabolic Traits Program, Icahn School of Medicine at Mount Sinai, New York, NY, USA.

30. Vth Department of Medicine, Medical Faculty Mannheim, Heidelberg University, Germany.
31. Department of Clinical Chemistry, Fimlab Laboratories and University of Tampere School of Medicine, Tampere, Finland.
32. Institute for Stroke and Dementia Research, Klinikum der Universität München, Ludwig-Maximilians University, München, Germany.
33. Laboratory of Genetics and Molecular Cardiology, Heart Institute, University of Sao Paulo, Sao Paulo, Brazil.
34. Stanford University, Stanford, CA, USA.
35. Heart and Lung Center HUS, Helsinki University Central Hospital, Helsinki, Finland.
36. University Hospital Basel, Switzerland.
37. Cardiovascular Research Institute Basel, Switzerland.
38. Population Health Research Institute, Hamilton, Canada.
39. Department of Pathology and Molecular Medicine, McMaster University, Hamilton, Canada.
40. Institute for Translational Genomics and Population Sciences, Department of Pediatrics, LABioMed at Harbor-UCLA Medical Center, Torrance, CA, USA.
41. Center for Human Genetics Research, Massachusetts General Hospital, Boston, MA, USA.
42. Interfaculty Institute for Genetics and Functional Genomics, University Medicine and Ernst-Moritz-Arndt-University Greifswald, Greifswald, Germany.
43. Institute for Community Medicine, University Medicine Greifswald, Greifswald, Germany.
44. Division of Cardiovascular Medicine, Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, USA.
45. Division of Cardiology, Department of Medicine, Duke University School of Medicine, Durham, NC, USA.
46. CTSU - Nuffield Department of Population Health, University of Oxford, Oxford, UK.
47. Inserm Center U1219 (Bordeaux Population Health Centre), Bordeaux, France.
48. University of Bordeaux, Bordeaux, France.
49. Department of Neurology, Bordeaux University Hospital, Bordeaux, France.
50. Department of Neurology, Boston University School of Medicine, Boston, MA, USA.
51. Biostatistics Department, School of Public Health, Boston University, Boston, MA, USA.
52. University of Virginia Health System, Departments of Neurology and Public Health Science, Charlottesville, VA, USA.
53. RIKEN Center for Integrative Medical Sciences, Yokohama, Japan.
54. Institute of Epidemiology II, Helmholtz Zentrum München - German Research Center for Environmental Health, Neuherberg, Germany.
55. Department of Epidemiology and Cardiovascular Health Research Unit, University of Washington, Seattle, WA, USA.
56. Group Health Research Institute, Group Health Cooperative, Seattle, WA, USA.
57. Department of Health Services, University of Washington, Seattle, WA, USA.
58. Department of Medicine, Boston University School of Medicine, Boston, MA, USA.
59. Laboratory of Epidemiology, Demography, and Biometry, National Institute on Aging, Bethesda, MD, USA.
60. Institute of Cardiovascular and Medical Sciences, BHF Glasgow Cardiovascular Research Centre, University of Glasgow, Glasgow, UK.
61. Fred Hutchinson Cancer Research Center, University of Washington, Seattle, WA, USA.
62. Cardiovascular Health Research Unit, Departments of Medicine and Biostatistics, University of Washington, Seattle, WA, USA.
63. Research unit of Molecular Epidemiology, Helmholtz Zentrum München - German Research Center for Environmental Health, Neuherberg, Germany.
64. Institute of Human Genetics, Helmholtz Zentrum München - German Research Center for Environmental Health, Neuherberg, Germany.
65. Institute for Medical Informatics, Biometry, and Epidemiology, University Hospital, University Duisburg-Essen, Germany.

66. Department of Clinical Physiology, Tampere University Hospital and University of Tampere School of Medicine, Tampere, Finland.
67. University Institute of Clinical Chemistry, University of Bern, Switzerland and labormedizinisches zentrum Dr. Risch, Schaan, Liechtenstein.
68. Heart Institute, University of Sao Paulo, Sao Paulo, Brazil.
69. German Center for Diabetes Research, Neuherberg, Germany.
70. Division of Population Health Sciences, University of Dundee, Scotland, UK.
71. Department of Medical Sciences, Cardiovascular Epidemiology, Uppsala University, Uppsala, Sweden.
72. Department of Genetics and Genomic Sciences , Icahn School of Medicine at Mount Sinai, New York, NY, USA.
73. Department of Pharmacology and Systems Therapeutics, Icahn School of Medicine at Mount Sinai, New York, NY, USA.
74. Department of Cardiology, Heart Hospital, Tampere University Hospital and University of Tampere School of Medicine, Tampere, Finland.
75. Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK.
76. Division of Cardiology, Hamilton Health Sciences, McMaster University, Hamilton, Ontario, Canada.
77. Boston VA Research Institute, Inc., Boston, MA, USA.
78. Department of Biostatistics, University of Liverpool, Liverpool, UK.
79. Robertson Center for Biostatistics, University of Glasgow, Glasgow, UK.
80. Department of Epidemiology, University of Washington, Seattle, WA, USA.
81. Cardiovascular Division, Department of Medicine, University of Minnesota Medical School, Minneapolis, MN, USA.
82. Division of Cardiology, University of Alberta, Edmonton, Canada.
83. Department of Epidemiology, Johns Hopkins University, Baltimore, MD, USA.
84. Division of Nephrology & Hypertension, Internal Medicine, School of Medicine, University of Utah, UT, USA.
85. Human Genome Sequencing Center, Baylor College of Medicine, Houston, TX, USA.
86. Department of Public Health and Caring Sciences, Geriatrics, Uppsala University, Uppsala, Sweden.
87. Acute Stroke Services, Massachusetts General Hospital, Boston, MA, USA.
88. Generation Scotland, Centre for Genomic and Experimental Medicine, Institute of Genetics and Molecular Medicine, University of Edinburgh, UK.
89. Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden.
90. Musculoskeletal Research Programme, Division of Applied Medicine, University of Aberdeen, Aberdeen, UK.
91. Transplantation Laboratory, Medicum, University of Helsinki, Helsinki, Finland.
92. Department of Clinical Sciences, Lund University, Malmö, Sweden.
93. Cardiovascular Genetics and Genomics Group, Atherosclerosis Research Unit, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden.
94. University of Illinois, Chicago, IL, USA.
95. Institute of Health and Wellbeing, College of Medical, Veterinary and Life Sciences, University of Glasgow, UK.
96. Institute of Human Genetics, University of Bonn, Germany.
97. Department of Genomics, Life & Brain Research Center, University of Bonn, Germany.
98. Cardiovascular Health Research Unit, University of Washington Medical Center, Seattle, WA, USA.
99. Epidemiological Cardiology Research Center (EPICARE), Wake Forest School of Medicine, Winston Salem, NC, USA.

100. Department of Epidemiology and Internal Medicine, Erasmus University Medical Center Rotterdam, the Netherlands.
101. Munich Cluster for Systems Neurology (SyNergy), München, Germany.
102. German Center for Neurodegenerative Diseases (DZNE), Munich, Germany.
103. Department of Medicine, Division of Cardiovascular Medicine, Stanford University School of Medicine, Stanford, CA, USA.
104. Department of Internal Medicine, Clinical Sciences, Lund University, Malmö, Sweden.
105. The Mindich Child Health and Development Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA.
106. Department of Cardio-Thoracic Surgery, Heart Hospital, Tampere University Hospital and University of Tampere School of Medicine, Tampere, Finland.
107. Laboratory of Genetics and Molecular Biology, Heart Institute, University of Sao Paulo, Sao Paulo, Brazil and Department of Genetics, Harvard Medical School, Boston, MA, USA.
108. Durrer Center for Cardiogenetic Research, Amsterdam, The Netherlands.
109. Interuniversity Cardiology Institute of the Netherlands, Utrecht, The Netherlands.
110. Institute for Translational Genomics and Population Sciences, Departments of Pediatrics and Medicine, LABioMed at Harbor-UCLA Medical Center, Torrance, CA, USA.
111. Clinical Institute of Medical and Chemical Laboratory Diagnostics, Medical University of Graz, Graz, Austria and Synlab Academy, Synlab Services GmbH, Mannheim, Germany.
112. Department of Epidemiology and Internal Medicine, Erasmus University Medical Center Rotterdam, the Netherlands and Inspectorate of Health Care, Utrecht, the Netherlands.
113. Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA, USA.
114. Divisions of Preventive Medicine and Genetics, Brigham and Women's Hospital & Harvard Medical School, Boston, MA, USA.
115. Department of Epidemiology, Boston University School of Public Health, Boston, MA, USA.
116. Laboratory for Cardiovascular Diseases, RIKEN Center for Integrative Medical Sciences, Yokohama, Japan.
117. Department of Human Genetics and Disease Diversity, Tokyo Medical and Dental University Graduate School of Medical and Dental Sciences, Tokyo, Japan.
118. Cardiac Arrhythmia Service, Massachusetts General Hospital, Boston, MA, USA.

CHARGE consortium:

Neurology - Stroke working group

Ganesh Chauhan (PhD), Audrey Y. Chu (PhD), Myriam Fornage (PhD), Joshua C. Bis (PhD), Aki S. Havulinna (DSc), Muralidharan Sargurupremraj (PhD), Albert Vernon Smith (PhD), Hieab H.H. Adams (MSc), Seung Hoan Choi (MA), Stella Trompet (PhD), Melissa E. Garcia (MPH), Ani Manichaikul (PhD), Alexander Teumer (PhD), Stefan Gustafsson (PhD), Traci M. Bartz (MS), Céline Bellenguez (PhD), Jean Sebastien Vidal (MD), Xueqiu Jian (PhD), Olafur Kjartansson (MD), Kerri L. Wiggins (MS), Claudia L. Satizabal (PhD), Flora Xue (MS), Samuli Ripatti (PhD), Yongmei Liu (PhD), Joris Deelen (PhD), Marcel den Hoed (PhD), Susan R. Heckbert (MD), Kenneth Rice (PhD), Nicholas L. Smith (PhD), Quenna Wong (MS), Hugo J. Aparicio (MD), Julie E. Buring (ScD), Paul M Ridker (MD), Claudine Berr (MD), Jean-François Dartigues (MD), Anders Hamsten (MD), Patrik K. Magnusson (PhD), Nancy L. Pedersen (PhD), Lars Lannfelt (MD), Lars Lind (MD), Cecilia M. Lindgren (PhD), Andrew P. Morris (PhD), Albert Hofman (MD), Peter J. Koudstaal (MD), Marileen LP. Portegies (MD), André G. Uitterlinden (PhD), Anton JM de Craen (PhD), Ian Ford (MD), J. Wouter Jukema (MD), David J Stott (MD), Norrina B. Allen (PhD), Michele M. Sale (PhD), Andrew D Johnson (PhD), David A. Bennett (MD), Philip L. De Jager (MD, PhD), Charles C. White (PhD), Hans Jörgen Grabe (MD), Marcello Ricardo Paulista Markus (MD), Ulf Schminke (MD), Oscar L Lopez (MD), Jerome I. Rotter (MD), Michael A. Nalls (PhD), Rebecca F. Gottesman (MD), Michael

E. Griswold (PhD), David S. Knopman (MD), B. Gwen Windham (MD), Alexa Beiser (PhD), Erkki Vartiainen (MD), Curtis R. French (PhD), Vilmundur Gudnason (MD), Tobias Kurth (MD), Bruce M. Psaty (MD), Tamara B. Harris (MD), Stephen S Rich (PhD), Anita L. deStefano (PhD), Carsten Oliver Schmidt (PhD), Veikko Salomaa (MD), Thomas H. Mosley (PhD), Erik Ingelsson (MD, PhD), Cornelia M. van Duijn (PhD), Christophe Tzourio (MD), Lenore J Launer (PhD), M. Arfan Ikram (MD), Daniel I. Chasman (PhD), William T. Longstreth, Jr. (MD), Sudha Seshadri (MD), Stéphanie Debette (MD)

University Medicine Greifswald, Institute for Community Medicine, SHIP-KEF, Greifswald, Germany (AT, COS); University Medicine Greifswald, Department of Neurology, Greifswald, Germany (US); University Medicine Greifswald, Department of Psychiatry and Psychotherapy, Greifswald, Germany (HJG); University Medicine Greifswald, Department of Internal Medicine B, DZHK (German Centre for Cardiovascular Research), partner site Greifswald, Greifswald, Germany (MRPM); Division of Preventive Medicine, Brigham and Women's Hospital, Boston, MA, USA (JEB, PMRi, DIC, AYC, TK); Harvard Medical School, Boston, MA, USA (JEB, PMRi, DIC) ; Inserm U1219, Bordeaux Population Health Center, Bordeaux University, France (MS, CT, JFD, GC, SD); Institute of Public Health, Charité - Universitätzmedizin, Berlin, Germany (TK); Northwestern University, Chicago, IL, USA (NBA); National institute for Health and Welfare, Helsinki, Finland (ASH, EV, VS); Public Health, University of Helsinki, Finland (SR); Institute for Molecular Medicine Finland (FIMM), University of Helsinki (SR); Wellcome Trust Sanger Institute, UK (SR); Department of Epidemiology, Erasmus MC, Rotterdam, The Netherlands (HHHA, MLP, AHo, CMvD, MAI); Department of Neurology, Erasmus MC, Rotterdam, The Netherlands (MLP, PJK); Department of Internal Medicine, Erasmus MC , Rotterdam, The Netherlands (AGU); Cardiovascular Health Research Unit, Department of Medicine, University of Washington, Seattle, WA, USA (JCB, BMP, KLW); Department of Epidemiology, University of Washington, Seattle, WA, USA (BMP, WTL, NLS, SRH); Group Health Research Institute, Group Health Cooperative, Seattle, WA, USA (SRH); Department of Health Services, University of Washington, Seattle, WA, USA (BMP); Group Health Research Institute, Group Health Cooperative, Seattle, WA, USA (BMP); Institute for Translational Genomics and Population Sciences, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, California, USA (JIR); Division of Genomic Outcomes, Department of Pediatrics, Harbor-UCLA Medical Center, California, USA (JIR); UCLA, California, USA (JIR); Department of Biostatistics, University of Washington, Seattle, WA, USA (TMB, KR, QW); Department of Neurology; University of Washington, Seattle, WA, USA (WTL); Seattle Epidemiologic Research and Information Center of the Department of Veterans Affairs Office of Research and Development, Seattle, WA, USA (NLS); Department of Cardiology, Leiden University Medical Center, Leiden The Netherlands (ST, JWJ); Department of Gerontology and Geriatrics, Leiden University Medical Center, Leiden, The Netherlands (ST, AJMdC); Department of Molecular Epidemiology, Leiden University Medical Center, Leiden, The Netherlands (JDe); Robertson Center for Biostatistics, University of Glasgow, United Kingdom (IF); Institute of Cardiovascular and Medical Sciences, Faculty of Medicine, University of Glasgow, United Kingdom (DJS); Center for Human Genetics, Division of Public Health Sciences, Wake Forest School of Medicine, Winston Salem, NC, USA (YL); Laboratory of Epidemiology and Population Sciences, National Institute on Aging, Bethesda, MD, USA (TBH, MEGa); Laboratory of Neurogenetics, National Institute on Aging, Bethesda, MD, USA (MAN); Department of Medical Sciences, Molecular Epidemiology and Science for Life Laboratory, Uppsala University, Uppsala, Sweden (SG, MdH, EI); Department of Medicine, Division of Cardiovascular Medicine, Stanford University School of Medicine, Stanford, CA 94305, USA (EI); Department of Medical Sciences, Uppsala University, Uppsala, Sweden (LLi); Department of Public Health and Caring Sciences, Uppsala University, Uppsala, Sweden (LLa); Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden (NLP, PKM); Genetic and Genomic Epidemiology Unit, Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK (CML, APM); Department of Biostatistics, University of Liverpool, Liverpool, UK (APM); Atherosclerosis Research Unit, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden (AHa); Inserm, U1167, F-59000 Lille, France (CeB), Institut Pasteur de Lille, F-

59000 Lille, France (CeB), Univ. Lille, U1167, F-59000 Lille, France (CeB); INSERM U1061, Montpellier, France (ClB); University Montpellier 1, Montpellier, France (ClB); Department of Neurology, Bordeaux University Hospital, Bordeaux, France (SD, JFD); Boston University School of Medicine, Boston, MA, USA (SD); IRP/NIA/NIH, Bethesda, MD, USA (LJL); Department of Neurology, University of Pittsburgh, PA, USA (OLL); Landspitali National University Hospital, Department of Radiology, Reykjavik, Iceland (OK); Icelandic Heart Association, Kópavogur, Iceland (VG, AVS); University of Iceland, Faculty of Medicine, Reykjavik, Iceland (VG); Institute of Molecular Medicine and Human Genetics Center; University of Texas Health Science Center at Houston, Houston, TX, USA (MF, XJ); Department of Neurology; Johns Hopkins University, Baltimore, MD, USA (RFG); Center of Biostatistics and Bioinformatics; University of Mississippi Medical Center, Jackson, MS, USA (MEGr); Department of Neurology; Mayo Clinic, Rochester, MN, USA (DSK); Department of Medicine, Division of Geriatrics; University of Mississippi Medical Center, Jackson, MS, USA (THM, BGW); CTSU, Nuffield Department of Population Health, University of Oxford, UK (JCH, RC); Ann Romney Center for Neurologic Diseases, Brigham and Women's Hospital, Boston, Massachusetts, USA (PLDJ, CCW), Rush Alzheimer's Disease Center, Rush University Medical Center, 600 S Paulina St, Chicago, IL 60612 (DAB), Hôpital Broca, Service de Gérontologie I, and Université Paris Descartes, Sorbonne Paris Cité, Paris, France (JSV), National Heart, Lung, and Blood Institute's Framingham Heart Study Population Sciences Branch, Framingham, Massachusetts, USA (ADJ), Department of Neurology, Boston University School of Medicine, Boston, Massachusetts, USA (AB, ALD, HJA, SS, CLS, SHC, FX), Department of Biostatistics, Boston University School of Public Health, Boston, Massachusetts, USA (AB, ALD, SS, SHC, FX), The National Heart, Lung, and Blood Institute's Framingham Heart Study, Framingham, Massachusetts, USA (AB, ADJ, ALD, AYC, HJA, SS, CLS, SHC, FX).

