

AMP-DCC Data Analysis Report

FUSION

Phase 2

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This document was generated using Loamstream [15] and the AMP-DCC Data Analysis Pipeline [16]

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1 Data

In order to run the data we received through our analysis pipeline in an efficient manner, the genotype arrays were each given a short code name; GWAS, EXBROAD, EXCIDR, and METABO. In Table 1, we list the corresponding filename of the data set we received, the format of the file set (*note: 'bfile' refers to binary Plink format [1]*), and a liftOver [2] chain file if it was required to remap the variants to GRCh37 / hg19 coordinates

See Figures 1 and 2 for intersection counts of samples and variants available for analysis. The counts for each genotype array have been broken down by inferred ancestry as well.

Table 1: Genotype array information

ID	Filename	Format	LiftOver
GWAS	FUSION_GWAS_portal.acgt	bfile	hg18ToHg19.over.chain.gz
EXBROAD	FUSION_exomechip_Broad_portal	bfile	N/A
EXCIDR	FUSION_exomechip_CIDR_portal	bfile	N/A
METABO	FUSION_metabohip_portal	bfile	hg18ToHg19.over.chain.gz

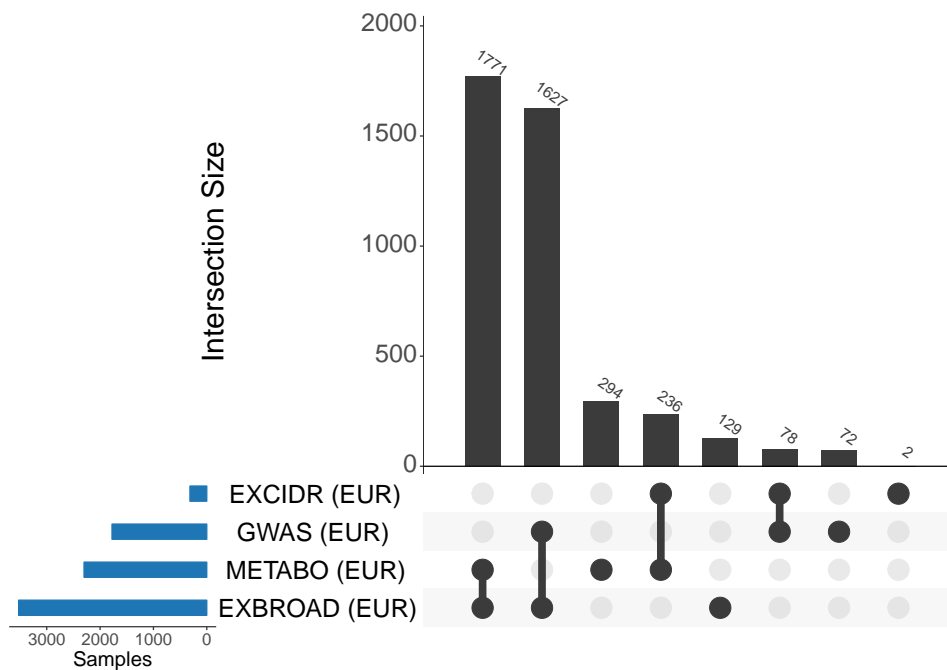


Figure 1: Samples remaining for analysis after quality control

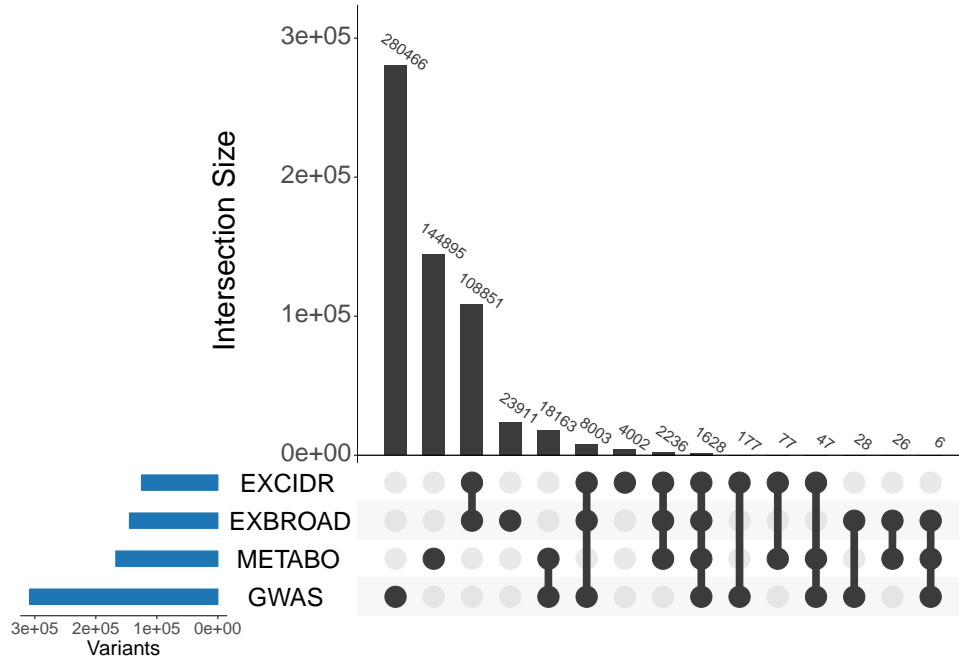


Figure 2: Variants remaining for analysis after quality control

2 Strategy

2.1 Sample structure and pipeline

The strategy we used to perform association testing can be found below. The 'ID' columns are the names used to identify each set of association test results in this document. The 'Report' columns indicate whether or not that particular set of association results will be presented in the tables and plots of the proceeding sections.

2.1.1 Cohort-level analysis

In Table 2, all of the cohorts available for analysis are defined. Each cohort was defined by a single array and one or more ancestral populations.

Table 2: Cohort-level analysis

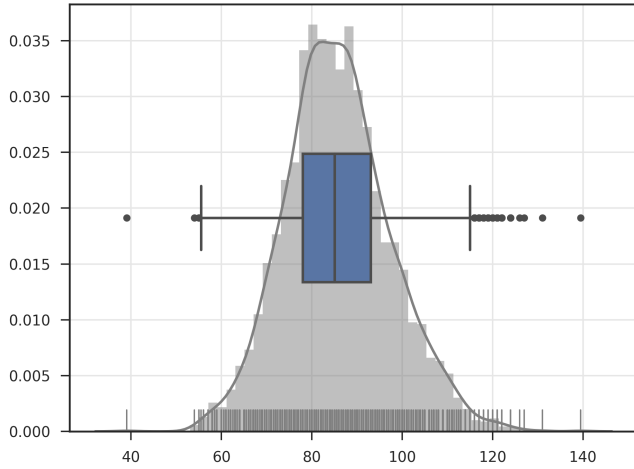
ID	Array	Ancestry	Report
GWAS_EUR	GWAS	EUR	YES
EXBROAD_EUR	EXBROAD	EUR	YES
METABO_EUR	METABO	EUR	YES

2.2 Ancestry Adjustment and Outlier Removal

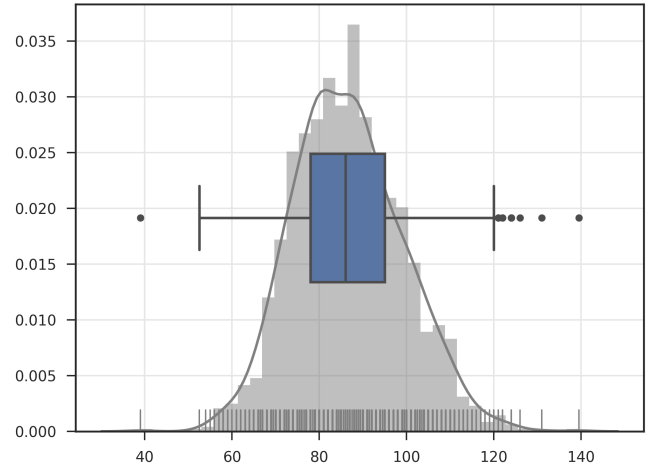
Adjusting the statistical models for underlying ancestry is often crucial to reduce or eliminate Type 1 error. Often analysts include principal components of ancestry as covariates in their models as a matter of convention. In our case, we undertook a more nuanced approach. First, the top 10 PC's were calculated for each cohort using the PC-AiR method [3]. Then, the phenotype of interest was regressed on the covariates to be used in the model and all of the PC's. If the N th PC exhibited a statistically significant p -value ($p \leq 0.05$), we selected PC's $1 - N$ to be included in association testing. Once determined, any sample lying outside 6 standard deviations from the mean on any of the N PC's was marked as an outlier and removed from the sample set. This process was repeated up to a maximum of ten times until no outliers were found, resulting in more homogeneous sample sets for each particular analysis. For this project, a hard minimum of 0 PC's to be included in analysis was set by the analyst.

