

SUPPLEMENTAL MATERIAL

Table S1. All 28 SNPs for serum urate from Köttgen et al study (1)

	SNP	chr	EA	OA	EAF	GX	SE_GX	pval	N	MAF	R2	F-statistic
1	rs10480300	7	T	C	0.280	0.035	0.006	4.10E-09	110,347	0.28	0.00030828	34.016363
2	rs10821905	10	A	G	0.180	0.057	0.007	7.40E-17	110,347	0.18	0.00060053	66.2645023
3	rs11264341	1	T	C	0.430	-0.050	0.006	6.20E-19	110,347	0.43	0.00062893	69.3988818
4	rs1165151	6	T	G	0.470	-0.091	0.005	7.00E-70	110,347	0.47	0.00299282	330.23968
5	rs1171614	10	T	C	0.220	-0.079	0.007	2.30E-28	110,347	0.22	0.00115291	127.217045
6	rs1178977	7	A	G	0.810	0.047	0.007	1.20E-12	110,347	0.19	0.00040838	45.0619972
7	rs12498742	4	A	G	0.770	0.373	0.006	1.00E-10	110,347	0.23	0.03383799	3733.81943
8	rs1260326	2	T	C	0.410	0.074	0.005	1.20E-44	110,347	0.41	0.00198108	218.600121
9	rs1394125	15	A	G	0.340	0.043	0.006	2.50E-13	110,347	0.34	0.00046523	51.3358205
10	rs1471633	1	A	C	0.460	0.059	0.005	1.20E-29	110,347	0.46	0.00126025	139.060742
11	rs17050272	2	A	G	0.430	0.035	0.006	1.60E-10	110,347	0.43	0.00030828	34.016363
12	rs17632159	5	C	G	0.310	-0.039	0.006	3.50E-11	110,347	0.31	0.00038274	42.2326812
13	rs17786744	8	A	G	0.580	-0.029	0.005	1.4E-08	110,347	0.42	0.00030476	33.6288335
14	rs2078267	11	T	C	0.510	-0.073	0.006	9.40E-38	110,347	0.49	0.00133968	147.825449
15	rs2231142	4	T	G	0.110	0.217	0.009	1.00E-134	110,347	0.11	0.00524073	578.28328
16	rs2941484	8	T	C	0.440	0.044	0.005	4.40E-17	110,347	0.44	0.00070129	77.3835879
17	rs3741414	12	T	C	0.240	-0.072	0.007	2.20E-25	110,347	0.24	0.00095784	105.69171
18	rs478607	11	A	G	0.840	-0.047	0.007	4.40E-11	110,347	0.16	0.00040838	45.0619972
19	rs653178	12	T	C	0.510	-0.035	0.005	7.20E-12	110,347	0.49	0.00044386	48.9769195
20	rs6598541	15	A	G	0.360	0.043	0.006	4.80E-15	110,347	0.36	0.00046523	51.3358205
21	rs675209	6	T	C	0.270	0.061	0.006	1.30E-23	110,347	0.27	0.00093582	103.261577
22	rs6770152	3	T	G	0.580	-0.044	0.005	2.60E-16	110,347	0.42	0.00070129	77.3835879
23	rs7188445	16	A	G	0.330	-0.032	0.005	1.60E-09	110,347	0.33	0.00037106	40.9436884

24	rs7193778	16	T	C	0.860	-0.046	0.008	8.20E-10	110,347	0.14	0.00029953	33.0516981
25	rs7224610	17	A	C	0.580	-0.042	0.005	5.40E-17	110,347	0.42	0.00063903	70.512993
26	rs729761	6	T	G	0.300	-0.047	0.006	8.00E-16	110,347	0.3	0.00055577	61.3253415
27	rs7953704	12	A	G	0.470	-0.029	0.005	2.6E-08	110,347	0.47	0.00030476	33.6288335
28	rs7976059	12	T	G	0.350	0.032	0.005	1.90E-09	110,347	0.35	0.00037106	40.9436884

SNP: each SNP's id; chr: chromosome; EA: effect allele; OA: other allele; EAF: effect allele frequency for GX; GX: beta for the SNP-urate relationship; SE_GX: standard error of GX; pval: p-value of GX; N: sample size of the study from which each SNP was found; MAF: minor allele frequency; R2: % of variance in cognition explained by each SNP, calculated by: $R2 = \frac{2 * GX^2 * MAF * (1 - MAF)}{2 * GX^2 * MAF * (1 - MAF) + SE_GX^2 * 2 * N * MAF * (1 - MAF)}$; F-statistic: a measurement of instrument's strength, calculated by: $F\text{-statistic} = \frac{R2 * (N - 2)}{1 - R2}$ (3)

Table S2. The 7 SNPs that are only associated with serum urate or/and gout (1) after excluding the pleiotropic SNPs using Phenoscanner (4)

	SNP	chr	EA	OA	EAF	GX	SE_GX	pval	R2	F-statistic
1	rs12498742	4	A	G	0.77	0.373	0.006	1.00E-10	0.03383799	3733.81943
2	rs1471633	1	A	C	0.46	0.059	0.005	1.20E-29	0.00126025	139.060742
3	rs2078267	11	T	C	0.51	-0.073	0.006	9.40E-38	0.00133968	147.825449
4	rs2941484	8	T	C	0.44	0.044	0.005	4.40E-17	0.00070129	77.3835879
5	rs6770152	3	T	G	0.58	-0.044	0.005	2.60E-16	0.00070129	77.3835879
6	rs7224610	17	A	C	0.58	-0.042	0.005	5.40E-17	0.00063903	70.512993
7	rs7976059	12	T	G	0.35	0.032	0.005	1.90E-09	0.00037106	40.9436884

SNP: each SNP's id; chr: chromosome; EA: effect allele; OA: other allele; EAF: effect allele frequency for GX; GX: beta for the SNP-urate relationship; SE_GX: standard error of GX; pval: p-value of GX

Table S3. Power calculations for all analyses using the 28 SNPs. The calculations were made using the mRnd power calculator (available at <http://cnsgenomics.com/shiny/mRnd/>) (5)

CHD						
% of variance in urate explained by the 28 SNPs	Type-I error rate	Sample size of the outcome dataset; CARDIoGRAMplusC4D 1000 Genomes-based GWAS (6)	Proportion of CAD cases		minimum OR to have >80% power	maximum OR to have >80% power
0.058	0.05	184,305	0.33		0.97	1.04
MI						
% of variance in urate explained by the 28 SNPs	Type-I error rate	Sample size of the outcome dataset; CARDIoGRAMplusC4D 1000 Genomes-based GWAS (6)	Proportion of MI cases		minimum OR to have >80% power	maximum OR to have >80% power
0.058	0.05	184,305	0.23		0.96	1.04
COGNITION						
% of variance in urate explained by the 28 SNPs	Type-I error rate	Sample size of the outcome dataset; (Lee et al) (7)	β OLS*	σ^2 (x)**	σ^2 (y)***	minimum beta to have >80% power
0.058	0.05	257,841	0	2.25	1	0.135
SBP						
% of variance in urate explained by the 28 SNPs	Type-I error rate	Sample size of the outcome dataset; SBP automated (UK biobank) (8)	β OLS*	σ^2 (x)**	σ^2 (y)***	minimum beta to have >80% power
0.058	0.05	473,891	0	2.25	1	0.096
ALZHEIMER						
% of variance in urate explained by the 28 SNPs	Type-I error rate	Sample size of the outcome dataset; IGAP 1st stage (9)	Proportion of Alzheimer cases		minimum OR to have >80% power	maximum OR to have >80% power
0.058	0.05	54,162	0.31		0.93	1.08
STROKE						
% of variance in urate explained by the 28 SNPs	Type-I error rate	Sample size of the outcome dataset; MEGASTROKE (10)	Proportion of any ischemic stroke cases		minimum OR to have >80% power	maximum OR to have >80% power

0.058	0.05	514,791	0.12	0.97	1.03
% of variance in urate explained by the 28 SNPs	Type-I error rate	Sample size of the outcome dataset; METASTROKE (10)	Proportion of CES stroke cases	minimum OR to have >80% power	maximum OR to have >80% power
0.058	0.05	514,791	0.02	0.92	1.08
% of variance in urate explained by the 28 SNPs	Type-I error rate	Sample size of the outcome dataset; METASTROKE (10)	Proportion of LAS stroke cases	minimum OR to have >80% power	maximum OR to have >80% power
0.058	0.05	514,791	0.013	0.91	1.10
% of variance in urate explained by the 28 SNPs	Type-I error rate	Sample size of the outcome dataset; METASTROKE (10)	Proportion of SVS stroke cases	minimum OR to have >80% power	maximum OR to have >80% power
0.058	0.05	514,791	0.023	0.92	1.07

* the observational association estimate of the exposure-outcome relationship

** variance of the exposure variable (x),

*** variance of the outcome variable (y)

CHD; coronary heart disease, MI; myocardial infraction, SBP; systolic blood pressure, CES; cardioembolic stroke, LAS; large vessels stroke, SVS; small vessels stroke

Table S4. Power calculations for all analyses using the 7 SNPs. The calculations were made using the mRnd power calculator (available at <http://cnsgenomics.com/shiny/mRnd/>) (5) .

CHD						
% of variance in urate explained by the 7 SNPs	Type-I error rate	Sample size of the outcome dataset; CARDIoGRAMplusC4D 1000 Genomes-based GWAS (6)	Proportion of CAD cases		minimum OR to have >80% power	maximum OR to have >80% power
0.039	0.05	184,305	0.33		0.95	1.05
MI						
% of variance in urate explained by the 7 SNPs	Type-I error rate	Sample size of the outcome dataset; CARDIoGRAMplusC4D 1000 Genomes-based GWAS (6)	Proportion of MI cases		minimum OR to have >80% power	maximum OR to have >80% power
0.039	0.05	184,305	0.23		0.95	1.05
COGNITION						
% of variance in urate explained by the 7 SNPs	Type-I error rate	Sample size of the outcome dataset; (Lee et al) (7)	β OLS*	σ^2 (x)**	σ^2 (y)***	minimum beta to have >80% power
0.039	0.05	257,841	0	2.25	1	0.250
SBP						
% of variance in urate explained by the 7 SNPs	Type-I error rate	Sample size of the outcome dataset; SBP automated (UK biobank) (8)	β OLS*	σ^2 (x)**	σ^2 (y)***	minimum beta to have >80% power
0.039	0.05	473,891	0	2.25	1	0.193
ALZHEIMER						
% of variance in urate explained by the 7 SNPs	Type-I error rate	Sample size of the outcome dataset; IGAP 1st stage (9)	Proportion of Alzheimer cases		minimum OR to have >80% power	maximum OR to have >80% power
0.039	0.05	54,162	0.31		0.91	1.10
STROKE						
% of variance in urate explained by the 7 SNPs	Type-I error rate	Sample size of the outcome dataset; MEGASTROKE (10)	Proportion of any ischemic stroke cases		minimum OR to have >80% power	maximum OR to have >80% power

0.039	0.05	514,791	0.12	0.96	1.04
% of variance in urate explained by the 7 SNPs	Type-I error rate	Sample size of the outcome dataset; METASTROKE (10)	Proportion of CES stroke cases	minimum OR to have >80% power	maximum OR to have >80% power
0.039	0.05	514,791	0.02	0.90	1.13
% of variance in urate explained by the 7 SNPs	Type-I error rate	Sample size of the outcome dataset; METASTROKE (10)	Proportion of LAS stroke cases	minimum OR to have >80% power	maximum OR to have >80% power
0.039	0.05	514,791	0.013	0.88	1.12
% of variance in urate explained by the 7 SNPs	Type-I error rate	Sample size of the outcome dataset; METASTROKE (10)	Proportion of SVS stroke cases	minimum OR to have >80% power	maximum OR to have >80% power
0.039	0.05	514,791	0.023	0.90	1.10

* the observational association estimate of the exposure-outcome relationship

** variance of the exposure variable (x),

*** variance of the outcome variable (y)

CHD; coronary heart disease, MI; myocardial infraction, SBP; systolic blood pressure, CES; cardioembolic stroke, LAS; large vessels stroke, SVS; small vessels stroke

Table S5. The association estimates of the 28 SNPs for urate (1) with cognitive performance (7)

	SNP	chr	EA	OA	EAF	GY	SE_GY	pval
1	rs10480300	7	C	T	0.704	-0.001	0.003	0.780
2	rs10821905	10	A	G	0.165	-0.001	0.004	0.856
3	rs11264341	1	T	C	0.412	0.000	0.003	0.878
4	rs1165151	6	G	T	0.551	-0.010	0.003	0.000
5	rs1171614	10	T	C	0.257	0.007	0.003	0.038
6	rs1178977	7	G	A	0.197	-0.007	0.004	0.047
7	rs12498742	4	A	G	0.779	-0.011	0.003	0.001
8	rs1260326	2	C	T	0.587	-0.003	0.003	0.237
9	rs1394125	15	G	A	0.645	-0.001	0.003	0.639
10	rs1471633	1	C	A	0.510	0.002	0.003	0.572
11	rs17050272	2	G	A	0.563	0.002	0.003	0.437
12	rs17632159	5	G	C	0.685	-0.003	0.003	0.389
13	rs17786744	8	G	A	0.439	0.003	0.003	0.348
14	rs2078267	11	C	T	0.442	0.003	0.003	0.249
15	rs2231142	4	G	T	0.893	0.001	0.005	0.886
16	rs2941484	8	T	C	0.422	-0.004	0.003	0.141
17	rs3741414	12	T	C	0.221	-0.010	0.003	0.002
18	rs478607	11	G	A	0.136	0.008	0.004	0.045
19	rs653178	12	C	T	0.473	-0.006	0.003	0.044
20	rs6598541	15	G	A	0.677	-0.004	0.003	0.197
21	rs675209	6	C	T	0.708	0.002	0.003	0.546
22	rs6770152	3	G	T	0.444	0.013	0.003	0.000
23	rs7188445	16	A	G	0.354	0.004	0.003	0.140
24	rs7193778	16	T	C	0.855	-0.009	0.004	0.032
25	rs7224610	17	A	C	0.585	0.004	0.003	0.136
26	rs729761	6	T	G	0.282	-0.006	0.003	0.054
27	rs7953704	12	A	G	0.481	0.003	0.003	0.272
28	rs7976059	12	G	T	0.645	0.006	0.003	0.050

SNP: each SNP's id; chr: chromosome; EA: effect allele, OA: other allele; EAF: effect allele frequency for GY; GY: beta for the SNP-cognition relationship; SE_GY: standard error of GY; pval: p-value of GY

Table S6. The association estimates of the 28 SNPs for urate (1) with Alzheimer's disease (9)

	SNP	chr	EA	OA	GY	SE_GY	pval
1	rs10480300	7	T	C	0.014	0.017	0.4349
2	rs10821905	10	A	G	-0.025	0.021	0.2371
3	rs11264341	1	T	C	0.005	0.017	0.7549
4	rs1165151	6	T	G	-0.004	0.016	0.8201
5	rs1171614	10	T	C	-0.004	0.019	0.8503
6	rs1178977	7	G	A	-0.011	0.021	0.6132
7	rs12498742	4	G	A	0.014	0.018	0.4517
8	rs1260326	2	T	C	-0.001	0.016	0.9608
9	rs1394125	15	A	G	0.028	0.017	0.09825
10	rs1471633	1	A	C	0.029	0.016	0.07095
11	rs17050272	2	A	G	0.005	0.017	0.7625
12	rs17632159	5	C	G	-0.012	0.017	0.4888
13	rs17786744	8	G	A	0.015	0.016	0.3461
14	rs2078267	11	C	T	-0.022	0.016	0.1722
15	rs2231142	4	T	G	0.025	0.026	0.3347
16	rs2941484	8	T	C	0.011	0.016	0.4893
17	rs3741414	12	T	C	0.009	0.019	0.6299
18	rs478607	11	G	A	0.018	0.022	0.4173
19	rs653178	12	C	T	0.027	0.016	0.09708
20	rs6598541	15	A	G	0.005	0.016	0.7584
21	rs675209	6	T	C	-0.011	0.018	0.5271
22	rs6770152	3	G	T	0.015	0.016	0.3378
23	rs7188445	16	A	G	0.016	0.017	0.3453
24	rs7193778	16	C	T	-0.005	0.023	0.8233
25	rs7224610	17	C	A	0.018	0.016	0.2631
26	rs729761	6	T	G	0.020	0.019	0.2834
27	rs7953704	12	A	G	0.012	0.016	0.4454
28	rs7976059	12	T	G	-0.031	0.017	0.07669

SNP: each SNP's id; chr: chromosome; EA: effect allele, OA: other allele; GY: beta for the SNP-Alzheimer's disease relationship; SE_GY: standard error of GY; pval: p-value of GY

Table S7. The association estimates of the 28 SNPs for urate (1) with coronary heart disease (CHD) (6)