Neurology – White matter hyperintensity burden working group

Benjamin F.J. Verhaaren, MD, PhD; Stéphanie Debette, MD, PhD; Joshua C. Bis, PhD; Jennifer A. Smith, PhD, MPH, MA; M. Kamran Ikram, MD, PhD; Hieab H. Adams, MSc; Ashley H. Beecham, MSc; Kumar B. Rajan, PhD; Lorna M. Lopez, PhD; Sandra Barral, PhD; Mark A. van Buchem, MD, PhD; Jeroen van der Grond, PhD; Albert V. Smith, PhD; Katrin Hegenscheid, MD; Neelum T. Aggarwal, MD; Mariza de Andrade, PhD; Elizabeth J. Atkinson, PhD; Marian Beekman, PhD; Alexa S. Beiser, PhD; Susan H. Blanton, PhD; Eric Boerwinkle, PhD; Adam M. Brickman, PhD; R. Nick Bryan, MD, PhD; Ganesh Chauhan, PhD; Christopher P.L.H. Chen, FRCP; Vincent Chouraki, MD, PhD; Anton J.M. de Craen, PhD; Fabrice Crivello, PhD; Ian J. Deary, PhD; Joris Deelen, MSc; Philip L. De Jager, MD, PhD; Carole Dufouil, PhD; Mitchell S.V. Elkind, MD, MSc; Denis A. Evans, MD; Paul Freudenberger, MSc; Rebecca F. Gottesman, MD, PhD; Vilmundur Guðnason, MD, PhD; Mohamad Habes, PhD; Susan R. Heckbert, MD, PhD; Gerardo Heiss, MD; Saima Hilal, MBBS; Edith Hofer, PhD; Albert Hofman, MD, PhD; Carla A. Ibrahim-Verbaas, MD; David S. Knopman, MD; Cora E. Lewis, MD, MSPH; Jiemin Liao, MSc; David C.M. Liewald, BSc; Michelle Luciano, PhD; Aad van der Lugt, MD, PhD; Oliver O. Martinez, PhD; Richard Mayeux, MD, MSc; Bernard Mazoyer, MD, PhD; Mike Nalls, PhD; Matthias Nauck, MD; Wiro J. Niessen, PhD; Ben A. Oostra, PhD; Bruce M. Psaty, MD, PhD; Kenneth M. Rice, PhD; Jerome I. Rotter, MD; Bettina von Sarnowski, MD; Helena Schmidt, MD, PhD; Pamela J. Schreiner, PhD; Maaike Schuur, MD, PhD; Stephen S. Sidney, MD, MPH; Sigurdur Sigurdsson, MSc; P. Eline Slagboom, PhD; David J.M. Stott, MD; John C. van Swieten, MD, PhD; Alexander Teumer, PhD; Anna Maria Töglhofer, MSc; Matthew Traylor, MSc; Stella Trompet, PhD; Stephen T. Turner, MD; Christophe Tzourio, MD, PhD; Hae-Won Uh, PhD; André G. Uitterlinden, PhD; Meike W. Vernooij, MD, PhD; Jing J. Wang, PhD; Tien Y. Wong, MD, PhD; Joanna M. Wardlaw, MD; B. Gwen Windham, MD; Katharina Wittfeld, MS; Christiane Wolf, PhD; Clinton B. Wright, MD; Qiong Yang, PhD; Wei Zhao, MD, PhD; Alex Zijdenbos, PhD; J. Wouter Jukema, MD, PhD; Ralph L. Sacco, MD; Sharon L.R. Kardia, PhD; Philippe Amouyel, MD, PhD; Thomas H. Mosley, PhD; W. T. Longstreth, Jr, MD, MPH; Charles C. DeCarli, MD; Cornelia M. van Duijn, PhD; Reinhold Schmidt, MD; Lenore J. Launer, PhD; Hans J. Grabe, MD; Sudha S. Seshadri, MD; M. Arfan Ikram, MD, PhD; Myriam Fornage, PhD

From the Departments of Epidemiology (B.F.J.V., H.H.A., A.H., C.A.I.-V., B.A.O., M.S., A.G.U., M.W.V., C.M.v.D., M.A.I.), Radiology (B.F.J.V., H.H.A., A.v.d.L., W.J.N., M.W.V., M.A.I.), Neurology (C.A.I.-V., M.S., J.C.v.S., M.A.I.), Medical Informatics (W.J.N.), Internal Medicine (A.G.U.), and Clinical Chemistry (A.G.U.), Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands; Inserm U897, Epidemiology and Biostatistics, Bordeaux, France (S.D., G.C., C.D., C.T., C.W.), CNRS-CEA UMR5296 (F.C., B.M.), Department of Neurology, Bordeaux University Hospitals, Bordeaux, France (S.D.); University of Bordeaux, France (S.D., G.C.); Department of Neurology (S.D., A.S.B., V.C., S.S.S.) and Department of Biostatistics, School of Public Health (A.S.B., J.J.W., Q.Y.), Boston University School of Medicine, MA; Cardiovascular Health Research Unit, Departments of Medicine (J.C.B., S.R.H., B.M.P.), Epidemiology (S.R.H., B.M.P., W.T.L.), Health Services (B.M.P.), Biostatistics (K.M.R.), and Neurology (W.T.L.), University of Washington, Seattle; Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor (J.A.S., W.Z., S.L.R.K.); Singapore Eye Research Institute, Singapore National Eye Centre, Singapore, Singapore (M.K.I., J.L., T.Y.W.); Department of Ophthalmology, National University Health System (M.K.I., J.L., T.Y.W.) and Memory Aging and Cognition Centre (M.K.I., C.P.L.H.C., S.H.), National University of Singapore, Singapore, Singapore; John P. Hussman Institute for Human Genomics, Miami, FL (A.H.B., S.H.B.); Department of Human Genetics, Dr. John T. Macdonald Foundation (S.H.B.), Neuroscience Program (S.H.B., C.B.W.), Department of Epidemiology and Public Health Sciences (C.B.W., R.L.S.), Department of Neurology (C.B.W., R.L.S.), Evelyn F. McKnight Brain Institute, Miller School of Medicine, University of Miami, FL (C.B.W., R.L.S.); Rush University Medical Center, Chicago, IL (K.B.R., N.T.A., D.A.E.); Centre for Cognitive Ageing and Cognitive Epidemiology, Psychology (L.M.L., I.J.D., D.C.M.L., M.L., J.M.W.) and Brain Research Imaging Centre, Scottish Imaging Network: A Platform for Scientific Excellence Collaboration, Centre for Clinical Brain Sciences (J.M.W.), University of Edinburgh, Edinburgh, United Kingdom; Department of Neurology (S.B.), G.H.Sergievsky Center, Taub Institute for Research on Alzheimer's Disease and Aging Brain (A.M.B., R.M.), Columbia University Medical Center, New York, NY; Departments of Radiology (M.A.v.B., J.v.d.G.), Molecular Epidemiology (M.B., J.D., P.E.S.), Gerontology and Geriatrics (A.J.M.d.C.), Cardiology (S.T., J.W.J.), Medical Statistics and Bioinformatics (H.-W.U.), Leiden University Medical Center, Leiden, The Netherlands; The Icelandic Heart Association, Kopavogur, Iceland (A.V.S., V.G., S.S.); Department of Diagnostic Radiology and Neuroradiology (K.H.), Institutes for Community Medicine (M.H.), Clinical Chemistry and Laboratory Medicine (M.N.), Interfaculty Institute for Genetics and Functional Genomics (A.T.), and Department of Psychiatry and Psychotherapy (H.J.G.), University Medicine Greifswald, Greifswald, Germany; Division of Biomedical Statistics and Informatics (M.d.A., E.J.A.), Department of Neurology (D.S.K.), Division of Nephrology and Hypertension (S.T.T.), Mayo Clinic, Rochester, MN; National Heart, Lung, & Blood Institute's Framingham Heart Study, Framingham, MA (A.S.B., V.C., J.J.W., Q.Y., S.S.S.); Human Genetics Center (E.B., M.F.) and Institute of Molecular Medicine (M.F.), University of Texas Health Science Center at Houston; Department of Radiology, Perelman School of Medicine, University of Pennsylvania Health System, Philadelphia (R.N.B., M.H.); Department of Neurology, Harvard University, Cambridge, MA (P.L.D.J.); Brigham and Women's Hospital, Boston, MA (P.L.D.J.); Department of Neurology, College of Physicians and Surgeons and Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY (M.S.V.E.); Institute of Molecular Biology and Biochemistry (P.F., A.M.T.), Clinical Division of Neurogeriatrics, Department of Neurology (E.H., R.S.), Institute for Medical Informatics, Statistics and Documentation (E.H.), Medical University Graz, Graz, Austria; Department of Neurology, School of Medicine, Johns Hopkins University, Baltimore, MD (R.F.G., H.S.); Faculty of Medicine, University of Iceland, Reykjavik, Iceland (V.G.); Department of Epidemiology, School of Public Health, University of North Carolina at Chapel Hill (G.H.); Division of Preventive Medicine, University of Alabama, Birmingham (C.E.L.); Alzheimer's Disease Center, Imaging of Dementia and Aging (IdeA) Laboratory, Department of Neurology, Center for Neuroscience, University of California, Davis (O.O.M., C.C.D.); Laboratory of Neurogenetics (M.N.), Laboratory of Epidemiology, Demography, and Biometry (L.J.L.), National Institute of Aging, The National Institutes of Health, Bethesda, MD; Faculty of Applied Sciences, Delft University of Technology,

Delft, The Netherlands (W.J.N.); Group Health Research Institute, Group Health Cooperative, Seattle, WA (B.M.P.); Division of Genomic Outcomes, Department of Pediatrics, Institute for Translational Genomics and Population Sciences, Los Angeles Biomedical Research Institute (J.I.R.), Harbor-UCLA Medical Center, Torrance; Department of Neurology, University Medicine of Greifswald, Greifswald, Germany (J.I.R., B.v.S.); Division of Epidemiology and Community Health, University of Minnesota, Minneapolis (P.J.S.); Kaiser Permanente Division of Research, Oakland, CA (S.S.S.); Institute of Cardiovascular and Medical Sciences, Faculty of Medicine, University of Glasgow, Glasgow, United Kingdom (D.J.M.S.); Research Centre for Stroke and Dementia, St. George's, University of London, London, United Kingdom (M.T.); Interuniversity Cardiology Institute of the Netherlands, Utrecht, The Netherlands (S.T., J.W.J.); Division of Geriatrics/Gerontology (B.G.W.), Department of Medicine, University of Mississippi Medical Center, Jackson (T.H.M.); German Center for Neurodegenerative Diseases (DZNE), Rostock/ Greifswald, Germany (K.W.); Biospective Inc, Montreal, Quebec, Canada (A.Z.); and Inserm, U744, Université Lille 2, Institut Pasteur de Lille, Centre Hospitalier Régional Universitaire de Lille, Lille, France (P.A.).

Subclinical atherosclerosis working group

Joshua C. Bis, PhD1,79, Maryam Kavousi, MD, MSc2,3,79, Nora Franceschini, MD, MPH4,79, Aaron Isaacs, PhD5,6,79, Gonçalo R Abecasis, PhD7,79, Ulf Schminke, MD8,79, Wendy Post, MD9,79, Albert V. Smith, PhD10,79, L. Adrienne Cupples, PhD11,12,79, Hugh S Markus, MD13, Reinhold Schmidt, MD14, Jennifer E. Huffman, MSc15, Terho Lehtimäki, MD, PhD16,17, Jens Baumert, PhD18, Thomas Münzel, MD19, Susan R. Heckbert, MD, PhD20,21, Abbas Dehghan, MD, PhD2,3, Kari North, PhD22, Ben Oostra, PhD6,23, Steve Bevan, PhD13, Eva-Maria Stoegerer, MD14, Caroline Hayward, PhD15, Olli Raitakari, MD, PhD24,25, Christa Meisinger, MD, MPH18, Arne Schillert, PhD26, Serena Sanna, PhD27, Henry Völzke, MD28, Yu-Ching Cheng, PhD29, Bolli Thorsson, MD10, Caroline S. Fox, MD, MS12,30,31, Kenneth Rice, PhD32, Fernando Rivadeneira, MD, PhD3,33, Vijay Nambi, MD34,35,36, Eran Halperin, PhD37,38, Katja E. Petrovic, MSc39, Leena Peltonen, MD, PhD40,41, H. Erich Wichmann, MD, PhD42, Renate B. Schnabel, MD, MSc19, Marcus Dörr, MD43, Afshin Parsa, MD, MPH44, Thor Aspelund, PhD10,45, Serkalem Demissie, PhD11, Sekar Kathiresan, MD46,47,48, Muredach P. Reilly, MBBCH, MSCE49, the CARDIoGRAM Consortium Kent Taylor, PhD50, Andre Uitterlinden, PhD2,3,33, David J. Couper, PhD51, Matthias Sitzer, MD52, Mika Kähönen, MD, PhD17,53, Thomas Illig, PhD54, Philipp S. Wild, MD19, Marco Orru, MD55, Jan Lüdemann, PhD56, Alan R. Shuldiner, MD57, Gudny Eiriksdottir, MSc10, Charles C. White, MPH11, Jerome I. Rotter, MD50, Albert Hofman, MD, PhD2,3, Jochen Seissler, MD58, Tanja Zeller, PhD19, Gianluca Usala, PhD27, Florian Ernst, PhD59, Lenore J. Launer, PhD60, Ralph B. D'Agostino Sr, PhD61, Daniel H. O'Leary, MD62, Christie Ballantyne, MD34, Joachim Thiery, MD, MBA63,64, Andreas Ziegler, Dr. rer. nat. habil.65, Edward G. Lakatta, MD66, Ravi Kumar Chilukoti, MSc59, Tamara B. Harris, MD, PhD60, Philip A. Wolf, MD12,67, Bruce M. Psaty, MD, PhD21,68, Joseph F Polak, MD, MPH69, Xia Li, MD, MPH4, Wolfgang Rathmann, MD, MSPH70, Manuela Uda, PhD27, Eric Boerwinkle, PhD71, Norman Klopp, PhD54, Helena Schmidt, MD PhD72, James F Wilson, DPhil73, Jorma Viikari, MD, PhD74,75, Wolfgang Koenig, MD76, Stefan Blankenberg, Prof Dr med19, Anne B. Newman, MD, MPH77,79, Jacqueline Witteman, PhD2,3,79, Gerardo Heiss, MD, PhD4,79, Cornelia van Duijn, PhD3,5,6,79, Angelo Scuteri, MD, PhD66,79, Georg Homuth, PhD59,79, Braxton D. Mitchell, PhD44,79, Vilmundur Gudnason, MD, PhD10,45,79, and Christopher J. O'Donnell, MD, MPH12,30,78,79

1Cardiovascular Health Research Unit and Department of Medicine, University of Washington, Seattle, WA, USA

2Department of Epidemiology, Erasmus Medical Center, Rotterdam, The Netherlands

3Netherlands Genomics Initiative (NGI)-Sponsored Netherlands Consortium for Healthy Aging (NCHA), Rotterdam, The Netherlands

4Department of Epidemiology, University of North Carolina Chapel Hill, Chapel Hill, NC, USA
5Genetic Epidemiology Unit, Dept. of Epidemiology, Erasmus University Medical Center, Rotterdam, The Netherlands

6Centre for Medical Systems Biology, Leiden, The Netherlands

7Center for Statistical Genetics, Department of Biostatistics, University of Michigan School of Public Health, Ann Arbor, MI, USA

8Department of Neurology, Ernst Moritz Arndt University Greifswald, Germany

9Division of Cardiology, Department of Medicine, Johns Hopkins University

10Icelandic Heart Association, Kopavogur, Iceland

11Department of Biostatistics, Boston University School of Public Health, Boston, MA, USA
12National Heart, Lung, and Blood Institute's Framingham Heart Study, Framingham MA, USA
13Clinical Neuroscience, St George's University of London, London, UK

14Department of Neurology, Medical University Graz, Austria

15MRC Human Genetics Unit, Institute of Genetics and Molecular Medicine, Western General Hospital, Crewe Road, Edinburgh, EH4 2XU, Scotland

16Department of Clinical Chemistry, University of Tampere, Finland

17Tampere University Hospital, Tampere, Finland

18Institute of Epidemiology II, Helmholtz Zentrum München, German Research Center for Environmental Health, Neuherberg, Germany

19Department of Medicine 2, University Medical Center Mainz, Mainz, Germany

20Cardiovascular Health Research Unit and Department of Epidemiology, University of Washington, Seattle, WA, USA

21Group Health Research Institute, Group Health, Seattle, WA, USA

22Carolina Center for Genome Sciences, University of North Carolina, Chapel Hill, NC, USA
23Department of Clinical Genetics, Erasmus University Medical Center, Rotterdam, The Netherlands
24Research Centre of Applied and Preventive Cardiovascular Medicine, University of Turku, Finland
25Department of Clinical Physiology, Turku University Hospital, Finland

26Institut für Medizinische Biometrie und Statistik, Universitätzu Lübeck, Universitätsklinikum Schleswig-Holstein, Campus Lübeck, Lübeck, Germany

27Istituto di Neurogenetica e Neurofarmacologia, Consiglio Nazionaledelle Ricerche, Cittadella Universitaria di Monserrato, Monserrato, Cagliari, Italy

28Institute for Community Medicine, Ernst Moritz Arndt University Greifswald, Germany

29Division of Endocrinology, Diabetes, and Nutrition, University of Maryland School of Medicine, Baltimore, MD, USA

30National Heart, Lung, and Blood Institute, Bethesda, MD, USA

31Division of Endocrinology, Metabolism, and Diabetes, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA

32Department of Biostatistics, University of Washington, Seattle, WA, USA

33Department of Internal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands

34Baylor College of Medicine, Houston, TX, USA

35Center for Cardiovascular Prevention, The Methodist DeBakey Heart and Vascular Center, Houston, TX, USA

36Ben Taub General Hospital, Houston, TX, USA

37The Blavatnik School of Computer Science, Tel-Aviv University, Israel

38The International Computer Science Institute, Berkeley, California, USA

39Department of Neurology, General Hospital and Medical University Graz, Austria

40Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge, UK
41Institute for Molecular Medicine Finland, Biomedicum, University of Helsinki and National Institute for Health and Welfare, Helsinki, Finland

42Institute of Epidemiology I, Helmholtz Zentrum München, German Research Center for Environmental Health, Neuherberg, Germany

43Department of Internal Medicine B, Ernst Moritz Arndt University Greifswald, Germany
44Departments of Medicine and Epidemiology & Public Health, University of Maryland School of Medicine, Baltimore, MD, USA

45University of Iceland, Reykjavik, Iceland

46Cardiovascular Research Center and Cardiology Division, Massachusetts General Hospital, Boston, MA, USA

47Center for Human Genetic Research, Massachusetts General Hospital, Boston, MA, USA
48Program in Medical and Population Genetics, Broad Institute of MIT and Harvard, Cambridge, MA, USA

49The Cardiovascular Institute, University of Pennsylvania, Philadelphia, Pennsylvania 19104, USA
50Medical Genetics Institute, Cedars-Sinai Medical Center, Los Angeles, CA, USA

51Department of Biostatistics, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

52Department of Neurology, Klinikum Herford, Germany

53Department of Clinical Physiology, University of Tampere, Finland

54Unit of Molecular Epidemiology, Helmholtz Zentrum München, German Research Center for Environmental Health, Neuherberg, Germany

55Unita Operativa Semplice Cardiologia, Divisione di Medicina, Presidio Ospedaliero Santa Barbara, Iglesias, Italy

56Institute of Clinical Chemistry and Laboratory Medicine, Ernst Moritz Arndt University Greifswald, Germany

57Program in Genetics and Genomic Medicine, and Division of Endocrinology, Diabetes and Nutrition, University of Maryland School of Medicine, Baltimore, MD, USA

58Ludwig-Maximilians University of Munich, Medical Clinic Innenstadt, Diabetes Center, Germany

59Interfaculty Institute for Genetics and Functional Genomics, Ernst Moritz Arndt University Greifswald, Germany

60Intramural Research Program, Laboratory of Epidemiology, Demography, and Biometry, National Institute on Aging, NIH, Bethesda MD, USA 61Mathematcs and Statistics Department, Boston University, Boston, MA, USA

62St. Elizabeth's Medical Center, Tufts University School of Medicine, Boston, MA, USA

63Institute of Laboratory Medicine, Clinical Chemistry and Molecular Diagnostics, University Hospital Leipzig, Germany

64Leipzig Research Center of Civilization Diseases, Medical Faculty, University of Leipzig, Germany 65Institut für Medizinische Biometrie und Statistik, Universitätzu Lübeck, Universitätsklinikum Schleswig-Holstein, Campus Lübeck, Lübeck, Germany

66Gerontology Research Center, National Institute on Aging, Baltimore, MD, USA

67Neurology, Boston University School of Medicine, Boston, MA, USA

68Cardiovascular Health Research Unit and Departments of Medicine, Epidemiology, and Health Services, University of Washington, Seattle, WA, USA

69Department of Radiology, Tufts University School of Medicine, Boston MA

70Institute of Biometrics and Epidemiology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf, Düsseldorf, Germany