3 Diastolic Blood Pressure (DBP10)

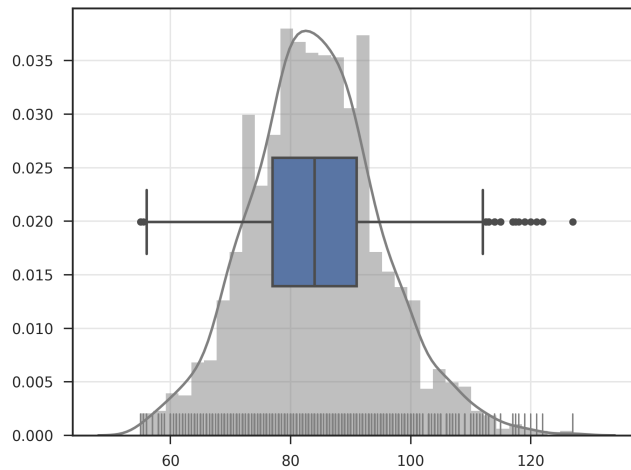
3.1 Summary



(a) EXBROAD_EUR



(b) GWAS_EUR



(c) METABO_EUR

Figure 3: Distribution of DBP10 in cohort-level analyses

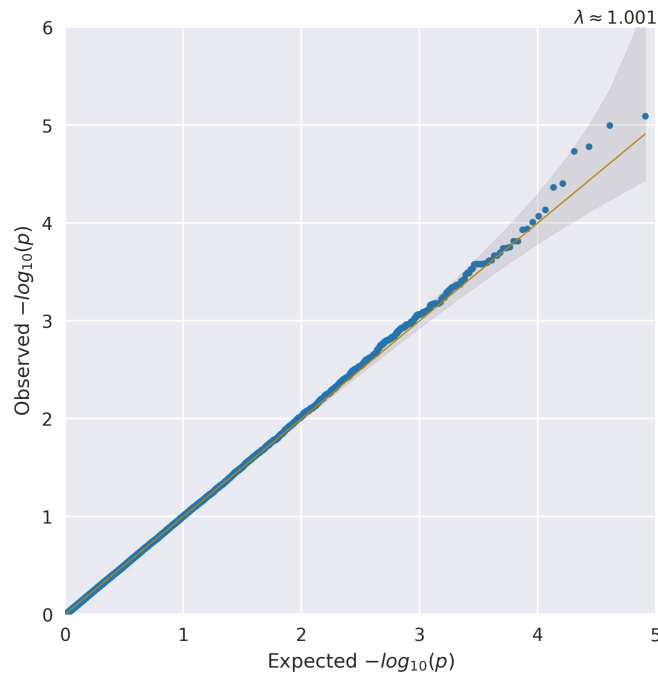
Table 3: Summary of samples removed from Diastolic Blood Pressure analysis by cohort and model

Cohort	Array	Ancestry	Trans	Covars	Total	-SampleQc	-missObs	-Kinship	-PcOutlier
EXBROAD_EUR	EXBROAD	EUR	invn	Age+Age2+SEX+BMI	3563	36	74	38	47
GWAS_EUR	GWAS	EUR	invn	Age+Age2+SEX+BMI	1796	19	61	103	0
METABO_EUR	METABO	EUR	invn	Age+Age2+SEX+BMI	2344	43	16	153	12

Table 4: Summary of samples remaining for Diastolic Blood Pressure analysis by cohort and model

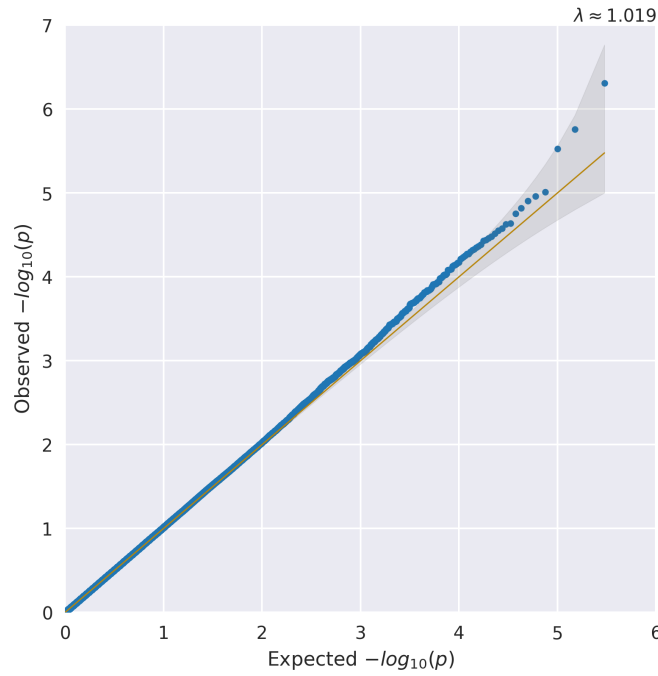
Cohort	Array	Ancestry	Trans	Covars	PCs	N	Male	Female	Max	Min	μ	\bar{x}	σ
EXBROAD_EUR	EXBROAD	EUR	invn	Age+Age2+SEX+BMI	2	3369	1905	1464	139.5	39.0	85.788	85.0	11.616
GWAS_EUR	GWAS	EUR	invn	Age+Age2+SEX+BMI	7	1614	875	739	139.5	39.0	86.761	86.0	12.445
METABO_EUR	METABO	EUR	invn	Age+Age2+SEX+BMI	3	2120	1178	942	127.0	55.0	84.338	84.0	10.909