	SNP	chr	EA	OA	EAF	GY	SE_GY	pval
1	rs10480300	7	C	T	0.758	0.017	0.011	0.1365408
2	rs10821905	10	G	A	0.820	0.023	0.012	0.055396
3	rs11264341	1	C	T	0.568	-0.017	0.010	0.081745
4	rs1165151	6	G	T	0.539	-0.016	0.009	0.0815358
5	rs1171614	10	C	T	0.762	-0.012	0.012	0.3340968
6	rs1178977	7	A	G	0.823	0.006	0.013	0.6071614
7	rs12498742	4	A	G	0.767	0.012	0.011	0.2830966
8	rs1260326	2	C	T	0.610	-0.003	0.010	0.7349392
9	rs1394125	15	G	A	0.691	-0.006	0.011	0.5658209
10	rs1471633	1	A	C	0.537	0.017	0.010	0.0749271
11	rs17050272	2	G	A	0.597	-0.006	0.010	0.5597656
12	rs17632159	5	G	C	0.691	-0.003	0.010	0.7899725
13	rs17786744	8	A	G	0.630	-0.005	0.010	0.6015566
14	rs2078267	11	C	T	0.540	0.001	0.010	0.9107651
15	rs2231142	4	G	T	0.887	0.024	0.015	0.1143624
16	rs2941484	8	C	T	0.563	-0.010	0.009	0.2861924
17	rs3741414	12	C	T	0.799	-0.012	0.012	0.3185743
18	rs478607	11	A	G	0.810	0.005	0.013	0.668657
19	rs653178	12	T	C	0.579	-0.064	0.010	5.15E-10
20	rs6598541	15	G	A	0.598	0.006	0.009	0.5183619
21	rs675209	6	C	T	0.645	0.016	0.010	0.1229597
22	rs6770152	3	T	G	0.573	-0.019	0.009	0.0409614
23	rs7188445	16	G	A	0.705	0.007	0.011	0.515785
24	rs7193778	16	T	C	0.836	-0.009	0.014	0.4928628
25	rs7224610	17	A	C	0.607	0.006	0.010	0.5373028
26	rs729761	6	G	T	0.718	-0.013	0.011	0.2615705
27	rs7953704	12	G	A	0.527	-0.009	0.009	0.3281571
28	rs7976059	12	G	T	0.632	0.004	0.010	0.6806164

SNP: each SNP's id; chr: chromosome; EA: effect allele, OA: other allele; EAF: effect allele frequency for GY; GY: beta for the SNP-CHD relationship; SE_GY: standard error of GY; pval: p-value of GY

Table S8. The association estimates of the 28 SNPs for urate (1) with myocardial infarction (MI) (6)

	SNP	chr	EA	OA	EAF	GY	SE_GY	pval
1	rs10480300	7	T	C	0.245	0.010	0.013	0.41820349
2	rs10821905	10	A	G	0.176	0.035	0.013	0.00932379
3	rs11264341	1	T	C	0.421	-0.016	0.011	0.13180104
4	rs1165151	6	G	T	0.533	-0.023	0.010	0.02632004
5	rs1171614	10	C	T	0.742	-0.002	0.014	0.87910941
6	rs1178977	7	G	A	0.172	0.007	0.014	0.63826783
7	rs12498742	4	G	A	0.228	0.013	0.012	0.29664083
8	rs1260326	2	T	C	0.422	-0.001	0.011	0.9166279
9	rs1394125	15	A	G	0.299	-0.002	0.012	0.88583215
10	rs1471633	1	C	A	0.452	0.016	0.011	0.13190286
11	rs17050272	2	A	G	0.378	0.005	0.011	0.64781176
12	rs17632159	5	C	G	0.298	-0.007	0.011	0.51468404
13	rs17786744	8	G	A	0.369	-0.005	0.011	0.65350967
14	rs2078267	11	T	C	0.438	-0.008	0.011	0.47673314
15	rs2231142	4	T	G	0.110	0.022	0.017	0.19174707
16	rs2941484	8	T	C	0.430	-0.018	0.010	0.07495691
17	rs3741414	12	T	C	0.193	0.003	0.014	0.82049052
18	rs478607	11	A	G	0.776	0.004	0.014	0.78504645
19	rs653178	12	T	C	0.558	-0.077	0.012	2.84E-11
20	rs6598541	15	G	A	0.580	0.010	0.011	0.35000693
21	rs675209	6	C	T	0.627	0.018	0.011	0.10676248
22	rs6770152	3	T	G	0.559	-0.017	0.010	0.11390205
23	rs7188445	16	A	G	0.291	0.005	0.012	0.65739895
24	rs7193778	16	T	C	0.811	0.003	0.015	0.83535075
25	rs7224610	17	A	C	0.587	0.003	0.011	0.78176886
26	rs729761	6	G	T	0.696	-0.018	0.012	0.14330225
27	rs7953704	12	G	A	0.513	-0.019	0.010	0.0648285
28	rs7976059	12	T	G	0.357	0.006	0.011	0.55745239

SNP: each SNP's id; chr: chromosome; EA: effect allele, OA: other allele; EAF: effect allele frequency for GY; GY: beta for the SNP-MI relationship; SE_GY: standard error of GY; pval: p-value of GY

Table S9. The association estimates of the 28 SNPs for urate (1) with systolic blood pressure (SBP) (8)

	SNP	chr	EA	OA	GY	SE_GY	pval
1	rs10480300	7	T	C	0.015	0.003	1.45E-07
2	rs10821905	10	A	G	0.009	0.003	0.00435053
3	rs11264341	1	T	C	-0.008	0.002	0.00082043
4	rs1165151	6	G	T	-0.006	0.002	0.00999244
5	rs1171614	10	C	T	-0.008	0.003	0.00897198
6	rs1178977	7	G	A	0.001	0.003	0.676104
7	rs12498742	4	G	A	0.004	0.003	0.21947
8	rs1260326	2	C	T	0.005	0.003	0.0439014
9	rs1394125	15	A	G	0.002	0.003	0.47681
10	rs1471633	1	C	A	0.002	0.002	0.313305
11	rs17050272	2	A	G	0.002	0.002	0.353964
12	rs17632159	5	C	G	0.003	0.003	0.348555
13	rs17786744	8	G	A	0.004	0.003	0.158785
14	rs2078267	11	T	C	0.000	0.002	0.998987
15	rs2231142	4	T	G	-0.011	0.004	0.00493599
16	rs2941484	8	T	C	0.008	0.002	0.00218681
17	rs3741414	12	T	C	-0.009	0.003	0.00195694
18	rs478607	11	A	G	-0.005	0.003	0.136448
19	rs653178	12	T	C	-0.021	0.002	1.16E-17
20	rs6598541	15	G	A	-0.001	0.003	0.618474
21	rs675209	6	C	T	-0.001	0.003	0.592666
22	rs6770152	3	T	G	-0.006	0.002	0.0220286
23	rs7188445	16	A	G	0.001	0.003	0.654585
24	rs7193778	16	T	C	-0.016	0.003	2.19E-06
25	rs7224610	17	A	C	-0.008	0.003	0.0024854
26	rs729761	6	G	T	0.002	0.003	0.506385
27	rs7953704	12	G	A	-0.004	0.002	0.124599
28	rs7976059	12	T	G	0.005	0.003	0.048739

SNP: each SNP's id; chr: chromosome; EA: effect allele, OA: other allele; GY: beta for the SNP-SBP relationship; SE_GY: standard error of GY; pval: p-value of GY

Table S10. The association estimates of the 28 SNPs for urate (1) with any ischemic stroke (IS) (10)

	SNP	chr	EA	OA	EAF	GY	SE_GY	pval
1	rs10480300	7	T	C	0.268	0.015	0.010	0.1382
2	rs10821905	10	A	G	0.193	-0.007	0.011	0.5244
3	rs11264341	1	T	C	0.468	-0.007	0.009	0.4156
4	rs1165151	6	T	G	0.432	-0.012	0.009	0.1708
5	rs1171614	10	T	C	0.226	-0.003	0.012	0.7939
6	rs1178977	7	A	G	0.811	0.008	0.012	0.5083
7	rs12498742	4	A	G	0.728	-0.010	0.011	0.366
8	rs1260326	2	T	C	0.414	0.006	0.009	0.5155
9	rs1394125	15	A	G	0.333	0.010	0.010	0.2888
10	rs1471633	1	A	C	0.537	0.007	0.010	0.4749
11	rs17050272	2	A	G	0.424	-0.010	0.009	0.2692
12	rs17632159	5	C	G	0.302	0.008	0.009	0.3547
13	rs17786744	8	A	G	0.624	-0.008	0.009	0.3781
14	rs2078267	11	T	C	0.491	0.021	0.010	0.03
15	rs2231142	4	T	G	0.175	-0.003	0.013	0.8286
16	rs2941484	8	T	C	0.454	-0.007	0.009	0.4401
17	rs3741414	12	T	C	0.227	-0.002	0.011	0.8872
18	rs478607	11	A	G	0.787	-0.017	0.011	0.1007
19	rs653178	12	T	C	0.543	-0.077	0.010	4.31E-14
20	rs6598541	15	A	G	0.409	0.011	0.009	0.1887
21	rs675209	6	T	C	0.346	-0.014	0.010	0.153
22	rs6770152	3	T	G	0.566	0.012	0.009	0.1693
23	rs7188445	16	A	G	0.312	-0.002	0.009	0.8374
24	rs7193778	16	T	C	0.861	-0.009	0.012	0.4761
25	rs7224610	17	A	C	0.631	0.002	0.009	0.8432
26	rs729761	6	T	G	0.247	-0.014	0.011	0.1802
27	rs7953704	12	A	G	0.487	-0.023	0.008	0.005882
28	rs7976059	12	T	G	0.414	-0.010	0.009	0.2491

SNP: each SNP's id; chr: chromosome; EA: effect allele, OA: other allele; EAF: effect allele frequency for GY; GY: beta for the SNP-IS relationship; SE_GY: standard error of GY; pval: p-value of GY

Table S11. The association estimates of the 28 SNPs for urate (1) with cardio-embolic stroke (CES) (10)

	SNP	chr	EA	OA	EAF	GY	SE_GY	pval
1	rs10480300	7	T	C	0.268	0.006	0.020	0.7797
2	rs10821905	10	A	G	0.194	0.022	0.023	0.3331
3	rs11264341	1	T	C	0.447	-0.034	0.017	0.05135
4	rs1165151	6	T	G	0.456	0.006	0.018	0.74
5	rs1171614	10	T	C	0.227	0.011	0.023	0.6229
6	rs1178977	7	A	G	0.814	0.014	0.024	0.5559
7	rs12498742	4	A	G	0.744	-0.019	0.021	0.3559
8	rs1260326	2	T	C	0.407	-0.013	0.019	0.4791
9	rs1394125	15	A	G	0.343	-0.006	0.020	0.7566
10	rs1471633	1	A	C	0.513	-0.005	0.018	0.7993
11	rs17050272	2	A	G	0.421	-0.007	0.018	0.6876
12	rs17632159	5	C	G	0.307	0.021	0.019	0.2671
13	rs17786744	8	A	G	0.612	0.007	0.018	0.7048
14	rs2078267	11	T	C	0.500	0.029	0.018	0.1192
15	rs2231142	4	T	G	0.147	0.002	0.028	0.9473
16	rs2941484	8	T	C	0.446	-0.002	0.017	0.9104
17	rs3741414	12	T	C	0.235	0.005	0.022	0.8014
18	rs478607	11	A	G	0.809	0.025	0.024	0.2943
19	rs653178	12	T	C	0.541	-0.058	0.020	0.003023
20	rs6598541	15	A	G	0.393	0.038	0.017	0.02562
21	rs675209	6	T	C	0.321	-0.013	0.021	0.513
22	rs6770152	3	T	G	0.572	-0.003	0.017	0.8761
23	rs7188445	16	A	G	0.315	-0.016	0.018	0.3768
24	rs7193778	16	T	C	0.858	-0.003	0.025	0.9134
25	rs7224610	17	A	C	0.610	0.011	0.018	0.5317
26	rs729761	6	T	G	0.258	0.008	0.022	0.7082
27	rs7953704	12	A	G	0.487	-0.024	0.017	0.1624
28	rs7976059	12	T	G	0.387	-0.015	0.018	0.4187

SNP: each SNP's id; chr: chromosome; EA: effect allele, OA: other allele; EAF: effect allele frequency for GY; GY: beta for the SNP-CE relationship; SE_GY: standard error of GY; pval: p-value of GY

Table S12. The association estimates of the 28 SNPs for urate (1) with large-artery atherosclerotic stroke (LAS) (10)

	SNP	chr	EA	OA	EAF	GY	SE_GY	pval
1	rs10480300	7	T	C	0.269	0.030	0.026	0.2486
2	rs10821905	10	A	G	0.183	0.015	0.028	0.6083
3	rs11264341	1	T	C	0.484	-0.032	0.021	0.1239
4	rs1165151	6	T	G	0.426	-0.032	0.022	0.1419
5	rs1171614	10	T	C	0.227	0.038	0.029	0.1838
6	rs1178977	7	A	G	0.823	0.023	0.028	0.4106
7	rs12498742	4	A	G	0.740	-0.027	0.026	0.3058
8	rs1260326	2	T	C	0.436	0.012	0.022	0.5781
9	rs1394125	15	A	G	0.324	0.045	0.024	0.06338
10	rs1471633	1	A	C	0.546	0.008	0.023	0.7251
11	rs17050272	2	A	G	0.431	-0.024	0.021	0.2399
12	rs17632159	5	C	G	0.304	0.011	0.022	0.6205
13	rs17786744	8	A	G	0.635	0.001	0.021	0.9619
14	rs2078267	11	T	C	0.496	0.028	0.024	0.2299
15	rs2231142	4	T	G	0.192	-0.008	0.029	0.7724
16	rs2941484	8	T	C	0.447	-0.001	0.020	0.9471
17	rs3741414	12	T	C	0.216	-0.009	0.027	0.7512
18	rs478607	11	A	G	0.799	-0.046	0.027	0.08713
19	rs653178	12	T	C	0.534	-0.094	0.026	0.000238
20	rs6598541	15	A	G	0.414	0.017	0.020	0.3917
21	rs675209	6	T	C	0.364	-0.025	0.025	0.3254
22	rs6770152	3	T	G	0.553	0.014	0.020	0.501
23	rs7188445	16	A	G	0.313	0.044	0.022	0.04303
24	rs7193778	16	T	C	0.862	-0.081	0.029	0.005975
25	rs7224610	17	A	C	0.639	0.025	0.022	0.2496
26	rs729761	6	T	G	0.244	-0.024	0.026	0.3675
27	rs7953704	12	A	G	0.490	-0.041	0.020	0.03757
28	rs7976059	12	T	G	0.437	0.016	0.021	0.4463

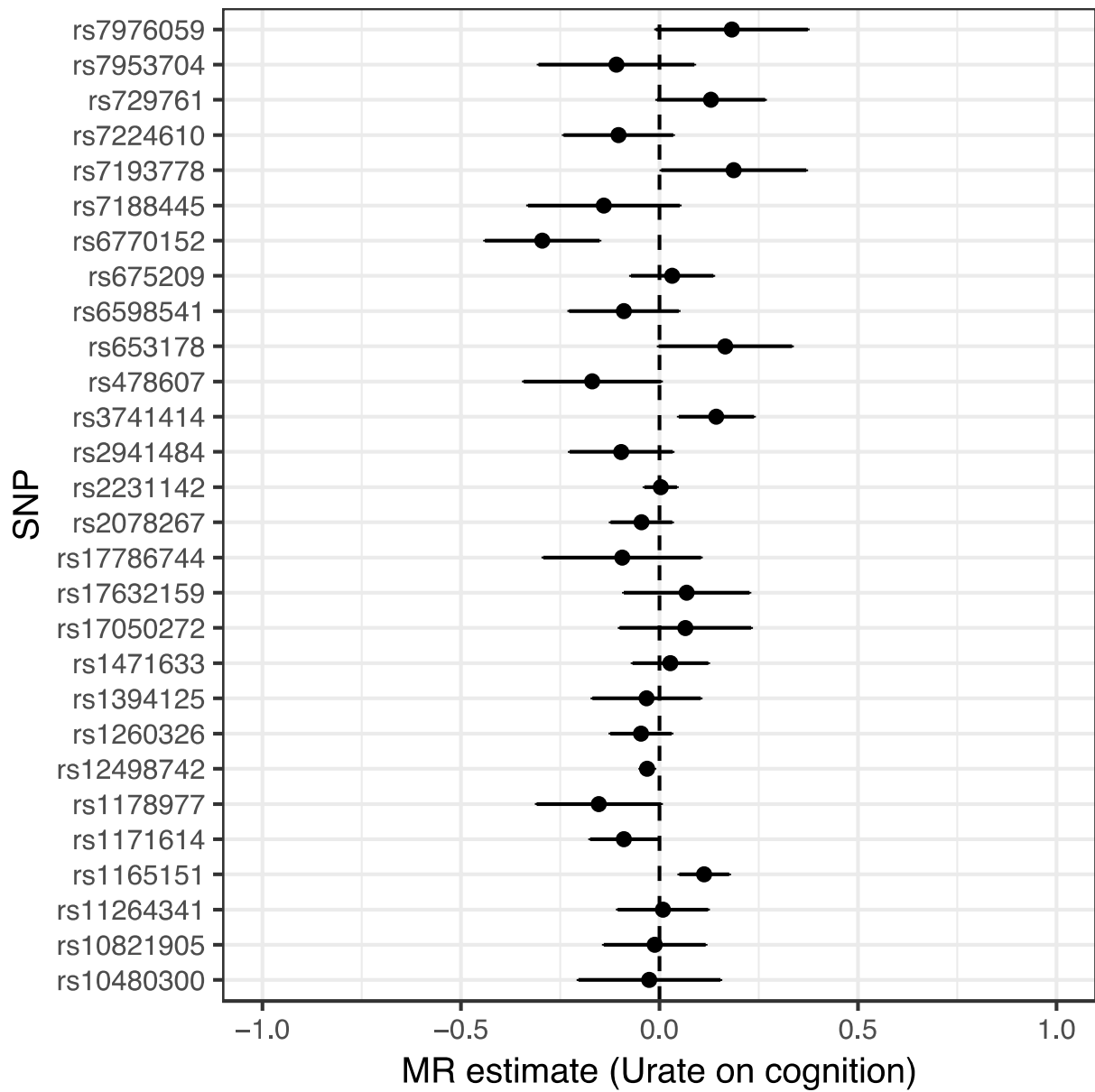
SNP: each SNP's id; chr: chromosome; EA: effect allele, OA: other allele; EAF: effect allele frequency for GY; GY: beta for the SNP-LAS relationship; SE_GY: standard error of GY; pval: p-value of GY