71University of Texas, School of Public Health, Human Genetics Center, Houston, TX, USA

72Institute of Molecular Biology and Biochemistry, Medical University Graz, Austria

73Centre for Population Health Sciences, University of Edinburgh, Teviot Place, Edinburgh, Scotland

74Department of Medicine, University of Turku, Finland

75Turku University Hospital, Finland

76Department of Internal Medicine II - Cardiology, University of Ulm Medical Center, Germany

77Graduate School of Public Health, Department of Epidemiology, and School of Medicine, Division of Geriatric Medicine, University of Pittsburgh, Pittsburg, PA, USA 78Cardiology Division, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston MA, USA

The International Genetics of Blood Pressure (iGEN-BP) Study

Norihiro Kato[1]*, Marie Loh[2,3]*, Fumihiko Takeuchi[1]*, Niek Verweij[4]*, Xu Wang[5]*, Weihua Zhang[3,6]*, Tanika N Kelly[7]*, Danish Saleheen[8,9,10]*, Benjamin Lehne[3]*, Irene Mateo Leach[4]*, Alexander Drong[11], James Abbott[12], Sian-Tsung Tan[6,13], William R Scott[3,13], Gianluca Campanella[3], Marc Chadeau-Hyam[3], Uzma Afzal[3,6], Peng Chen[5], Todd L Edwards[14], Tõnu Esko[15,16,17,18], Min Jin Go[19], Sarah E Harris[20,21], Jaana Hartiala[22,23], Anuradhani Kasturiratne[24], Chiea-Chuen Khor[5,25,26,27], Marcus E Kleber[28], Huaixing Li[29], Masahiro Nakatochi[30], Richa Saxena[31], Alexandre FR Stewart[32,33], Yasuharu Tabara[34], Ying Wu[35], Jer-Yuarn Wu[36,37], Yi Zhang[38,39], Tarunveer S Ahluwalia[40], Imke Aits[41], Alexessander Da Silva Couto Alves[42], Shikta Das[42], Rajkumar Dorajoo[25], Jemma C Hopewell[43], Yun Kyoung Kim[19], Robert W Koivula[44], Leo-Pekka Lyytikäinen[45,46], Quang N Nguyen[47], Mark A Pereira[48], Iris Postmus[49,50], Olli T Raitakari[51,52], Robert A Scott[53], Rossella Sorice[54], Vinicius Tragante[55], Michela Traglia[56,57], Jon White[58], Ken Yamamoto[59], Yonghong Zhang[60], Linda S Adair[61], Koichi Akiyama[1], Rasheed Asif[8], Tin Aung[62], Inês Barroso[63,64,65], Andrew Bjonnes[31], Timothy R Braun[66], Hui Cai[67], Li-Ching Chang[36], Chien-Hsiun Chen[36,37], Ching-Yu Cheng[5,26,68,69], Rory Collins[43], Regina Courtney[67], Gail Davies[70,71], Graciela Delgado[28], Loi D Do[47], Pieter A Doevendans[55], Lude Franke[72], Ron T Gansevoort[73], Yu-Tang Gao[74], Tanja B Grammer[28], Niels Grarup[40], Jagvir Grewal[3,6], Dongfeng Gu[75], Wander S Gurpreet[76], Anna-Liisa Hartikainen[77,78], Stanley L Hazen[79,80], Jing He[81], Chew-Kiat Heng[82], James E Hixson[83], Chris Hsu[84], Wei Huang[85], Lise LN Husemoen[86], Joo-Yeon

Hwang[19], Sahoko Ichihara[87], Michiya Igase[88], Masato Isono[1], Johanne M Justesen[40], Tomohiro Katsuya[89,90], Young Jin Kim[19], Miyako Kishimoto[91], Woon-Puay Koh[5,92], Katsuhiko Kohara[88], Meena Kumari[93], Nanette R Lee[94], Jeannette Lee[5], Jiemin Liao[26,68], Wolfgang Lieb[41], David CM Liewald[70,71], Tatsuaki Matsubara[95], Yumi Matsushita[91], Evelin Mihailov[15], Lili Milani[15], Rebecca Mills[6], Nina Mononen[45,46], Toru Nabika[96], Eitaro Nakashima[97,98], Kjell Nikus[99], Teresa Nutile[54], Takayoshi Ohkubo[100], Keizo Ohnaka[101], Sarah Parish[43], Hao Peng[60], Son T Pham[47], Mohitha J Pinidiyapathirage[24], Hiromi Rakugi[90], Olov Rolandsson[102], Daniela Ruggiero[54], Cinzia F Sala[56], Ralhan Sarju[76], Kazuro Shimokawa[1], Harold Snieder[103], Thomas HW Spasø[40], Wilko Spiering[104], John M Starr[21,105], David J Stott[106], Daniel O Stram[84], Takao Sugiyama[107], Silke Szymczak[108], W.H. Wilson Tang[79,80], Stella Trompet[109], Väinö Turjanmaa[110,111], Hirotsugu Ueshima[112], Satoshi Umemura[113], Marja Vaarasmaki[114], Rob M van Dam[5], Wiek H van Gilst[4], Dirk J van Veldhuisen[4], Jorma S Viikari[115,116], Yiqin Wang[29], Aili Wang[60], Tien-Yin Wong[26,68], Yong-Bing Xiang[74], Shuhei Yamaguchi[117], Xingwang Ye[29], Robin D Young[9], Terri L Young[118,119], Jian-Min Yuan[120], Xueya Zhou[121], Folkert W Asselbergs[55,122,123], Marina Ciullo[54], Robert Clarke[43], Panos Deloukas[124,125], Andre Franke[108], Paul W Franks[44,102,126], Steve Franks[127], Yechiel Friedlander[128], Myron D Gross[129], Zhirong Guo[60], Torben Hansen[40], Marjo-Riitta Jarvelin[2,42,130,131,132], Torben Jørgensen[86], Wouter J Jukema[109,122,133], Mika Kähönen[110,111], Hiroshi Kajio[91], Mika Kivimaki[93], Jong-Young Lee[134], Terho Lehtimäki[45,46], Allan Linneberg[86], Tetsuro Miki[88], Oluf Pedersen[40], Nilesh J Samani[135,136], Ryoichi Takayanagi[137], Daniela Toniolo[56,138], CARDIoGRAMplusC4D, LifeLines Cohort Study, The InterAct Consortium, Hooman Allayee[22,23], Yuan-Tson Chen[36,139], John Danesh[9], Ian J Deary[21,70], Bong-Jo Kim[19], Xu Lin[29], Jianjun Liu[5,25], Winfried März[28,140,141], Andres Metspalu[15], Karen L Mohlke[35], Dharambir K Sanghera[66], Xiao-Ou Shu[67], Eranga Vithana[26,68,118], Ananda R Wickremasinghe[24], Cisca Wijmenga[72], Bruce HW Wolffenbuttel[142], Mitsuhiro Yokota[143], Wei Zheng[67], Dingliang Zhu[38,39], Paolo Vineis[3], Soterios A Kyrtopoulos[144], Jos CS Kleinjans[145], Mark I McCarthy[11,146], James Scott[13], Yik-Ying Teo[5,25,68,147,148,149]*, Jiang He[7]*, Paul Elliott[3]*, E Shyong Tai[5,92,150]*, Pim van der Harst[4,72,122]*, Jaspal S Kooner[6,13,151]*, John C Chambers[3,6,151]*.

1. Department of Gene Diagnostics and Therapeutics, Research Institute, National Center for Global Health and Medicine, Tokyo, 1628655, Japan.
2. Institute of Health Sciences, P.O.Box 5000, FI-90014 University of Oulu, Finland.
3. Department of Epidemiology and Biostatistics, Imperial College London, London W2 1PG, UK.
4. University of Groningen, University Medical Center Groningen, Department of Cardiology, Hanzeplein 1, 9713 GZ Groningen, The Netherlands.
5. Saw Swee Hock School of Public Health, National University of Singapore and National University Health System, Singapore 117597.
6. Ealing Hospital NHS Trust, Middlesex UB1 3HW, UK.
7. Department of Epidemiology, Tulane University School of Public Health and Tropical Medicine, 1440 Canal Street, Suite 2000, New Orleans, LA 70112.
8. Center for Non-Communicable Diseases, Karachi, Pakistan.
9. Department of Public Health and Primary Care University of Cambridge Strangeways Research Laboratory Cambridge CB1 8RN.
10. Cardiovascular Institute, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania, PA 19104.
11. Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK.
12. Bioinformatics Support Service, Imperial College London, South Kensington, London, SW7 2AZ, UK.
13. National Heart and Lung Institute, Imperial College London, London W12 0NN, UK.
14. Vanderbilt Epidemiology Center, Center for Human Genetics Research, Division of Epidemiology, Department of Medicine, Vanderbilt University, Nashville, TN, 37203.
15. Estonian Genome Center, University of Tartu, Riia 23c, 51010, Tartu, Estonia.
16. Division of Endocrinology, Children's Hospital Boston, Longwood 300, 02115, Boston, MA, USA.
17. Department of Genetics, Harvard Medical School, 77 Avenue Louis Pasteur, 02115, Boston, MA, USA.
18. Program in Medical and Population Genetics, Broad Institute, 7 Cambridge Center, 02142, Cambridge, MA, USA.

19. Center for Genome Science, National Institute of Health, Osong Health Technology Administration Complex, Chungcheongbuk-do, Republic of Korea, 363-951.
20. Medical Genetics Section, University of Edinburgh Molecular Medicine Centre and MRC Institute of Genetics and Molecular Medicine, Western General Hospital, Crewe Road, Edinburgh EH4 2XU, UK.
21. Centre for Cognitive Aging and Cognitive Epidemiology, University of Edinburgh, EH8 9JZ, UK.
22. Department of Preventive Medicine, USC Keck School of Medicine, Los Angeles, CA 90033, USA.
23. Institute for Genetic Medicine, USC Keck School of Medicine, Los Angeles, CA 90033, USA.
24. Department of Public Health, Faculty of Medicine, University of Kelaniya, P.O. Box 6, Thalagolla Road, Ragama 11010, Sri Lanka.
25. Genome Institute of Singapore, Agency for Science, Technology and Research, 60 Biopolis Street, #02-01 Genome, Singapore 138672.
26. Department of Ophthalmology, National University of Singapore, Singapore 119228.
27. Department of Paediatrics, National University of Singapore, Singapore 119228.
28. Medical Clinic V, Mannheim Medical Faculty, University of Heidelberg, Theodor-Kutzer-Ufer 1-3, 68167 Mannheim, Germany.
29. Key Laboratory of Nutrition and Metabolism, Institute for Nutritional Sciences, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai 200031.
30. Center for Advanced Medicine and Clinical Research, Nagoya University Hospital, Nagoya 466-8560, Japan.
31. Massachusetts General Hospital, Harvard Medical School, Boston, MA, 02114, USA.
32. University of Ottawa Heart Institute, Cardiovascular Research Methods Centre Ontario, Canada.
33. Ruddy Canadian Cardiovascular Genetics Centre, Ontario, Canada.
34. Center for Genomic Medicine, Kyoto University Graduate School of Medicine, Sakyo-ku, Kyoto 606-8507, Japan.
35. Department of Genetics, University of North Carolina, Chapel Hill, NC, USA.
36. Institute of Biomedical Sciences, Academia Sinica, 128 Academia Road, Section 2, Nankang, Taipei 115, Taiwan.
37. School of Chinese Medicine, China Medical University, 91 Hsueh-Shih Road,Taichung, Taiwan 40402, R.O.C.
38. State Key Laboratory of Medical Genetics, Shanghai Ruijin Hospital, Shanghai JiaoTong University School of Medicine, Shanghai 200025, China.
39. Shanghai Institute of Hypertension, Shanghai 200025, China.
40. Novo Nordisk Foundation Centre for Basic Metabolic Research, Section of Metabolic Genetics, Faculty of Health and Medical Sciences, University of Copenhagen, 2100 Copenhagen, Denmark.
41. Institute of Epidemiology and Biobank popgen, Christian-Albrechts-University of Kiel, 24105 Kiel, Germany.
42. Department of Epidemiology and Biostatistics, MRC Health Protection Agency (HPE) Centre for Environment and Health, School of Public Health, Imperial College London, UK.
43. Clinical Trial Service Unit & Epidemiological Studies Unit, University of Oxford, Richard Doll Building, Old Road Campus, Roosevelt Drive, Oxford, OX3 7LF, UK.
44. Department of Clinical Sciences, Genetic and Molecular Epidemiology Unit, Skåne University Hospital Malmö, SE-20502 Malmö, Sweden.
45. Department of Clinical Chemistry, Fimlab Laboratories, Tampere 33520, Finland.
46. Department of Clinical Chemistry, University of Tampere School of Medicine, Tampere 33014, Finland.
47. Bach Mai Hospital, 78 Giai Phong, Hanoi, Vietnam.
48. School of Public Health, University of Minnesota, Minneapolis, MN 55454. .
49. Department of Gerontology and Geriatrics, Leiden University Medical Center, 2300 RC Leiden, The Netherlands.
50. Netherlands Consortium for Healthy Ageing, Leiden, The Netherlands.

51. Department of Clinical Physiology and Nuclear Medicine, Turku University Hospital, Turku 20521, Finland.
52. Research Centre of Applied and Preventive Cardiovascular Medicine, University of Turku, Turku 20520, Finland.
53. MRC Epidemiology Unit, Institute of Metabolic Science, University of Cambridge, CB2 0QQ, UK.
54. Institute of Genetics and Biophysics A. Buzzati-Traverso, CNR, 80131 Naples, Italy.
55. Department of Cardiology, Division Heart and Lungs, University Medical Center Utrecht, 3508 GA, Utrecht, The Netherlands.
56. Division of Genetics and Cell Biology, San Raffaele Scientific Institute, 20132 Milano, Italy.
57. Institute for Maternal and Child Health - IRCCS ''Burlo Garofolo''- Trieste, 34137 Trieste, Italy.
58. UCL Genetics Institute, Department of Genetics, Environment and Evolution UCL, London, WC1E 6BT, UK.
59. Division of Genomics, Medical Institute of Bioregulation, Kyushu University, Japan, 812-8582.
60. Department of Epidemiology, School of Public Health, Medical College of Soochow University, Suzhou 215123, China.
61. Department of Nutrition, University of North Carolina, Chapel Hill, NC, USA.
62. Singapore Eye Research Institute, Singapore National Eye Centre, Singapore 168751.
63. Metabolic Disease Group, The Wellcome Trust Sanger Institute, Cambridge CB10 1SA, UK.
64. NIHR Cambridge Biomedical Research Centre, Institute of Metabolic Science, Addenbrooke's Hospital Cambridge, UK.
65. University of Cambridge Metabolic Research Laboratories, Institute of Metabolic Science, Addenbrooke's Hospital Cambridge, UK.
66. Department of Pediatrics, University of Oklahoma HSC, Oklahoma City, 73104, USA.
67. Vanderbilt Epidemiology Center and Vanderbilt-Ingram Cancer Center, Division of Epidemiology, Department of Medicine, Vanderbilt University, Nashville, TN, 37203.
68. Singapore Eye Research Institute, Singapore National Eye Center, Singapore 168751.
69. Centre for Quantitative Medicine, Office of Clinical Sciences, Duke-NUS Graduate Medical School, Singapore 169857.
70. Department of Psychology, University of Edinburgh, 7 George Square, Edinburgh EH8 9JZ, UK.
71. Mohanraj, L. *et al.* IGFBP-3 inhibits cytokine-induced insulin resistance and early manifestations of atherosclerosis. *PLoS One* **8**, e55084 (2013).
72. University of Groningen, University Medical Center Groningen, Department of Genetics, Hanzeplein 1, 9713 GZ Groningen, The Netherlands.
73. University of Groningen, University Medical Center Groningen, Department of Internal Medicine, Hanzeplein 1, 9713 GZ Groningen, The Netherlands.
74. Department of Epidemiology, Shanghai Cancer Institute, Shanghai, People's Republic of China.
75. Fu Wai Hospital & Cardiovascular Institute, Chinese Academy of Medical Sciences & Peking Union Medical College, 167 Beilishi Rd, Beijing, 100037, China.
76. Department of Cardiology, Hero DMC Heart Institute, Ludhiana, Punjab, India.
77. Department of Obstetrics and Gynecology University Hospital of Oulu, University of Oulu, Finland.
78. Department of Clinical Sciences/Obsterics and Gynecology, University of Oulu, Oulu, Finland.
79. Center for Cardiovascular Diagnostics and Prevention, Cleveland Clinic, Cleveland, OH 44195, USA.
80. Department of Cellular and Molecular Medicine, Lerner Research Institute, Cleveland Clinic, Cleveland, OH 44195, USA.
81. Department of Biostatistics, Vanderbilt University, Nashville, TN, 37204.
82. Yong Loo Lin School of Medicine, Dept of Paediatrics, 1E Kent Ridge Road, NUHS Tower Blk Level 12, Singapore 119228.

83. Human Genetics Center, UT-Houston School of Public Health, 1200 Hermann Pressler, Houston, TX 77030.
84. Keck School of Medicine, Univ. of Souther California, Los Angeles, CA 90089.
85. Department of Genetics, Chinese National Human Genomic Center, Shanghai 201203, China.
86. Research Centre for Prevention and Health, Glostrup University Hospital, 2600 Glostrup, Denmark.
87. Graduate School of Regional Innovation Studies, Mie University, Tsu 514-8507, Japan.
88. Department of Geriatric Medicine, Ehime University Graduate School of Medicine, Toon, Ehime 791-0295, Japan.
89. Department of Clinical Gene Therapy, Osaka University Graduate School of Medicine, Suita, Japan, 565-0871.
90. Department of Geriatric Medicine and Nephrology, Osaka University Graduate School of Medicine, Suita, Japan, 565-0871.
91. National Center for Global Health and Medicine, 1-21-1 Toyama,162-8655, Japan.
92. Duke-NUS Graduate Medical School, Singapore.
93. Department of Epidemiology and Public Health, UCL, London, WC1E 6BT, UK.
94. Office of Population Studies Foundation, University of San Carlos, Cebu City, Philippines.
95. Department of Internal Medicine, Aichi-Gakuin University School of Dentistry, Nagoya 464-8651, Japan.
96. Department of Functional Pathology, Shimane University Faculty of Medicine, Izumo 693-8501, Japan.
97. Division of Endocrinology and Diabetes, Department of Internal Medicine, Nagoya University Graduate School of Medicine, Nagoya, Japan, 466-8550.
98. Department of Diabetes and Endocrinology, Chubu Rosai Hospital, Nagoya, Japan, 455-8530.
99. Heart Centre, Department of Cardiology, Tampere University Hospital, and University of Tampere School of Medicine, Tampere 33521, Finland.
100. Department of Hygiene and Public Health, Teikyo University School of Medicine, Itabashi-ku, Tokyo 173-8605, Japan.
101. Department of Geriatric Medicine, Graduate School of Medical Sciences, Kyushu University, Japan, 812-8582.
102. Department of Public Health & Clinical Medicine, Section for Family Medicine, Umeå universitet, SE-90185 Umeå, Sweden.
103. University of Groningen, University Medical Center Groningen, Department of Epidemiology, Hanzeplein 1, 9713 GZ Groningen, The Netherlands.
104. Department of Vascular Medicine, University Medical Center Utrecht, 3508 GA, Utrecht, The Netherlands.
105. Alzheimer Scotland Dementia Research Centre, University of Edinburgh, 7 George Square, Edinburgh, EH8 9JZ UK.
106. Academic Section of Geriatric Medicine, Institute of Cardiovascular and Medical Sciences, Faculty of Medicine, University of Glasgow, Glasgow G4 0SF, UK.
107. Institute for Adult Diseases, Asahi Life Foundation, Tokyo, Japan, 100-0005.
108. Institute of Clinical Molecular Biology, Christian-Albrechts-University of Kiel, Kiel, Germany.
109. Department of Cardiology, Leiden University Medical Center, 2300 RC Leiden, The Netherlands.
110. Department of Clinical Physiology, Tampere University Hospital, Tampere 33521, Finland.
111. Department of Clinical Physiology, University of Tampere School of Medicine, Tampere 33014, Finland.
112. Department of Health Science, and Center for Epidemiologic Research in Asia, Shiga University of Medical Science,Seta Tsukinowa-cho, Otsu 520-2121, Japan.
113. Department of Medical Science and Cardiorenal Medicine, Yokohama City University Graduate School of Medicine, Kanazawa-ku, Yokohama 236-0004, Japan.
114. Department of Obstetrics and Gynecology, Oulu University Hospital, PO Box 23, FIN-90029 OYS Oulu, Finland.
115. Department of Medicine, Turku University Hospital, Turku 20521, Finland.
116. Department of Medicine, University of Turku, Turku 20014, Finland.