3.2 Calibration



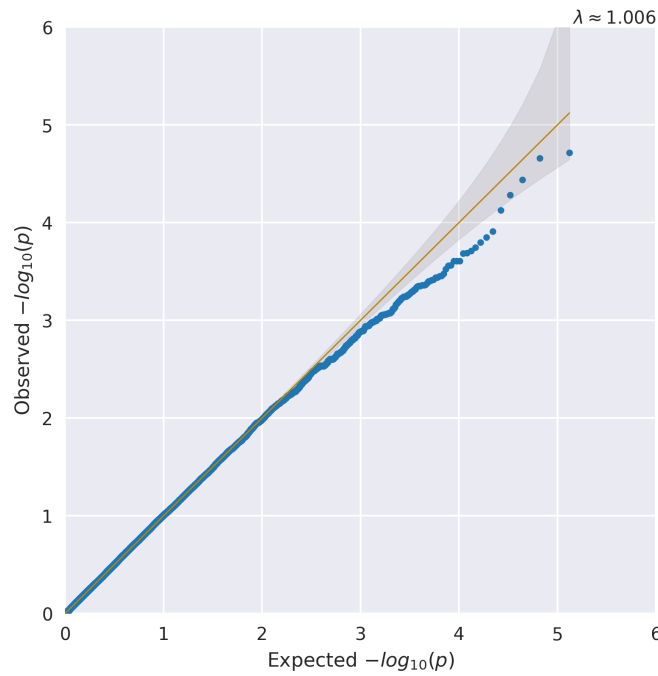
(a) invn Adjusted Age+Age2+SEX+BMI

Figure 4: QQ plots for DBP10 in the EXBROAD_EUR analysis



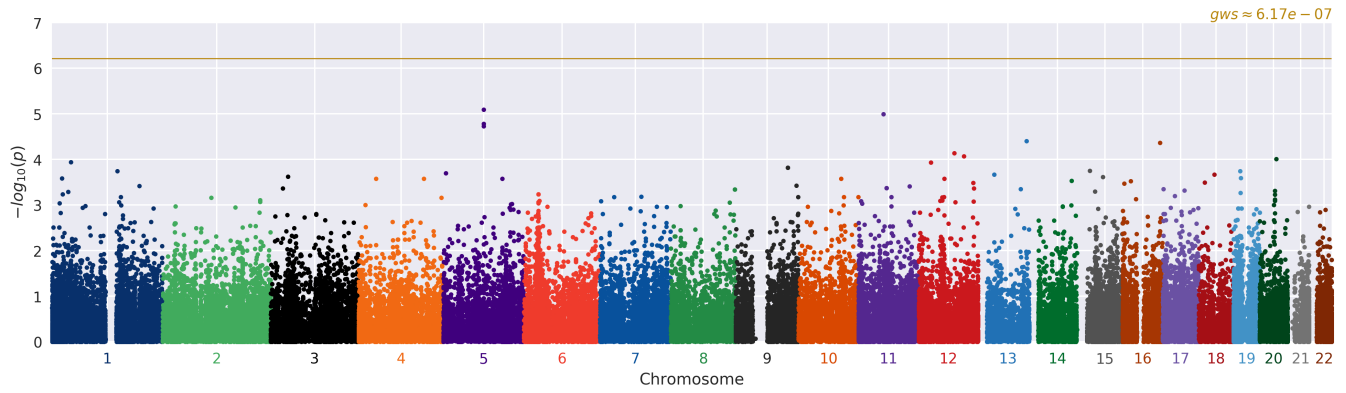
(a) invn Adjusted Age+Age2+SEX+BMI

Figure 5: QQ plots for DBP10 in the GWAS_EUR analysis



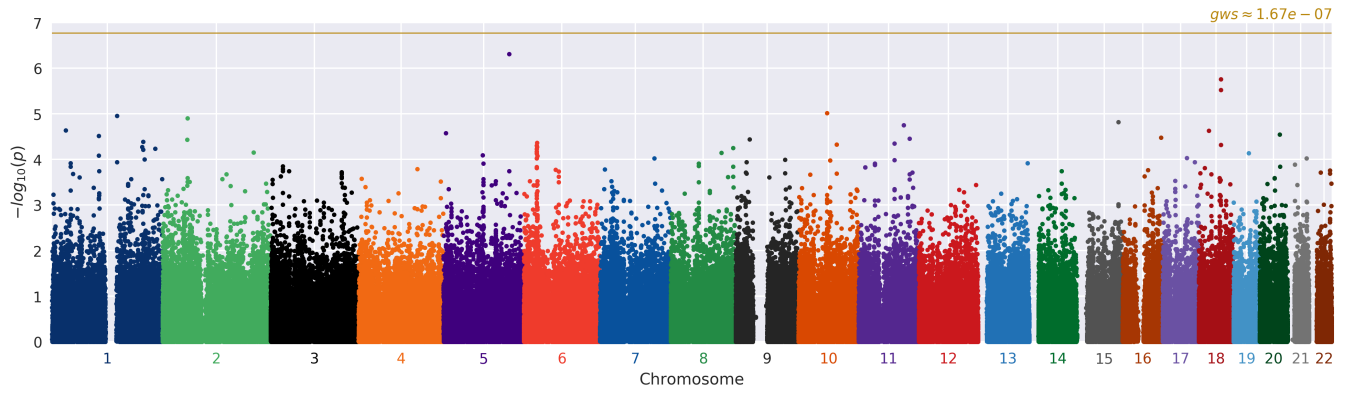
(a) invn Adjusted Age+Age2+SEX+BMI

Figure 6: QQ plots for DBP10 in the METABO_EUR analysis



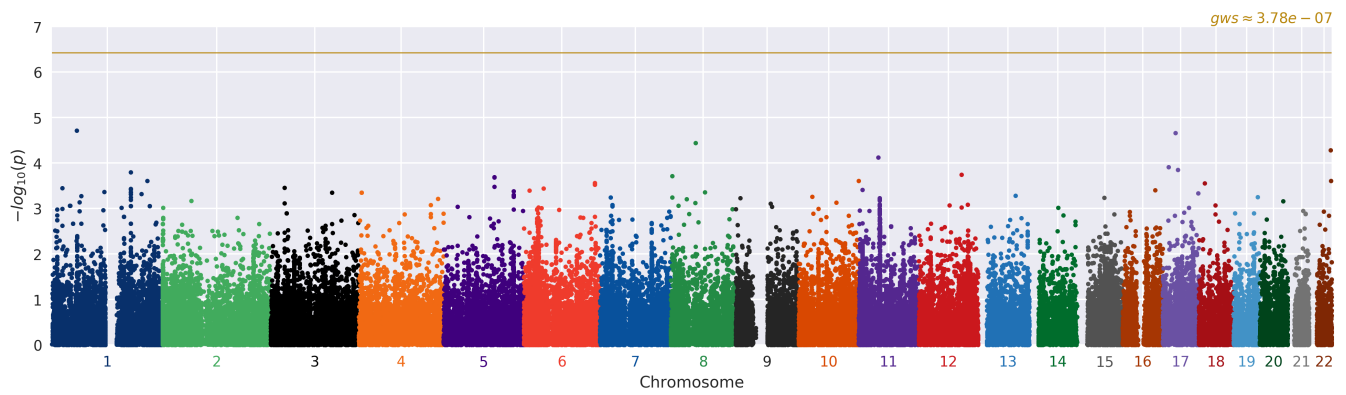
(a) invn Adjusted Age+Age2+SEX+BMI

Figure 7: Manhattan plots for DBP10 in the EXBROAD_EUR analysis



(a) invn Adjusted Age+Age2+SEX+BMI

Figure 8: Manhattan plots for DBP10 in the GWAS_EUR analysis



(a) invn Adjusted Age+Age2+SEX+BMI

Figure 9: Manhattan plots for DBP10 in the METABO_EUR analysis

3.3 Top associations

Table 5: Top variants in the EXBROAD_EUR invn Adjusted Age+Age2+SEX+BMI model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	GENE _{CLOSEST}	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
5	89943571	rs2366777	T	G	ADGRV1	3,369	1,905	1,464	2,264	0.336	0.115	$2.58 \cdot 10^{-2}$	$8.12 \cdot 10^{-6}$
11	55861234	rs147380855	G	A	OR8I2	3,369	1,905	1,464	6	0.999	1.804	0.408	$1.01 \cdot 10^{-5}$
13	108658557	rs9520691	G	A	FAM155A	3,369	1,905	1,464	3,334	0.505	0.102	$2.47 \cdot 10^{-2}$	$3.95 \cdot 10^{-5}$
16	84227713	rs78344060	T	C	ADAD2	3,369	1,905	1,464	158	0.977	0.328	$8 \cdot 10^{-2}$	$4.31 \cdot 10^{-5}$
12	80062230	rs7297018	A	G	PAWR	3,369	1,905	1,464	1,173	0.174	0.126	$3.18 \cdot 10^{-2}$	$7.3 \cdot 10^{-5}$
12	101763659	rs149603349	G	A	UTP20	3,369	1,905	1,464	6	0.999	1.606	0.408	$8.54 \cdot 10^{-5}$
20	36977952	exm1540342	G	A	LBP	3,369	1,905	1,464	6	0.999	1.592	0.408	$9.74 \cdot 10^{-5}$
1	42806191	rs913426	G	A	FOXJ3	3,369	1,905	1,464	3,036	0.451	$9.49 \cdot 10^{-2}$	$2.46 \cdot 10^{-2}$	$1.15 \cdot 10^{-4}$
12	27540204	rs71541528	A	G	ARNTL2	3,369	1,905	1,464	130	0.981	0.342	$8.88 \cdot 10^{-2}$	$1.17 \cdot 10^{-4}$
9	117139110	rs145721525	T	C	AKNA	3,369	1,905	1,464	3	1	2.186	0.577	$1.53 \cdot 10^{-4}$
15	28520072	exm1143812	C	G	HERC2	3,369	1,905	1,464	12	0.998	1.085	0.289	$1.76 \cdot 10^{-4}$
19	15273335	rs115582213	C	T	NOTCH3	3,369	1,905	1,464	131	0.981	0.334	$8.91 \cdot 10^{-2}$	$1.8 \cdot 10^{-4}$
1	147131553	rs143920833	T	C	ACP6	3,369	1,905	1,464	54	0.992	0.515	0.137	$1.81 \cdot 10^{-4}$
5	5183783	rs10037656	G	A	ADAMTS16	3,369	1,905	1,464	1,050	0.844	0.124	$3.33 \cdot 10^{-2}$	$2 \cdot 10^{-4}$
18	34740290	rs140424487	A	C	KIAA1328	3,369	1,905	1,464	61	0.991	0.48	0.129	$2.15 \cdot 10^{-4}$
13	35747681	rs41292197	A	G	NBEA	3,369	1,905	1,464	137	0.98	0.318	$8.59 \cdot 10^{-2}$	$2.15 \cdot 10^{-4}$
3	39178808	rs73070244	G	A	TTC21A	3,369	1,905	1,464	131	0.981	0.328	$8.91 \cdot 10^{-2}$	$2.4 \cdot 10^{-4}$
15	57836690	rs149850139	G	A	CGNL1	3,369	1,905	1,464	11	0.998	1.109	0.302	$2.42 \cdot 10^{-4}$
19	16884009	rs149897388	C	G	NWD1	3,369	1,905	1,464	3	1	2.112	0.577	$2.55 \cdot 10^{-4}$
1	23198619	rs4655134	G	T	EPHB2	3,369	1,905	1,464	588	$8.73 \cdot 10^{-2}$	0.157	$4.29 \cdot 10^{-2}$	$2.6 \cdot 10^{-4}$

Table 6: Top variants in the GWAS_EUR invn Adjusted Age+Age2+SEX+BMI model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	GENE _{CLOSEST}	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
5	147557190	rs4259160	A	G	SPINK14	1,614	875	739	1,490	0.462	0.177	$3.5 \cdot 10^{-2}$	$4.91 \cdot 10^{-7}$
18	49675410	rs9962572	G	T	DCC	1,614	875	739	550	0.83	0.221	$4.6 \cdot 10^{-2}$	$1.74 \cdot 10^{-6}$
10	64487073	rs224149	C	T	ZNF365	1,614	875	739	1,570	0.486	0.155	$3.49 \cdot 10^{-2}$	$9.71 \cdot 10^{-6}$
1	146508774	rs1853782	T	C	NBPF12	1,613	875	738	775	0.24	0.18	$4.08 \cdot 10^{-2}$	$1.1 \cdot 10^{-5}$
2	55819752	rs6737995	C	T	PPP4R3B	1,614	875	739	785	0.757	0.178	$4.05 \cdot 10^{-2}$	$1.24 \cdot 10^{-5}$
15	93251289	rs8025706	T	G	FAM174B	1,599	867	732	711	0.778	0.184	$4.24 \cdot 10^{-2}$	$1.52 \cdot 10^{-5}$
11	101255789	rs2508358	T	C	TRPC6	1,614	875	739	682	0.211	0.188	$4.36 \cdot 10^{-2}$	$1.77 \cdot 10^{-5}$
1	31267470	rs12726862	G	A	LAPTM5	1,614	875	739	416	0.871	0.217	$5.11 \cdot 10^{-2}$	$2.3 \cdot 10^{-5}$
18	22683541	rs4129316	G	T	ZNF521	1,614	875	739	598	0.815	0.193	$4.56 \cdot 10^{-2}$	$2.35 \cdot 10^{-5}$
5	5192861	rs8711122	T	C	ADAMTS16	1,614	875	739	552	0.829	0.191	$4.53 \cdot 10^{-2}$	$2.66 \cdot 10^{-5}$
20	44950851	rs2425866	T	C	CDH22	1,614	875	739	1,138	0.647	0.153	$3.65 \cdot 10^{-2}$	$2.82 \cdot 10^{-5}$
1	106179205	rs4553248	G	A	PRMT6	1,613	874	739	870	0.73	0.164	$3.93 \cdot 10^{-2}$	$3.05 \cdot 10^{-5}$
16	86763202	rs10514618	C	T	FOXL1	1,607	871	736	95	0.97	0.421	0.101	$3.3 \cdot 10^{-5}$
11	114233785	rs7927378	G	A	C11orf71	1,613	875	738	1,196	0.371	0.152	$3.67 \cdot 10^{-2}$	$3.48 \cdot 10^{-5}$
9	31612603	rs1412339	T	C	ACO1	1,614	875	739	498	0.846	0.201	$4.86 \cdot 10^{-2}$	$3.65 \cdot 10^{-5}$
1	205415348	rs10793730	C	T	LEMD1	1,614	875	739	296	$9.17 \cdot 10^{-2}$	0.249	$6.05 \cdot 10^{-2}$	$4.13 \cdot 10^{-5}$
6	29230577	rs3117328	A	C	OR14J1	1,614	875	739	1,314	0.407	0.15	$3.65 \cdot 10^{-2}$	$4.3 \cdot 10^{-5}$
11	80241068	rs4945417	G	A	TENM4	1,614	875	739	371	0.885	0.222	$5.43 \cdot 10^{-2}$	$4.48 \cdot 10^{-5}$
10	85826201	rs3999209	C	T	GHITM	1,614	875	739	542	0.832	0.188	$4.6 \cdot 10^{-2}$	$4.69 \cdot 10^{-5}$
6	28751727	rs1233627	T	C	TRIM27	1,614	875	739	1,397	0.567	0.147	$3.62 \cdot 10^{-2}$	$5.01 \cdot 10^{-5}$