Table S13. The association estimates of the 28 SNPs for urate (1) with small-vessel stroke (SVS) (10)

	SNP	chr	EA	OA	EAF	GY	SE_GY	pval
1	rs10480300	7	T	C	0.265	-0.021	0.024	0.3765
2	rs10821905	10	A	G	0.178	-0.017	0.025	0.489
3	rs11264341	1	T	C	0.521	0.014	0.017	0.4048
4	rs1165151	6	T	G	0.388	-0.041	0.019	0.03197
5	rs1171614	10	T	C	0.228	-0.004	0.026	0.8896
6	rs1178977	7	A	G	0.822	0.011	0.023	0.6485
7	rs12498742	4	A	G	0.721	0.018	0.024	0.4411
8	rs1260326	2	T	C	0.453	0.021	0.018	0.2346
9	rs1394125	15	A	G	0.304	-0.032	0.021	0.126
10	rs1471633	1	A	C	0.578	0.007	0.020	0.7272
11	rs17050272	2	A	G	0.436	-0.031	0.017	0.07663
12	rs17632159	5	C	G	0.297	0.042	0.018	0.02171
13	rs17786744	8	A	G	0.653	0.010	0.018	0.5885
14	rs2078267	11	T	C	0.486	0.020	0.022	0.3554
15	rs2231142	4	T	G	0.219	0.005	0.023	0.8172
16	rs2941484	8	T	C	0.452	-0.008	0.017	0.6376
17	rs3741414	12	T	C	0.204	0.021	0.023	0.3575
18	rs478607	11	A	G	0.771	-0.035	0.021	0.09941
19	rs653178	12	T	C	0.544	-0.104	0.023	8.42E-06
20	rs6598541	15	A	G	0.434	0.004	0.017	0.7922
21	rs675209	6	T	C	0.408	-0.014	0.022	0.5217
22	rs6770152	3	T	G	0.539	0.013	0.017	0.4429
23	rs7188445	16	A	G	0.309	0.004	0.018	0.8338
24	rs7193778	16	T	C	0.865	-0.016	0.025	0.5174
25	rs7224610	17	A	C	0.669	-0.007	0.019	0.7091
26	rs729761	6	T	G	0.226	-0.055	0.022	0.01285
27	rs7953704	12	A	G	0.491	-0.008	0.016	0.6139
28	rs7976059	12	T	G	0.483	-0.023	0.018	0.1978

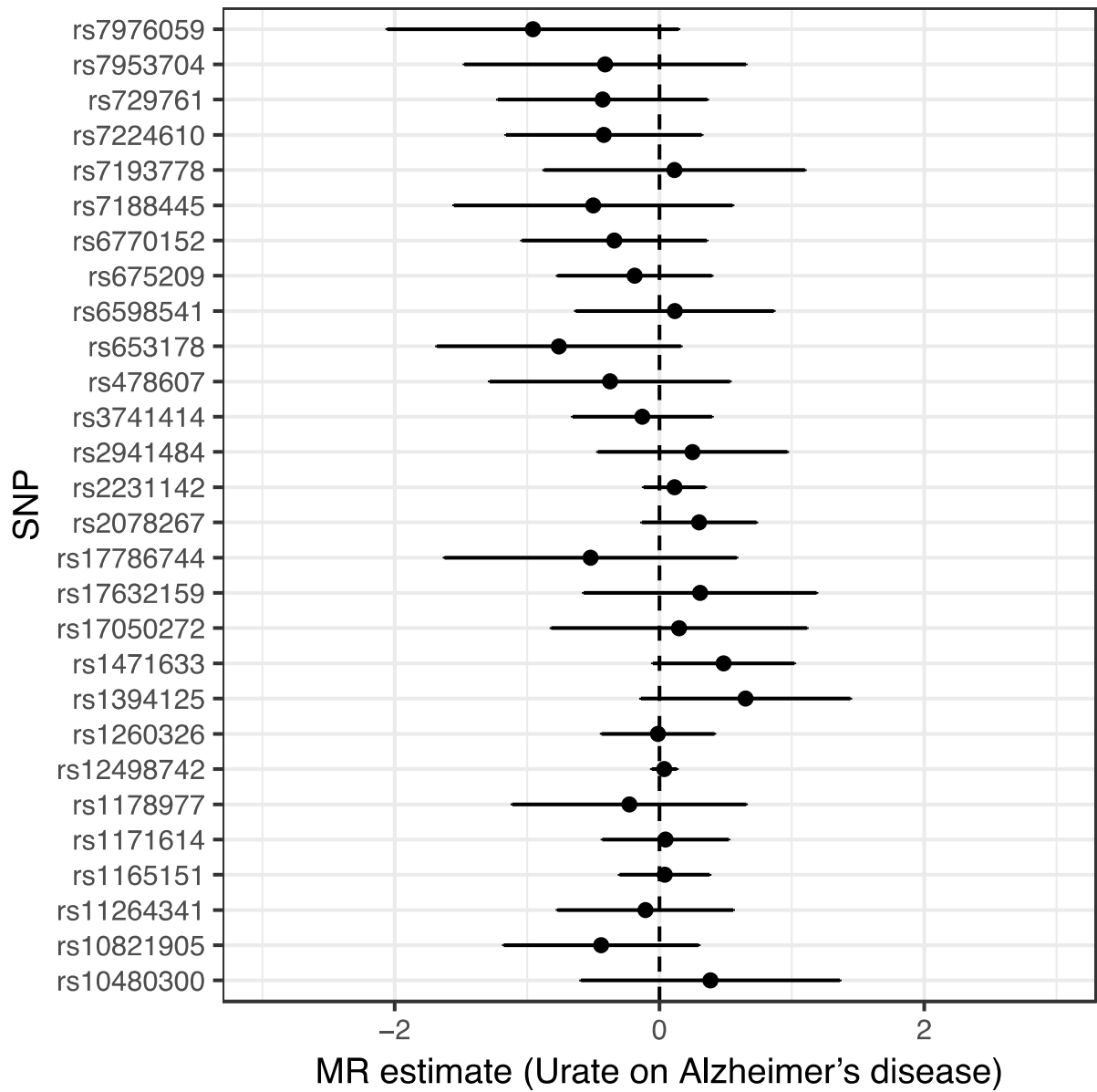
SNP: each SNP's id; chr: chromosome; EA: effect allele, OA: other allele; EAF: effect allele frequency for GY; GY: beta for the SNP-SVS relationship; SE_GY: standard error of GY; pval: p-value of GY

Figure S1. Forest plot of the 28 MR estimates of the urate-cognitive performance relationship.



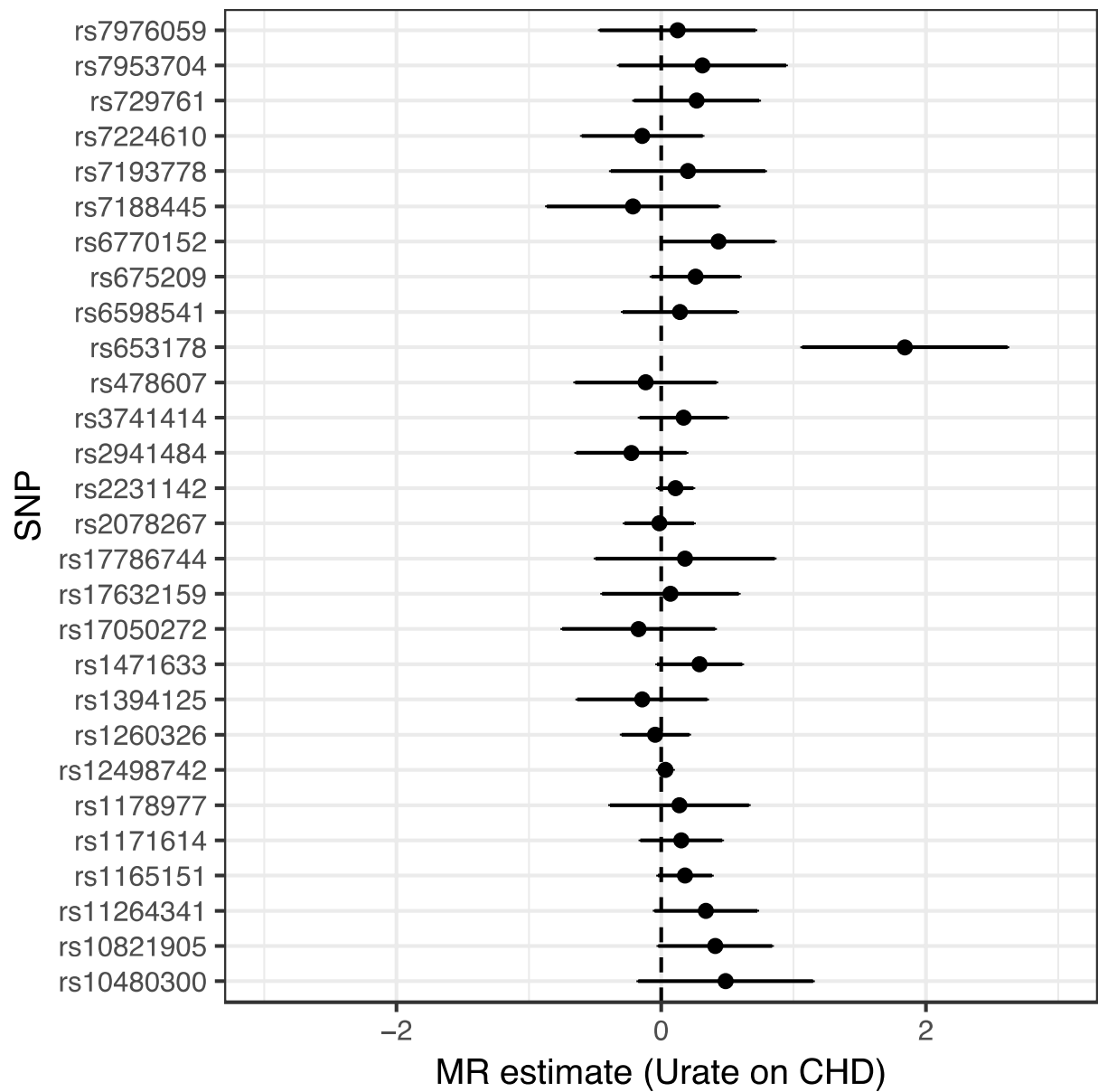
Each dot indicates the effect estimate of each SNP with horizontal lines represent the 95% confidence interval (CI) of this estimate.

Figure S2. Forest plot of the 28 MR estimates of the urate-Alzheimer's disease relationship.



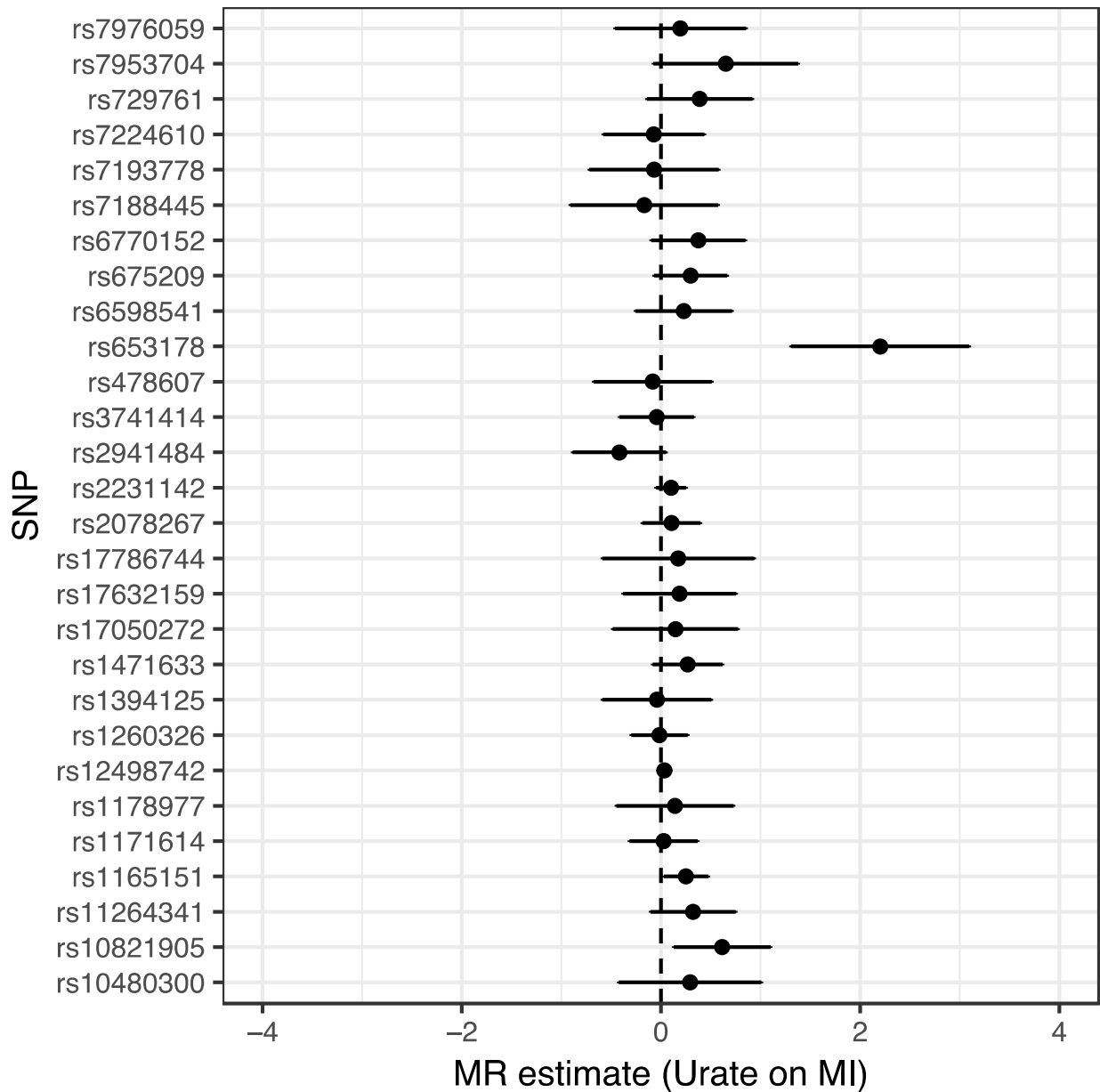
Each dot indicates the effect estimate (logOR) of each SNP with horizontal lines represent the 95% confidence interval (CI) of this estimate.

Figure S3. Forest plot of the 28 MR estimates of the urate-coronary heart disease (CHD) relationship.



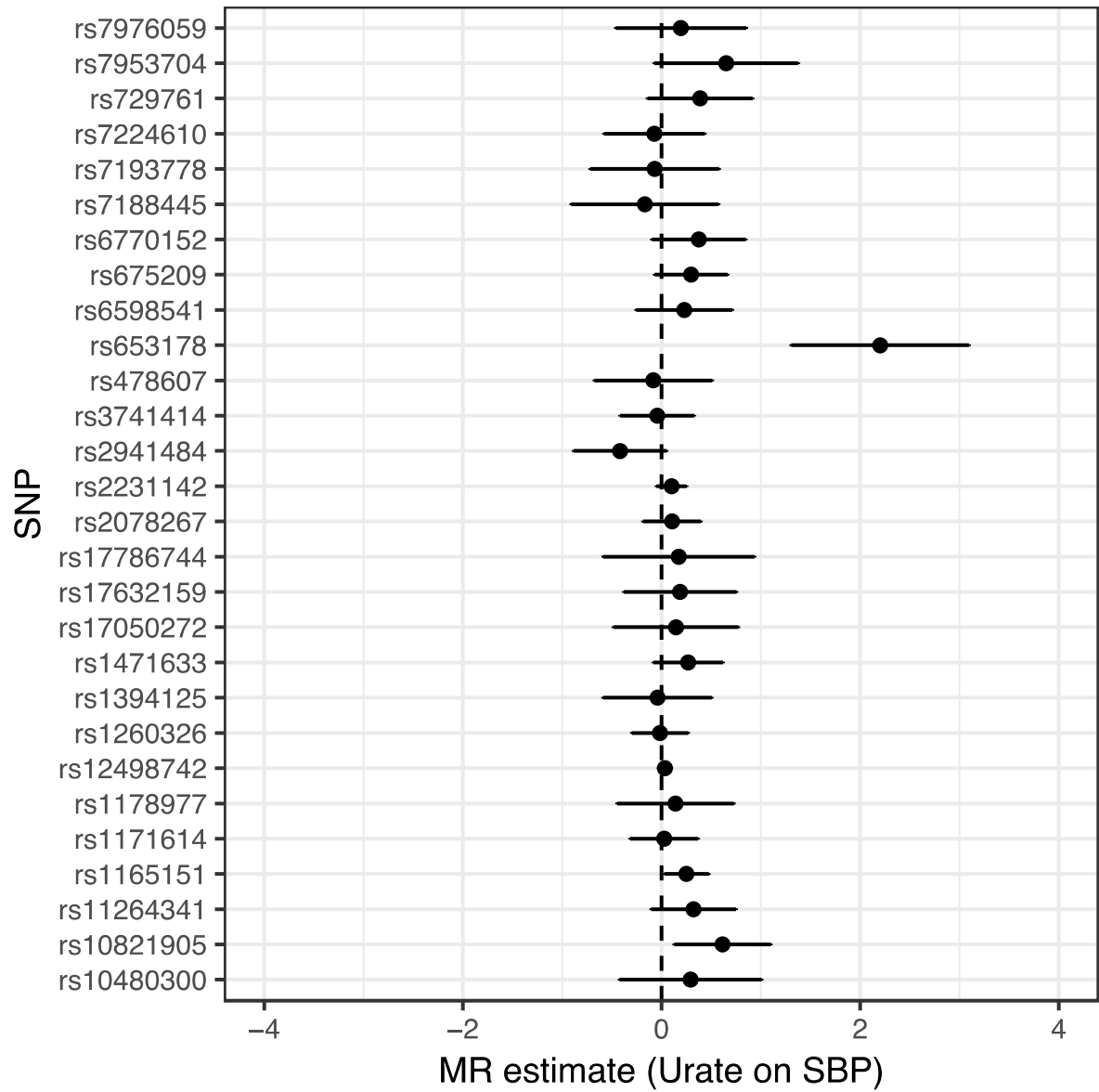
Each dot indicates the effect estimate (logOR) of each SNP with horizontal lines represent the 95% confidence interval (CI) of this estimate.

