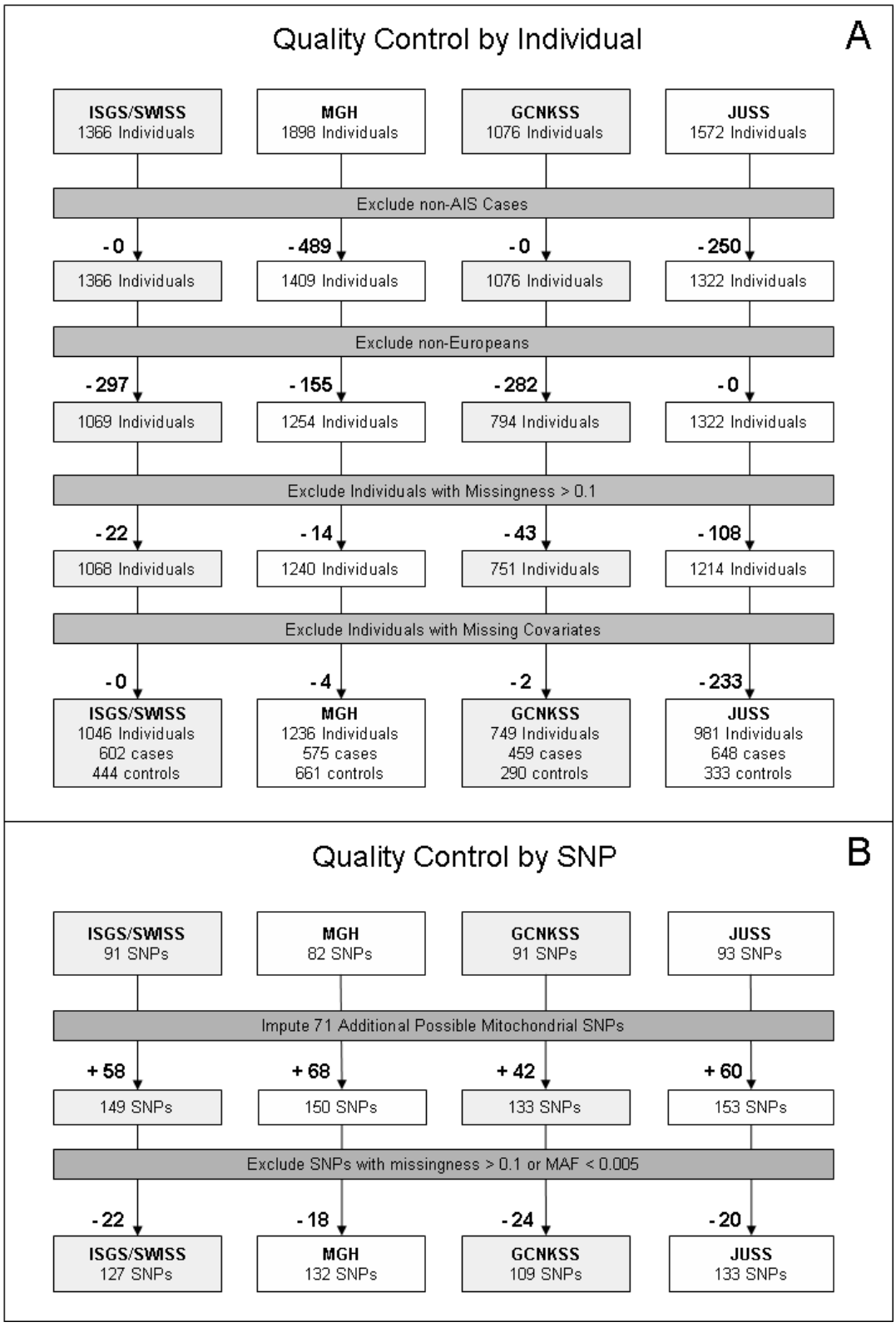
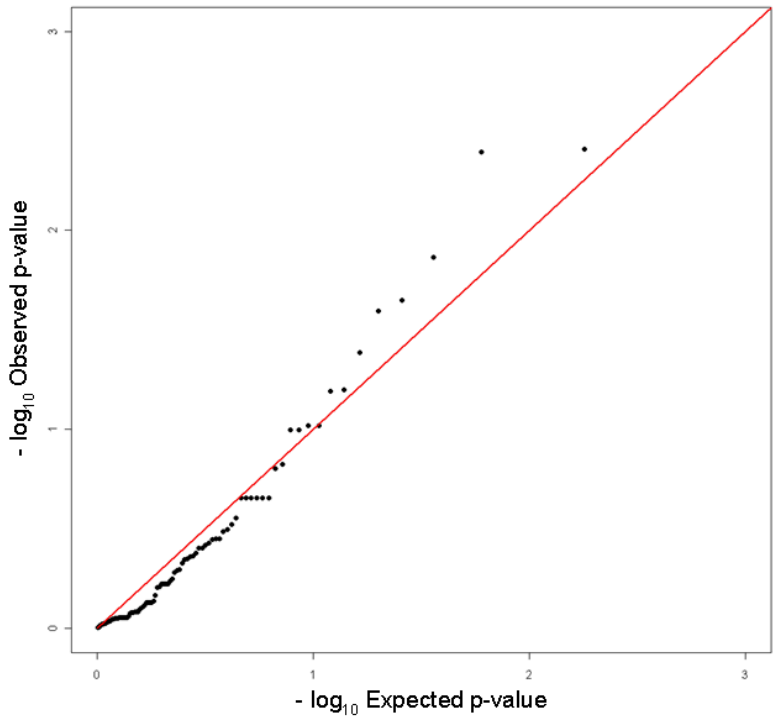
Supplementary Figure S1. Quality control methods and results, by individual and SNP.