Table 7: Top variants in the METABO_EUR invn Adjusted Age+Age2+SEX+BMI model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	GENE _{CLOSEST}	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
1	56434233	rs6658481	A	G	PLPP3	2,120	1,178	942	1,562	0.368	0.135	$3.15 \cdot 10^{-2}$	$1.93 \cdot 10^{-5}$
17	29189830	rs7342938	A	G	ATAD5	2,120	1,178	942	408	$9.62 \cdot 10^{-2}$	0.218	$5.12 \cdot 10^{-2}$	$2.19 \cdot 10^{-5}$
8	56282834	rs4738099	T	G	XKR4	2,120	1,178	942	1,725	0.407	0.128	$3.1 \cdot 10^{-2}$	$3.64 \cdot 10^{-5}$
22	48888255	rs1034435	G	A	FAM19A5	2,120	1,178	942	1,506	0.355	0.129	$3.19 \cdot 10^{-2}$	$5.24 \cdot 10^{-5}$
11	43939626	rs11823586	T	C	ALKBH3	2,120	1,178	942	12	$2.83 \cdot 10^{-3}$	1.148	0.289	$7.5 \cdot 10^{-5}$
17	13663208	rs16948423	T	C	HS3ST3A1	2,120	1,178	942	792	0.187	0.152	$3.95 \cdot 10^{-2}$	$1.23 \cdot 10^{-4}$
17	33890976	rs12452797	G	C	SLFN14	2,117	1,176	941	266	$6.28 \cdot 10^{-2}$	0.237	$6.22 \cdot 10^{-2}$	$1.41 \cdot 10^{-4}$
1	177766495	rs12074250	C	T	SEC16B	2,120	1,178	942	176	$4.15 \cdot 10^{-2}$	0.291	$7.7 \cdot 10^{-2}$	$1.59 \cdot 10^{-4}$
12	96129363	rs17288038	C	A	NTN4	2,120	1,178	942	667	0.157	0.154	$4.1 \cdot 10^{-2}$	$1.79 \cdot 10^{-4}$
8	3586074	rs2623745	T	C	CSMD1	2,120	1,178	942	452	0.893	0.185	$4.95 \cdot 10^{-2}$	$1.95 \cdot 10^{-4}$
5	113984474	rs2681530	T	C	KCNN2	2,118	1,176	942	1,021	0.241	0.131	$3.51 \cdot 10^{-2}$	$2.04 \cdot 10^{-4}$
10	135093673	rs12778349	T	C	TUBGCP2	2,120	1,178	942	946	0.223	0.135	$3.67 \cdot 10^{-2}$	$2.47 \cdot 10^{-4}$
1	214329866	rs12135339	A	G	PROX1	2,119	1,177	942	54	$1.27 \cdot 10^{-2}$	0.494	0.135	$2.48 \cdot 10^{-4}$
6	159643696	rs2782552	A	C	FNDC1	2,120	1,178	942	1,134	0.267	0.124	$3.41 \cdot 10^{-2}$	$2.74 \cdot 10^{-4}$
18	13430168	rs11663519	C	T	LDLRAD4	2,120	1,178	942	2,074	0.511	0.11	$3.02 \cdot 10^{-2}$	$2.77 \cdot 10^{-4}$
3	30730239	rs2276768	T	C	TGFBR2	2,120	1,178	942	468	0.11	0.176	$4.92 \cdot 10^{-2}$	$3.49 \cdot 10^{-4}$
1	23714665	rs1212034	C	T	TCEA3	2,112	1,174	938	493	0.883	0.17	$4.76 \cdot 10^{-2}$	$3.54 \cdot 10^{-4}$
6	44451814	rs7755190	G	A	CDC5L	2,119	1,177	942	870	0.795	0.136	$3.81 \cdot 10^{-2}$	$3.65 \cdot 10^{-4}$
11	8682465	rs10840103	T	C	TRIM66	2,120	1,178	942	1,755	0.414	0.111	$3.11 \cdot 10^{-2}$	$3.87 \cdot 10^{-4}$
16	73090039	rs8048267	A	G	ZFH3	2,120	1,178	942	1,142	0.731	0.122	$3.44 \cdot 10^{-2}$	$3.96 \cdot 10^{-4}$

3.4 Previously identified risk loci

Table 8 shows statistics from the EXBROAD_EUR cohort for 21 loci that were shown to be significantly associated with Diastolic Blood Pressure in the 2011 Nature paper by Ehret et al [9]. Where a previously reported variant was not genotyped in the study (indicated by $\bar{R}^2 < 1$), if available, a tagging variant in LD with the reported variant ($\bar{R}^2 \geq 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. None of the variants shows even nominal significance ($p < 0.05$) in this study. Out of the 14 variants in both studies, 7 exhibit the same direction of effect with the known result (binomial test $p = 0.605$).

Table 8: Top known loci in EXBROAD_EUR model invn Adjusted Age+Age2+SEX+BMI (**bold** variants indicate matching direction of effect)

CHR	POS	ID	EA	OA	N	FREQ	EFFECT	STDERR	P	GENE _{CLOSEST}	R ²	ID _{KNOWN}	N _{KNOWN}	EFFECT _{KNOWN}	STDERR _{KNOWN}	P _{KNOWN}
12	112007756	rs653178	C	T	3,369	0.416	$2.89 \cdot 10^{-2}$	$2.47 \cdot 10^{-2}$	0.242	ATXN2	1	rs653178	$2 \cdot 10^5$	-0.48	$6.26 \cdot 10^{-2}$	$1.64 \cdot 10^{-14}$
12	111884608	rs3184504	T	C	3,369	0.409	$2.51 \cdot 10^{-2}$	$2.48 \cdot 10^{-2}$	0.31	SH2B3	1	rs3184504	$2 \cdot 10^5$	0.48	$6.29 \cdot 10^{-2}$	$2.33 \cdot 10^{-14}$
12	112072424	rs11065987	G	A	3,369	0.614	$2.07 \cdot 10^{-2}$	$2.49 \cdot 10^{-2}$	0.405	BRAP	1	rs11065987	$2 \cdot 10^5$	0.449	$6.46 \cdot 10^{-2}$	$3.43 \cdot 10^{-12}$
15	75077367	rs1378942	C	A	3,369	0.451	$3.86 \cdot 10^{-2}$	$2.47 \cdot 10^{-2}$	0.119	CSK	1	rs1378942	$2 \cdot 10^5$	0.445	$6.4 \cdot 10^{-2}$	$3.47 \cdot 10^{-12}$
12	112486818	rs17696736	G	A	3,369	0.598	$2.76 \cdot 10^{-2}$	$2.46 \cdot 10^{-2}$	0.263	NAA25	1	rs17696736	$2 \cdot 10^5$	0.422	$6.34 \cdot 10^{-2}$	$2.8 \cdot 10^{-11}$
12	112871372	rs11066301	G	A	3,368	0.597	$2.38 \cdot 10^{-2}$	$2.46 \cdot 10^{-2}$	0.332	PTPN11	1	rs11066301	$2 \cdot 10^5$	0.414	$6.34 \cdot 10^{-2}$	$6.59 \cdot 10^{-11}$
15	75125645	rs6495122	A	C	3,369	0.53	$4.2 \cdot 10^{-2}$	$2.46 \cdot 10^{-2}$	$8.84 \cdot 10^{-2}$	CPLX3	1	rs6495122	$2 \cdot 10^5$	-0.383	$6.23 \cdot 10^{-2}$	$8.41 \cdot 10^{-10}$
15	75044238	rs2472304	G	A	3,369	0.442	$3.91 \cdot 10^{-2}$	$2.47 \cdot 10^{-2}$	0.113	CYP1A2	1	rs2472304	$2 \cdot 10^5$	0.393	$6.45 \cdot 10^{-2}$	$1.18 \cdot 10^{-9}$
12	90008959	rs2681472	A	G	3,369	0.921	$2.93 \cdot 10^{-2}$	$4.57 \cdot 10^{-2}$	0.521	ATP2B1	1	rs2681472	$2 \cdot 10^5$	-0.492	$8.36 \cdot 10^{-2}$	$3.9 \cdot 10^{-9}$
10	63524591	rs1530440	T	C	3,369	0.797	$3.45 \cdot 10^{-3}$	$3.01 \cdot 10^{-2}$	0.909	C10orf107	1	rs1530440	$2 \cdot 10^5$	0.459	$7.92 \cdot 10^{-2}$	$6.71 \cdot 10^{-9}$
1	11862778	rs17367504	A	G	3,369	0.859	$4.33 \cdot 10^{-2}$	$3.46 \cdot 10^{-2}$	0.211	MTHFR	1	rs17367504	$2 \cdot 10^5$	-0.49	$8.61 \cdot 10^{-2}$	$1.29 \cdot 10^{-8}$
6	26107463	rs198846	A	G	3,369	0.111	$3.7 \cdot 10^{-2}$	$3.86 \cdot 10^{-2}$	0.338	HIST1H1T	1	rs198846	$2 \cdot 10^5$	-0.487	$8.85 \cdot 10^{-2}$	$3.8 \cdot 10^{-8}$
6	26107463	rs198846	A	G	3,369	0.111	$3.7 \cdot 10^{-2}$	$3.86 \cdot 10^{-2}$	0.338	HIST1H2BC	1	rs198833	$2 \cdot 10^5$	-0.485	$8.88 \cdot 10^{-2}$	$4.58 \cdot 10^{-8}$
15	75189930	rs1130741	A	G	3,369	0.57	$1.4 \cdot 10^{-2}$	$2.44 \cdot 10^{-2}$	0.568	MPI	1	rs7495739	$2 \cdot 10^5$	-0.335	$6.15 \cdot 10^{-2}$	$5.02 \cdot 10^{-8}$
15	75189930	rs1130741	A	G	3,369	0.57	$1.4 \cdot 10^{-2}$	$2.44 \cdot 10^{-2}$	0.568	SCAMP2	0.981	rs11072511	$2 \cdot 10^5$	-0.339	$6.16 \cdot 10^{-2}$	$3.6 \cdot 10^{-8}$
1	11862778	rs17367504	A	G	3,369	0.859	$4.33 \cdot 10^{-2}$	$3.46 \cdot 10^{-2}$	0.211	CLCN6	0.976	rs12567136	$2 \cdot 10^5$	0.488	$8.56 \cdot 10^{-2}$	$1.15 \cdot 10^{-8}$
15	75189930	rs1130741	A	G	3,369	0.57	$1.4 \cdot 10^{-2}$	$2.44 \cdot 10^{-2}$	0.568	COX5A	0.931	rs1133323	$2 \cdot 10^5$	0.337	$6.17 \cdot 10^{-2}$	$4.52 \cdot 10^{-8}$
12	112486818	rs17696736	G	A	3,369	0.598	$2.76 \cdot 10^{-2}$	$2.46 \cdot 10^{-2}$	0.263	TRAFD1	0.922	rs17630235	$2 \cdot 10^5$	0.447	$6.4 \cdot 10^{-2}$	$2.92 \cdot 10^{-12}$
12	112486818	rs17696736	G	A	3,369	0.598	$2.76 \cdot 10^{-2}$	$2.46 \cdot 10^{-2}$	0.263	HECTD4	0.913	rs11066188	$2 \cdot 10^5$	0.447	$6.41 \cdot 10^{-2}$	$3.06 \cdot 10^{-12}$
12	90060586	rs17249754	G	A	3,369	0.921	$3.37 \cdot 10^{-2}$	$4.56 \cdot 10^{-2}$	0.46	POC1B-GALNT4	0.904	rs11105328	$2 \cdot 10^5$	0.487	$8.66 \cdot 10^{-2}$	$1.83 \cdot 10^{-8}$
15	75033400	rs2472299	A	G	3,369	0.32	$1.47 \cdot 10^{-2}$	$2.65 \cdot 10^{-2}$	0.577	LMAN1L	0.778	rs7162232	$2 \cdot 10^5$	-0.416	$6.89 \cdot 10^{-2}$	$1.58 \cdot 10^{-9}$