Figure S4. Forest plot of the 28 MR estimates of the urate-myocardial infarction (MI) relationship.



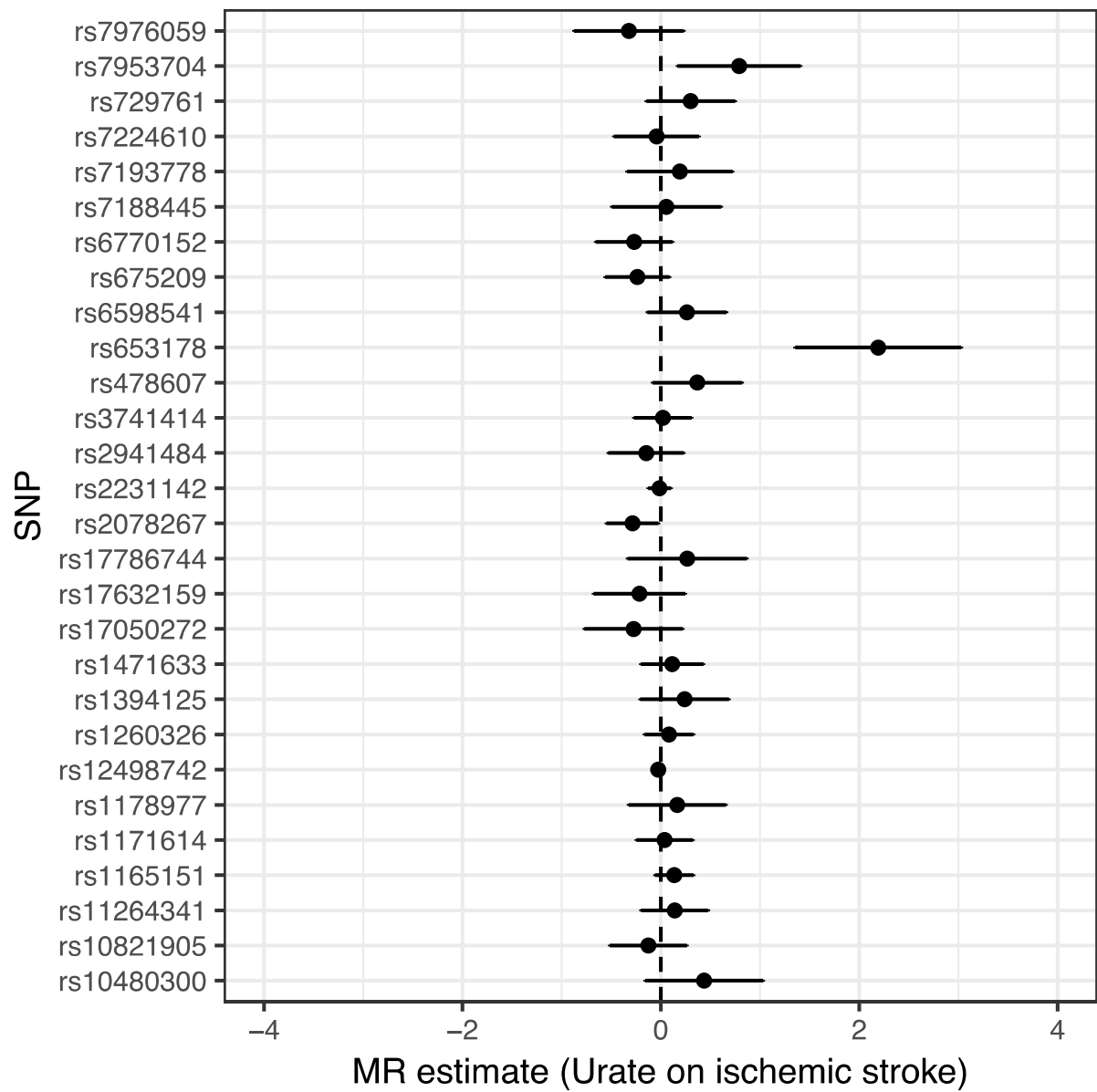
Each dot indicates the effect estimate (logOR) of each SNP with horizontal lines represent the 95% confidence interval (CI) of this estimate.

Figure S5. Forest plot of the 28 MR estimates of the urate-systolic blood pressure (SBP) relationship.



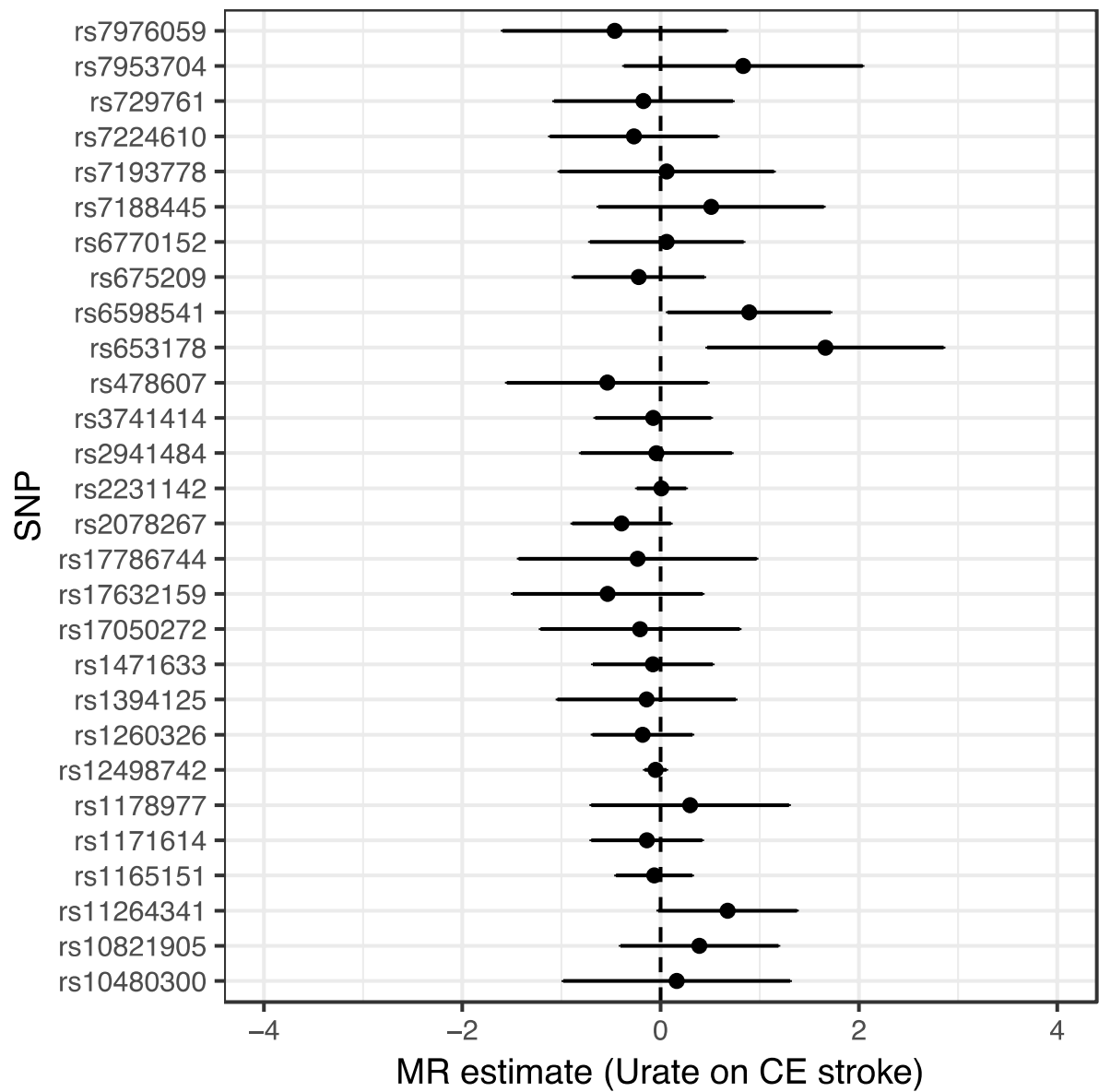
Each dot indicates the effect estimate of each SNP with horizontal lines represent the 95% confidence interval (CI) of this estimate.

Figure S6. Forest plot of the 28 MR estimates of the urate- any ischemic stroke relationship.



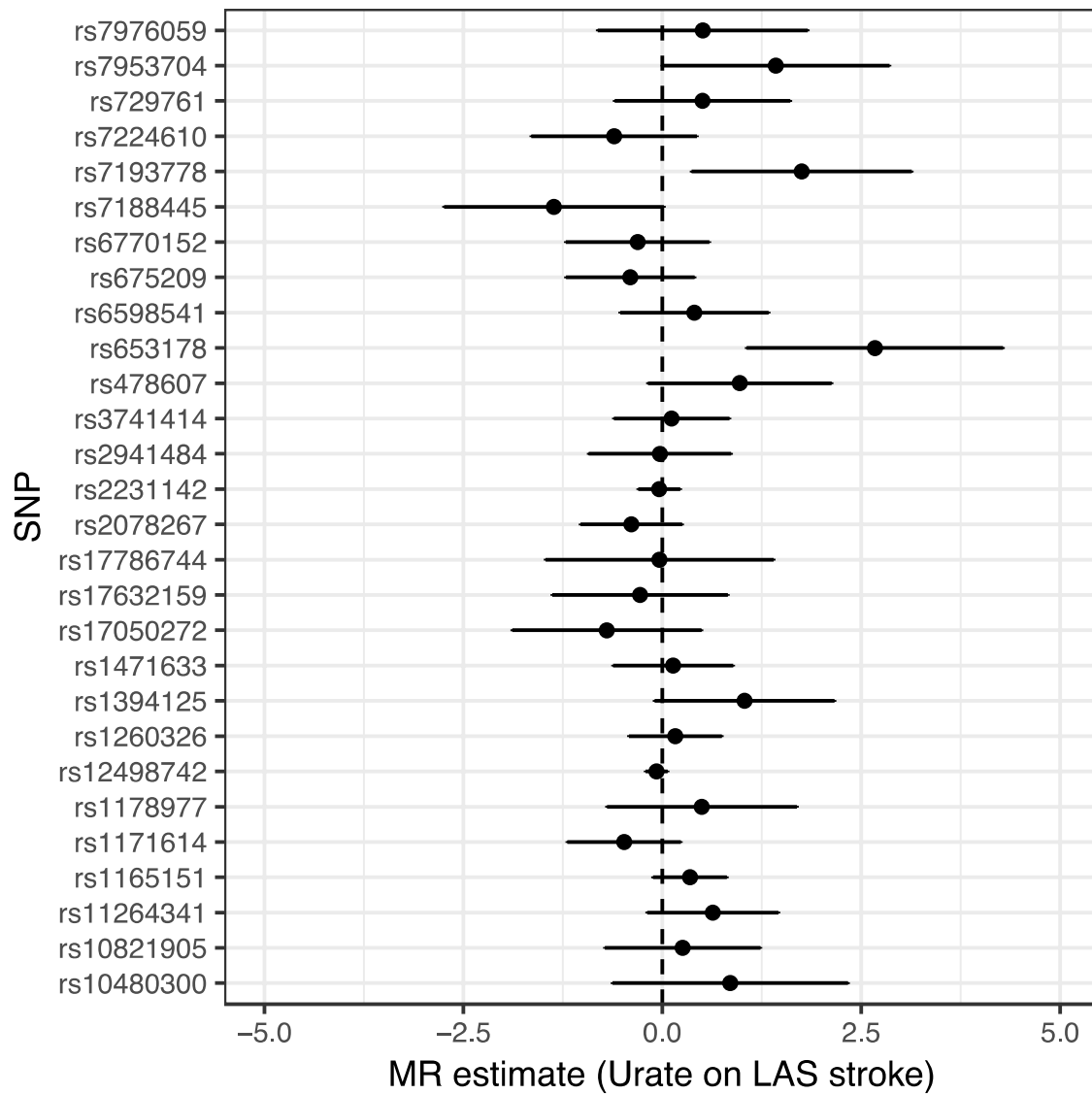
Each dot indicates the effect estimate (logOR) of each SNP with horizontal lines represent the 95% confidence interval (CI) of this estimate.

Figure S7. Forest plot of the 28 MR estimates of the urate- cardioembolic stroke ischemic stroke (CES) relationship.



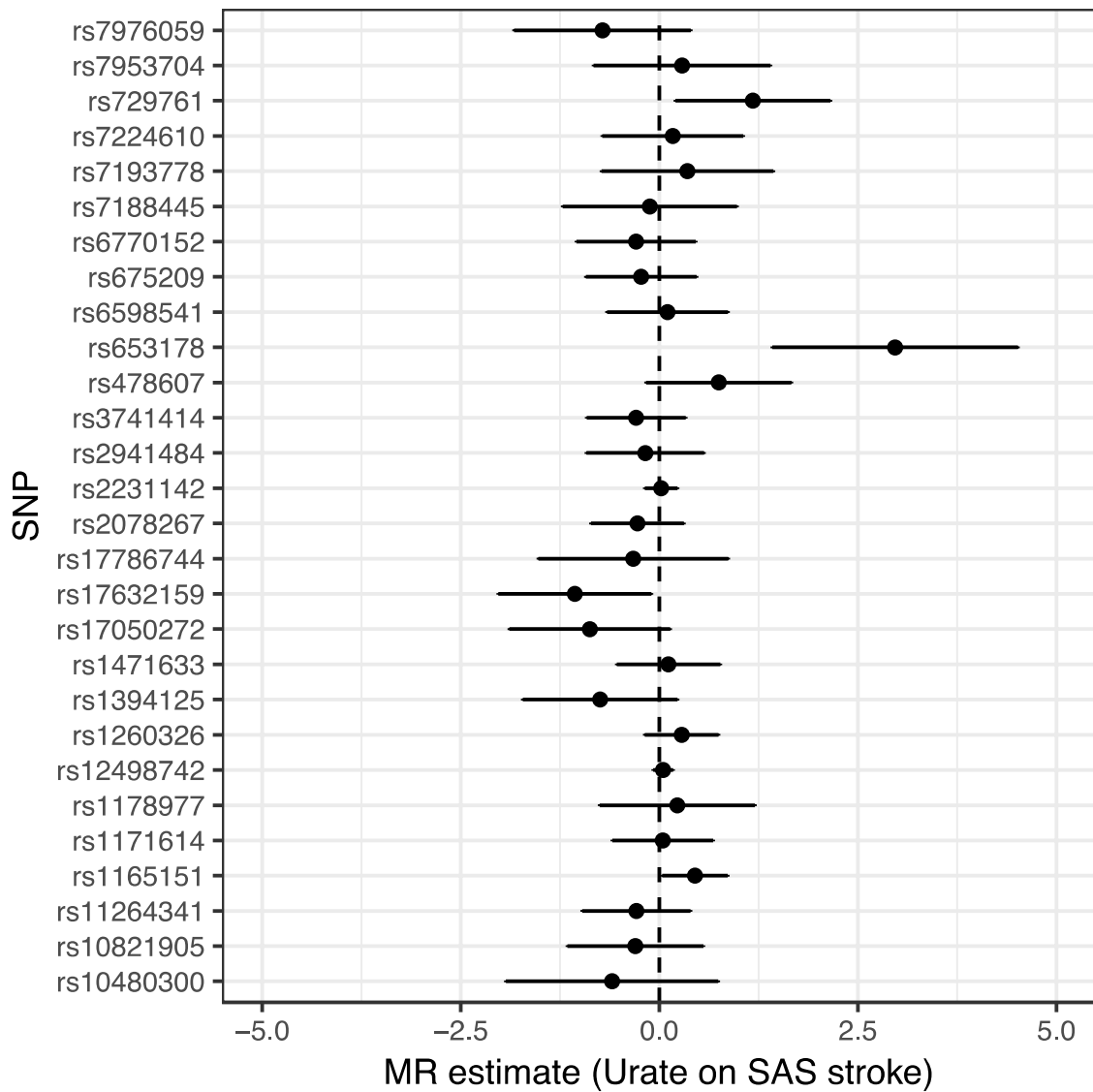
Each dot indicates the effect estimate (logOR) of each SNP with horizontal lines represent the 95% confidence interval (CI) of this estimate.

Figure S8. Forest plot of the 28 MR estimates of the urate- large-artery atherosclerotic ischemic stroke (LAS) relationship.



Each dot indicates the effect estimate (logOR) of each SNP with horizontal lines represent the 95% confidence interval (CI) of this estimate.