117. The Third Department of Internal Medicine, Shimane University Faculty of Medicine, Izumo 693-8501, Japan.
118. Neuroscience and Behavioural Disorders (NBD) Program, Duke-NUS Graduate Medical School, Singapore 169857.
119. Duke Eye Center, Duke University Medical Center, Durham, North Carolina 27710, USA.
120. Cancer Control and Population Sciences, University of Pittsburgh Cancer Institute; and Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, 5150 Centre Avenue, Pittsburgh, Pennsylvania 15232, USA.
121. Bioinformatics Division and Center for Synthetic and Systems Biology, TNLIST, MOE Key Lab of Bioinformatics / Department of Automation, Tsinghua University, Beijing, 100084, China.
122. Durrer Center for Cardiogenetic Research, ICIN-Netherlands Heart Institute, 3511 GC Utrecht, The Netherlands.
123. Institute of Cardiovascular Science, faculty of Population Health Sciences, University College London, WC1E 6BT, London, UK.
124. William Harvey Research Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, EC1M 6BQ, UK.
125. King Abdulaziz University, Jeddah 21589, Saudi Arabia.
126. Department of Nutrition, Harvard School of Public Health, Boston, MA 02115, USA.
127. Institute of Reproductive and Developmental Biology, Imperial College London, Hammersmith Hospital, London, UK.
128. Hebrew University, School of Public Health, POB 12272, Jerusalem 91120, Israel.
129. School of Medicine, University of Minnesota, Minneapolis, MN 55455.
130. Biocenter Oulu, P.O.Box 5000, Aapistie 5A, FI-90014 University of Oulu, Finland.
131. Unit of Primary Care, Oulu University Hospital, Kajaanintie 50, P.O.Box 20, FI-90220 Oulu, 90029 OYS, Finland.
132. Department of Children and Young People and Families, National Institute for Health and Welfare, Aapistie 1, Box 310, FI-90101 Oulu, Finland.
133. Interuniversity Cardiology Institute of the Netherlands, Utrecht, The Netherlands.
134. Ministry of Health and Welfare, Seoul, South Korea, 110-793.
135. Department of Cardiovascular Sciences, University of Leicester, Glenfield Hospital, Leicester, LE3 9QP, UK.
136. National Institute for Health Research Leicester Cardiovascular Biomedical Research Unit, Glenfield Hospital, Leicester LE3 9QP, UK.
137. Department of Medicine and Bioregulatory Science, Graduate School of Medical Sciences, Kyushu University, Japan, 812-8582.
138. Institute of Molecular Genetics.CNR, 27100 Pavia, Italy.
139. Department of Pediatrics, Duke University Medical Center, T901/Children's Health Center, Durham, NC 27705, USA.
140. Clinical Institute of Medical and Chemical Laboratory Diagnostics, Medical University of Graz, Auenbruggerplatz 15, 8036 Graz, Austria.
141. Synlab Academy, Synlab Services GmbH, Gottlieb-Daimler-Straße 25, 68165 Mannheim, Germany.
142. University of Groningen, University Medical Center Groningen, Department of Endocrinology, Hanzeplein 1, 9713 GZ Groningen, The Netherlands.
143. Department of Genome Science, Aichi-Gakuin University School of Dentistry, Nagoya 464-8651, Japan.
144. National Hellenic Research Foundation, Institute of Biological Research and Biotechnology, Athens, Greece.
145. Department of Toxicogenomics, Maastricht University, Universiteitssingel 50, 6229ER Maastricht, The Netherlands.
146. Oxford Centre for Diabetes Endocrinology and Metabolism, University of Oxford, Oxford, UK.
147. NUS Graduate School for Integrative Science and Engineering, National University of Singapore, Singapore 117456.
148. Life Sciences Institute, National University of Singapore, Singapore 117456.

149. Department of Statistics and Applied Probability, National University of Singapore, Singapore 117546.
150. Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore 119228.
151. Imperial College Healthcare NHS Trust, London W12 0HS, UK.

* These authors contributed equally to this work

Correspondence to

John C Chambers
Department of Epidemiology and Biostatistics, Imperial College London, London W2 1PG, UK.
john.chambers@ic.ac.uk

Paul Elliott
Department of Epidemiology and Biostatistics, Imperial College London, London W2 1PG, UK.
p.elliott@ic.ac.uk

Pim van der Harst
University of Groningen, University Medical Center Groningen, Department of Cardiology, Hanzeplein 1, 9713 GZ Groningen, The Netherlands.
p.van.der.harst@umcg.nl

Jiang He
Department of Epidemiology, Tulane University School of Public Health and Tropical Medicine, 1440 Canal Street, Suite 2000, New Orleans, LA 70112, USA.
jhe@tulane.edu

Norihiro Kato
Department of Gene Diagnostics and Therapeutics, Research Institute, National Center for Global Health and Medicine, Tokyo, 1628655, Japan.
nokato@ri.ncgm.go.jp

Jaspal S Kooner
National Heart and Lung Institute, Imperial College London, London W12 0NN, UK.
j.kooner@ic.ac.uk

E Shyong Tai
Saw Swee Hock School of Public Health, National University of Singapore and National University Health System, Singapore 117597
e_shyong_tai@nuhs.edu.sg

INVENT Consortium

Philippe Amouyel,[1] Mariza de Andrade,[2] Saonli Basu,[3] Claudine Berr,[4] Jennifer A Brody,[5] Daniel I Chasman,[6] Jean-Francois Dartigues,[7] Aaron R Folsom,[8] Marine Germain,[9] Hugoline de Haan,[10] John Heit,[11] Jeanine Houwing-Duitermaat,[12] Christopher Kabrhel,[13] Peter Kraft,[14] Grégoire Legal,[15,16] Sara Lindström,[14] Ramin Monajemi,[12] Pierre-Emmanuel Morange,[17] Bruce M Psaty,[5,18] Pieter H Reitsma,[19] Paul M Ridker,[20] Lynda M Rose,[21] Frits R Rosendaal,[10] Noémie Saut,[17] Eline Slagboom,[22] , David Smadja[23] Nicholas L Smith,[18,24,25] Pierre Suchon,[17] Weihong Tang,[8] Kent D Taylor,[26] David-Alexandre Trégouët,[9] Christophe Tzourio,[27] Marieke CH de Visser,[19] Astrid van Hylckama Vlieg,[10] Lu-Chen Weng,[8] Kerri L Wiggins,[24]

Affiliations

[1] Institut Pasteur de Lille, Université de Lille Nord de France, INSERM UMR_S 744, Lille, France; Centre Hospitalier Régional Universitaire de Lille, Lille, France.

[2] Division of Biomedical Statistics and Informatics Mayo Clinic, Rochester, MN, USA.

[3] University of Minnesota, Division of Biostatistics, Minneapolis, MN, USA.

[4] INSERM Research Unit U1061 , University of Montpellier I , Montpellier, France.

[5] Cardiovascular Health Research Unit, Departments of Medicine, Epidemiology, and Health Services, University of Washington, Seattle, WA, USA.

[6] Division of Preventive Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA 02215, USA.

[7] INSERM Research Center U897, University of Bordeaux, Bordeaux, France.

[8] University of Minnesota, Division of Epidemiology and Community Health Minneapolis, MN, USA.

[9] Institut National pour la Santé et la Recherche Médicale (INSERM), Unité Mixte de Recherche en Santé (UMR_S) 1166, F-75013, Paris, France; Sorbonne Universités, Université Pierre et Marie Curie (UPMC Univ Paris 06), UMR_S 1166, Team Genomics & Pathophysiology of Cardiovascular Diseases, F-75013, Paris, France; Institute for Cardiometabolism and Nutrition (ICAN), F-75013, Paris, France.

[10] Department of Thrombosis and Hemostasis, Leiden University Medical Center, Leiden, The Netherlands; Department of Clinical Epidemiology, Leiden University Medical Center, Leiden, The Netherlands.

[11] Division of Cardiovascular Diseases, Mayo Clinic, Rochester, MN, USA.

[12] Department of Medical Statistics and Bioinformatics, Leiden University Medical Center, 2300 RC Leiden, Netherlands.

[13] Department of Emergency Medicine, Massachusetts General Hospital, Channing Network Medicine, Harvard Medical School, Boston, MA 2114, USA.

[14] Program in Genetic Epidemiology and Statistical Genetics, Department of Epidemiology, Harvard School of Public Health, Boston, MA 2115, USA.

[15] Université de Brest, EA3878 and CIC1412, Brest, France.

[16] Ottawa Hospital Research Institute at the University of Ottawa, Ottawa, ON, Canada.

[17] Laboratory of Haematology, La Timone Hospital, F-13385, Marseille, France; INSERM, UMR_S 1062, Nutrition Obesity and Risk of Thrombosis,F-13385, Marseille, France; Aix-Marseille University, UMR_S 1062, Nutrition Obesity and Risk of Thrombosis, F-13385, Marseille, France.

[18] Group Health Research Institute, Group Health Cooperative, Seattle WA 98101, USA.

[19] Einthoven Laboratory for Experimental Vascular Medicine, Department of Thrombosis and Hemostasis, Leiden University Medical Center, Leiden,2300 RC, Netherlands.

[20] Division of Preventive Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA 02215, USA.

[21] Division of Preventive Medicine, Brigham and Women's Hospital, Boston, MA 02215, USA.

[22] Department of Molecular Epidemiology, Leiden University Medical Center, 2300 RC Leiden, Netherlands.

[23] Université Paris Descartes, Sorbonne Paris Cité, Paris, France; AP-HP, Hopital Européen Georges Pompidou, Service d'hématologie Biologique, Paris, France; INSERM, UMR_S 1140, Faculté de Pharmacie, Paris, France.

[24] Department of Epidemiology, University of Washington, Seattle WA 98195, USA.

[25] Seattle Epidemiologic Research and Information Center, VA Office of Research and Development, Seattle WA 98108, USA.

[26] Los Angeles Biomedical Research Institute and Department of Pediatrics, Harbor-UCLA Medical Center, Torrence CA 90502, USA.

[27] INSERM Research Center U897, University of Bordeaux, Bordeaux, France.

STARNET

Johan LM Bjorkegren (PI) [1,2], Eric E Schadt [1], Simon Koplev [1], Arno Ruusalepp (co-PI) [3], Raili Ermel [3], Katyayani Sukhavasi [4]

1 Department of Genetics and Genomic Sciences, Icahn Institute for Genomics and Multiscale Biology, Icahn School of Medicine at Mount Sinai, New York, NY, USA
2 Integrated Cardio Metabolic Centre, Department of Medicine, Karolinska Institutet, Huddinge, Sweden
3 Department of Cardiac Surgery, Tartu University Hospital,Tartu, Estonia
4 Department of Physiology, Institute of Biomedicine and Translation Medicine,University of Tartu, Tartu, Estoni

BioBank Japan Cooperative Hospital Group

Michiaki Kubo,[1] Yoichiro Kamatani,[2] Koichi Matsuda,[3,4] Makoto Hirata,[5] Akiko Nagai,[6] Kaori Muto,[6] Taisei Mushiroda,[7] Yukihide Momozawa,[8] Yoshinori Murakami,[9] Koichiro Yuji,[10] Yoichi Furukawa,[11] Hitoshi Zembutsu,[3] Toshihiro Tanaka,[12] Masaki Shiono,[13] Kazuo Misumi,[13] Reiji Kaieda,[13] Hiromasa Harada,[13] Shiro Minami,[14] Mitsuru Emi,[14] Naoya Emoto,[14] Hajime Arai,[15] Ken Yamaji,[15] Yoshimune Hiratsuka,[15] Satoshi Asai,[16] Mitsuhiko Moriyama,[16] Yasuo Takahashi,[16] Tomoaki Fujioka,[17] Wataru Obara,[17] Seijiro Mori,[18] Hideki Ito,[18] Satoshi Nagayama,[19] Yoshio Miki,[19] Akihide Masumoto,[20] Akira Yamada,[20] Yasuko Nishizawa,[21] Ken Kodama,[21] Hiromu Kutsumi,[22] Yoshihisa Sugimoto,[22] Yukihiro Koretsune,[23] Hideo Kusuoka,[23] Takashi Yoshiyama,[24] Yozo Ohnishi,[12] Yusuke Nakamura[3]

Affiliations

1. RIKEN Center for Integrative Medical Sciences, Yokohama, Japan
2. Laboratory for Statistical Analysis, RIKEN Center for Integrative Medical Sciences, Yokohama, Japan
3. Laboratory of Molecular Medicine, Institute of Medical Science, The University of Tokyo, Tokyo, Japan
4. Laboratory of Clinical Genome Sequencing, Graduate School of Frontier Sciences, The University of Tokyo, Tokyo, Japan
5. Laboratory of Genome Technology, Institute of Medical Science, The University of Tokyo, Tokyo, Japan
6. Department of Public Policy, Institute of Medical Science, The University of Tokyo, Tokyo, Japan
7. Laboratory for Pharmacogenomics, RIKEN Center for Integrative Medical Sciences, Yokohama, Japan
8. Laboratory for Genotyping Development, RIKEN Center for Integrative Medical Sciences, Yokohama, Japan
9. Division of Molecular Pathology, Institute of Medical Science, The University of Tokyo, Tokyo, Japan
10. Project Division of International Advanced Medical Research, Institute of Medical Science, The University of Tokyo, Tokyo, Japan
11. Division of Clinical Genome Research, Institute of Medical Science, The University of Tokyo, Tokyo, Japan
12. SNP Research Center, RIKEN Yokohama Institute, Japan
13. Tokushukai Hospitals, Japan
14. Nippon Medical School, Tokyo, Japan
15. Juntendo University, Tokyo, Japan
16. Nihon University, Tokyo, Japan
17. Iwate Medical Universitym Iwate, Japan
18. Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan
19. The Cancer Institute Hospital of JFCR, Tokyo, Japan
20. Aso Iizuka Hospital, Fukuoka, Japan
21. Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Japan
22. Shiga University of Medical Science, Shiga, Jpana

23. National Hospital Organization, Osaka National Hospital, Osaka, Japan
24. Fukujuji Hospital, Tokyo, Japan

COMPASS consortium

Adolfo Correa [1], Alexander P Reiner [2,3], Bradford B Worrall [4], Braxton D Mitchell [5,6], Bruce M Psaty [7,8,9], Cara L Carty [10], Cathryn M Lewis [11,12], Charles Kooperberg [13], Daniel Woo [14], Fang-Chi Hsu [15], Guillaume Pare [16], Hugh S Markus [17,18], Hyacinth I Hyacinth [19], James F Meschia [20], James G Wilson [21], Jeffrey Haessler [13], Jerome I Rotter [22,23], Joshua C Bis [7], Keith L Keene [24,25], Kenneth Rice [26], Leslie Lange [27], Martin J O'Donnell [16,28], Michael A Nalls [29,30], Michael Chong [16], Michele M Sale [31], Myriam Fornage [32,33], Qing Duan [34], Rebecca F Gottesman [35], Salim Yusuf [16], Stephen S Rich [36], Steven J Kittner [37], Thomas H Mosley [38,39], Traci M Bartz [7], W T Longstreth, Jr [40,41], Wei-Min Chen [42], Xueqiu Jian [32], Yu-ching Cheng [43]

1 Department of Medicine and Pediatrics University of Mississippi Medical Center, Jackson, MS, USA
2 Department of Epidemiology, University of Washington, Seattle, WA, USA
3 Fred Hutchinson Cancer Research Center, University of Washington, Seattle, WA, USA
4 Departments of Neurology and Public Health Sciences, University of Virginia School of Medicine, Charlottesville, VA, USA
5 Department of Medicine, University of Maryland School of Medicine, MD, USA
6 Geriatrics Research and Education Clinical Center, Baltimore Veterans Administration Medical Center, Baltimore, MD, USA
7 Cardiovascular Health Research Unit, Department of Medicine, University of Washington, Seattle, WA, USA
8 Department of Epidemiology, University of Washington, Seattle, WA
9 Department of Health Services, University of Washington, Seattle, WA, USA
10 Children's Research Institute, Children's National Medical Center, Washington, DC, USA
11 Department of Medical and Molecular Genetics, King's College London, London, UK
12 SGDP Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK
13 Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA, USA
14 University of Cincinnati College of Medicine, Cincinnati, OH, USA
15 Department of Biostatistical Sciences, Wake Forest School of Medicine, Winston-Salem, NC, USA
16 Population Health Research Institute, McMaster University, Hamilton, Canada
17 Stroke Research Group, Division of Clinical Neurosciences, University of Cambridge, UK
18 Department of Clinical Neurosciences,Cambridge Biomedical Campus,Cambridge CB2 0QQ,UK
19 Aflac Cancer and Blood Disorder Center, Department of Pediatrics, Emory University School of Medicine, Atlanta, GA, USA
20 Department of Neurology, Mayo Clinic, Jacksonville, FL, USA
21 Department of Physiology and Biophysics, University of Mississippi Medical Center, Jackson, MS, USA
22 Institute for Translational Genomics and Population Sciences, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA, USA
23 Division of Genomic Outcomes, Department of Pediatrics, Harbor-UCLA Medical Center, Torrance, CA, USA

24 Department of Biology, East Carolina University, Greenville, NC, USA
25 Center for Health Disparities, East Carolina University, Greenville, NC, USA
26 Department of Biostatistics, University of Washington, Seattle, WA, USA
27 University of Colorado, Denver, CO, USA
28 Clinical Research Facility, Department of Medicine, NUI Galway, Galway, Ireland
29 Laboratory of Neurogenetics, National Institute on Aging, National institutes of Health, Bethesda, MD, USA
30 Data Tecnica International, Glen Echo MD, USA
31 Center for Public Health Genomics, University of Virginia, Charlottesville, VA, USA
32 Brown Foundation Institute of Molecular Medicine, University of Texas Health Science Center at Houston, Houston, TX, USA
33 Human Genetics Center, University of Texas Health Science Center at Houston, Houston, TX, USA
34 Department of Genetics, University of North Carolina, Chapel Hill, NC, USA
35 Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, 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, MD, USA
38 Division of Geriatrics, School of Medicine, University of Mississippi Medical Center, Jackson, MS, USA
39 Memory Impairment and Neurodegenerative Dementia Center, University of Mississippi Medical Center, Jackson, MS, USA
40 Department of Neurology University of Washington, Seattle, WA
41 Department of Epidemiology University of Washington, Seattle, WA
42 Center for Public Health Genomics, Department of Public Health Sciences, University of Virginia School of Medicine, Charlottesville, VA, USA
43 Department of Medicine, University of Maryland School of Medicine, Baltimore, MD, USA