Table 9 shows statistics from the GWAS_EUR cohort for 21 loci that were shown to be significantly associated with Diastolic Blood Pressure in the 2011 Nature paper by Ehret et al [9]. Where a previously reported variant was not genotyped in the study (indicated by $\bar{R}^2 < 1$), if available, a tagging variant in LD with the reported variant ($\bar{R}^2 \geq 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. There are 4 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 12 variants in both studies, 3 exhibit the same direction of effect with the known result (binomial test $p = 0.981$).

Table 9: Top known loci in GWAS_EUR model invn Adjusted Age+Age2+SEX+BMI (**bold** variants indicate matching direction of effect)

CHR	POS	ID	EA	OA	N	FREQ	EFFECT	STDERR	P	GENE _{CLOSEST}	R ²	ID _{KNOWN}	N _{KNOWN}	EFFECT _{KNOWN}	STDERR _{KNOWN}	P _{KNOWN}
12	112007756	rs653178	C	T	1,614	0.41	$8.58 \cdot 10^{-2}$	$3.52 \cdot 10^{-2}$	$1.49 \cdot 10^{-2}$	ATXN2	1	rs653178	$2 \cdot 10^5$	-0.48	$6.26 \cdot 10^{-2}$	$1.64 \cdot 10^{-14}$
12	111884608	rs3184504	T	C	1,606	0.4	$8.82 \cdot 10^{-2}$	$3.54 \cdot 10^{-2}$	$1.29 \cdot 10^{-2}$	SH2B3	1	rs3184504	$2 \cdot 10^5$	0.48	$6.29 \cdot 10^{-2}$	$2.33 \cdot 10^{-14}$
4	81164723	rs1458038	T	C	1,613	0.651	$3.03 \cdot 10^{-2}$	$3.65 \cdot 10^{-2}$	0.406	FGF5	1	rs1458038	$2 \cdot 10^5$	0.503	$7.02 \cdot 10^{-2}$	$7.91 \cdot 10^{-13}$
15	75077367	rs1378942	C	A	1,609	0.452	$1.62 \cdot 10^{-2}$	$3.6 \cdot 10^{-2}$	0.653	CSK	1	rs1378942	$2 \cdot 10^5$	0.445	$6.4 \cdot 10^{-2}$	$3.47 \cdot 10^{-12}$
12	112906415	rs11066320	A	G	1,614	0.39	$8.66 \cdot 10^{-2}$	$3.54 \cdot 10^{-2}$	$1.46 \cdot 10^{-2}$	PTPN11	1	rs11066320	$2 \cdot 10^5$	-0.413	$6.32 \cdot 10^{-2}$	$6.32 \cdot 10^{-11}$
15	75057203	rs4886406	G	T	1,614	0.296	$2.97 \cdot 10^{-3}$	$3.94 \cdot 10^{-2}$	0.94	CYP1A2	1	rs4886406	$2 \cdot 10^5$	-0.426	$6.85 \cdot 10^{-2}$	$4.83 \cdot 10^{-10}$
15	75125645	rs6495122	A	C	1,606	0.531	$2 \cdot 10^{-3}$	$3.56 \cdot 10^{-2}$	0.955	CPLX3	1	rs6495122	$2 \cdot 10^5$	-0.383	$6.23 \cdot 10^{-2}$	$8.41 \cdot 10^{-10}$
12	90008959	rs2681472	A	G	1,614	0.919	0.117	$6.46 \cdot 10^{-2}$	$7.09 \cdot 10^{-2}$	ATP2B1	1	rs2681472	$2 \cdot 10^5$	-0.492	$8.36 \cdot 10^{-2}$	$3.9 \cdot 10^{-9}$
1	11862778	rs17367504	A	G	1,614	0.856	$9.55 \cdot 10^{-2}$	$5.05 \cdot 10^{-2}$	$5.9 \cdot 10^{-2}$	MTHFR	1	rs17367504	$2 \cdot 10^5$	-0.49	$8.61 \cdot 10^{-2}$	$1.29 \cdot 10^{-8}$
10	63507669	rs10509158	C	T	1,614	0.781	$1.25 \cdot 10^{-2}$	$4.28 \cdot 10^{-2}$	0.769	C10orf107	1	rs10509158	$2 \cdot 10^5$	-0.43	$7.63 \cdot 10^{-2}$	$1.74 \cdot 10^{-8}$
12	111798553	rs3742004	A	G	1,608	0.789	$5.29 \cdot 10^{-2}$	$4.28 \cdot 10^{-2}$	0.217	FAM109A	1	rs3742004	$2 \cdot 10^5$	-0.429	$7.66 \cdot 10^{-2}$	$2.15 \cdot 10^{-8}$
15	75234610	rs11072518	C	T	1,614	0.466	$4.49 \cdot 10^{-2}$	$3.51 \cdot 10^{-2}$	0.201	COX5A	1	rs11072518	$2 \cdot 10^5$	-0.355	$6.45 \cdot 10^{-2}$	$3.78 \cdot 10^{-8}$
15	75196176	rs4886636	A	G	1,612	0.571	$4.27 \cdot 10^{-2}$	$3.57 \cdot 10^{-2}$	0.233	MPI	0.992	rs7495739	$2 \cdot 10^5$	-0.335	$6.15 \cdot 10^{-2}$	$5.02 \cdot 10^{-8}$
15	75199892	rs11856413	G	A	1,614	0.597	$2.68 \cdot 10^{-2}$	$3.61 \cdot 10^{-2}$	0.458	SCAMP2	0.981	rs11630918	$2 \cdot 10^5$	-0.358	$6.27 \cdot 10^{-2}$	$1.16 \cdot 10^{-8}$
1	11862778	rs17367504	A	G	1,614	0.856	$9.55 \cdot 10^{-2}$	$5.05 \cdot 10^{-2}$	$5.9 \cdot 10^{-2}$	CLCN6	0.976	rs12567136	$2 \cdot 10^5$	0.488	$8.56 \cdot 10^{-2}$	$1.15 \cdot 10^{-8}$
12	111798553	rs3742004	A	G	1,608	0.789	$5.29 \cdot 10^{-2}$	$4.28 \cdot 10^{-2}$	0.217	CUX2	0.976	rs10219736	$2 \cdot 10^5$	0.414	$7.58 \cdot 10^{-2}$	$4.88 \cdot 10^{-8}$
15	75092384	rs2301249	T	C	1,614	0.315	$1.03 \cdot 10^{-2}$	$3.88 \cdot 10^{-2}$	0.791	LMAN1L	0.966	rs7162232	$2 \cdot 10^5$	-0.416	$6.89 \cdot 10^{-2}$	$1.58 \cdot 10^{-9}$
12	90008959	rs2681472	A	G	1,614	0.919	0.117	$6.46 \cdot 10^{-2}$	$7.09 \cdot 10^{-2}$	POC1B-GALNT4	0.897	rs11105328	$2 \cdot 10^5$	-0.487	$8.66 \cdot 10^{-2}$	$1.83 \cdot 10^{-8}$
12	112007756	rs653178	C	T	1,614	0.41	$8.58 \cdot 10^{-2}$	$3.52 \cdot 10^{-2}$	$1.49 \cdot 10^{-2}$	BRAP	0.811	rs11065987	$2 \cdot 10^5$	0.449	$6.46 \cdot 10^{-2}$	$3.43 \cdot 10^{-12}$
6	26125342	rs129128	C	T	1,613	$8.96 \cdot 10^{-2}$	0.104	$6.17 \cdot 10^{-2}$	$9.26 \cdot 10^{-2}$	HIST1H1T	0.808	rs198846	$2 \cdot 10^5$	0.487	$8.85 \cdot 10^{-2}$	$3.8 \cdot 10^{-8}$
6	26125342	rs129128	C	T	1,613	$8.96 \cdot 10^{-2}$	0.104	$6.17 \cdot 10^{-2}$	$9.26 \cdot 10^{-2}$	HIST1H2BC	0.808	rs198833	$2 \cdot 10^5$	0.485	$8.88 \cdot 10^{-2}$	$4.58 \cdot 10^{-8}$