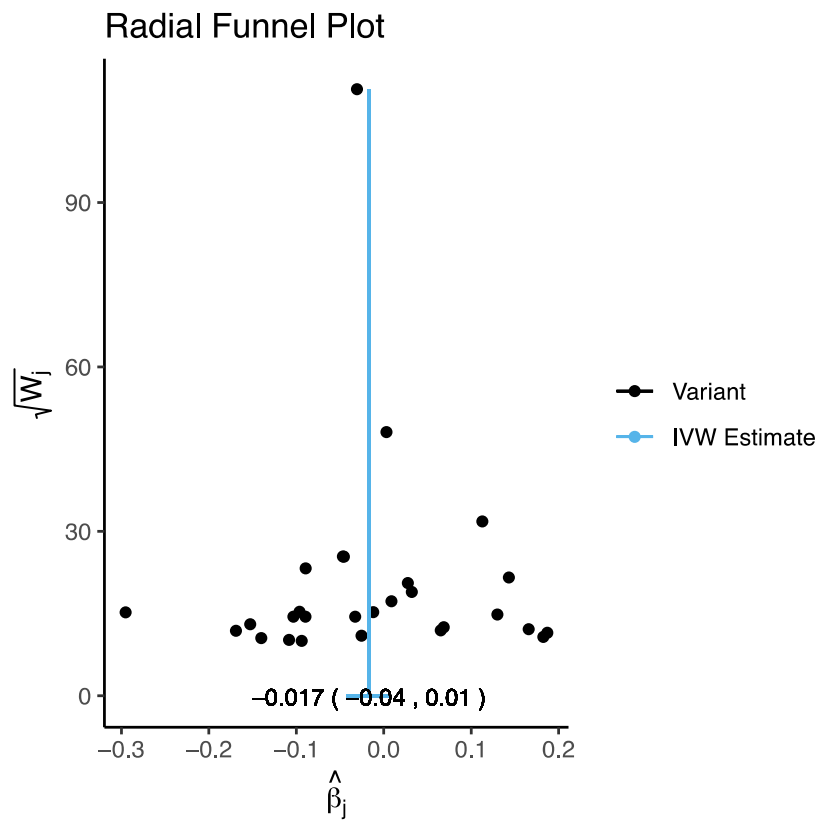
Figure S9. Forest plot of the 28 MR estimates of the urate- small-artery stroke ischemic stroke (SAS) relationship.



Each dot indicates the effect estimate (logOR) of each SNP with horizontal lines represent the 95% confidence interval (CI) of this estimate.

Figure S10. Funnel plot (A) and radial plot (B) for the urate-cognitive performance relationship.

(A)



(B)

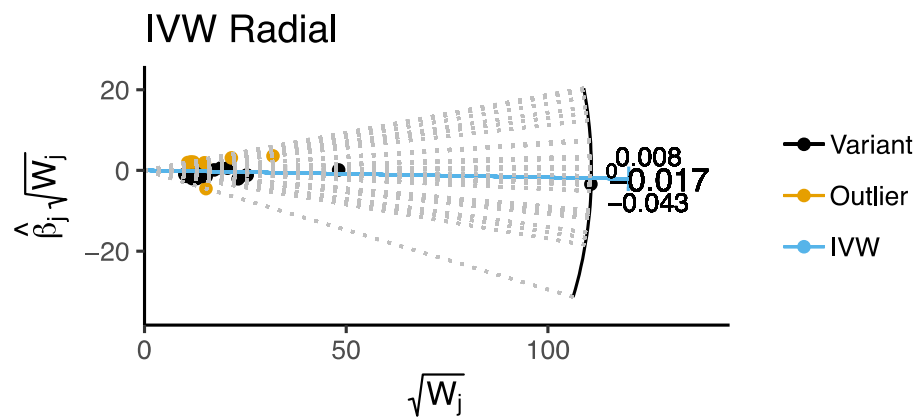
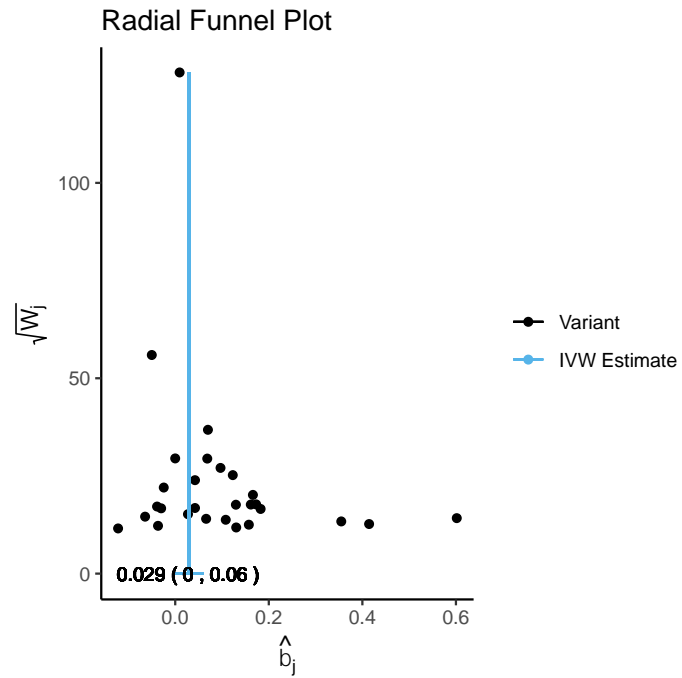


Figure S11. Funnel plot (A) and radial plot (B) for the urate-Alzheimer's disease relationship.

(A)



(B)

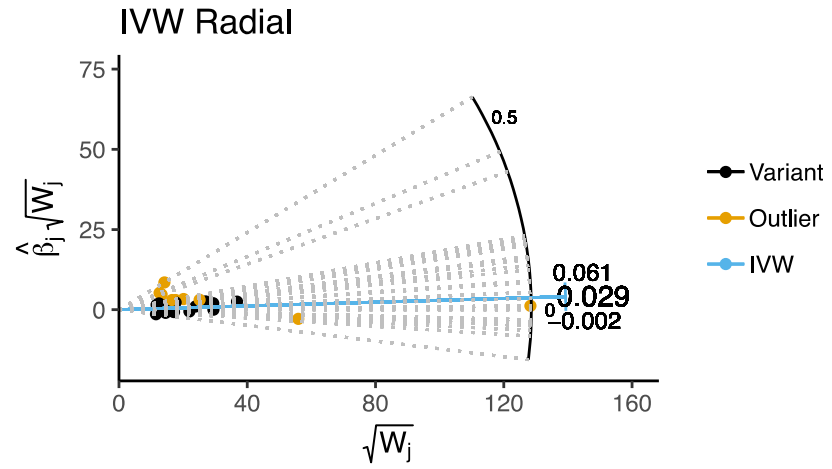
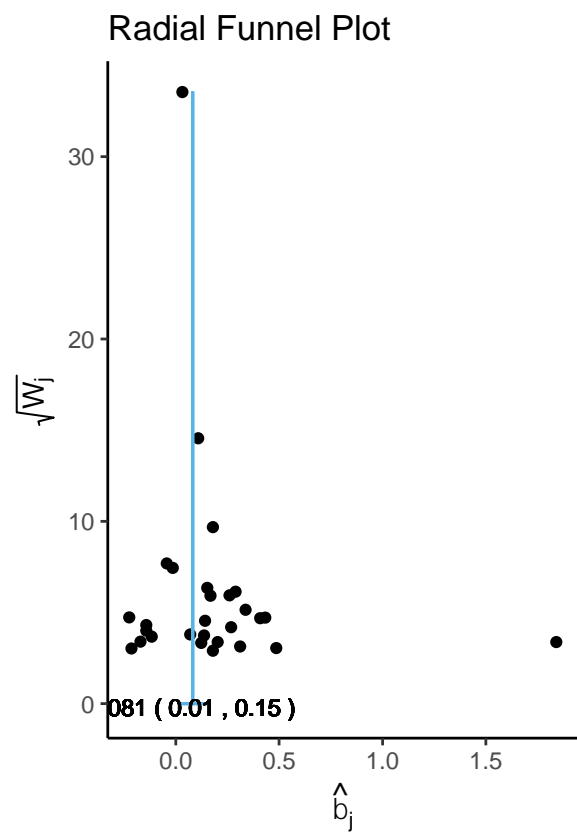


Figure S12. Funnel plot (A) and radial plot (B) for the urate-coronary heart disease (CHD) relationship.

(A)



(B)

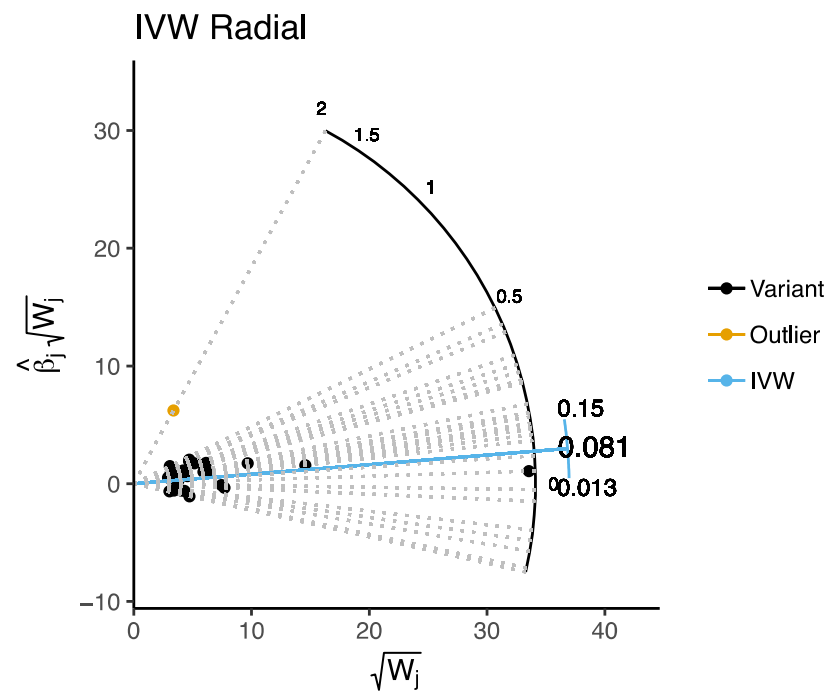
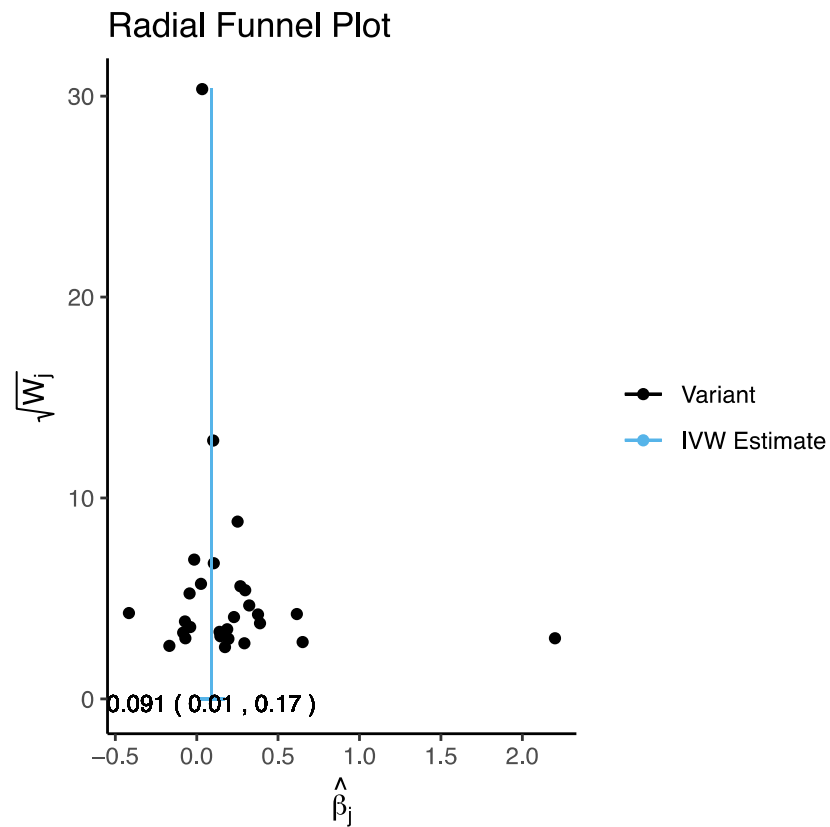


Figure S13. Funnel plot (A) and radial plot (B) for the urate-myocardial infarction (MI) relationship.

(A)



(B)

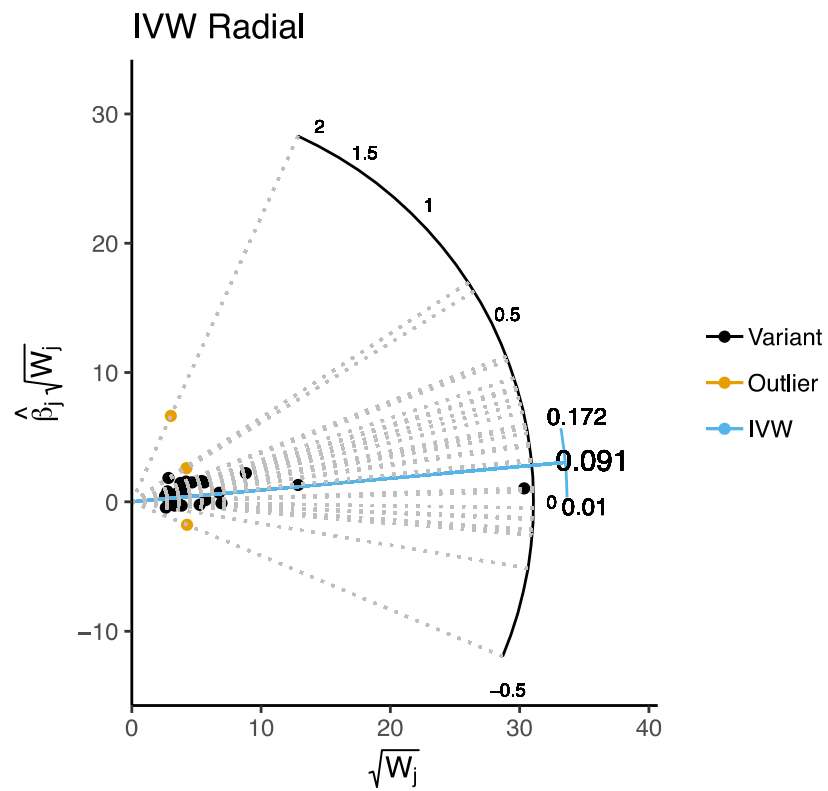
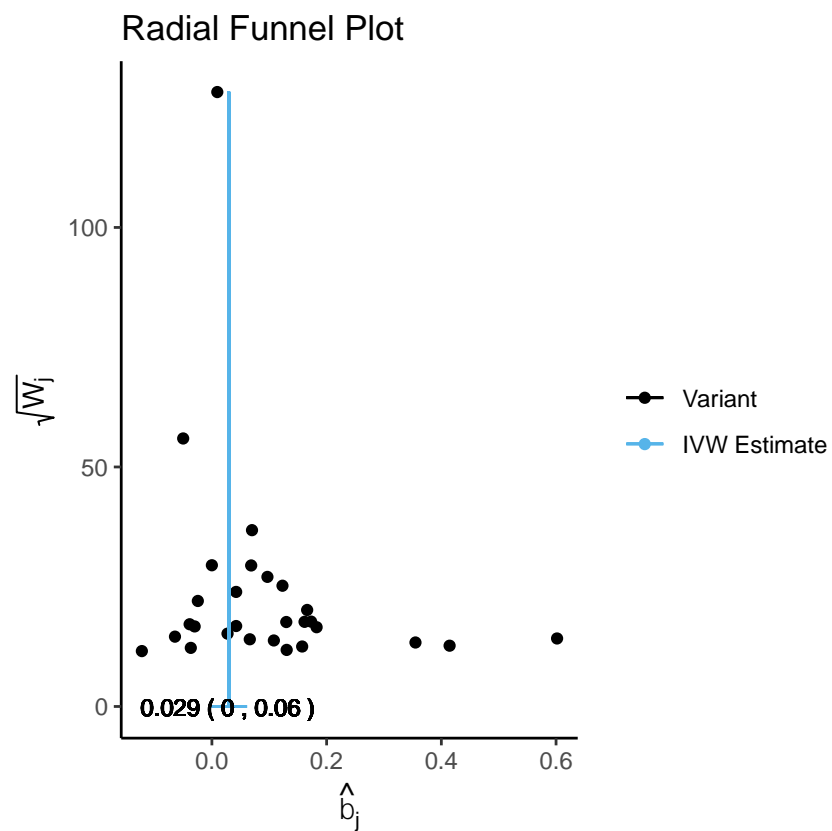


Figure S14. Funnel plot (A) and radial plot (B) for the urate- systolic blood pressure (SBP) relationship.