Supplementary Figure S1 Legend. A – Quality control by individual for each of the cohorts included in the present study. B – Quality control by SNP for each of the cohorts included in the present study. AIS = Acute Ischemic Stroke, GCNKSS = Greater Cincinnati Northern Kentucky Stroke Study, ISGS/SWISS = Ischemic Stroke Genetic Study/Siblings with Ischemic Stroke Study, JUSS = Jagiellonian University Stroke Study, MAF = Minor Allele Frequency, MGH = Massachusetts General Hospital Ischemic Stroke Genome-wide Association Study

Supplementary Figure S2. QQ – plot and mitochondrial genomic inflation factors after quality control



Study	mtGIF
ISGS/SWISS	1.00
MGH	1.11
GCNKSS	1.00
JUSS	1.00
All Studies	**1.00**

Covariates:

age, sex, site (when applicable), and PC 1-5

Supplementary Figure S2 Legend. GCNKSS = Greater Cincinnati Northern Kentucky Stroke Study, ISGS/SWISS = Ischemic Stroke Genetic Study/Siblings with Ischemic Stroke Study, JUSS = Jagiellonian University Stroke Study, MAF = Minor Allele Frequency, MGH = Massachusetts General Hospital Ischemic Stroke Genome-wide Association Study, mtGIF = mitochondrial Genomic Inflation Factor, PC = Principal Component

Supplementary Table S1. Single Nucleotide Polymorphism IDs, reference alleles, and beta coefficients for association with ischemic stroke.