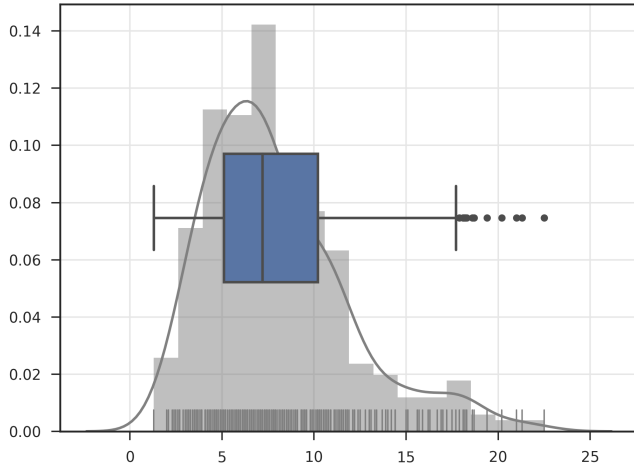
Table 10 shows statistics from the METABO_EUR cohort for 27 loci that were shown to be significantly associated with Diastolic Blood Pressure in the 2011 Nature paper by Ehret et al [9]. Where a previously reported variant was not genotyped in the study (indicated by $\bar{R}^2 < 1$), if available, a tagging variant in LD with the reported variant ($\bar{R}^2 \geq 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. None of the variants shows even nominal significance ($p < 0.05$) in this study. Out of the 26 variants in both studies, 15 exhibit the same direction of effect with the known result (binomial test $p = 0.279$).

Table 10: Top known loci in METABO_EUR model invn Adjusted Age+Age2+SEX+BMI (**bold** variants indicate matching direction of effect)

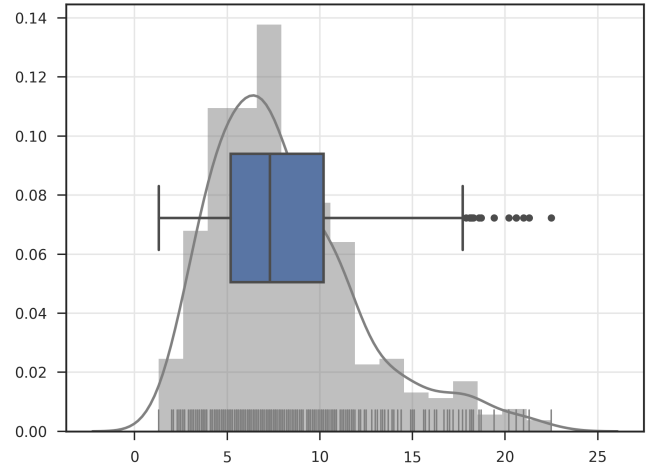
CHR	POS	ID	EA	OA	N	FREQ	EFFECT	STDERR	P	GENE _{CLOSEST}	R ²	ID _{KNOWN}	N _{KNOWN}	EFFECT _{KNOWN}	STDERR _{KNOWN}	P _{KNOWN}
12	112007756	rs653178	T	C	2,122	0.413	$2.73 \cdot 10^{-3}$	$3.13 \cdot 10^{-2}$	0.93	ATXN2	1	rs653178	$2 \cdot 10^5$	0.48	$6.26 \cdot 10^{-2}$	$1.64 \cdot 10^{-14}$
12	111884608	rs3184504	C	T	2,122	0.406	$8.75 \cdot 10^{-3}$	$3.13 \cdot 10^{-2}$	0.78	SH2B3	1	rs3184504	$2 \cdot 10^5$	-0.48	$6.29 \cdot 10^{-2}$	$2.33 \cdot 10^{-14}$
4	81164723	rs1458038	T	C	2,118	0.645	$6.22 \cdot 10^{-2}$	$3.29 \cdot 10^{-2}$	$5.85 \cdot 10^{-2}$	FGF5	1	rs1458038	$2 \cdot 10^5$	0.503	$7.02 \cdot 10^{-2}$	$7.91 \cdot 10^{-13}$
12	112591686	rs17630235	G	A	2,122	0.616	$1.84 \cdot 10^{-2}$	$3.15 \cdot 10^{-2}$	0.558	TRAFD1	1	rs17630235	$2 \cdot 10^5$	0.447	$6.4 \cdot 10^{-2}$	$2.92 \cdot 10^{-12}$
12	112610714	rs11066188	G	A	2,122	0.616	$1.84 \cdot 10^{-2}$	$3.15 \cdot 10^{-2}$	0.558	HECTD4	1	rs11066188	$2 \cdot 10^5$	0.447	$6.41 \cdot 10^{-2}$	$3.06 \cdot 10^{-12}$
12	112072424	rs11065987	A	G	2,122	0.615	$1.76 \cdot 10^{-2}$	$3.15 \cdot 10^{-2}$	0.576	BRAP	1	rs11065987	$2 \cdot 10^5$	-0.449	$6.46 \cdot 10^{-2}$	$3.43 \cdot 10^{-12}$
15	75077367	rs1378942	C	A	2,122	0.444	$3.47 \cdot 10^{-2}$	$3.06 \cdot 10^{-2}$	0.257	CSK	1	rs1378942	$2 \cdot 10^5$	0.445	$6.4 \cdot 10^{-2}$	$3.47 \cdot 10^{-12}$
12	112486818	rs17696736	A	G	2,122	0.596	$1.95 \cdot 10^{-2}$	$3.14 \cdot 10^{-2}$	0.533	NAA25	1	rs17696736	$2 \cdot 10^5$	-0.422	$6.34 \cdot 10^{-2}$	$2.8 \cdot 10^{-11}$
12	112906415	rs11066320	G	A	2,122	0.402	$1.95 \cdot 10^{-2}$	$3.14 \cdot 10^{-2}$	0.533	PTPN11	1	rs11066320	$2 \cdot 10^5$	0.413	$6.32 \cdot 10^{-2}$	$6.32 \cdot 10^{-11}$
15	75125645	rs6495122	A	C	2,122	0.529	$5.58 \cdot 10^{-2}$	$3.05 \cdot 10^{-2}$	$6.73 \cdot 10^{-2}$	CPLX3	1	rs6495122	$2 \cdot 10^5$	-0.383	$6.23 \cdot 10^{-2}$	$8.41 \cdot 10^{-10}$
15	75044238	rs2472304	G	A	2,122	0.434	$3.24 \cdot 10^{-2}$	$3.07 \cdot 10^{-2}$	0.291	CYP1A2	1	rs2472304	$2 \cdot 10^5$	0.393	$6.45 \cdot 10^{-2}$	$1.18 \cdot 10^{-9}$
15	75115895	rs7162232	G	A	2,122	0.335	$5.86 \cdot 10^{-2}$	$3.23 \cdot 10^{-2}$	$6.98 \cdot 10^{-2}$	LMAN1L	1	rs7162232	$2 \cdot 10^5$	0.416	$6.89 \cdot 10^{-2}$	$1.58 \cdot 10^{-9}$
10	63467553	rs4590817	C	G	2,122	0.872	$4.74 \cdot 10^{-2}$	$4.58 \cdot 10^{-2}$	0.301	C10orf107	1	rs4590817	$2 \cdot 10^5$	-0.507	$8.42 \cdot 10^{-2}$	$1.77 \cdot 10^{-9}$
7	2512545	rs2969070	G	A	2,121	0.332	$5.29 \cdot 10^{-2}$	$3.25 \cdot 10^{-2}$	0.103	GRIFIN	1	rs2969070	$2 \cdot 10^5$	0.386	$6.47 \cdot 10^{-2}$	$2.57 \cdot 10^{-9}$
12	90008959	rs2681472	A	G	2,122	0.925	$6.48 \cdot 10^{-3}$	$5.86 \cdot 10^{-2}$	0.912	ATP2B1	1	rs2681472	$2 \cdot 10^5$	-0.492	$8.36 \cdot 10^{-2}$	$3.9 \cdot 10^{-9}$
15	75140854	rs3765066	G	A	2,122	0.422	$2.62 \cdot 10^{-2}$	$3.06 \cdot 10^{-2}$	0.392	SCAMP2	1	rs3765066	$2 \cdot 10^5$	0.382	$6.51 \cdot 10^{-2}$	$4.17 \cdot 10^{-9}$
1	11883731	rs12567136	C	T	2,122	0.862	$1.84 \cdot 10^{-2}$	$4.33 \cdot 10^{-2}$	0.672	CLCN6	1	rs12567136	$2 \cdot 10^5$	-0.488	$8.56 \cdot 10^{-2}$	$1.15 \cdot 10^{-8}$
1	11862778	rs17367504	A	G	2,122	0.861	$1.94 \cdot 10^{-2}$	$4.33 \cdot 10^{-2}$	0.655	MTHFR	1	rs17367504	$2 \cdot 10^5$	-0.49	$8.61 \cdot 10^{-2}$	$1.29 \cdot 10^{-8}$
15	75129594	rs2290573	G	A	2,121	0.543	$5 \cdot 10^{-2}$	$3.06 \cdot 10^{-2}$	0.102	ULK3	1	rs2290573	$2 \cdot 10^5$	0.361	$6.42 \cdot 10^{-2}$	$1.85 \cdot 10^{-8}$
12	111798553	rs3742004	G	A	2,122	0.777	$3.09 \cdot 10^{-2}$	$3.76 \cdot 10^{-2}$	0.411	FAM109A	1	rs3742004	$2 \cdot 10^5$	0.429	$7.66 \cdot 10^{-2}$	$2.15 \cdot 10^{-8}$
15	75234610	rs11072518	T	C	2,122	0.467	$4.71 \cdot 10^{-2}$	$3.02 \cdot 10^{-2}$	0.119	COX5A	1	rs11072518	$2 \cdot 10^5$	0.355	$6.45 \cdot 10^{-2}$	$3.78 \cdot 10^{-8}$
6	26107463	rs198846	A	G	2,122	0.113	$1.08 \cdot 10^{-2}$	$4.81 \cdot 10^{-2}$	0.822	HIST1H1T	1	rs198846	$2 \cdot 10^5$	-0.487	$8.85 \cdot 10^{-2}$	$3.8 \cdot 10^{-8}$
6	26114508	rs198833	G	A	2,122	0.113	$1.08 \cdot 10^{-2}$	$4.81 \cdot 10^{-2}$	0.822	HIST1H2BC	1	rs198833	$2 \cdot 10^5$	0.485	$8.88 \cdot 10^{-2}$	$4.58 \cdot 10^{-8}$
6	26091179	rs1799945	G	C	2,116	0.888	$9.09 \cdot 10^{-3}$	$4.82 \cdot 10^{-2}$	0.851	HFE	1	rs1799945	$2 \cdot 10^5$	-0.482	$8.82 \cdot 10^{-2}$	$4.78 \cdot 10^{-8}$
12	111788402	rs10219736	T	C	2,122	0.779	$3.04 \cdot 10^{-2}$	$3.77 \cdot 10^{-2}$	0.421	CUX2	1	rs10219736	$2 \cdot 10^5$	0.414	$7.58 \cdot 10^{-2}$	$4.88 \cdot 10^{-8}$
15	75185670	rs7495739	A	G	2,122	0.574	$5.75 \cdot 10^{-2}$	$3.03 \cdot 10^{-2}$	$5.8 \cdot 10^{-2}$	MPI	1	rs7495739	$2 \cdot 10^5$	-0.335	$6.15 \cdot 10^{-2}$	$5.02 \cdot 10^{-8}$
12	90026523	rs11105354	A	G	2,122	0.924	$1.46 \cdot 10^{-2}$	$5.84 \cdot 10^{-2}$	0.802	POC1B-GALNT4	0.904	rs11105328	$2 \cdot 10^5$	-0.487	$8.66 \cdot 10^{-2}$	$1.83 \cdot 10^{-8}$