(A)



(B)

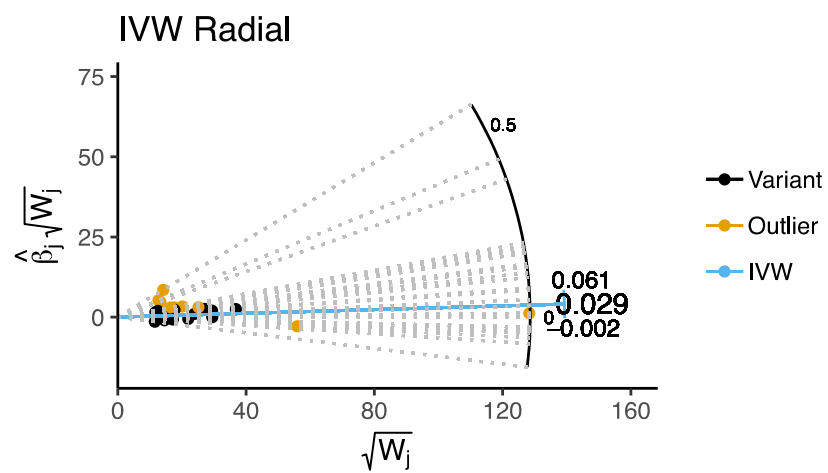
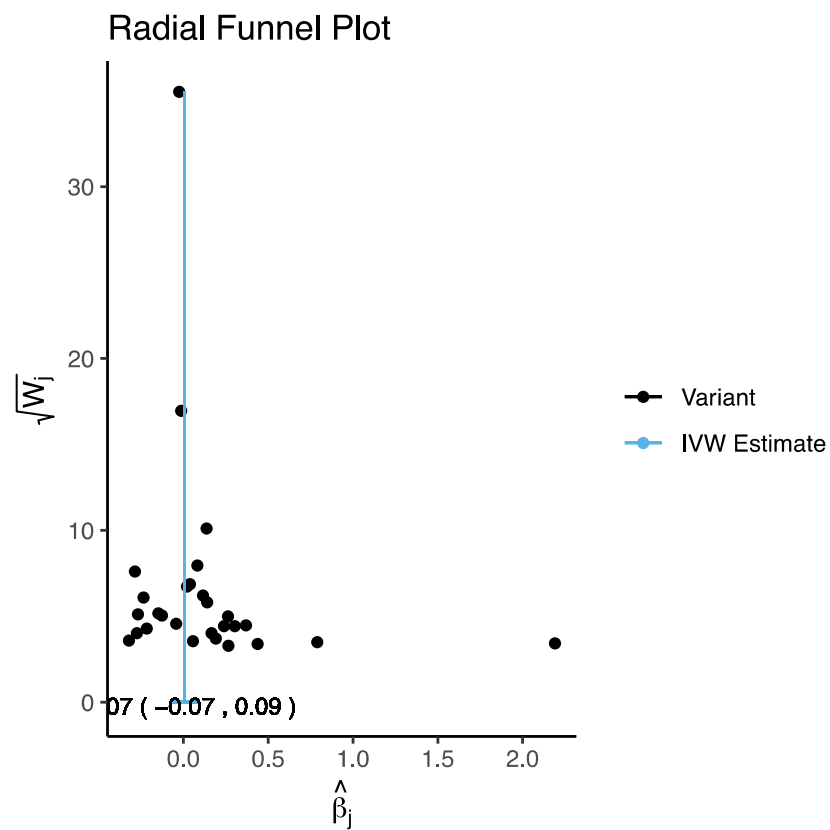


Figure S15. Funnel plot (A) and radial plot (B) for the urate-any ischemic stroke relationship.

(A)



(B)

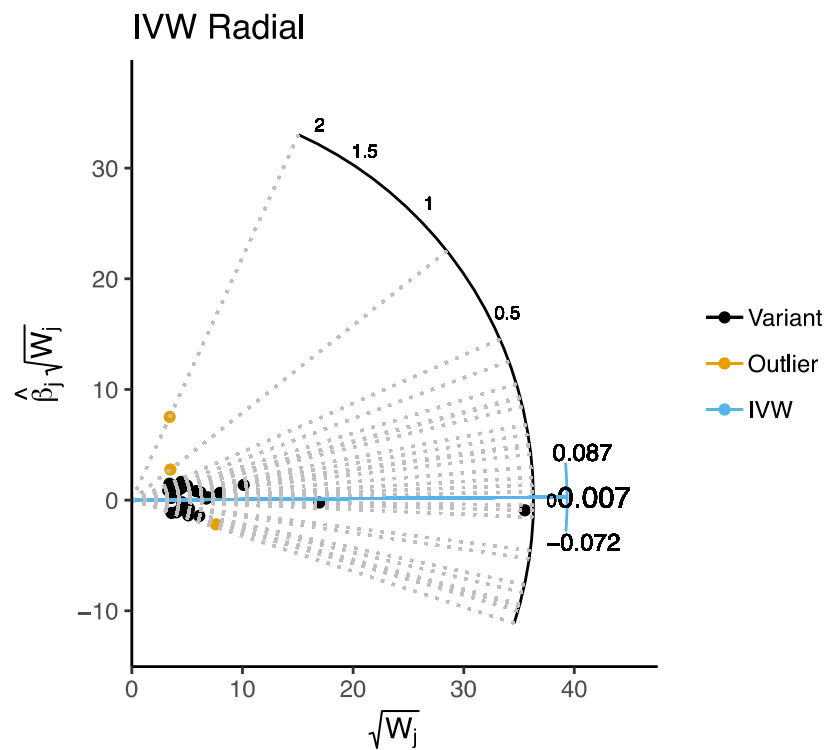
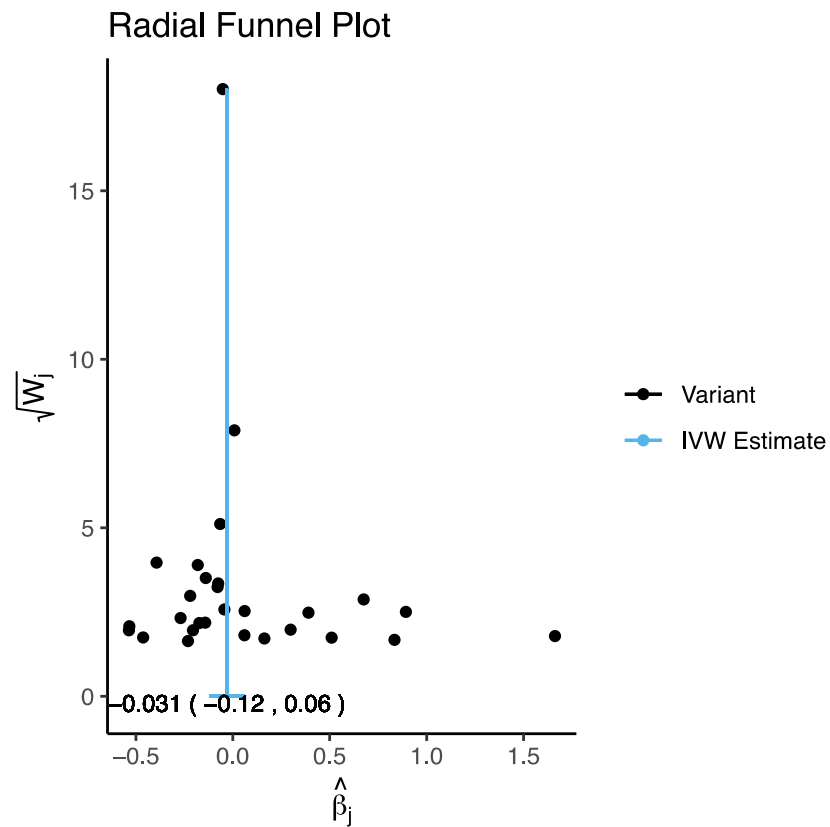


Figure S16. Funnel plot (A) and radial plot (B) for the urate- cardioembolic ischemic stroke (CES) relationship.

(A)



(B)

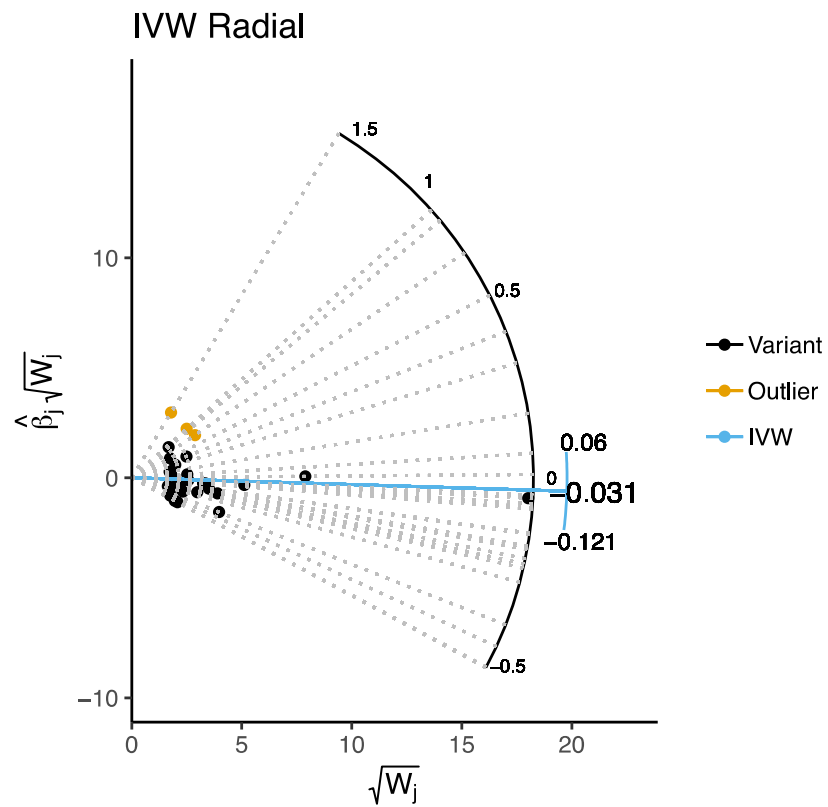
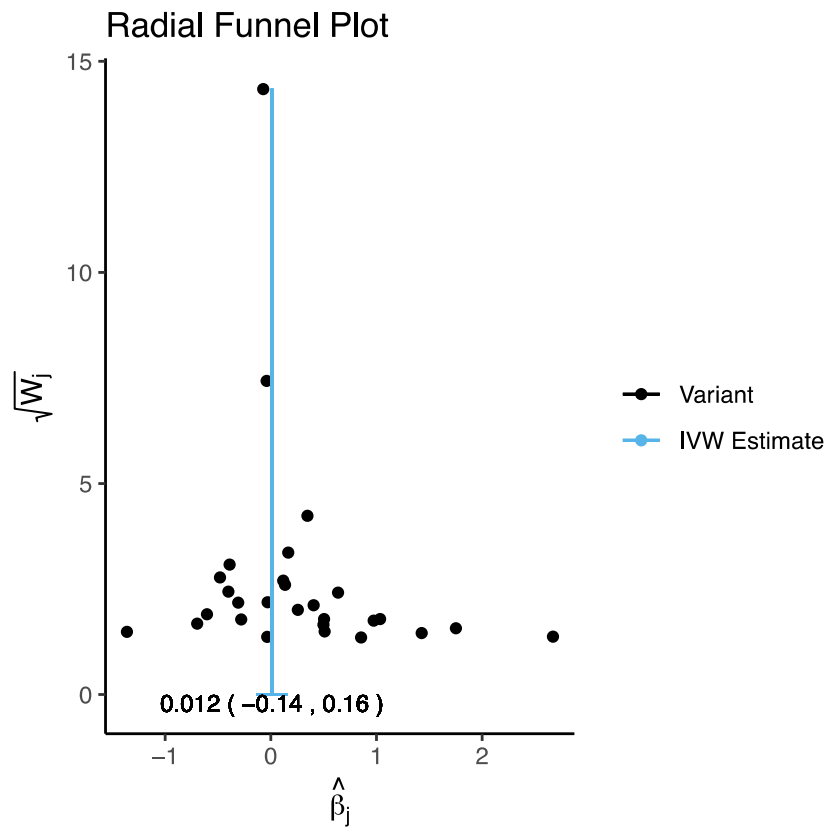


Figure S17. Funnel plot (A) and radial plot (B) for the urate- large-artery atherosclerotic ischemic stroke (LAS) relationship.

(A)



(B)

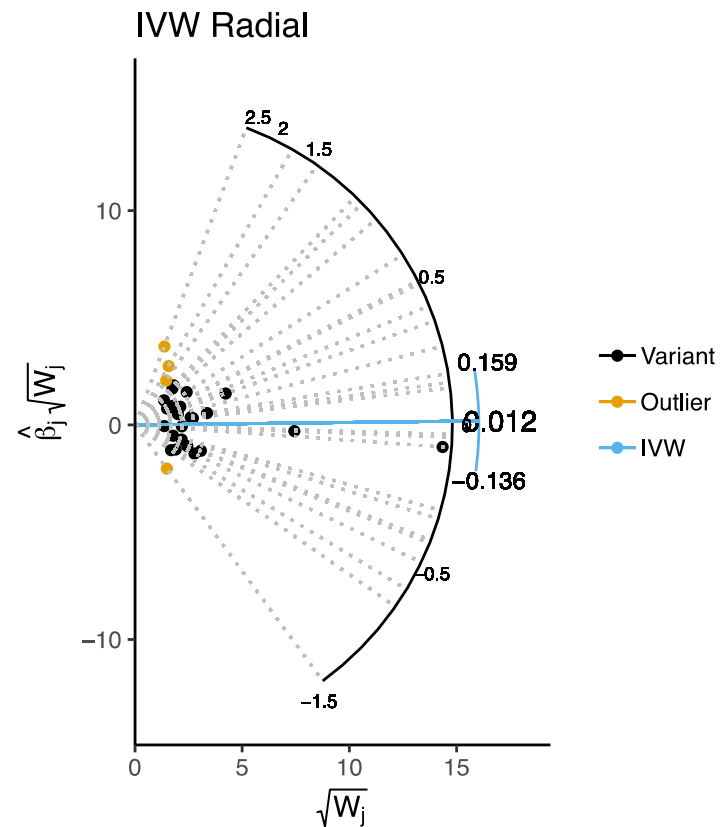
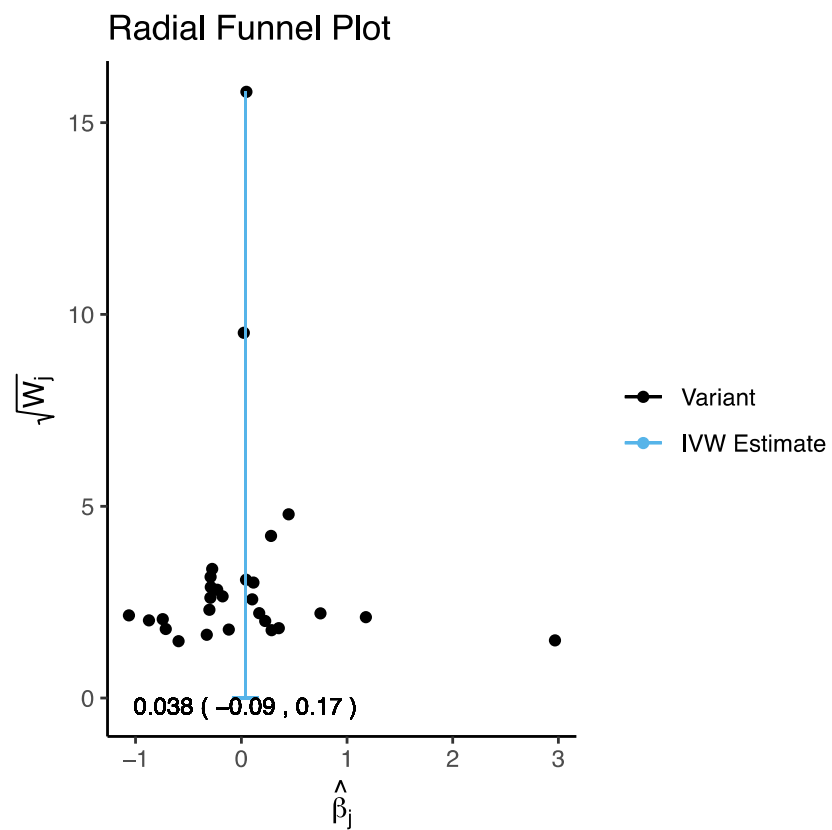


Figure S18. Funnel plot (A) and radial plot (B) for the urate- small-artery ischemic stroke (SVS) relationship.