SNP	ALLELE	BETA
mt150	4	-0.001
mt709	1	-0.05119
mt750	1	0.101654
mt930	1	-0.20371
mt1189	2	-0.03957
mt1243	2	0.076961
mt1719	1	-0.13662
mt1811	3	-0.03263
mt1888	1	0.026642
mt2706	1	0.24998
mt3010	1	-0.03407
mt3197	2	0.020783
mt3394	2	0.175633
mt3480	3	-0.21159
mt3505	3	0.076961
mt3915	1	-0.07764
mt4216	2	0.109751
mt4336	2	-0.00682
mt4529	1	0.01094
mt4580	1	-0.22602
mt4793	3	-0.01745
mt4917	3	0.026642
mt5046	3	-0.03097
mt5147	3	-0.1879
mt5495	2	-0.01857
mt5656	3	0.032467
mt6221	2	-0.20543
mt6776	2	0.072321
mt7028	2	0.249201
mt7476	2	0.096219
mt7768	1	0.099845
mt8251	3	0.030529
mt8697	1	0.026642
mt8994	3	-0.03097
mt9055	1	-0.21159
mt9123	1	0.005982
mt9477	1	0.020783
mt9667	3	0.09349
mt9698	2	-0.21159
mt9716	2	-0.10993
mt9899	2	0.08158
mt10034	2	0.00995
mt10238	2	0.002996
mt10398	3	0.131905
mt10550	3	-0.21159
mt10915	2	0.309688
mt11251	1	0.156149

Supplementary Table S1 (continued).

SNP	ALLELE	BETA
mt11299	2	-0.21159
mt11377	1	-0.02604
mt11467	1	-0.014
mt11485	2	-0.04972
mt11674	4	0.076961
mt11719	3	-0.01288
mt11812	3	-0.19614
mt11914	1	-0.08219
mt11947	1	-0.03097
mt12007	1	-0.01349
mt12308	1	-0.014
mt12372	1	-0.04751
mt12414	2	-0.00884
mt12705	4	-0.15047
mt13020	2	-0.11777
mt13105	3	-0.13513
mt13368	1	0.026642
mt13617	2	0.020783
mt13708	1	-0.04825
mt13734	2	-0.05996
mt13780	1	0.067659
mt13934	4	0.129272
mt13965	2	-0.05774
mt13966	3	-0.28316
mt14167	4	-0.21159
mt14182	2	0.168899
mt14233	3	-0.19614
mt14687	3	-0.05774
mt14766	4	-0.02634
mt14793	3	-0.0715
mt14798	2	-0.02634
mt14905	1	0.026642
mt15043	1	-0.00612
mt15218	3	-0.04615
mt15257	1	0.103459
mt15452	2	0.156149
mt15607	3	0.026642
mt15758	3	-0.02163
mt15833	4	0.033435
mt15904	2	-0.15362
mt15924	3	-0.01359
mt15928	1	0.026642
mt16189	2	-0.07032

Supplementary Table S1 Legend. Beta coefficients expressed as the natural logarithm of the odds ratio.

Allele 1 = Adenine, Allele 2 = Cytosine, Allele 3 = Guanine, Allele 4 = Thiamine.

Supplementary Table S2. Power calculations for haplogroup association tests in ischemic stroke.

Haplogroup	Expected Frequency in Controls[1]	Frequency in Cases to Detect Association[2]		Minimum Effect Size (OR) Detectable[3]	
		Risk Variants	*Protective Variants*	*Risk Variants*	*Protective Variants*
H	0.41	0.45	0.37	1.18	0.84
H1	0.14	0.17	0.12	1.24	0.81
H2	0.26	0.30	0.23	1.21	0.83
J	0.11	0.14	0.085	1.35	0.74
K	0.08	0.10	0.06	1.33	0.75
preHV	0.06	0.13	0.03	2.52	0.40
T	0.13	0.16	0.11	1.24	0.81
U	0.15	0.18	0.13	1.24	0.81
WX	0.04	0.10	0.016	2.58	0.39
I	0.02	0.05	0.007	2.80	0.36

Supplementary Table S2 Legend. All power calculations assume α = 0.05, statistical power = 0.80

[1] Based on published data compiled in MitoMap (www.mitomap.org)

[2] For risk variants, this field reports the lowest haplogroup frequency in cases that can generate an association at α = 0.05 with statistical power = 0.80. For protective variants, the highest haplogroup frequency in cases compatible with an association at α = 0.05 with statistical power = 0 is reported.

[3] The weakest haplogroup-related odds ratio compatible with an association at α = 0.05 with statistical power = 0.80 is reported, as determined by comparison of reported haplogroup frequency.