4 Urinary Creatinine (CREAT_URINARY)

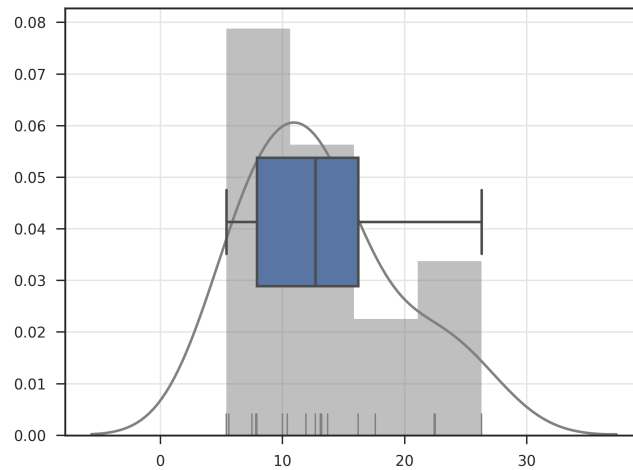
4.1 Summary



(a) EXBROAD_EUR



(b) GWAS_EUR



(c) METABO_EUR

Figure 10: Distribution of CREAT_URINARY in cohort-level analyses

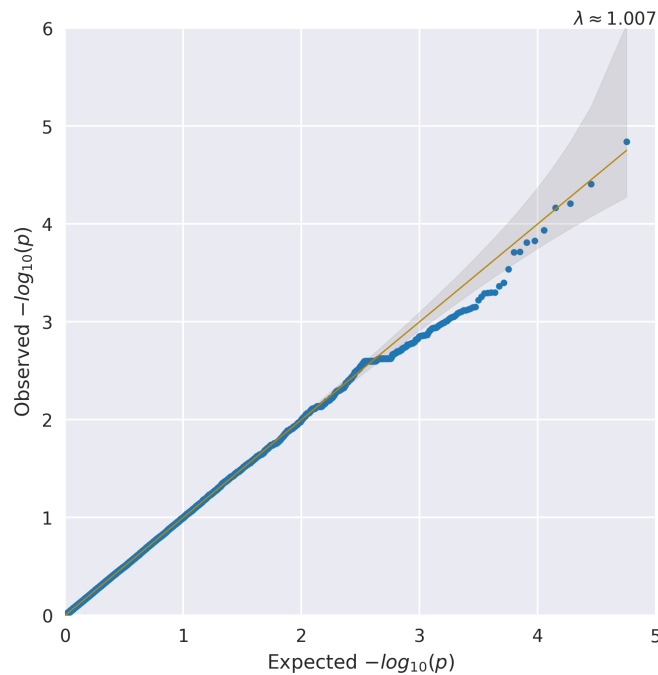
Table 11: Summary of samples removed from Urinary Creatinine analysis by cohort and model

Cohort	Array	Ancestry	Trans	Covars	Total	-SampleQc	-missObs	-Kinship	-PcOutlier
EXBROAD_EUR	EXBROAD	EUR	invn	Age+SEX	3563	36	3178	2	0
GWAS_EUR	GWAS	EUR	invn	Age+SEX	1796	19	1394	27	0
METABO_EUR	METABO	EUR	invn	Age+SEX	2344	43	2326	8	0

Table 12: Summary of samples remaining for Urinary Creatinine analysis by cohort and model

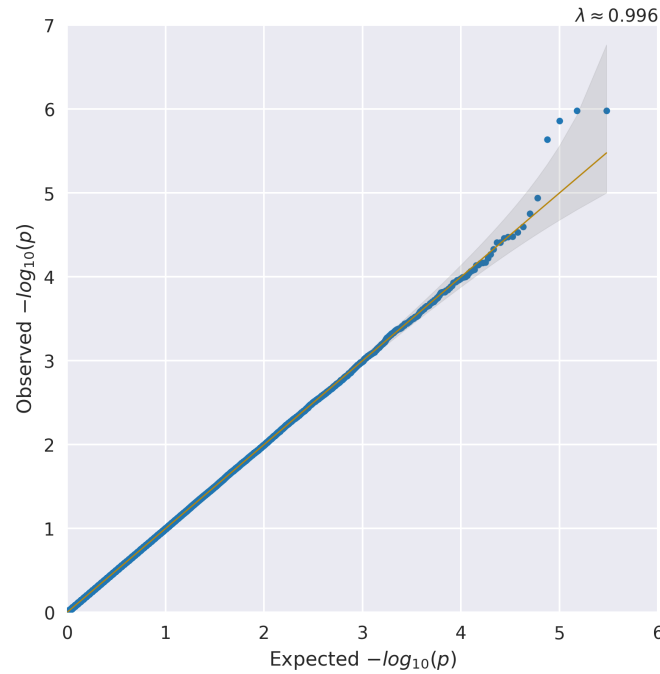
Cohort	Array	Ancestry	Trans	Covars	PCs	N	Male	Female	Max	Min	μ	\bar{x}	σ
EXBROAD_EUR	EXBROAD	EUR	invn	Age+SEX	0	380	205	175	22.5	1.3	7.951	7.2	3.925
GWAS_EUR	GWAS	EUR	invn	Age+SEX	9	373	199	174	22.5	1.3	8.083	7.3	3.987
METABO_EUR	METABO	EUR	invn	Age+SEX	0	9	4	5	17.6	5.4	11.1	10.4	3.753