(A)



(B)

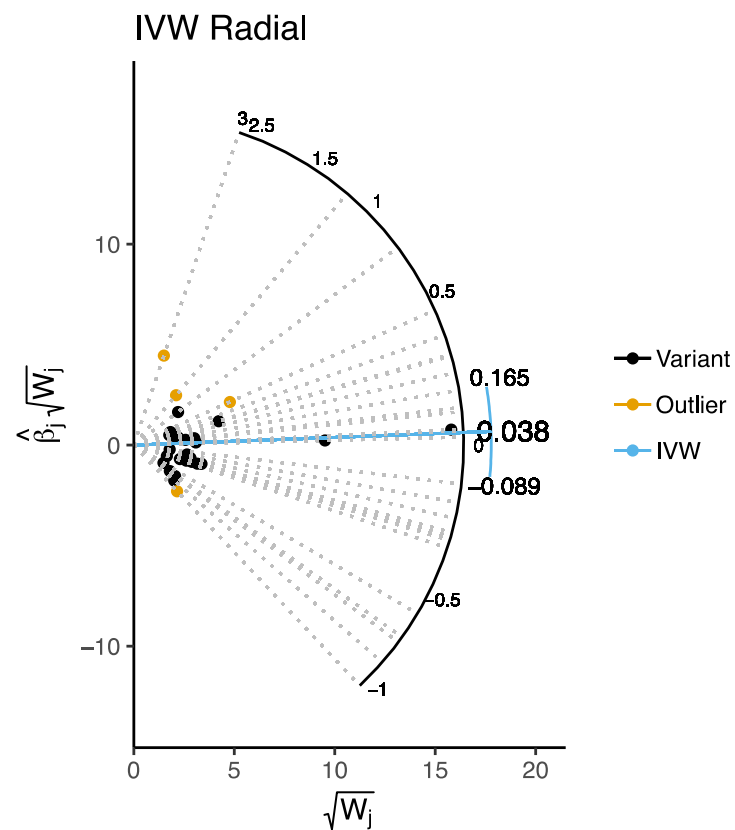
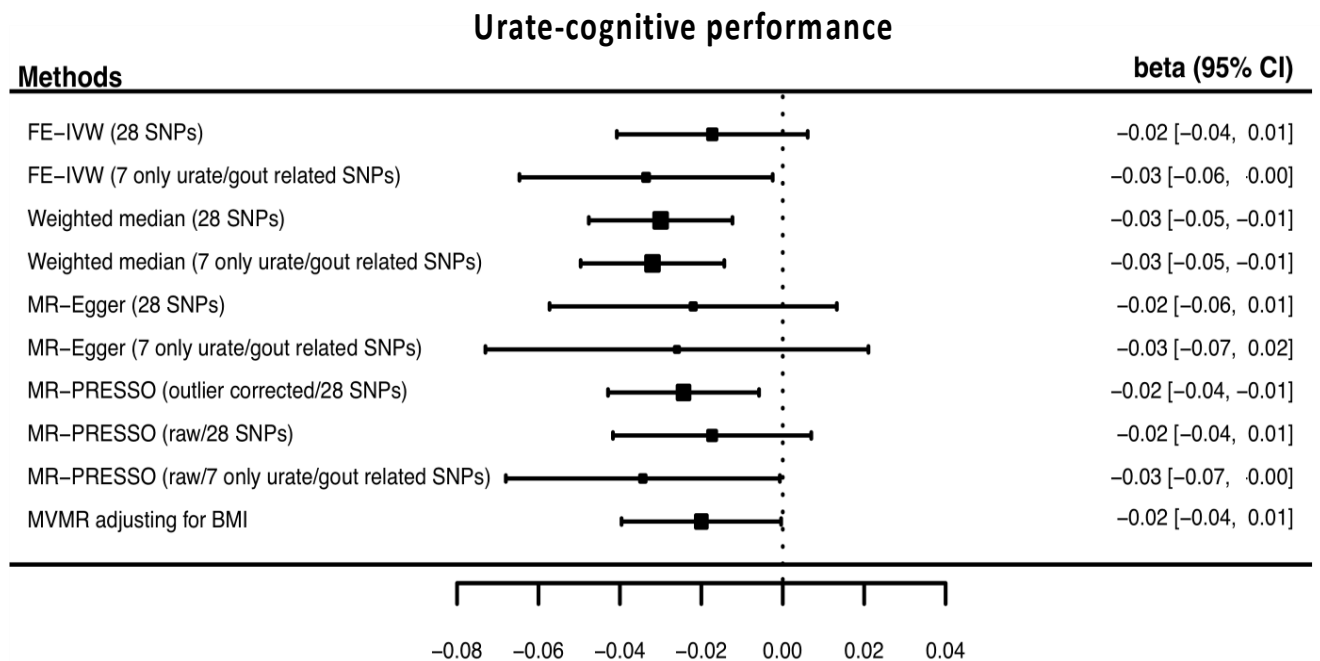
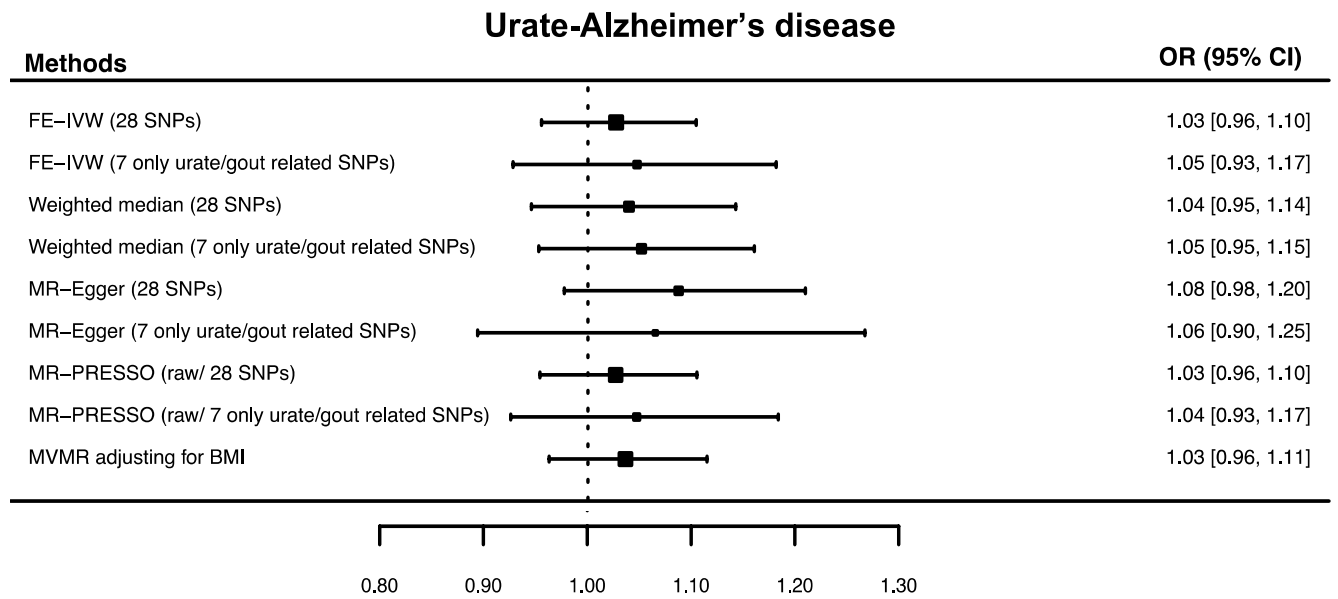


Figure S19. Forest plot for the association of uric acid with cognitive performance.



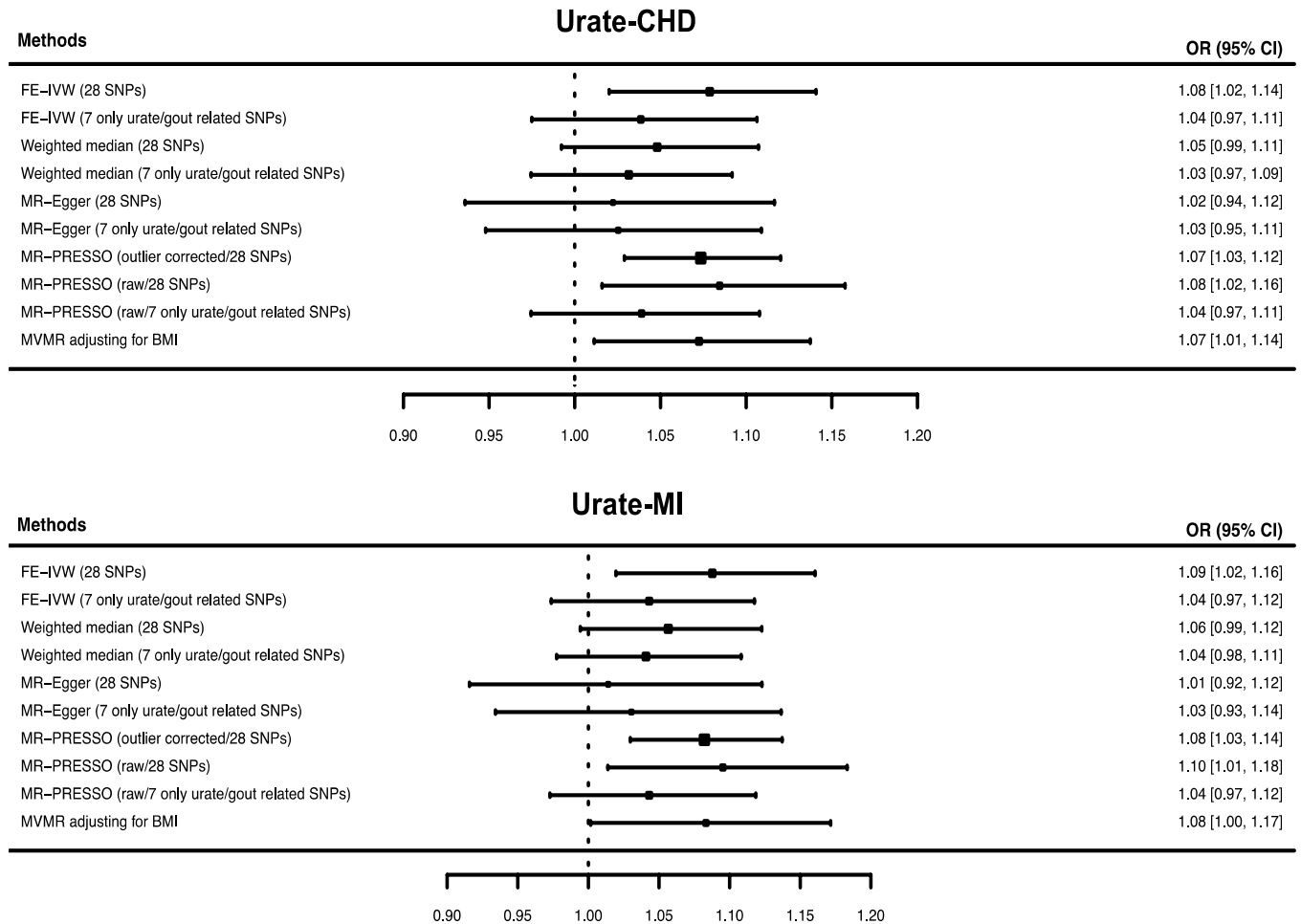
All methods performed in this study are included. Each box indicates the effect estimate (beta) calculated by each method with horizontal lines represent the 95% confidence interval (CI) of this estimate.

Figure S20. Forest plot for the association of uric acid with Alzheimer’s disease.



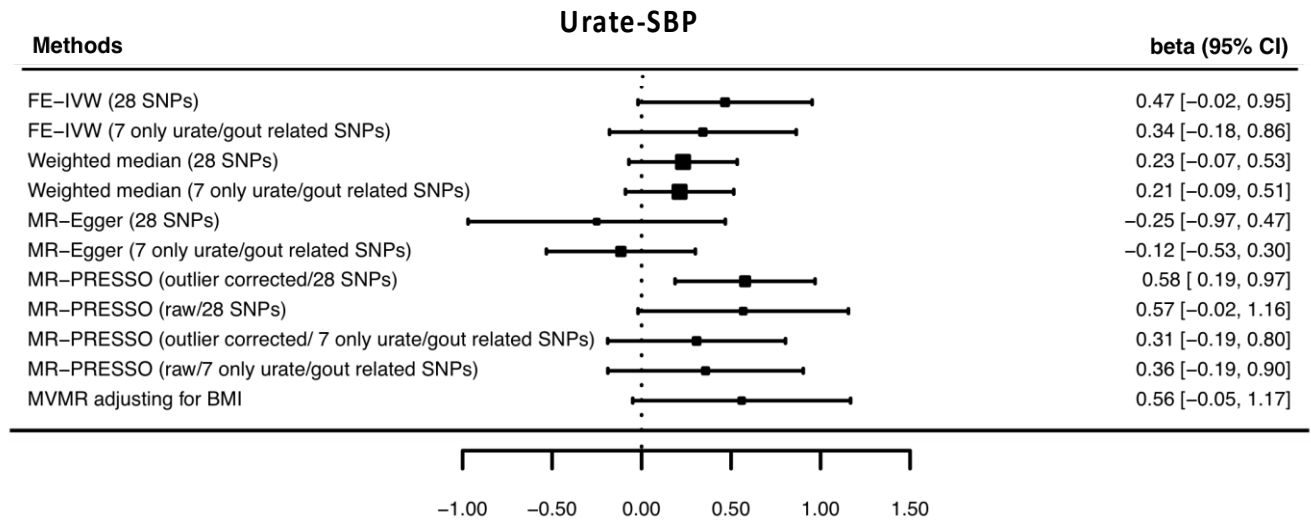
All methods performed in this study are included. Each box indicates the effect estimate (odds ratio [OR]) calculated by each method with horizontal lines represent the 95% confidence interval (CI) of this estimate.

Figure S21. Forest plots for the association of uric acid with coronary heart disease (CHD), myocardial infarction (MI).



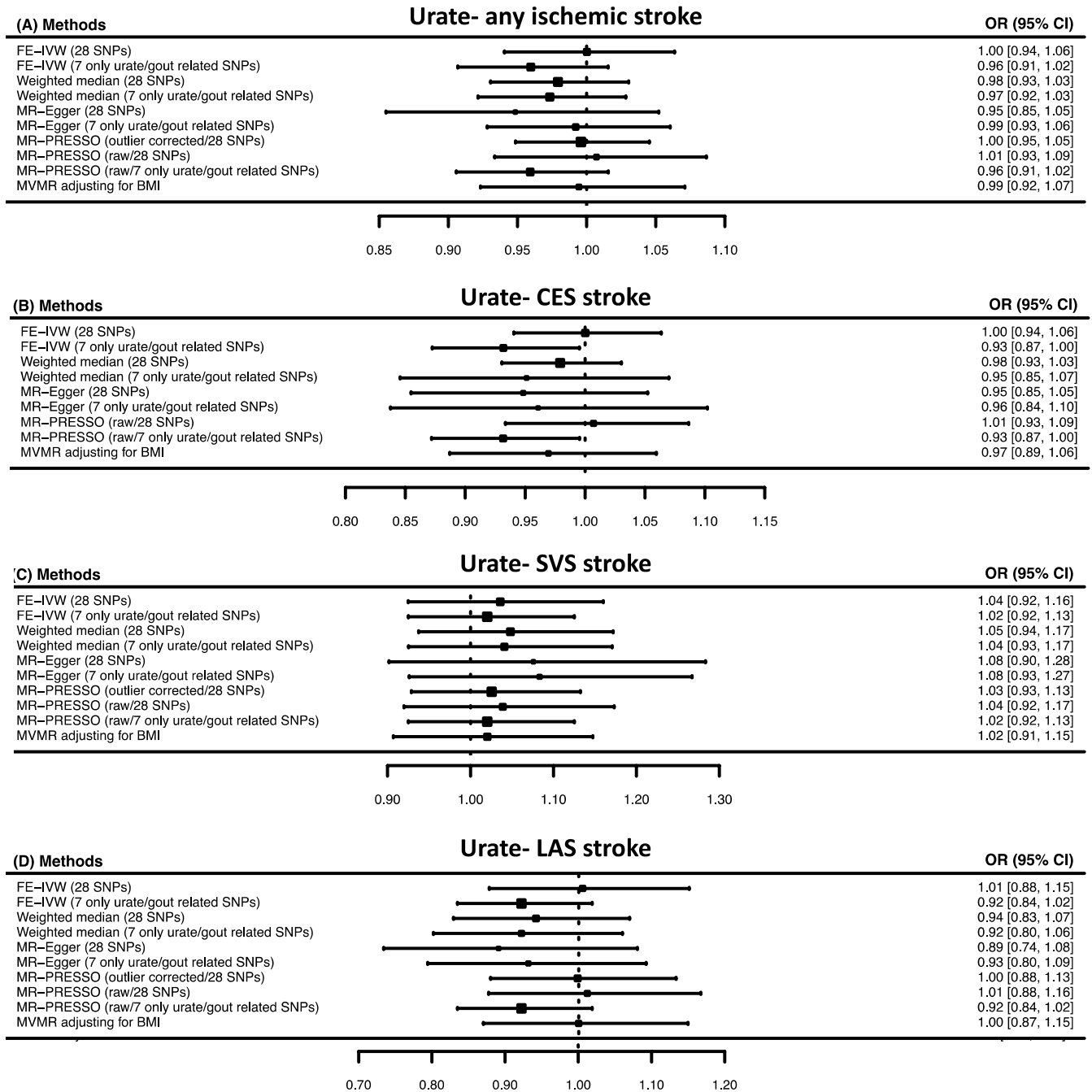
All methods performed in this study are included. Each box indicates the effect estimate (odds ratio [OR]) calculated by each method with horizontal lines represent the 95% confidence interval (CI) of this estimate.

Figure S22. Forest plot for the association of uric acid with systolic blood pressure (SBP).



All methods performed in this study are included. Each box indicates the effect estimate (beta) calculated by each method with horizontal lines represent the 95% confidence interval (CI) of this estimate.

Figure S23. Forest plots for the association of uric acid with ischemic stroke (any type) and its subtypes (cardioembolic stroke [CES], stroke caused by small-vessel disease (small-vessel stroke [SVS]) and large-artery atherosclerotic stroke [LAS]).



All methods performed in this study are included. Each box indicates the effect estimate (odds ratio [OR]) calculated by each method with horizontal lines represent the 95% confidence interval (CI) of this estimate.