EPIC-CVD consortium

Kim Overvad[1,2], Anne Tjønneland[3], Francoise Clavel-Chapelon[4], Rudolf Kaaks[5], Heiner Boeing[6], Antonia Trichopoulou[7,8], Pietro Ferrari[9], Domenico Palli[10], Vittorio Krogh[11], Salvatore Panico[12], Rosario Tumino[13], Giuseppe Matullo[14,15], Jolanda Boer[16], Yvonne van. der Schouw[17], Elisabete Weiderpass[18,19,20,21], J. Ramon Quiros[22], María-José Sánchez[23,24], Carmen Navarro[25], Conchi Moreno-Iribas[26], Larraitz Arriola[27], Olle Melander[28], Patrik Wennberg[29], Nicholas J. Wareham[30], Timothy J. Key[31], Elio Riboli[32], Adam S. Butterworth[33,34], Joanna M M Howson[33], John Danesh[33,34,35]

1. Department of Public Health, Section for Epidemiology, Aarhus University, Aarhus, Denmark
2. Department of Cardiology, Aalborg University Hospital, Aalborg, Denmark
3. Diet, Genes and Environment, Danish Cancer Society Research Center, Copenhagen, Denmark
4. INSERM, Centre for Research in Epidemiology and Population Health (CESP), U1018, Nutrition, Hormones, and Women's Health Team, Institut Gustave Roussy, Villejuif, France
5. Division of Cancer Genetic Epidemiology, German Cancer Research Centre (DKFZ), im Neuenheimer Feld 581, 69120 Heidelberg, Germany
6. Department of Epidemiology, German Institute of Human Nutrition (DIfE), Potsdam-Rehbrücke, Germany
7. WHO Collaborating Center for Nutrition and Health, Unit of Nutritional Epidemiology and

Nutrition in Public Health, Department of Hygiene, Epidemiology and Medical Statistics, University of Athens Medical School, Athens, Greece
8. Hellenic Health Foundation, Athens, Greece
9. International Agency for Research on Cancer, Lyon, France
10. Molecular and Nutritional Epidemiology Unit, Centro per lo Studio e la Prevenzione Oncologica-Scientific Institute of Tuscany, Florence, Italy
11. Epidemiology and Prevention Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy
12. Dipartimento di Medicina Clinica e Chirurgia, Federico II University, Naples, Italy
13. Cancer Registry and Histopathology Unit, Civic- M.P.Arezzo Hospital, ASP Ragusa, Italy
14. Human Genetics Foundation, Turin, Italy
15. Department of Medical Sciences, University of Turin, Italy
16. Centre for Nutrition, Prevention and Health Services, National Institute for Public Health and the Environment (RIVM), Bilthoven, the Netherlands
17. Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, the Netherlands
18. Department of Community Medicine, Faculty of Health Sciences, University of Tromsø, The Arctic University of Norway, Tromsø, Norway
19. Department of Research, Cancer Registry of Norway, Institute of Population-Based Cancer Research, Oslo, Norway
20. Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden
21. Genetic Epidemiology Group, Folkhälsan Research Center, Helsinki, Finland
22. Public Health Directorate, Asturias, Spain
23. Escuela Andaluza de Salud Pública, Instituto de Investigación Biosanitaria ibs.GRANADA. Hospitales Universitarios de Granada/Universidad de Granada, Granada, Spain
24. CIBER de Epidemiología y Salud Pública (CIBERESP), Madrid, Spain
25. Epidemiology Department, Murcia Health Authority, Murcia, Spain
26. Public Health Institute of Navarra, Pamplona, Spain
27. Public Health Division of Gipuzkoa, Instituto Bio-Donostia, Basque Government, CIBERESP, Spain
28. Department of Clinical Sciences, Hypertension & Cardiovascular Disease, Clinical Research Centre, Malmö University Hospital, Malmö, Sweden
29. Department of Public Health and Clinical Medicine, Family Medicine, Umeå University, Umeå, Sweden
30. Medical Research Council Epidemiology Unit, University of Cambridge, Cambridge, UK
31. Cancer Epidemiology Unit, Nuffield Department of Population Health, University of Oxford, UK
32. School of Public Health, Imperial College London, UK
33. MRC/BHF Cardiovascular Epidemiology Unit, Department of Public Health & Primary Care, University of Cambridge, UK
34. The National Institute for Health Research Blood and Transplant Unit (NIHR BTRU) in Donor Health and Genomics at the University of Cambridge, UK
35. Wellcome Trust Sanger Institute, Genome Campus, Hinxton, UK

EPIC-InterAct consortium

Claudia Langenberg[1], Robert A Scott[1], Stephen J Sharp[1], Nita G Forouhi[1], Nicola D Kerrison[1], Matt Sims[1], Debora ME Lucarelli[1], InÍs Barroso[2,3], Panos Deloukas[2], Mark I McCarthy[4,5,6], Larraitz Arriola[7,8,9], Beverley Balkau[10,11], Aurelio Barricarte[12,13,9], Heiner Boeing[14], Paul W Franks[15,16], Carlos Gonzalez[17], Sara Grioni[18], Rudolf Kaaks[19], Timothy J Key[20], Carmen Navarro[21,9,22], Peter M Nilsson[15], Kim Overvad[23,24], Domenico Palli[25], Salvatore Panico[26], J. RamÛn QuirÛs[27], Olov Rolandsson[16],

Carlotta Sacerdote[28,29], MarÌa-JosÈ S·nchez[30,9,31], Nadia Slimani[32], Anne Tjonneland[33], Rosario Tumino[34], Daphne L van der A[35], Yvonne T van der Schouw[36], Elio Riboli[37], Nicholas J Wareham[1]
(1) MRC Epidemiology Unit, University of Cambridge, Cambridge, United Kingdom, (2) The Wellcome Trust Sanger Institute, Cambridge, United Kingdom
(3) University of Cambridge Metabolic Research Laboratories, Cambridge, UK,
(4) Oxford Centre for Diabetes, Endocrinology and Metabolism (OCDEM), University of Oxford, UK,
(5) Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK,
(6) Oxford NIHR Biomedical Research Centre, Oxford, UK,
(7) Public Health Division of Gipuzkoa, San Sebastian, Spain,
(8) Instituto BIO-Donostia, Basque Government, San Sebastian, Spain,
(9) CIBER EpidemiologÌa y Salud P˙blica (CIBERESP), Spain,
(10) Inserm, CESP, U1018, Villejuif, France,
(11) Univ Paris-Sud, UMRS 1018, Villejuif, France,
(12) Navarre Public Health Institute (ISPN), Pamplona, Spain,
(13) Navarra Institute for Health Research (IdiSNA) Pamplona, Spain,
(14) German Institute of Human Nutrition Potsdam-Rehbruecke, Germany,
(15) Lund University, Malmˆ, Sweden,
(16) UmeÂ University, UmeÂ, Sweden,
(17) Catalan Institute of Oncology (ICO), Barcelona, Spain,
(18) Epidemiology and Prevention Unit, Milan, Italy,
(19) German Cancer Research Centre (DKFZ), Heidelberg, Germany,
(20) University of Oxford, United Kingdom,
(21) Department of Epidemiology, Murcia Regional Health Council, IMIB-Arrixaca, Murcia, Spain,
(22) Unit of Preventive Medicine and Public Health, School of Medicine, University of Murcia, Spain,
(23) Department of Public Health, Section for Epidemiology, Aarhus University, Aarhus, Denmark,
(24) Aalborg University Hospital, Aalborg, Denmark,
(25) Cancer Research and Prevention Institute (ISPO), Florence, Italy,
(26) Dipartimento di Medicina Clinica e Chirurgia, Federico II University, Naples, Italy,
(27) Public Health Directorate, Asturias, Spain,
(28) Unit of Cancer Epidemiology, Citta' della Salute e della Scienza Hospital-University of Turin and Center for Cancer Prevention (CPO), Torino, Italy,
(29) Human Genetics Foundation (HuGeF), Torino, Italy,
(30) Andalusian School of Public Health, Granada, Spain,
(31) Instituto de InvestigaciÛn Biosanitaria de Granada (Granada.ibs), Granada (Spain),
(32) International Agency for Research on Cancer, Lyon, France,
(33) Danish Cancer Society Research Center, Copenhagen, Denmark,
(34) ASP Ragusa, Italy,
(35) National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands,
(36) University Medical Center Utrecht, Utrecht, the Netherlands,
(37) School of Public Health, Imperial College London, UK

International Stroke Genetics consortium (ISGC)

Sudha Seshadri,Department of Neurology,Boston University School of Medicine ,Framingham Heart Study, Boston, MA ,USA
Laura Kilarski,University of Cologne,Germany
Hyacinth I Hyacinth,Aflac Cancer and Blood Disorder Center, Department of Pediatrics,Emory University School of Medicine,Atlanta, GA,USA

Jamary Oliveira-Filho,Stroke and Cardiomyopathy Clinics,Federal University of Bahia, Brazilian National Research Committee (CNPq), Instituto Nacional de Ciencia e Tecnologia em Doencas Tropicais (INCT-DT),Salvador,Brazil
Sandro Marini, Center for Human Genetic Research,Harvard Medical School,Boston, MA,USA
Sunaina Yadav, Imperial College Cerebrovascular Research Unit, Department of Clinical Neuroscience,Imperial College London,London,UK
Paul Nyquist,Department of Anesthesiology and Critical Care Medicine,Johns Hopkins Medicine,Baltimore, MD,USA
Cathryn Lewis,Department of Medical and Molecular Genetics ,King's College London, SGDP Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London,London,UK
Bjorn Hansen ,Department of Clinical Sciences Lund, Neurology,Lund University,Department of Neurology and Rehabilitation Medicine, Skåne University Hospital,Lund,Sweden
Bo Norrving,Sahlgrenska Academy at University of Gothenburg ,Lund University,Department of Neurology and Rehabilitation Medicine,Skåne University Hospital,Lund,Sweden
Gustav Smith ,Department of Clinical Sciences Lund, Cardiology,Lund University ,The Section for Heart Failure and Valvular Disease, VO Heart and Lung medicine,Skane University Hospital,Lund,Sweden
Jonathan Rosand,Department of Neurology,Massachusetts General Hospital,Center for Human Genetic Research,Massachusetts General Hospital (MGH),Boston, MA,USA
Alessandro Biffi,Division of Behavioral Neurology, Department of Neurology,Massachusetts General Hospital,Center for Human Genetic Research,Massachusetts General Hospital (MGH),Boston, MA,USA
Christina Kourkoulis,Department of Neurology,Massachusetts General Hospital,Center for Human Genetic Research,Massachusetts General Hospital (MGH),Boston, MA,USA
Chris Anderson ,Center for Genomic Medicine,Massachusetts General Hospital (MGH),J. Philip Kistler Stroke Research Center, Department of Neurology, Massachusetts General Hospital (MGH),Boston, MA,USA
Anne-Katrin Giese,Department of Neurology,Massachusetts General Hospital, Harvard Medical School, Department of Neurology,J. Philip Kistler Stroke Research Center, MGH,Boston, MA,USA
Ralph Sacco,Department of Neurology,Miller School of Medicine, University of Miami,Miami, FL,USA
Pankaj Sharma,Institute of Cardiovascular Research,Royal Holloway University of London,London,UK
Oh Young Bang,Department of Neurology,Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul ,Korea
Jong-Won Chung,Department of Neurology,Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul ,USA
Gyeong-Moon Kim,Department of Neurology,Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul ,Korea
Qishuai Zhuang,Department of Pharmacology,School of Life Science and Biopharmaceutical Sciences, Shenyang Pharmaceutical University,Shenyang,China
Wayne Sheu,Department of Internal Medicine,Taichung Veterans General Hospital, Taichung,Taiwan
Steven Lubitz,Department of Cardiology,Massachusetts General Hospital, Harvard Medical School,Boston, MA,USA
David Werring,Stroke Research Centre, Department of Brain Repair and Rehabilitation,University College London Institute of Neurology,London,UK
John Hardy,Reta Lila Weston Institute, UCL Institute of Neurology,University College London,London,UK
June Smalley,Reta Lila Weston Institute, UCL Institute of Neurology,University College London,London,UK
Romain Bourcier,Department of Neuroradiology,University Hospital of Nantes,Nantes,France

Joanna Howson,MRC/BHF Cardiovascular Epidemiology Unit, Department of Public Health and Primary Care,University of Cambridge,Cambridge,UK
Alessandra Granata, Department of Clinical Neurosciences ,University of Cambridge,Cambridge,UK
Anna Drazyk,Department of Clinical Neurosciences,University of Cambridge,Cambridge,UK
Hugh Markus,Stroke Research Group, Division of Clinical Neurosciences,University of Cambridge ,Cambridge,UK
Joanna Wardlaw,Neuroimaging Sciences,University of Edinburgh ,Centre for Clinical Brain Sciences,University of Edinburgh , Edinburgh,UK
Braxton Mitchell,Department of Medicine,University of Maryland School of Medicine ,Geriatrics Research and Education Clinical Center,Baltimore Veterans Administration Medical Center,Baltimore, MD,USA
John Cole,Department of Neurology,University of Maryland School of Medicine and Baltimore VAMC,Baltimore, MD,USA
Anbupalam Thalamuthu,Centre for Healthy Brain Ageing, Psychiatry,University of New South Wales (UNSW),Sydney,Australia
Jemma Hopewell,Clinical Trial Service Unit and Epidemiological Studies Unit, Nuffield Department of Population Health,University of Oxford,Oxford,UK
Robin Walters,Clinical Trial Service Unit and Epidemiological Studies Unit, Nuffield Department of Population Health,University of Oxford,Oxford,UK
Iain Turnbull,Clinical Trial Service Unit and Epidemiological Studies Unit, Nuffield Department of Population Health,University of Oxford,Oxford,UK
Bradford Worrall,Departments of Neurology and Public Health Sciences,University of Virginia School of Medicine,Charlottesville, VA,USA
Josh Bis,Cardiovascular Health Research Unit, Department of Medicine,University of Washington ,Seattle, WA,USA
David Tirschwell,Comprehensive Stroke Care at the UW Medicine Stroke Center at Harborview Medical Center,University of Washington , Seattle, WA,USA
Alex Reiner,Department of Epidemiology,University of Washington ,Fred Hutchinson Cancer Research Center, University of Washington, Seattle, WA,USA
Raj Dhar,Department of Neurology,Washington University School of Medicine,St. Louis, MO,USA
Laura Heitsch,Department of Neurology, Radiology, and Biomedical Engineering,Washington University School of Medicine,St. Louis, MO,USA
Jin-Moo Lee,Department of Neurology, Radiology, and Biomedical Engineering, Washington University School of Medicine,St. Louis, MO,USA
Janne Mortenson,Department of Neurology,Aarhus University Hospital,Aarhus,Denmark
Sylvia Wassertheil-Smoller ,Department of Epidemiology and Population Health,Albert Einstein College of Medicine,New York, NY,USA
Kameshwar Prasad,Department of Neurology and Stroke Unit;and Director of Clinical Epidemiology,,All India Institute of Medical Sciences (AIIMS),New Delhi,India
Mark Fisher,Department of Neurology,University of Massachusetts Medical School ,Worchester, MA,USA
Christopher Traenka,Neurology Clinic,Basel University Hospital,Basel,Switzerland
Xingwu Wang,Beijing Hypertension League Institute,Beijing,China
Yongjun Wang,Center of Stroke,Beijing Insitute for Brain Disorders,Department of Neurology ,Beijing Tiantan Hospital, Capital Medical University,Beijing,China
Francois Rouanet,Department of Neurology,Bordeaux University Hospital,Bordeaux,France
Igor Sibon,Department of Neurology,Bordeaux University Hospital,Bordeaux,France
Chloé Sarnowski,Department of Biostatistics,Boston University,Boston,USA
Pauline Maillard,Department of Neurology,University of California at Davis,Sacramento, CA,USA
Aleksandra Pikula,Department of Neurology,University of Toronto,Toronto,USA
Hugo Javier Aparicio,Department of Neurology,Boston University School of Medicine,Boston,USA
Philip Wolf,Boston University School of Medicine,Boston,USA

Josee Dupuis,Boston University School of Public Health,Boston,USA
Qiong Yang,Boston University School of Public Health,Boston,USA
Gustavo Luvizutto,Rehabilitation department,Botucatu Medical School,Botucatu School of Medicine,University Estadual Paulista Júlio de Mesquita Filho, District of Rubião Junior,Botucatu,Brazil
Daniel Chasman,Division of Preventive Medicine,Brigham and Women's Hospital,Harvard Medical School,Boston, MA,USA
Kathryn Rexrode,Department of Medicine,Brigham and Women's Hospital,Harvard Medical School,Boston,USA
Andrea Harriot,Department of Neurology,Brigham and Women's Hospital, Massachusetts General Hospital,Boston, MA,USA
Chia-Ling Phuah,Center for Human Genetic Research, Massachusetts General Hospital (MGH),Division of Neurocritical Care and Emergency Neurology, Department of Neurology,Boston, MA,USA
Gustavo Santo ,Stroke Unit,Centro Hospitalar e Universitário de Coimbra, CHUC,Coimbra,Portugal
Ales Tomek,Department of Neurology, 2nd Faculty of Medicine,Charles University in Prague and Motol University Hospital,Prague,Czech Republic
Jen Gerard,Department of Cardiology,Children's Hospital of Wisconsin,Milwaukee,USA
Cara Carty,Children's Research Institute,Children's National Medical Center,Center for Translational Science,George Washington University,Washington,USA
Guiyou Liu,Chinese Academy of Sciences (CAS),Beijing,China
Sanjith Aaron,Department of Neurological Sciences,Christian Medical College,Vellore,India
Christhunesa S. Christudass,Department of Neurological Sciences,Christian Medical College,Vellore,India
BSB Salomi,Department of Neurological Sciences,Christian Medical College,Vellore,India
Dharambir Sanghera,Department of Pediatrics,College of Medicine, University of Oklahoma Health Sciences Center,Department of Pharmaceutical Sciences,College of Pharmacy, University of Oklahoma Health Sciences Center,Oklahoma City,USA
Amelia Boehme,Department of Neurology,Columbia University,New York,USA
Mitchell Elkind,Neurological Institute of New York,Columbia University College,New York,USA
Gudmar Thorleifsson,deCODE genetics/AMGEN inc,Reykjavik,Iceland
Solveig Gretarsdottir,deCODE genetics/AMGEN inc,Reykjavik,Iceland
Leslie Lange,University of Colorado Denver - Anschutz Medical Campus,Denver, CO,USA
Natalia Rost,Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA,Department of Neurology, J. Philip Kistler Stroke Research Center, MGH,Boston, MA,USA
Michael James,Translational Acute Brain Injury Research Center,Duke University,Durham,USA
Jill Stewart ,Department of Neurology,Duke University School of Medicine,Durham,USA
Larry Goldstein,Department of Medicine, Duke Stroke Center,Duke Univesrity School of Medicine,Durham, NC ,USA
Salina Waddy,Cardiovascular and Stroke Genetics Working Group,Emory University,Atlanta,USA
Carla Ibrahim-Verbaas,Department of Neurology,Erasmus MC ,Rotterdam,Netherlands
Dina Vojinovic,Department of Epidemiology,Erasmus MC, University Medical Center Rotterdam,Clinic for Neurology and Psychiatry for Children and Youth,University of Belgrade, Faculty of Medicine,Rotterdam,Netherlands
Arfan Ikram,Department of Epidemiology,Erasmus University Medical Center,Rotterdam,Netherlands
Hieab Adams,Department of Epidemiology,Erasmus University Medical Center,Rotterdam,Netherlands
Fadi Charchar,L.E.W. Carty Cardiovascular Genomics laboratory,Federation University Australia,Ballarat,Australia
Vincent Thijs,Stroke Division,Florey Institute of Neuroscience and Mental Health,Department of Neurology,Austin Health,Heidelberg,Australia

Eugenio Parati,Laboratory of Cellular Neurobiology,Fondazione IRCCS Istituto Neurologico C. Besta, Cerebrovascular Disease Unit,Cerebrovascular Disease Unit,Fondazione IRCCS Istituto Neurologico C. Besta,Milan,Italy
Giorgio Boncoraglio,Department of Cerebrovascular Diseases,Fondazione IRCCS Istituto Neurologico Carlo Besta,Milan,Italy
Charles Kooperberg,Division of Public Health Sciences,Fred Hutchinson Cancer Research Center,Seattle,USA
Sherrine Abboud,Laboratory of Experimental Neurology,Free University of Brussels (ULB),Brussels,Belgium
Ramin Zand,Department of Neuroscience,Geisinger Health System,Danville,USA
Philippe Bijlenga,Departement des neurosciences cliniques, Clinique de neurochirurgie,Geneva University Hospital,Geneva,Switzerland
Magdy Selim ,Beth Israel Deaconess Medical Center,Harvard Medical School,Boston,USA
caspar Grond-Ginsbach,Department of Neurology,Heidelberg University Hospital,Heidelberg,Germany
Olli Happola,Department of Neurology,Helsinki University Central Hospital ,Helsinki,Finland
Daniel Strbian,Department of Neurology,Helsinki University Central Hospital ,Clinical Neurosciences, Neurology,University of Helsinki,Helsinki,Finland
Liisa Tomppo,Department of Neurology,Helsinki University Central Hospital ,Helsinki,Finland
Hanne Sallinen,Department of Neurology,Helsinki University Hospital ,Helsinki,Finland
Abhishek Pathak,Department of Neurology,Heritage Hospital,Department of Neurology,Neuro Expert Clinic,Varanasi,India
Dorothea Pfeiffer,Department of Neurology,Hiedelberg University Hospital,Heidelberg,Germany
Pablo Bonardo,Department of Neurology,Hospital Británico de Buenos Aires,Ciudad Autónoma de Buenos Aires,Argentina
Joao Jose Freitas de Carvalho,Hospital Geral de Fortaleza/SUS Fortaleza,Ceará,Brazil
Priscila Ribeiro,Hospital Governador Celso Ramos,Florianópolis,Brazil
Nuria Torres,Stroke Pharmacogenomics and Genetics,Hospital Mútua de Terrassa, Fundació Docència i Recerca Mútua Terrassa,Terrassa,Spain
Miguel Barboza,Department of Neurology,Hospital Rafael A. Calderon Guardia,San Jose,Costa Rica
Melanie Laarman,Cardiac Development and Genetics Group,Hubrecht Institute,Utrecht,Netherlands
Roberta Carriero,Inflammation and immunology laboratory,Humanitas Clinical Institute,Pavia,Italy
Elizabeth Holliday,Public Health Stream,Hunter Medical Research Institute,Faculty of Health and Medicine,University of Newcastle,New Lambton,Australia
Androniki Plomaritoglou,Neurology,Hygeia Hospital,Marousi,Greece
Johan Bjorkegren,Department of Genetic and Genomic Sciences,Icahn School of Medicine,New York,USA
Yu-Feng Yvonne Chan,Department of Genetic and Genomic Sciences,Icahn School of Medicine, Mount Sinai,New York,USA
Villi Gudnason,Icelandic Heart Association Research Institute,Faculty of Medicine,University of Iceland,Kopavogur,Iceland
Jordi Jimenez-Conde,Neurovascular Research Group (NEUVAS). Neurology Department. ,IMIM - Hospital del Mar,Barcelona,Spain
Carolina Soriano,Department of Neurology, Neurovascular Research Group,IMIM-Hospital del Mar,Barcelona,Spain
Jaume Roquer,Neurology Service,IMIM-Hospital del Mar, Institut Hospital del Mar d'investigacions Mèdiques,Barcelona,Spain
Paul Bentley,Faculty of Medicine, Department of Medicine ,Imperial College London,London,UK
Dipender Gill,Centre for Pharmacology and Therapeutics,Imperial College London ,London,UK
Ganesh Chauhan,Centre for Brain Research,Indian Institute of Science,Bangalore,India
Elisabeth Tournier-Lasserve ,UMR-S 740,INSERM,Paris,France
Sara Kaffashian,INSERM U1219 Bordeaux Population Health Research Center,Bordeaux,France

Cecilia Samieri,INSERM U1219 Bordeaux Population Health Research Center,ISPED,University of Bordeaux,Bordeaux,France
Carole Dufouil ,INSERM U1219 Bordeaux Population Health Research Center,Department of Public Health,CHU Bordeaux,Bordeaux,France
Stephanie Debette,INSERM U1219 Bordeaux Population Health Research Center, Bordeaux, France,University of Bordeaux,France
Aniket Mishra,INSERM U1219 Bordeaux Population Health Research Center, Bordeaux, France,University of Bordeaux,France
Lawrence Wee,Data Analytics Department,Institute for Infocomm Research (I2R),Singapore,Singapore
Saima Siddiqi,Institute of Biomedical And Genetic Engineering,Islamabad,Pakistan
Jer-Yuarn Wu,Institute of Biomedical Sciences, Academia Sinica ,Taipei,Taiwan
Tai-Ming Ko,Institute of Biomedical Sciences, Academia Sinica , Graduate Institute of Integrated Medicine, China Medical University,Taipei,Taiwan
Silvia Bione,Computational Biology Unit,Institute of Molecular Genetics-National Research Council,Pavia,Italy
Katarina Jood,Department of Clinical Neuroscience ,Institute of Neuroscience and Physiology, Sahlgrenska Academy at University of Gothenburg ,Gothenburg,Sweden
Turgut Tatlisumak,Department of Clinical Neuroscience ,Institute of Neuroscience and Physiology, Sahlgrenska Academy at University of Gothenburg , Sahlgrenska University Hospital,Gothenburg,Sweden
Lukas Holmegaard,Department of Clinical Neuroscience,Institute of Neuroscience and Physiology, Sahlgrenska Academy at University of Gothenburg ,Gothenburg,Sweden
Antonio Arauz,Stroke Clinic,Instituto Nacional de Neurologia y Neurocirugia, Manuel Velasco Suarez,Mexico City,Mexico
Michal Korostynski,Department of Molecular Neuropharmacology,Polish Academy of Sciences,Warsaw,Poland
Lenore Launer,Laboratory of Epidemiology and Population Science,Intramural Research Program, National Institutes of Health, National Institute on Aging,Bethesda,USA
Suo Yue,Ion Torrent by Life Technologies (company),Carnegie Mellon University,San Francisco,USA
anna bersano,Cerebrovascular Unit,IRCCS Foundation C. Besta Neurological Institute,Milan,Italy
Tomasz Dziedzic,Department of Neurology,Jagiellonian University,Krakow,Poland
Karol Józef Juchniewicz ,Jagiellonian University,Krakow,Poland
Adamski Mateusz,Jagiellonian Centre for Experimental Therapeutics,Jagiellonian University ,Krakow,Poland
Joanna Pera,Department of Neurology,Jagiellonian University Medical College,Krakow,Poland
Agnieszka Slowik,Department of Neurology,Jagiellonian University Medical College,Krakow,Poland
Andrzej Urbanik ,Department of Radiology,Jagiellonian University Medical College,Krakow,Poland
Jerzy Gasowski,Department of Internal Medicine and Gerontology,Jagiellonian University Medical College,Krakow,Poland
Rafa? Olszanecki,Faculty of Medicine,Jagiellonian University Medical College,Krakow,Poland
Marcin Wnuk,Jagiellonian University Medical College,Poland
Christopher Levi,John Hunter Hospital, Hunter Medical Research Institute and University of Newcastle,Newcastle,Australia
Aaron Gusdon,Department of Neurology,Johns Hopkins Medicine,University of Pittsburgh School of Medicine,Baltimore,USA
Konstantinos Kostulas,Department of Clinical Neuroscience ,Karolinska Institute,Stockholm,Sweden
Milita Crisby,Division of Clinical Geriatrics, Neurobiology Care Sciences and Society,Karolinska Institute,Huddinge,Sweden
Lina Keller,Karolinska Institutet,Stockholm,Sweden
Kristina Schlicht,Institut für Medizinische Informatik und Statistik,Kiel University,Kiel,Germany

Jessye Maxwell,Social genetic and Developmental Psychiatry,King's College London,London,
Christof Haffner,Institute for Stroke and Dementia Research,Klinikum der Universität München,Munich,Germany
Marco Duering,Institute for Stroke and Dementia Research,Klinikum der Universität München, Ludwig-Maximilians-University LMU,Munich,Germany
Jeremiasz Jagiella,Krakow University Hospital,Krakow,Poland
Robin Lemmens,Department of Neurosciences, Experimental Neurology,KU Leuven – University of Leuven,Department of Neurology,University Hospitals Leuven, VIB Center for Brain & Disease Research ,Leuven,Belgium
Jun Hata,Department of Epidemiology and Public Health,Kyushu University, Graduate School of Medical Sciences,Fukuoka,Japan
Toshiharu Ninomiya,Department of Epidemiology and Public Health,Kyushu University, Graduate School of Medical Sciences ,Fukuoka,Japan
Vinh Nguyen,School of Psychological Science,La Trobe University,Melbourne,Australia
Bjorn Logi Thorarinsson,Department of Neurology,Landspítali Háskólasjúkrahús,Reykjavík,Iceland
Saskia Lesnik Oberstein,Department of Clinical Genetics,Leiden University Medical Center,Leiden,Netherlands
Tsong-Hai Lee,Neurology department and Stroke center ,Linkou Chang Gung Memorial Hospital,Taipei,Taiwan
Alexandr Rakitko,Lomonosov Moscow State University,Moscow,Russia
Rainer Malik,Institute for Stroke and Dementia Research,Ludwig-Maximilians-University, Klinikum der Universität München,Munich,Germany
Martin Dichgans,Institute for Stroke and Dementia Research,Ludwig-Maximilians-University, Klinikum der Universität München ,Munich Cluster for Systems Neurology (SyNergy),Munich,Germany
Arne Lindgren,Department of Clinical Sciences Lund, Neurology,Lund University,Department of Neurology and Rehabilitation Medicine,Skåne University Hospital,Lund,Sweden
Johan Wasselius,Department of Clinical Sciences Malmö,Lund University,Vascular Center,Skåne University Hospital,Malmö,Sweden
Mattias Drake,Diagnostic Radiology,Lund University,Lund,Sweden
Olle Melander,Department of Clinical Sciences,Lund University,Lund,sweden
Martin Stenman,Geriatric Medicine,Lund University,Lund,Sweden
Andreea Ilinca,Neurology,Lund University,Lund,Sweden
Julie Staals,Department of Neurology,Maastricht University Medical Center (MUMC+), Cardiovascular Research Institute Maastricht (CARIM),Maastricht,Netherlands
Ariane Sadr-Nabavi,Medical Genetics Research Center (MGRC),Mashhad University of Medical Sciences (MUMS), School of Medicine,Department of Medical Genetics,Mashhad University of Medical Sciences (MUMS), Faculty of Medicine,Mashhad,Iran
Katherine Crawford,Center for Genomic Medicine ,Massachusetts General Hospital,Boston, MA,USA
Jose Florez,Center for Human Genetic Research, MGH,Massachusetts General Hospital, Harvard Medical School ,Boston, MA,USA
Umme Lena,Massachusetts General Hospital,South Hadley, MA,USA
Farrah Mateen,Department of Neurology,Massachusetts General Hospital,Boston, MA,USA
Hakan Ay,Department of Neurology,Massachusetts General Hospital,Boston, MA,USA
Ona Wu,Department of Neurology, JPK Stroke Research Center,Massachusetts General Hospital and Harvard Medical School, Department of Radiology ,Athinoula A. Martinos Center for Biomedical Imaging, MGH,Boston, MA,USA
Markus Schirmer,Department of Neurology, J. Philip Kistler Stroke Research Centre,Massachusetts General Hospital and Harvard Medical School,Boston,USA
Javier Romero,Division of Neurocritical Care and Emergency Neurology, Department of Neurology,Massachusetts General Hospital, Harvard Medical School,J. P. Kistler Stroke Research Center,Massachusetts General Hospital, Harvard Medical School,Boston, MA,USA

Rebecca Jackson,Center for women's health,Ohio State University Wexner Medical Center,Colombus,USA
Eva Giralt,Parc de Salut Mar,Barcelona,Spain
Danish Saleheen,Department of Genetics,Perelman School of Medicine, University of Pennsylvania,Pennsylvania, PA,USA
Frank-Erik de Leeuw,Department of Neurology,Radboud University Medical Center,Nijmegen,Netherlands
Karin Klijn,Department of Neurology,Radboud University Medical Centre, Donders Institute for Brain, Cognition and Behaviour,Department of Neurology and Neurosurgery,University Medical Center, Brain Center Rudolf Magnus,Nijmegen,Netherlands
Jes Olesen,Department of Clinical Medicine,Rigshospitalet - Neurocentret,Glostrup,Denmark
Yoichiro Kamatani,Laboratory for Statistical Analysis,RIKEN Center for Integrative Medical Sciences,Center for Genomic Medicine ,Kyoto University Graduate School of Medicine,Yokohama,Japan
Michiaki Kubo,RIKEN Center for Integrative Medical Sciences,Yokohama,Japan
Yukinori Okada,Laboratory for Statistical Analysis,RIKEN Center for Integrative Medical Sciences,Department of Statistical Genetics, Osaka University Graduate School of Medicine,Yokohama,Japan
David Spence,Stroke Prevention & Atherosclerosis Research Centre,Robarts Research,London (ON),Canada
Annie Pedersen,Västra Vötalandsregionen,Sahlgrenska Academy at University of Gothenburg,Gothenburg,Sweden
Maja Olsson,Department of Medical and Clinical Genetics, Institute of Biomedicine,Sahlgrenska Academy at University of Gothenburg ,Gothenburg,Sweden
Turgut Tatlisumak,Department of Clinical Neurosciences/Neurology,Sahlgrenska Academy at University of Gothenburg, Institute of Neuroscience and Physiology,Sahlgrenska University Hospital,Gothenburg,Sweden
Giacomo Giacalone,Neurology Department,San Raffaele Scientific Institute,University Vita-Salute San Raffaele,Milan,Italy
Juan José Martín,Department of Neurology,Sanatorio Allende,Cordoba,Argentina
Rodrigo Bazan,Department of Neurology,São Paulo State University (Unesp) Botucatu Medical School,Botucatu,Brazil
Gabriel Braga,Hospital das Clínicas,São Paulo State University (Unesp) Botucatu Medical School,Botucatu,Brazil
Steve Bevan,School of Life Science, University of Lincoln,Lincoln,UK
Huichun Xu,Medicine department,School of Medicine, University of Maryland,Baltimore,USA
Tim Assimes,Cardiovascular Medicine,School of Medicine, University of Stanford,Stanford,USA
Jamie Wright ,Anderson Cancer Center, MD Anderson
Clinical Cancer Genetics,School of Medicine, University of Texas,Houston,USA
Anton Raskurazhev,Scientific Center of Neurology,Moscow,Russia
Wei Ling Lee,National Neuroscience Institute,Singapore General Hospital,Department of Pediatrics,National University of Singapore, Yong Loo Lin School of Medicine,Singapore,Singapore
Eng King Tan,Department of Neurology,Singapore General Hospital, National Neuroscience Institute,Neuroscience and Behavioral Disorders Program,Duke-National University of Singapore Graduate Medical School,Singapore,Singapore
Philippe Burri,Department of Cardiology,Skane University Hospital,Malmö,Sweden
Petrea Frid,Critical Care Neurology,Skåne University Hospital, Lund university,Malmö,Sweden
Christian Opherk,Department of Neurology,SLK-Kliniken Heilbronn GmbH,Heilbronn,Germany
Chaeyoung Lee,Department of Bioinformatics and Life Science,Soongsil University,Seoul,Korea
David Tregouet,Team Genomics and Pathophysiology of Cardiovascular Diseases,Sorbonne Universités, UPMC Univ. Paris 06, INSERM, UMR_S 1166,ICAN Institute for Cardiometabolism and Nutrition,Paris,France

Zhen Deng,Department of Neurology,Southern Medical University, FIMMU,Guangzhou,China
Hung Yi Chiou,School of Public Health, College of Public Health and Nutrition,Taipei Medical University,Taipei,Taiwan
Mahdi Habibi-koolaee,Department of Health Information Management,Tehran University of Medical Sciences (TUMS),Tehr?n,Iran
Murali Vijayan,Garrison Institute on Aging,Texas Tech University Health Sciences Center,Lubbock,USA
Thomas Leung,Division of Neurology, Department of Medicine and Therapeutics,The Chinese University of Hong Kong,Hong-Kong,Hong-Kong
Lawrence Wong,Division of Neurology, Department of Medicine and Therapeutics,The Chinese University of Hong Kong,Hong-Kong,Hong-Kong
Vincent Mok,Department of Medicine and Therapeutics,The Chinese University of Hong Kong,Hong-Kong,Hong-Kong
Richard Choy,Department of Obstetrics and Gynecology,The Chinese University of Hong Kong,Hong-Kong,Hong-Kong
Christina Jern,Department of Pathology and Genetics,The Sahlgrenska Academy at University of Gothenburg, Institute of Biomedicine,Gothenburg,Sweden
Elena Lebedeva,Department of Neurology and Neurosurgery,The Urals State Medical University,International Headache Center 'Europe-Asia',Yekaterinburg,Russia
Martin Farrall,Department of Cardiovascular Medicine,The Wellcome Trust Centre for Human Genetics,Oxford,UK
Xu Jiayuan,Department of radiology,Tianjin Medical University (TIJMU),Tianjin,China
Keat Wei Loo,Tunku Abdul Rahman University, UTAR,Kampar Perak,Malaysia
Isabel Hostettler,Stroke Research Center,UCL Institue of Neurology,London,UK
Gabriel Rinkel,Department of Neurology and Neurosurgery,UMC Utrecht, Brain Center Rudolf Magnus,Utrecht,Netherlands
Anderson Goncalves,Universidade da Região de Joinville,Joinville,Brazil
Paulo Franca,Department of Medicine,Universidade da Região de Joinville – Univille,Joinville,Brazil
Norberto Cabral,Department of Medicine,Universidade da Região de Joinville (Univille),Joinville,Brazil
Iscia Cendes,Molecular Genetics Laboratory,Universidade Estadual de Campinas, Faculdade de Ciências Médicas,Campinas,Brazil
Caty Carrera,Neurovascular Research Laboratory, Vall d'Hebron Institut of Research, Neurology and Medicine Departments,Universitat Autònoma de Barcelona, Vall d'Hebrón Hospital,Stroke Pharmacogenomics and Genetics,Fundacio Docència i Recerca Mutua Terrassa,Spain
Israel Fernandez-Cadenas,Neurovascular Research Laboratory, Vall d'Hebron Institut of Research, Neurology and Medicine Departments,Universitat Autònoma de Barcelona, Vall d'Hebrón Hospital,Stroke Pharmacogenomics and Genetics,Fundacio Docència i Recerca Mutua Terrassa,Barcelona,Spain
Joan Montaner ,Neurovascular Research Laboratory,Universitat Autònoma de Barcelona, Vall d'Hebron Institute of Research,Neurology Department,Hospital Vall d'Hebron,Barcelona,Spain
Helen Kim ,Institute for Human Genetics, The Center for Cerebrovascular Research (CCR),Université de Californie,San Francisco,USA
Arndt Rolfs,Albrecht Kossel Institute,University Clinic of Rostock,Rostock,Germany
Mayowa Owolabi,Department of Neurology,University College Hospital,Ibadan,Nigeria
Reecha Sofat,Metabolism & Experi Therapeutics, Div of Medicine, Faculty of Medical Sciences,University College London,London,UK
Mark Bakker,University Medical Center Utrecht,Utrecht,Netherlands
Dominique PV de Kleijn,Laboratory of Experimental Cardiology,University Medical Center Utrecht,ICIN-Netherlands Heart Institute,Utrecht,Netherlands