Supplemental References:

1. Köttgen A, Albrecht E, Teumer A, Vitart V, Krumsiek J, Hundertmark C, Pistis G, Ruggiero D, O'Seaghdha CM, Haller T, Yang Q, Tanaka T, Johnson AD, Kutalik Z, Smith AV, Shi J, Struchalin M, Middelberg RP, Brown MJ, Gaffo AL, Pirastu N, Li G, Hayward C, Zemunik T, Huffman J, Yengo L, Zhao JH, Demirkan A, Feitosa MF, Liu X, Malerba G, Lopez LM, van der Harst P, Li X, Kleber ME, Hicks AA, Nolte IM, Johansson A, Murgia F, Wild SH, Bakker SJ, Peden JF, Dehghan A, Steri M, Tenesa A, Lagou V, Salo P, Mangino M, Rose LM, Lehtimäki T, Woodward OM, Okada Y, Tin A, Müller C, Oldmeadow C, Putku M, Czamara D, Kraft P, Frogger L, Thun GA, Grotevendt A, Gislason GK, Harris TB, Launer LJ, McArdle P, Shuldiner AR, Boerwinkle E, Coresh J, Schmidt H, Schallert M, Martin NG, Montgomery GW, Kubo M, Nakamura Y, Tanaka T, Munroe PB, Samani NJ, Jacobs DR Jr, Liu K, D'Adamo P, Ulivi S, Rotter JI, Psaty BM, Vollenweider P, Waeber G, Campbell S, Devuyst O, Navarro P, Kolcic I, Hastie N, Balkau B, Froguel P, Esko T, Salumets A, Khaw KT, Langenberg C, Wareham NJ, Isaacs A, Kraja A, Zhang Q, Wild PS, Scott RJ, Holliday EG, Org E, Viigimaa M, Bandinelli S, Metter JE, Lupo A, Trabetti E, Sorice R, Döring A, Lattka E, Strauch K, Theis F, Waldenberger M, Wichmann HE, Davies G, Gow AJ, Bruinenberg M; LifeLines Cohort Study, Stolk RP, Kooner JS, Zhang W, Winkelmann BR, Boehm BO, Lucae S, Penninx BW, Smit JH, Curhan G, Mudgal P, Plenge RM, Portas L, Persico I, Kirin M, Wilson JF, Mateo Leach I, van Gilst WH, Goel A, Ongen H, Hofman A, Rivadeneira F, Uitterlinden AG, Imboden M, von Eckardstein A, Cucca F, Nagaraja R, Piras MG, Nauck M, Schurmann C, Budde K, Ernst F, Farrington SM, Theodoratou E, Prokopenko I, Stumvoll M, Jula A, Perola M, Salomaa V, Shin SY, Spector TD, Sala C, Ridker PM, Kähönen M, Viikari J, Hengstenberg C, Nelson CP; CARDIoGRAM Consortium; DIAGRAM Consortium; ICBP Consortium; MAGIC Consortium, Meschia JF, Nalls MA, Sharma P, Singleton AB, Kamatani N, Zeller T, Burnier M, Attia J, Laan M, Klopp N, Hillege HL, Kloiber S, Choi H, Pirastu M, Tore S, Probst-Hensch NM, Völzke H, Gudnason V, Parsa A, Schmidt R, Whitfield JB, Fornage M, Gasparini P, Siscovick DS, Polašek O, Campbell H, Rudan I, Bouatia-Naji N, Metspalu A, Loos RJ, van Duijn CM, Borecki IB, Ferrucci L, Gambaro G, Deary IJ, Wolfenbutter BH, Chambers JC, März W, Pramstaller PP, Snieder H, Gyllenstein U, Wright AF, Navis G, Watkins H, Witteman JC, Sanna S, Schipf S, Dunlop MG, Tönjes A, Ripatti S, Soranzo N, Toniolo D, Chasman DI, Raitakari O, Kao WH, Ciullo M, Fox CS, Caulfield M, Bochud M, Gieger C. Genome-wide association analyses identify 18 new loci associated with serum urate concentrations. *Nat Genet.* 2013; 45:145–54.
2. Palmer TM, Lawlor DA, Harbord RM, Sheehan NA, Tobias JH, Timpson NJ, Davey Smith G, Sterne J. Using multiple genetic variants as instrumental variables for modifiable risk factors. *Stat Methods Med Res.* 2012; 21:223–42.
3. Teslovich TM, Musunuru K, Smith AV, Edmondson AC, Stylianou IM, Koseki M, Pirruccello JP, Ripatti S, Chasman DI, Willer CJ, Johansen CT, Fouchier SW, Isaacs A, Peloso GM, Barbalic M, Ricketts SL, Bis JC, Aulchenko YS, Thorleifsson G, Feitosa MF, Chambers J, Orho-Melander M, Melander O, Johnson T, Li X, Guo X, Li M, Shin Cho Y, Jin Go M, Jin Kim Y, Lee JY, Park T, Kim K, Sim X, Twee-Hee Ong R, Croteau-Chonka DC, Lange LA, Smith JD,

- Song K, Hua Zhao J, Yuan X, Luan J, Lamina C, Ziegler A, Zhang W, Zee RY, Wright AF, Witteman JC, Wilson JF, Willemsen G, Wichmann HE, Whitfield JB, Waterworth DM, Wareham NJ, Waeber G, Vollenweider P, Voight BF, Vitart V, Uitterlinden AG, Uda M, Tuomilehto J, Thompson JR, Tanaka T, Surakka I, Stringham HM, Spector TD, Soranzo N, Smit JH, Sinisalo J, Silander K, Sijbrands EJ, Scuteri A, Scott J, Schlessinger D, Sanna S, Salomaa V, Saharinen J, Sabatti C, Ruukonen A, Rudan I, Rose LM, Roberts R, Rieder M, Psaty BM, Pramstaller PP, Pichler I, Perola M, Penninx BW, Pedersen NL, Pattaro C, Parker AN, Pare G, Oostra BA, O'Donnell CJ, Nieminen MS, Nickerson DA, Montgomery GW, Meitinger T, McPherson R, McCarthy MI, McArdle W, Masson D, Martin NG, Marroni F, Mangino M, Magnusson PK, Lucas G, Luben R, Loos RJ, Lokki ML, Lettre G, Langenberg C, Launer LJ, Lakatta EG, Laaksonen R, Kyvik KO, Kronenberg F, König IR, Khaw KT, Kaprio J, Kaplan LM, Johansson A, Jarvelin MR, Janssens AC, Ingelsson E, Igl W, Kees Hovingh G, Hottenga JJ, Hofman A, Hicks AA, Hengstenberg C, Heid IM, Hayward C, Havulinna AS, Hastie ND, Harris TB, Haritunians T, Hall AS, Gyllenstein U, Guiducci C, Groop LC, Gonzalez E, Gieger C, Freimer NB, Ferrucci L, Erdmann J, Elliott P, Ejebe KG, Döring A, Dominiczak AF, Demissie S, Deloukas P, de Geus EJ, de Faire U, Crawford G, Collins FS, Chen YD, Caulfield MJ, Campbell H, Burt NP, Bonnycastle LL, Boomsma DI, Boekholdt SM, Bergman RN, Barroso I, Bandinelli S, Ballantyne CM, Assimes TL, Quertermous T, Altshuler D, Seielstad M, Wong TY, Tai ES, Feranil AB, Kuzawa CW, Adair LS, Taylor HA Jr, Borecki IB, Gabriel SB, Wilson JG, Holm H, Thorsteinsdottir U, Gudnason V, Krauss RM, Mohlke KL, Ordovas JM, Munroe PB, Kooner JS, Tall AR, Hegele RA, Kastelein JJ, Schadt EE, Rotter JI, Boerwinkle E, Strachan DP, Mooser V, Stefansson K, Reilly MP, Samani NJ, Schunkert H, Cupples LA, Sandhu MS, Ridker PM, Rader DJ, van Duijn CM, Peltonen L, Abecasis GR, Boehnke M, Kathiresan S. Biological, clinical and population relevance of 95 loci for blood lipids. *Nature*. 2010; 466:707–13.
4. Staley JR, Blackshaw J, Kamat MA, Ellis S, Surendran P, Sun BB, Paul DS, Freitag D, Burgess S, Danesh J, Young R, Butterworth AS. PhenoScanner: a database of human genotype–phenotype associations. *Bioinformatics*. 2016; 32:3207–9.
 5. Brion M-JA, Shakhbazov K, Visscher PM. Calculating statistical power in Mendelian randomization studies. *Int J Epidemiol*. 2013; 42:1497–501.
 6. Nikpay M, Goel A, Won H-H, Hall LM, Willenborg C, Kanoni S, Saleheen D, Kyriakou T, Nelson CP, Hopewell JC, Webb TR, Zeng L, Dehghan A, Alver M, Armasu SM, Auro K, Bjornes A, Chasman DI, Chen S, Ford I, Franceschini N, Gieger C, Grace C, Gustafsson S, Huang J, Hwang SJ, Kim YK, Kleber ME, Lau KW, Lu X, Lu Y, Lyytikäinen LP, Mihailov E, Morrison AC, Pervjakova N, Qu L, Rose LM, Salfati E, Saxena R, Scholz M, Smith AV, Tikkanen E, Uitterlinden A, Yang X, Zhang W, Zhao W, de Andrade M, de Vries PS, van Zuydam NR, Anand SS, Bertram L, Beutner F, Dedoussis G, Frossard P, Gauguier D, Goodall AH, Gottesman O, Haber M, Han BG, Huang J, Jalilzadeh S, Kessler T, König IR, Lannfelt L, Lieb W, Lind L, Lindgren CM, Lokki ML, Magnusson PK, Mallick NH, Mehra N, Meitinger T, Memon FU, Morris AP, Nieminen MS, Pedersen NL, Peters A, Rallidis LS, Rasheed A, Samuel M, Shah SH, Sinisalo J, Stirrups KE, Trompet S, Wang L, Zaman KS, Ardisino D, Boerwinkle E, Borecki IB, Bottinger EP, Buring JE, Chambers JC,

- Collins R, Cupples LA, Danesh J, Demuth I, Elosua R, Epstein SE, Esko T, Feitosa MF, Franco OH, Franzosi MG, Granger CB, Gu D, Gudnason V, Hall AS, Hamsten A, Harris TB, Hazen SL, Hengstenberg C, Hofman A, Ingelsson E, Iribarren C, Jukema JW, Karhunen PJ, Kim BJ, Kooner JS, Kullo IJ, Lehtimäki T, Loos RJF, Melander O, Metspalu A, März W, Palmer CN, Perola M, Quertermous T, Rader DJ, Ridker PM, Ripatti S, Roberts R, Salomaa V, Sanghera DK, Schwartz SM, Seedorf U, Stewart AF, Stott DJ, Thiery J, Zalloua PA, O'Donnell CJ, Reilly MP, Assimes TL, Thompson JR, Erdmann J, Clarke R, Watkins H, Kathiresan S, McPherson R, Deloukas P, Schunkert H, Samani NJ, Farrall M. A comprehensive 1000 Genomes–based genome-wide association meta-analysis of coronary artery disease. *Nat Genet.* 2015; 47:1121–30.
7. Lee JJ, Wedow R, Okbay A, Kong E, Maghziyan O, Zacher M, Nguyen-Viet TA, Bowers P, Sidorenko J, Karlsson Linnér R, Fontana MA, Kundu T, Lee C, Li H, Li R, Royer R, Timshel PN, Walters RK, Willoughby EA, Yengo L; 23andMe Research Team; COGENT (Cognitive Genomics Consortium); Social Science Genetic Association Consortium, Alver M, Bao Y, Clark DW, Day FR, Furlotte NA, Joshi PK, Kemper KE, Kleinman A, Langenberg C, Mägi R, Trampush JW, Verma SS, Wu Y, Lam M, Zhao JH, Zheng Z, Boardman JD, Campbell H, Freese J, Harris KM, Hayward C, Herd P, Kumari M, Lencz T, Luan J, Malhotra AK, Metspalu A, Milani L, Ong KK, Perry JRB, Porteous DJ, Ritchie MD, Smart MC, Smith BH, Tung JY, Wareham NJ, Wilson JF, Beauchamp JP, Conley DC, Esko T, Lehrer SF, Magnusson PKE, Oskarsson S, Pers TH, Robinson MR, Thom K, Watson C, Chabris CF, Meyer MN, Laibson DI, Yang J, Johannesson M, Koellinger PD, Turley P, Visscher PM, Benjamin DJ, Cesarini D. Gene discovery and polygenic prediction from a genome-wide association study of educational attainment in 1.1 million individuals. *Nat Genet.* 2018; 50:1112–21.
 8. UK Biobank — Neale lab [Internet]. [cited 2018 Dec 14]. Available from: <http://www.nealelab.is/uk-biobank/>
 9. Lambert J-C, Ibrahim-Verbaas CA, Harold D, Naj AC, Sims R, Bellenguez C, DeStafano AL, Bis JC, Beecham GW, Grenier-Boley B, Russo G, Thornton-Wells TA, Jones N, Smith AV, Chouraki V, Thomas C, Ikram MA, Zelenika D, Vardarajan BN, Kamatani Y, Lin CF, Gerrish A, Schmidt H, Kunkle B, Dunstan ML, Ruiz A, Bihoreau MT, Choi SH, Reitz C, Pasquier F, Cruchaga C, Craig D, Amin N, Berr C, Lopez OL, De Jager PL, Deramecourt V, Johnston JA, Evans D, Lovestone S, Letenneur L, Morón FJ, Rubinsztein DC, Eiriksdottir G, Sleegers K, Goate AM, Fiévet N, Huentelman MW, Gill M, Brown K, Kamboh MI, Keller L, Barberger-Gateau P, McGuinness B, Larson EB, Green R, Myers AJ, Dufouil C, Todd S, Wallon D, Love S, Rogaeva E, Gallacher J, St George-Hyslop P, Clarimon J, Lleo A, Bayer A, Tsuang DW, Yu L, Tsolaki M, Bossù P, Spalletta G, Proitsi P, Collinge J, Sorbi S, Sanchez-Garcia F, Fox NC, Hardy J, Deniz Naranjo MC, Bosco P, Clarke R, Brayne C, Galimberti D, Mancuso M, Matthews F; European Alzheimer's Disease Initiative (EADI); Genetic and Environmental Risk in Alzheimer's Disease; Alzheimer's Disease Genetic Consortium; Cohorts for Heart and Aging Research in Genomic Epidemiology, Moebus S, Mecocci P, Del Zompo M, Maier W, Hampel H, Pilotto A, Bullido M, Panza F, Caffarra P, Nacmias B, Gilbert JR, Mayhaus M, Lannefelt L, Hakonarson H, Pichler S, Carrasquillo MM, Ingelsson M, Beekly D, Alvarez V, Zou F, Valladares O, Younkin SG, Coto E, Hamilton-Nelson KL, Gu W,

- Razquin C, Pastor P, Mateo I, Owen MJ, Faber KM, Jonsson PV, Combarros O, O'Donovan MC, Cantwell LB, Soininen H, Blacker D, Mead S, Mosley TH Jr, Bennett DA, Harris TB, Fratiglioni L, Holmes C, de Bruijn RF, Passmore P, Montine TJ, Bettens K, Rotter JI, Brice A, Morgan K, Foroud TM, Kukull WA, Hannequin D, Powell JF, Nalls MA, Ritchie K, Lunetta KL, Kauwe JS, Boerwinkle E, Riemenschneider M, Boada M, Hiltunen M, Martin ER, Schmidt R, Rujescu D, Wang LS, Dartigues JF, Mayeux R, Tzourio C, Hofman A, Nöthen MM, Graff C, Psaty BM, Jones L, Haines JL, Holmans PA, Lathrop M, Pericak-Vance MA, Launer LJ, Farrer LA, van Duijn CM, Van Broeckhoven C, Moskvina V, Seshadri S, Williams J, Schellenberg GD, Amouyel P. Meta-analysis of 74,046 individuals identifies 11 new susceptibility loci for Alzheimer's disease. *Nat Genet.* 2013; 45:1452–8.
10. Malik R, Chauhan G, Traylor M, Sargurupremraj M, Okada Y, Mishra A, Rutten-Jacobs L, Giese AK, van der Laan SW, Gretarsdottir S, Anderson CD, Chong M, Adams HHH, Ago T, Almgren P, Amouyel P, Ay H, Bartz TM, Benavente OR, Bevan S, Boncoraglio GB, Brown RD Jr, Butterworth AS, Carrera C, Carty CL, Chasman DI, Chen WM, Cole JW, Correa A, Cotlarciuc I, Cruchaga C, Danesh J, de Bakker PIW, DeStefano AL, den Hoed M, Duan Q, Engelter ST, Falcone GJ, Gottesman RF, Grewal RP, Gudnason V, Gustafsson S, Haessler J, Harris TB, Hassan A, Havulinna AS, Heckbert SR, Holliday EG, Howard G, Hsu FC, Hyacinth HI, Ikram MA, Ingelsson E, Irvin MR, Jian X, Jiménez-Conde J, Johnson JA, Jukema JW, Kanai M, Keene KL, Kissela BM, Kleindorfer DO, Kooperberg C, Kubo M, Lange LA, Langefeld CD, Langenberg C, Launer LJ, Lee JM, Lemmens R, Leys D, Lewis CM, Lin WY, Lindgren AG, Lorentzen E, Magnusson PK, Maguire J, Manichaikul A, McArdle PF, Meschia JF, Mitchell BD, Mosley TH, Nalls MA, Ninomiya T, O'Donnell MJ, Psaty BM, Pulit SL, Rannikmäe K, Reiner AP, Rexrode KM, Rice K, Rich SS, Ridker PM, Rost NS, Rothwell PM, Rotter JI, Rundek T, Sacco RL, Sakaue S, Sale MM, Salomaa V, Sapkota BR, Schmidt R, Schmidt CO, Schminke U, Sharma P, Slowik A, Sudlow CLM, Tanislav C, Tatlisumak T, Taylor KD, Thijs VNS, Thorleifsson G, Thorsteinsdottir U, Tiedt S, Trompet S, Tzourio C, van Duijn CM, Walters M, Wareham NJ, Wassertheil-Smoller S, Wilson JG, Wiggins KL, Yang Q, Yusuf S; AFGen Consortium; Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium; International Genomics of Blood Pressure (iGEN-BP) Consortium; INVENT Consortium; STARNET, Bis JC, Pastinen T, Ruusalepp A, Schadt EE, Koplev S, Björkegren JLM, Codoni V, Civelek M, Smith NL, Trégouët DA, Christophersen IE, Roselli C, Lubitz SA, Ellinor PT, Tai ES, Kooner JS, Kato N, He J, van der Harst P, Elliott P, Chambers JC, Takeuchi F, Johnson AD; BioBank Japan Cooperative Hospital Group; COMPASS Consortium; EPIC-CVD Consortium; EPIC-InterAct Consortium; International Stroke Genetics Consortium (ISGC); METASTROKE Consortium; Neurology Working Group of the CHARGE Consortium; NINDS Stroke Genetics Network (SiGN); UK Young Lacunar DNA Study; MEGASTROKE Consortium, Sanghera DK, Melander O, Jern C, Strbian D, Fernandez-Cadenas I, Longstreth WT Jr, Rolfs A, Hata J, Woo D, Rosand J, Pare G, Hopewell JC, Saleheen D, Stefansson K, Worrall BB, Kittner SJ, Seshadri S, Fornage M, Markus HS, Howson JMM, Kamatani Y, Debette S, Dichgans. Multiancestry genome-wide association study of 520,000 subjects identifies 32 loci associated with stroke and stroke subtypes. *Nat Genet.* 2018; 50:524–37.