Ynte Ruigrok,Department of Neurology and Neurosurgery,University Medical Center Utrecht, Brain Center Rudolf Magnus,The Dutch Parelsnoer Institute-Cerebrovascular accident (CVA) Study Group,Utrecht,Netherlands
Allard Hauer,Department of Neurology and Neurosurgery,University Medical Center Utrecht, Brain Center Rudolf Magnus,Utrecht,Netherlands
Sara L. Pulit,Department of Neurology,University Medical Center Utrecht, Brain Center Rudolf Magnus,Utrecht,Netherlands
Ale Algra,Department of Neurology and Neurosurgery,University Medical Center Utrecht, Brain Center Rudolf Magnus,Julius Center for Health Sciences and Primary Care,University Medical Center Utrecht,Utrecht,Netherlands
Sander W. van der Laan,Laboratory of Experimental Cardiology,University Medical Center Utrecht, Division of Heart and Lungs ,Utrecht,Netherlands
Mary Macleod,Dept of Medicine & Therapeutics,University of Aberdeen, King's College,Aberdeen,UK
George Howard,School of Public Health,University of Alabama,Birmingham, AL,USA
Hemant Tiwari,Department of Biostatistics,University of Alabama,Birmingham, AL,USA
Ryan Irvin,Department of Epidemiology,University of Alabama at Birmingham,Birmingham, AL,USA
Karen C. Albright,Neurology,University Of Alabama Hospital, Spectrum Health - Butterworth Campus,Birmingham, AL,USA
Rodney Perry,Department of Epidemiology,University of Alabama School of Medicine,Birmingham, AL,USA
Chelsea Kidwell,Department of Neurology,University of Arizona,Stroke Center at Georgetown,University of Georgetown,Tucson, AZ,USA
Aleksandra Pavlovic,Neurology Clinic, Clinical Center of Serbia,University of Belgrade, Faculty of Medicine,Belgrade,Serbia
Christophe Tzourio,University of Bordeaux,INSERM U1219,Bordeaux,France
Murali Sargurupremraj,INSERM U1219 Bordeaux Population Health Research Center ,University of Bordeaux,Bordeaux,France
Sabrina Schilling,University of Bordeaux,Bordeaux,
Alessandro Padovani,Department of Clinical and Experimental Sciences,University of Brescia,Brescia,Italy
Alessandro Pezzini,Department of Clinical and Experimental Sciences,University of Brescia, Neurology Clinic,Brescia,Italy
Foad Abd-Allah,Department of Neurology,University of Cairo,Cairo,Egypt
Charles DeCarli,Alzheimer’s Disease Center,University of Californa Davis,Sacramento, CA ,USA
Yuqi Zhao,Department of Integrative Biology and Physiology,University of California, Los Angeles, CA,USA
David Liebeskind,Department of Neurology,University of California, Los Angeles, CA,USA
Matthew Traylor,Stroke Research Group, Division of Clinical Neurosciences,University of Cambridge,Cambridge,UK
Rhea Tan,Department of Clinical Neurosciences,University of Cambridge,Cambridge,England
John Danesh,MRC/BHF Cardiovascular Epidemiology Unit, Department of Public Health and Primary Care, ,University of Cambridge ,The National Institute for Health Research Blood and Transplant Research Unit in Donor Health and Genomics, Wellcome Trust Sanger Institute,Cambridge,UK
Susanna C. Larsson, Department of Clinical Neurosciences, Neurology Unit,University of Cambridge,Cambridge,UK
Loes Rutten-Jacobs,Stroke Research Group,University of Cambridge, Division of Clinical Neurosciences,DZNE,Cambdrige,UK
Amanda Donatti,School of Medical Sciences, FCM,University of Campinas, UNICAMP,São Paulo,Brazil

Wagner Avelar,Department of Neurology,University of Campinas, UNICAMP,São Paulo,Brazil
Joseph Broderick,Gardner Neuroscience Institute, Comprehensive Stroke Center,University of Cincinnati,Cincinnati, OH,USA
Daniel Woo,University of Cincinnati College of Medicine,Cincinnati, OH,USA
Brett Kissela,Department of Neurology and Rehabilitation Medicine,University of Cincinnati Gardner Neuroscience Institute, Comprehensive Stroke Center,Cincinnati, OH,USA
Laura Garcia Ibenez,Institute for Cancer Genetics,University of Columbia,New York,USA
Rustam Salman,Centre for Clinical Brain Sciences,University of Edinburgh, Edinburgh,UK
Cathie Sudlow,Department of Neurology,University of Edinburgh, Edinburgh,UK
Kristiina Rannikmae,Department of Neurology,University of Edinburgh,Edinburgh,UK
Caitrin Wheeler McDonough,College of Pharmacy,University of Florida,Gainesville, FL,USA
Scott Silliman,Department of Neurology,University of Florida College of Medicine,Jacksonville, FL,USA
Oyunbileg Magvanjav,Department of Pharmacotherapy and Translational Research and Center for Pharmacogenomics,University of Florida, College of Pharmacy,Gainesville, FL,Japan USA
Tom van Agtmael,Insittute of Cardiovascular and Medical Sciences,University of Glasgow,Glasgow,UK
Matthew Walters,School of Medicine, Dentistry and Nursing,University of Glasgow,Glasgow,UK
Martin Söderholm,Bioinformatics Core Facility,University of Gothenburg,Gothenburg,Sweden
Erik Lorentzen,Bioinformatics Core Facility,University of Gothenburg,Gothenburg,Sweden
Sandra Olsson,University of Gothenburg,Gothenburg,Sweden
Tara Stanne,University of Gothenburg,Gothenburg,Sweden
Martina Olsson,University of Gothenburg,Gothenburg,Sweden
Kazuma Nakagawa,University of Hawaii, John A. Burns School of Medicine,Department of Neurology,The Queen's Medical Center,Honolulu,USA
Rufus Akinyemi,Institute for Advanced Medical Research and Training,University of Ibadan, College of Medicine ,Ibadan,Nigeria
Ioana Cotlatciuc,Institute of Cardiovascular Research Royal Holloway,University of London ,London,UK
Jeff O'Connell,Medicine department,University of Maryland,Animal Genetics Improvement Laboratory,United States Department of Agriculture,Baltimore, MD,USA
Mary Sparks ,Department of Neurology,University of Maryland,Baltimore, MD,USA
John Sorkin,Department of Neural and Pain Sciences,University of Maryland,Baltimore, MD,USA
Patrick McArdle,Division of Endocrinology, Diabetes and Nutrition,University of Maryland School of Medicine,Baltimore, MD,USA
Tushar Dave,Bioinformatics,University of Maryland School of Medicine,Baltimore, MD,USA
Colin Stine,Epidemiology & Public Health,University of Maryland School of Medicine,Baltimore, MD,USA
Steven Kittner,Department of Neurology,University of Maryland School of Medicine and Baltimore VAMC, MD, USA,Baltimore, MD,USA
Jill Naylor,University of Melbourne,Melbourne,Australia
Devin Brown,Department of Neurovascular,University of Michigan Medical School,Ann Arbor,USA
Mario Di Napoli,Department of Neurology,University of Naples,Naples,Italy
Rose Du,Comprehensive Cancer Center,University of New Mexico, Albuquerque, NM,USA
Tobias B. Kulik,Neurology,University of New Mexico,Albuquerque, NM ,USA
John Attia,School of Medicine and Public Health,University of Newcastle,New Lambton,Australia
Shahbaz Zamani,University of Newcastle,Newcastle,Australia
James E Faber,Cell Biology and Physiology,University of North Carolina,Chapel Hill,USA
Peter Rothwell,Nuffield Department of Clinical Neurosciences,University of Oxford,Oxford,UK
Iona Millwood,Nuttfield Department of Population Health,University of Oxford,Oxford,UK
Elsa Valdés Márquez,CTSU-Clinical Trial Service Unit and Epidemiological Studies Unit,University of Oxford,Oxford,UK

Michelangelo Mancuso,Department of Neurology,University of Pisa,Pisa,Italy
Doralina Brum Souza,Department of Neurology,University of Sao Paulo,Ribeirao Preto,Brazil
Ranil de Silva,Genetic, Diagnostic and Research Laboratory, Department of Anatomy,University of Sri Jayewardenepura, Faculty of Medical Sciences,Nugegoda,Sri Lanka
Riina Vibo,Department of Neurology and Neurosurgery,University of Tartu,Tartu,Estonia
Janika Korv ,Department of Neurology and Neurosurgery,University of Tartu,Tartu,Estonia
Jane Maguire,Faculty of Health,University of Technology Sydney,Ultimo,Australia
Myriam Fornage,Brown Foundation Institute of Molecular Medicine // Human Genetics Center,University of Texas Health Science Center at Houston,Houston, TX,USA
Kachikwu Illoh,University of Texas Medical School,Houston, TX,USA
Dianna Milewicz,Division of Medical Genetics,University of TexasHealth Science Center, McGovern Medical School,Department of Internal Medicine,University of TexasHealth Science Center, McGovern Medical School,Houston, TX,USA
Jennifer Majersik,Neurology,University of Utah,Salt Lake City, UT,USA
Adam DeHavenon,Department of Neurology,University of Utah,Salt Lake City, UT,USA
Yashar Kalani,Neurobiology and Anatomy ,University of Utah School of Medicine,Salt Lake City, UT,USA
Matthew Alexander,Radiology and Imaging Sciences,University of Utah School of Medicine,Neurosurgery ,University of Utah School of Medicine,Salt Lake City, UT,USA
Mary Cushman,Department of Hematology and oncology,University of Vermont, Medical Center,Colchester,USA
Michele Sale,Center for Public Health Genomics,University of Virginia,Charlottesville, VA,USA
Andrew Southerland ,Departments of Neurology and Public Health Sciences,University of Virginia,Charlottesville, VA,USA
Debra Owens,Newborn Intensive Care Units,University of Virginia Children's Hospital,Charlottesville, VA,USA
Keith Keene,Center for Public Health Genomics,University of Virginia School of Medicine,Charlottesville, VA,USA
Stephen Rich,Center for Public Health Genomics,University of Virginia School of Medicine,Charlottesville, VA,USA
Bruce Psaty,Cardiovascular Health Research Unit, Department of Medicine,University of Washington,Department of Epidemiology,University of Washington,Seattle, WA,USA
Will Longstreth,Department of Epidemiology,University of Washington,Department of Neurology,University of Washington,Seattle,USA
Masharip Atadzhanov,Department of Neurology,University Teaching Hospital,Lusaka,Zambia
Stacey Quintero Wolfe,Wake Forest Baptist Health,Winston-Salem, NC ,USA
Carl Langefeld,Center for Public Health Genomics and Department of Biostatistical Sciences,Wake Forest School of Medicine,Winston-Salem, NC,USA
Cheryl Bushnell,Department of Neurology,Wake Forest University Medical Center,Winston-Salem, NC,USA
Carlos Cruchaga,Department of Psychiatry,The Hope Center Program on Protein Aggregation and Neurodegeneration (HPAN),Washington University School of Medicine,Department of Developmental Biology, Washington University School of Medicine,St. Louis, MO,USA
Jan Konrad,Department of Psychiatry,The Hope Center Program on Protein Aggregation and Neurodegeneration (HPAN),Washington University, School of Medicine,St. Louis, MO,USA
Junfeng Liu,West China Medical School, Sichuan University,Sichuan,China
Kevin Sheth ,Department of Neurology, Neuro Intensive Care & Neurological Emergencies ,Yale School of Medicine,Nw Haven, CT,USA
Guido Falcone,Department of Neurology,Yale University School of Medicine, Program in Medical and Population Genetics,The Broad Institute of Harvard and MIT,New Haven, CT ,USA
Kathleen Donahue,J. Philip Kistler Stroke Research Center,Massachusetts General Hospital,USA

METASTROKE consortium

Agnieszka Slowik [1], Albert Hofman [2], Ale Algra [3], Alex P Reiner [4], Alexander S F Doney [5], Andreas Gschwendtner [6], Andreea Ilinca [7], Anne-Katrin Giese [8], Arne Lindgren [9], Astrid M Vicente [10], Bo Norrving [11], Børge G Nordestgaard [12], Braxton D Mitchell [13], Bradford B Worrall [14], Bruce M Psaty [15], Cara L Carty [16], Cathie Sudlow [17], Christopher D Anderson [18], Christopher Levi [19], Claudia L Satizabal [20], Colin N A Palmer [5], Dale M Gamble [21], Daniel Woo [22], Danish Saleheen [23], E Bernd Ringelstein [24], Einar Valdimarsson [25], Elizabeth Holliday [26], Gail Davies [27], Ganesh Chauhan [28], Gerard Pasterkamp [29], Giorgio Boncoraglio [30], Gregor Kuhlenbäumer [31], Gudmar Thorleifsson [32], Guido J Falcone [33], Guillame Pare [34], Helena Schmidt [35], Hossein Delavaran [11], Hugh S Markus [36], Hugo J Aparicio [37], Ian Dreary [27], Ioana Cotlarciuc [38], Israel Fernandez-Cadenas [39], James Meschia [21], Jemma C Hopewell [40], Jingmin Liu [41], Joan Montaner [42], Joanna Pera [1], John Cole [43], John R Attia [44], Jonathan Rosand [18], Jose M Ferro [45], Joshua Bis [46], Karen Furie [47], Kari Stefansson [48], Klaus Berger [49], Konstantinos Kostulas [50], Kristina Rannikmae [51], M Arfan Ikram [52], Marianne Benn [12], Martin Dichgans [53], Martin Farrall [54], Massimo Pandolfo [55], Matthew Traylor [36], Matthew Walters [56], Michele Sale [57], Mike Nalls [58], Myriam Fornage [59], Natalie R van Zuydam [5], Pankaj Sharma [38], Patricia Abrantes [60], Paul IW de Bakker [61], Peter Higgins [62], Peter Lichtner [63], Peter M Rothwell [64], Philippe Amouyel [65], Qiong Yang [66], Rainer Malik [53], Reinhold Schmidt [67], Robert Clarke [40], Robin Lemmens [68], Sander W van der Laan [69], Sara L Pulit [70], Sherine Abboud [55], Sofia A Oliveira [71], Solveig Gretarsdottir [32], Stephanie Debette [72], Stephen R Williams [73], Steve Bevan [74], Steven J Kittner [43], Sudha Seshadri [75], Thomas Mosley [76], Thomas WK Battey [77], Turgut Tatlisumak [78], Unnur Thorsteinsdottir [48], Vincent NS Thijs [79], W T Longstreth [80], Wei Zhao [23], Wei-Min Chen [81], Yu-Ching Cheng [82]

1 Department of Neurology, Jagiellonian University, Krakow, Poland
2 Department of Epidemiology, Erasmus MC University Medical Center, Rotterdam, Netherlands
3 Department of Neurology and Neurosurgery, Utrecht Stroke Center, Rudolf Magnus Institute of Neuroscience, University Medical Center Utrecht, Utrecht, Netherlands
4 Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA, USA
5 Medical Research Institute, Ninewells Hospital and Medical School, University of Dundee, Dundee, UK
6 Institute for Stroke and Dementia Research, Klinikum der Universität München, Ludwig-Maximilians-Universität, and Munich Cluster for Systems Neurology (SyNergy), Munich, Germany
7 Department of Clinical Sciences Lund, Neurology, Lund University, Sweden
8 Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; J. Philip Kistler Stroke Research Center, Department of Neurology, MGH, Boston, MA, USA
9 Department of Clinical Sciences Lund, Neurology, Lund University, Lund, Sweden; Department of Neurology and Rehabilitation Medicine, Skåne University Hospital, Lund, Sweden
10 Departamento Promoção da Saúde e Doenças Crónicas, Instituto Nacional de Saúde Dr Ricardo Jorge, Lisbon, Portugal
11 Department of Clinical Sciences Lund, Neurology, Lund University, and Department of Neurology, Skåne University Hospital, Lund, Sweden
12 Department of Clinical Biochemistry and The Copenhagen General Population Study, Herlev Hospital, Copenhagen University Hospital, and Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark
13 Department of Medicine, University of Maryland School of Medicine, MD, USA; Geriatrics Research and Education Clinical Center, Baltimore Veterans Administration Medical Center, Baltimore, MD, USA
14 Departments of Neurology and Public Health Sciences, University of Virginia School of Medicine, Charlottesville, VA, USA
15 Cardiovascular Health Research Unit, Department of Medicine; Department of Epidemiology; Department of Health Services, University of Washington, Seattle, WA, USA; Kaiser Permanente Washington Health Research Institute, Seattle, WA, USA
16 Children's Research Institute, Children's National Medical Center, Washington, DC, USA; Center for Translational Science, George Washington University, Washington, DC, USA

17 University of Edinburgh, Edinburgh, UK
18 Center for Genomic Medicine, Massachusetts General Hospital (MGH), Boston, MA, USA; J. Philip Kistler Stroke Research Center, Department of Neurology, MGH, Boston, MA, USA; Program in Medical and Population Genetics, Broad Institute, Cambridge, MA, USA
19 Sydney Partnership for Health Education Research & Enterprise (SPHERE), University of NSW (Sydney), NSW, Australia and Priority Research Centre for Stroke & Brain Injury, University of Newcastle, NSW, Australia
20 Boston University School of Medicine, Boston, MA, USA
21 Department of Neurology, Mayo Clinic, Jacksonville, FL, USA
22 University of Cincinnati College of Medicine, Cincinnati, OH, USA
23 Department of Genetics, Perelman School of Medicine, University of Pennsylvania, PA, USA
24 Department of Neurology, University of Münster, Münster, Germany
25 Landspitali, University Hospital, Reykjavik, Iceland
26 Public Health Stream, Hunter Medical Research Institute, New Lambton, Australia; Faculty of Health and Medicine, University of Newcastle, Newcastle, Australia
27 Department of Psychology, and Centre for Cognitive Ageing and Cognitive Epidemiology, University of Edinburgh, Edinburgh, UK
28 Centre for Brain Research, Indian Institute of Science, Bangalore, India
29 Laboratory of Experimental Cardiology, University Medical Center Utrecht, Utrecht, Netherlands
30 Department of Cerebrovascular Diseases, Fondazione IRCCS Istituto Neurologico Carlo 85 Besta, Milano, Italy
31 Institute for Experimental Medicine, University of Kiel, Germany
32 deCODE genetics/AMGEN inc, Reykjavik, Iceland
33 Division of Neurocritical Care and Emergency Neurology, Department of Neurology, Yale University School of Medicine, New Haven, CT, USA; Program in Medical and Population Genetics, The Broad Institute of Harvard and MIT, Cambridge, MA, USA
34 Population Health Research Institute, McMaster University, Hamilton, Canada
35 Institute of Molecular Biology and Biochemistry, Medical University Graz, Graz, Austria
36 Stroke Research Group, Division of Clinical Neurosciences, University of Cambridge, UK
37 Department of Neurology, Boston University School of Medicine, Boston, MA, USA; NHLBI's Framingham Heart Study, Framingham, MA, USA
38 Institute of Cardiovascular Research, Royal Holloway University of London, UK
39 Neurovascular Research Laboratory, Vall d'Hebron Institut of Research, Neurology and Medicine Departments-Universitat Autònoma de Barcelona, Vall d'Hebrón Hospital, Barcelona, Spain; Stroke Pharmacogenomics and Genetics, Fundacio Docència i Recerca MutuaTerrassa, Terrassa, Spain
40 CTSU, Nuffield Department of Population Health, University of Oxford, UK
41 Fred Hutchinson Cancer Research Center, Seattle, WA, USA
42 Neurovascular Research Laboratory, Neurology and Medicine Departments, Universitat Autònoma de Barcelona and Institute of Research Vall d'Hebrón Hospital, Barcelona, Spain
43 Department of Neurology, University of Maryland School of Medicine and Baltimore VAMC, MD, USA
44 Hunter Medical Research Institute Public Health Research Program, Newcastle, Australia
45 Serviço de Neurologia, Centro de Estudos Egas Moniz, Hospital de Santa Maria, Lisbon, Portugal
46 Cardiovascular Health Research Unit, Department of Medicine, University of Washington, Seattle, WA, USA
47 Department of Neurology, Massachusetts General Hospital, Boston, MA, USA
48 deCODE genetics/AMGEN inc, Reykjavik, Iceland; Faculty of Medicine, University of Iceland, Reykjavik, Iceland
49 Institute of Epidemiology and Social Medicine, University of Münster, Germany
50 Department of Neurology, Karolinska Institutet at Karolinska University Hospital, Huddinge, Sweden
51 Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, UK
52 Department of Epidemiology, Erasmus University Medical Center, Rotterdam, Netherlands

53 Institute for Stroke and Dementia Research, Klinikum der Universität München, Ludwig-51 Maximilians-University, Munich, Germany
54 Department of Cardiovascular Medicine, University of Oxford, Oxford, UK
55 Laboratory of Experimental Neurology, Brussels, Belgium
56 School of Medicine, Dentistry and Nursing at the University of Glasgow, Glasgow, UK
57 Center for Public Health Genomics, University of Virginia, Charlottesville, VA, USA
58 Laboratory of Neurogenetics, National Institute on Aging, National institutes of Health, Bethesda, MD, USA; Data Tecnica International, Glen Echo MD, USA
59 Brown Foundation Institute of Molecular Medicine, University of Texas Health Science Center at Houston, Houston, TX, USA; Human Genetics Center, University of Texas Health Science Center at Houston, Houston, TX, USA
60 Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Portugal
61 Department of Medical Genetics, University Medical Center Utrecht, Utrecht, Netherlands; Department of Epidemiology, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, Netherlands
62 Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, UK
63 Helmholtz Zentrum München and Technische Universität München, Institut für Humangenetik, Munich, Germany
64 Nuffield Department of Clinical Neurosciences, University of Oxford, UK
65 INSERM U1167, Institut Pasteur de Lille, Lille, France; Department of Public Health, Lille University Hospital, Lille, France
66 Boston University School of Public Health, Boston, MA, USA
67 Department of Neurology, Medical University of Graz, Graz, Austria
68 KU Leuven – University of Leuven, Department of Neurosciences, Experimental Neurology, Leuven, Belgium; VIB Center for Brain & Disease Research, University Hospitals Leuven, Department of Neurology, Leuven, Belgium
69 Laboratory of Experimental Cardiology, Division of Heart and Lungs, University Medical Center Utrecht, Utrecht, Netherlands
70 Brain Center Rudolf Magnus, Department of Neurology, University Medical Center Utrecht, Utrecht, The Netherlands
71 Instituto de Medicina Molecular, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal
72 INSERM U1219 Bordeaux Population Health Research Center, Bordeaux, France; University of Bordeaux, Bordeaux, France
73 Department of Neurology, University of Virginia, Charlottesville, VA, USA
74 School of Life Science, University of Lincoln, Lincoln, UK
75 Department of Neurology, Boston University School of Medicine, Boston, MA, USA; Framingham Heart Study, Framingham, MA, USA
76 Division of Geriatrics, School of Medicine, University of Mississippi Medical Center, Jackson, MS, USA; Memory Impairment and Neurodegenerative Dementia Center, University of Mississippi Medical Center, Jackson, MS, USA
77 Division of Neurocritical Care and Emergency Neurology, Department of Neurology, Center for Human Genetic Research, Massachusetts General Hospital, Boston, USA
78 Department of Clinical Neurosciences/Neurology, Institute of Neuroscience and Physiology, Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden
79 Stroke Division, Florey Institute of Neuroscience and Mental Health, Heidelberg, Australia; Austin Health, Department of Neurology, Heidelberg, Australia
80 Department of Epidemiology, University of Washington, Seattle, WA, USA; Department of Neurology, University of Washington, Seattle, WA, USA
81 Center for Public Health Genomics, Department of Public Health Sciences, University of Virginia School of Medicine, Charlottesville, VA, USA
82 Department of Medicine, University of Maryland School of Medicine, Baltimore, USA

NINDS-SiGN

Peter Almgren, MSC
Department of Clinical Sciences, Malmo, Lund University, Malmo, Sweden

Christopher D. Anderson, MD
Department of Neurology Massachusetts General Hospital, Broad Institute

Donna K. Arnett, PhD, MSPH
University of Kentucky College of Public Health, Lexington, Kentucky

John Attia, MD, PhD, FRACP, FRCPC
Hunter Medical Research Institute, New Lambton NSW 2305 Australia

Hakan Ay, MD
AA Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA. Stroke Service, Department of Neurology.

Oscar R. Benavente, MD
Division of Neurology, Faculty of Medicine, Brain Research Center, University of British Columbia, Vancouver, British Columbia, Canada

Steve Bevan, PhD
University of Lincoln, Lincoln, UK

Robert D. Brown, MD
Department of Neurology, Mayo Clinic Rochester, Rochester, MN, USA

Mariana Bustamante, PhD
Centre for Research in Environmental Epidemiology, Barcelona, Spain

Yu-Ching Cheng, PhD
Department of Medicine, University of Maryland School of Medicine

John W. Cole, MD, MS
Department of Neurology, Baltimore Veterans Affairs Medical Center and University of Maryland School of Medicine

Ioana Cotlarciuc, PhD
Institute of Cardiovascular Research Royal Holloway University of London (ICR2UL)

Carlos Cruchaga, PhD
Department of Psychiatry, Washington University School of Medicine

Paul IW. de Bakker, PhD
Department of Medical Genetics, University Medical Center Utrecht, Utrecht, Netherlands

Hossein Delavaran, MD, PhD
Department of Clinical Sciences Lund, Neurology; Lund University; Lund; Sweden Department of Neurology and Rehabilitation Medicine; Skåne University Hospital; Lund; Sweden

Martin Dichgans, MD
Institute for Stroke and Dementia Research, Ludwig-Maximilians-Universität München, Munich, Germany

Gunnar Engström, MD, PHD, PROF

DEPT OF CLINICAL SCIENCES, MALMÖ, LUND UNIVERSITY, MALMÖ, SWEDEN
Department of Clinical Sciences, Malmö, Lund University, Malmö, Sweden

Myriam Fornage, PhD
Institute of Molecular Medicine, University of Texas Health Science Center at Houston

Raji P. Grewal, MD
Neuroscience Institute, SF Medical Center, Trenton, NJ, USA

Laura Heitsch, MD
Division of Emergency Medicine, and Department of Neurology, Washington University School of Medicine

Elizabeth Holliday, MSc, PhD
HMRI Administration, Locked Bag 1000, New Lambton NSW 2305, Australia

Laure Ibanez, PhD
Department of Psychiatry, Washington University School of Medicine

Andreea Ilinca, MD
Department of Clinical Sciences Lund, Neurology; Lund University; Lund; Sweden Department of Neurology and Rehabilitation Medicine; Skåne University Hospital; Lund; Sweden

Marguerite R. Irvin, PhD
Epidemiology, School of Public Health, University of Alabama at Birmingham

Rebecca D. Jackson, MD
Department of Internal Medicine and the Center for Clinical and Translational Science, The Ohio State University, Columbus, OH

Christina Jern, MD, PhD
Institute of Biomedicine, the Sahlgrenska Academy at University of Gothenburg, Goteborg, SWEDEN

Jordi Jimenez-Conde, MD, PhD
Department of Neurology, Neurovascular Research Group, Hospital del Mar, Barcelona

Julie A. Johnson, PharmD
Department of Pharmacotherapy and Translational Research and Center for Pharmacogenomics, College of Pharmacy, University of Florida

Katarina Jood, MD, PhD
Institute of Neuroscience and Physiology, the Sahlgrenska Academy at University of Gothenburg, Goteborg SWEDEN

Brett M. Kissela, MD, MS
Department of Neurology, University of Cincinnati College of Medicine

Steven J. Kittner, MD
Department of Neurology, Baltimore Veterans Affairs Medical Center and University of Maryland School of Medicine

Dawn O. Kleindorfer, MD, MS
Department of Neurology, University of Cincinnati College of Medicine

Daniel Labovitz, MD
Department of Neurology, Albert Einstein College of Medicine, Montefiore Medical Center

Cathy C. Laurie, PhD
Department of Biostatistics, University of Washington, Seattle, WA, USA

Jin-Moo Lee, MD, PhD
Department of Neurology, Radiology, and Biomedical Engineering, Washington University School of Medicine,

Robin Lemmens, MD PhD
KU Leuven – University of Leuven, Department of Neurosciences, Experimental Neurology VIB Center for Brain & Disease Research; University Hospitals Leuven, Department of Neurology, Leuven, Belgium

Christopher Levi, MBBS B Med Sci FRACP
John Hunter Hospital, Hunter Medical Research Institute and University of Newcastle

Linxin Li, DPhil
Centre for Prevention of Stroke and Dementia, Nuffield Department of Clinical Neurosciences, University of Oxford, UK

Arne G. Lindgren, MD, PhD
Department of Clinical Sciences Lund, Neurology; Lund University; Lund; Sweden Department of Neurology and Rehabilitation Medicine; Skåne University Hospital; Lund; Sweden

Jane Maguire, PhD
University of Newcastle, Faculty of Health and Medicine, School of Nursing and Midwifery, University Drive, Callaghan NSW 2308 Australia

Hugh S. Markus, FRCP
University of Cambridge, Cambridge, UK

Patrick F. McArdle, PhD
Department of Medicine, University of Maryland School of Medicine

Olle Melander, MD, PHD, PROF
Department of Clinical Sciences, Malmö, Lund University, Malmö, Sweden

James F. Meschia, MD
Mayo Clinic, Department of Neurology, Jacksonville, FL 32224, USA

Braxton D. Mitchell, PhD
Department of Medicine, University of Maryland School of Medicine

Martina Müller-Nurasyid, PhD

Institute of Genetic Epidemiology, Helmholtz Zentrum München - German Research Center for Environmental Health, Neuherberg, Germany Department of Medicine I, Ludwig-Maximilians-University Munich, Munich, Germany

Bo Norrving, MD, PhD
Department of Clinical Sciences Lund, Neurology; Lund University; Lund; Sweden Department of Neurology and Rehabilitation Medicine; Skåne University Hospital; Lund; Sweden

Leema Reddy Peddareddygari, MD
Neuroscience Institute, SF Medical Center, Trenton, NJ, USA

Joanna Pera, MD, PhD
Department of Neurology, Jagiellonian University, Krakow Poland

Sara L. Pulit, PhD
Brain Center Rudolf Magnus, Department of Neurology, University Medical Center Utrecht, Utrecht, The Netherlands

Kathryn Rexrode, MD, MPH
Department of Medicine, Brigham and Women's Hospital

Marta Ribasés, PhD, BSc
Psychiatric Genetics Unit, Group of Psychiatry, Mental Health and Addictions, Vall d'Hebron Research Institute (VHIR), Universitat Autònoma de Barcelona, Barcelona, Spain

Jaume Roquer, MD, PhD
Department of Neurology, Neurovascular Research Group, Hospital del Mar, Barcelona IMIM (Hospital del Mar Medical Research Institute), Barcelona

Jonathan Rosand, MD, MSc
Department of Neurology Massachusetts General Hospital, Broad Institute

Natalia S. Rost, MD
Department of Neurology Massachusetts General Hospital

Peter M. Rothwell, FMedSci
Centre for Prevention of Stroke and Dementia, Nuffield Department of Clinical Neurosciences, University of Oxford, UK

Tatjana Rundek, MD PhD
Department of Neurology, Miller School of Medicine, University of Miami

Ralph L. Sacco, MD MS
Department of Neurology, Miller School of Medicine, University of Miami

Reinhold Schmidt, MD
Department of Neurology, Clinical Division of Neurogeriatrics, Medical University Graz, Austria

Pankaj Sharma, MD PhD
Institute of Cardiovascular Research Royal Holloway University of London (ICR2UL) Ashford & St Peters NHS Foundation Trust

Agnieszka Slowik, MD, PhD
Department of Neurology, Jagiellonian University, Krakow Poland

Carolina Soriano-Tárraga, BSc, PhD
IMIM (Hospital del Mar Medical Research Institute), Barcelona

Tara Stanne, PhD
Institute of Biomedicine, the Sahlgrenska Academy at University of Gothenburg, Box 445, S-405 30 Goteborg, SWEDEN

Konstantin Stauch, PhD
Institute of Genetic Epidemiology, Helmholtz Zentrum München

O C. Stine, PhD
Department of Epidemiology, University of Maryland School of Medicine

Cathie LM. Sudlow, BMBCh, MSc, DPhil, FRCP (Ed)
Centre for Clinical Brain Sciences & Institute of Genetics and Molecular Medicine, University of Edinburgh

Vincent N.S.Thijs, MD,PhD
Stroke Division, Florey Institute of Neuroscience and Mental Health, Heidelberg, Victoria, Australia; Austin Health, Department of Neurology, Heidelberg, Victoria, Australia

Sylvia Wassertheil-Smoller, PhD
Department of Epidemiology and Population Health, Albert Einstein College of Medicine

David Weir, PhD
Survey Research Center, University of Michigan

Stephen R. Williams, PhD
University of Virginia Department of Neurology; Charlottesville, VA

Quenna Wong, PhD
Department of Biostatistics, University of Washington, Seattle, WA, USA

Daniel Woo, MD, MS
Department of Neurology, University of Cincinnati College of Medicine

Bradford B. Worrall, MD, MSc
University of Virginia Departments of Neurology and Health Evaluation Sciences; Charlottesville, VA

Huichun Xu, MD, PhD
Department of Medicine, University of Maryland School of Medicine

UK Young Lacunar Stroke DNA Study (DNA Lacunar)
Study managers: Josie Monaghan; Alan Zanich, Samantha Febrey, Eithne Smith, Jenny Lennon, St George's University of London
Database cleaning: Loes Rutten-Jacobs, University of Cambridge
Participating centres (number of enrolled patients per centre; local investigators):

Aberdeen Royal Infirmary, Aberdeen (12; Mary Macleod). Addenbrooke's Hospital, Cambridge (54; Jean-Claude Baron, Elizabeth Warburton, Diana J Day, Julie White). Airedale General Hospital, Steeton (4; Samantha Mawer). Barnsley Hospital, Barnsley (3; Mohammad Albazzaz, Pravin Torane, Keith Elliott, Kay Hawley). Bart's and the London, London (2; Patrick Gompertz). Basingstoke and North Hampshire Hospital, Basingstoke (13; Elio Giallombardo, Deborah Dellafera). Blackpool Victoria Hospital, Blackpool (11; Mark O'Donnell). Bradford Royal Infirmary, Bradford (1; Chris Patterson). Bristol Royal Infirmary, Bristol (8; Sarah Caine). Charing Cross Hospital, London (12; Pankaj Sharma). Cheltenham General and Gloucester Royal Hospitals, Cheltenham and Gloucester (10; Dipankar Dutta). Chesterfield Royal Hospital, Chesterfield (4; Sunil Punnoose, Mahmud Sajid). Countess of Chester Hospital, Chester (22; Kausik Chatterjee). Derriford Hospital, Plymouth (4; Azlisham Mohd Nor). Dorset County Hospital NHS Foundation Trust, Dorchester (6; Rob Williams). East Kent Hospitals University NHS Foundation Trust, Kent (22; Hardeep Baht, Guna Gunathilagan). Eastbourne District General Hospital, Eastbourne (4; Conrad Athulathmudali). Frenchay Hospital, Bristol (1; Neil Baldwin). Frimley Park Hospital NHS Foundation Trust, Frimley (6; Brian Clarke). Guy's and St Thomas' Hospital, London (14; Tony Rudd). Institute of Neurology, London (25; Martin Brown). James Paget University Hospital, Great Yarmouth (1; Peter Harrison). King's College Hospital, London (16; Lalit Kalra). Leeds Teaching Hospitals NHS Trust, London (125; Ahamad Hassan). Leicester General Hospital and Royal Infirmary, Leicester (9; Tom Robinson, Amit Mistri). Luton and Dunstable NHSFT University Hospital, Luton (16; Lakshmanan Sekaran, Sakthivel Sethuraman, Frances Justin). Maidstone and Tunbridge Wells NHS Trust (3; Peter Maskell). Mayday University Hospital, Croydon (14; Enas Lawrence). Medway Maritime Hospital, Gillingham (5; Sam Sanmuganathan). Milton Keynes Hospital, Milton Keynes (1; Yaw Duodu). Musgrove Park Hospital, Taunton (9; Malik Hussain). Newcastle Hospitals NHS Foundation Trust, Newcastle upon Tyne (12; Gary Ford). Ninewells Hospital, Dundee (5; Ronald MacWalter). North Devon District Hospital, Barnstaple (8; Mervyn Dent). Nottingham University Hospitals, Nottingham (17; Philip Bath, Fiona Hammonds). Perth Royal Infirmary, Perth (2; Stuart Johnston). Peterborough City Hospital, Peterborough (1; Peter Owusu-Agyei). Queen Elizabeth Hospital, Gateshead (5; Tim Cassidy, Maria Bokhari). Radcliffe Infirmary, Oxford (5; Peter Rothwell). Rochdale Infirmary, Rochdale (4; Robert Namushi). Rotherham General Hospital, Rotherham (1; James Okwera). Royal Cornwall Hospitals NHS Trust, Truro (11; Frances Harrington, Gillian Courtauld). Royal Devon and Exeter Hospital, Exeter (22; Martin James). Royal Hallamshire Hospital, Sheffield (1; Graham Venables). Royal Liverpool University Hospital and Broadgreen Hospital, Liverpool (9; Aravind Manoj). Royal Preston Hospital, Preston (18; Shuja Punekar). Royal Surrey County Hospital, Guildford (23; Adrian Blight, Kath Pasco). Royal Sussex County Hospital, Brighton (14; Chakravarthi Rajkumar, Joanna Breeds). Royal United Hospital, Bath (6; Louise Shaw, Barbara Madigan). Salford Royal Hospital, Salford (16; Jane Molloy). Southampton General Hospital, Southampton (1; Giles Durward). Southend Hospital, Westcliff-on-Sea (26; Paul Guyler). Southern General Hospital, Glasgow (34; Keith Muir, Wilma Smith). St George's Hospital, London (108; Hugh Markus). St Helier Hospital, Carshalton (10; Val Jones). Stepping Hill Hospital, Stockport (4; Shivakumar Krishnamoorthy). Sunderland Royal Hospital, Sunderland (1; Nikhil Majumdar). The Royal Bournemouth Hospital, Bournemouth (15; Damian Jenkinson). The Walton Centre, Liverpool (15; Richard White). Torbay Hospital, Torquay (19; Debs Kelly). University Hospital Aintree, Liverpool (19; Ramesh Durairaj). University Hospital of North Staffordshire, Stoke-on-trent (16; David Wilcock). Wansbeck General Hospital and North Tyneside Hospital, Ashington and North Shields (6; Christopher Price). West Cumberland Hospital, Whitehaven (6; Olu Orugun, Rachel Glover). West Hertfordshire Hospital, Watford (20; David Collas). Western General Hospital, Edinburgh (12; Cathie Sudlow). Western Infirmary, Glasgow (33; Kennedy R. Lees, Jesse Dawson). Wycombe Hospital and Stoke Mandeville, High Wycombe (20; Dennis Briley and Matthew Burn). Yeovil District Hospital, Yeovil (46; Khalid Rashed). York Teaching Hospital, York (1; John Coyle).