4.2 Calibration



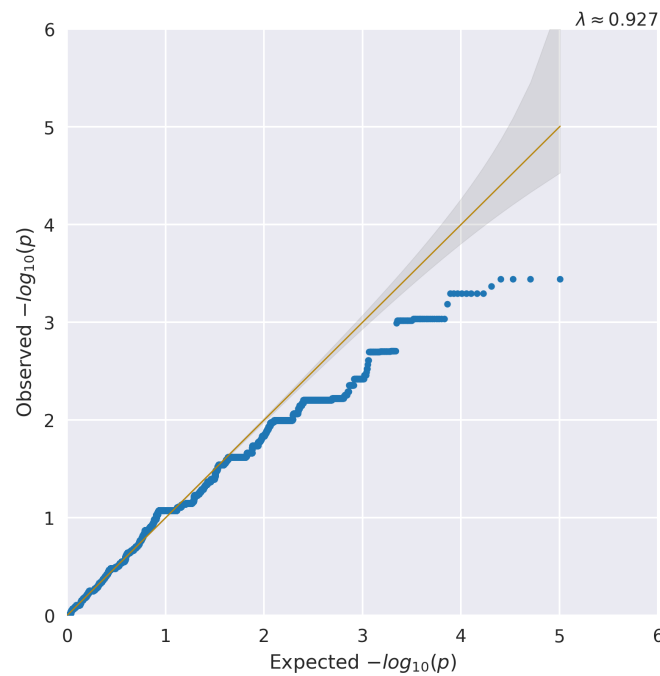
(a) invn Adjusted Age+SEX

Figure 11: QQ plots for CREAT_URINARY in the EXBROAD_EUR analysis



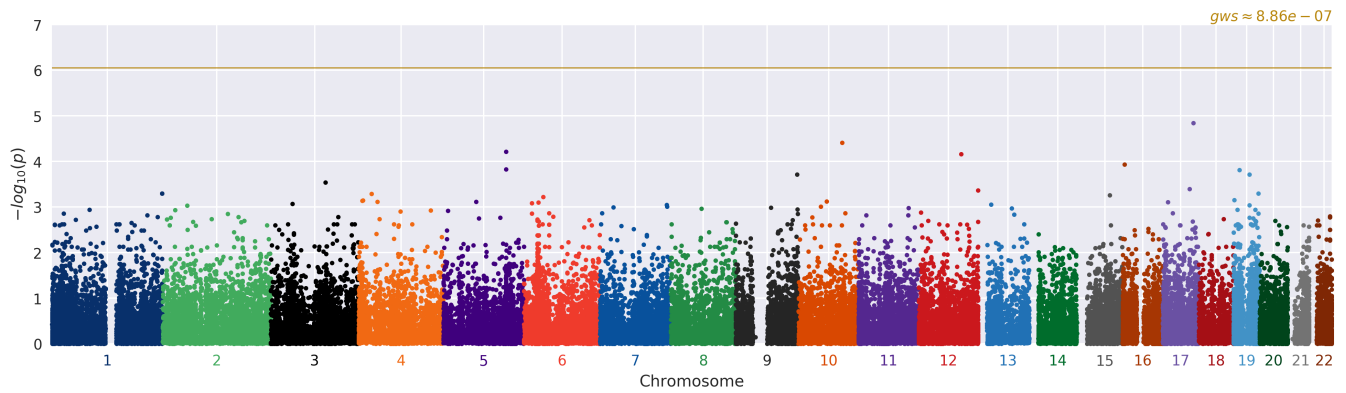
(a) invn Adjusted Age+SEX

Figure 12: QQ plots for CREAT_URINARY in the GWAS_EUR analysis



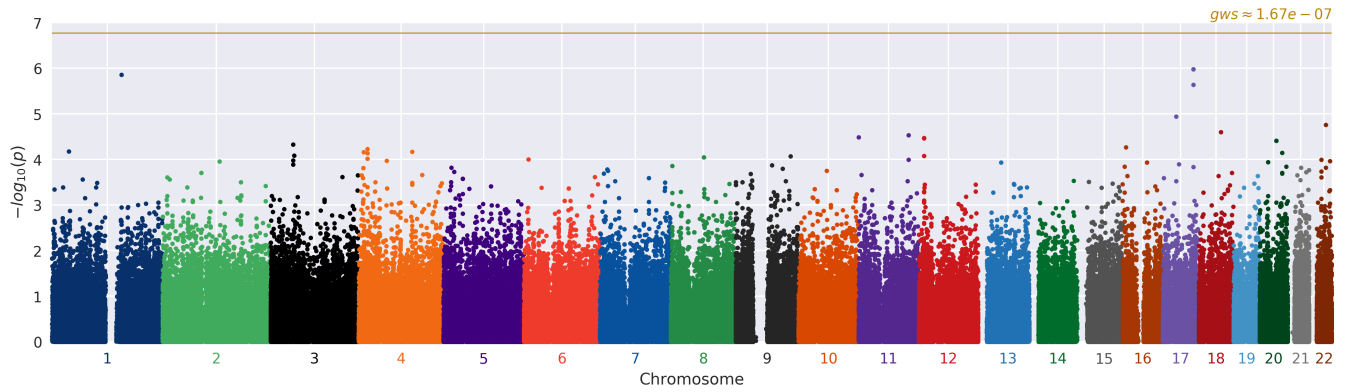
(a) invn Adjusted Age+SEX

Figure 13: QQ plots for CREAT_URINARY in the METABO_EUR analysis



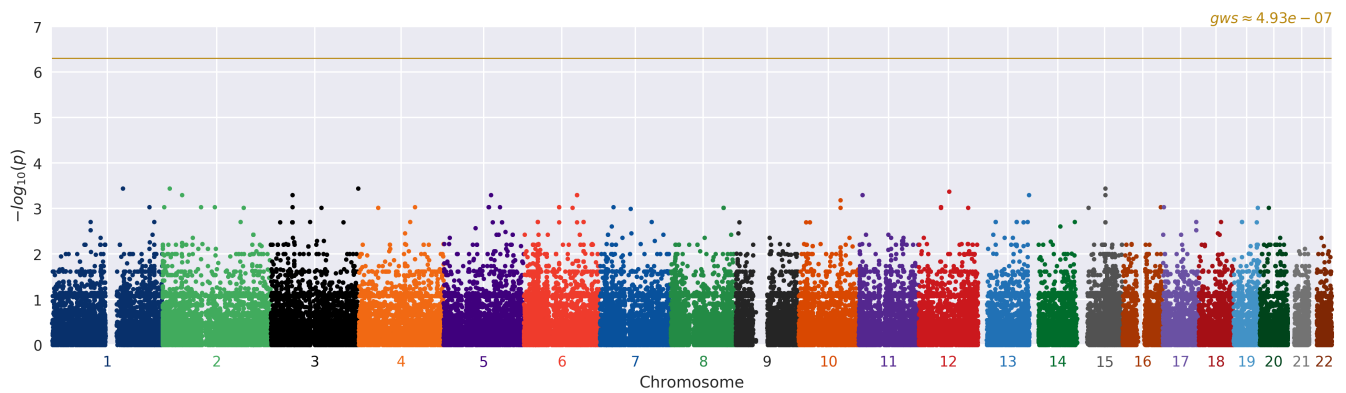
(a) invn Adjusted Age+SEX

Figure 14: Manhattan plots for CREAT_URINARY in the EXBROAD_EUR analysis



(a) invn Adjusted Age+SEX

Figure 15: Manhattan plots for CREAT_URINARY in the GWAS_EUR analysis



(a) invn Adjusted Age+SEX

Figure 16: Manhattan plots for CREAT_URINARY in the METABO_EUR analysis

4.3 Top associations

Table 13: Top variants in the EXBROAD_EUR invn Adjusted Age+SEX model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	GENE _{CLOSEST}	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
17	69233083	rs8076167	C	T	AC007461	380	205	175	105	0.138	0.452	0.103	$1.44 \cdot 10^{-5}$
10	98172999	rs41291632	T	C	TLL2	380	205	175	13	$1.71 \cdot 10^{-2}$	1.149	0.276	$3.9 \cdot 10^{-5}$
5	140567264	rs2740588	G	T	PCDHB9	380	205	175	183	0.241	0.342	$8.43 \cdot 10^{-2}$	$6.16 \cdot 10^{-5}$
12	95694111	rs17855934	G	T	VEZT	380	205	175	62	$8.16 \cdot 10^{-2}$	0.518	0.129	$6.86 \cdot 10^{-5}$
16	4445327	rs3747579	T	C	CORO7-PAM16	380	205	175	245	0.678	0.289	$7.41 \cdot 10^{-2}$	$1.16 \cdot 10^{-4}$
5	140530529	rs3776096	G	A	PCDHB6	380	205	175	176	0.232	0.329	$8.59 \cdot 10^{-2}$	$1.49 \cdot 10^{-4}$
19	14000196	rs61732721	T	G	C19orf57	380	205	175	2	$2.63 \cdot 10^{-3}$	2.66	0.696	$1.55 \cdot 10^{-4}$
9	138378685	rs199680517	G	A	PPP1R26	380	205	175	10	$1.32 \cdot 10^{-2}$	1.185	0.315	$1.92 \cdot 10^{-4}$
19	36352906	rs144457307	G	A	KIRREL2	380	205	175	2	$2.63 \cdot 10^{-3}$	2.621	0.696	$1.94 \cdot 10^{-4}$
3	123453061	rs3796164	A	G	MYLK	380	205	175	25	$3.29 \cdot 10^{-2}$	0.688	0.188	$2.9 \cdot 10^{-4}$
17	60767015	rs2429387	A	G	MRC2	380	205	175	5	0.993	1.582	0.443	$4.01 \cdot 10^{-4}$
12	133428242	rs2306541	A	G	CHFR	380	205	175	117	0.154	0.344	$9.7 \cdot 10^{-2}$	$4.33 \cdot 10^{-4}$
1	248004775	rs10888256	T	C	OR11L1	380	205	175	67	0.912	0.457	0.13	$5.03 \cdot 10^{-4}$
19	56369314	rs16986718	A	G	NLRP4	380	205	175	167	0.22	0.297	$8.45 \cdot 10^{-2}$	$5.06 \cdot 10^{-4}$
4	28872833	rs10049756	G	A	STIM2	380	205	175	53	$6.97 \cdot 10^{-2}$	0.511	0.146	$5.13 \cdot 10^{-4}$
15	73616159	rs62641689	T	C	HCN4	380	205	175	6	$7.89 \cdot 10^{-3}$	1.411	0.405	$5.55 \cdot 10^{-4}$
6	43155718	rs145911635	A	G	CUL9	380	205	175	6	$7.89 \cdot 10^{-3}$	1.403	0.405	$6.01 \cdot 10^{-4}$
19	2405404	exm1403971	A	G	TMPRSS9	380	205	175	4	$5.26 \cdot 10^{-3}$	1.692	0.495	$7.04 \cdot 10^{-4}$
4	10027542	rs6820230	T	C	SLC2A9	380	205	175	203	0.267	0.274	$8.03 \cdot 10^{-2}$	$7.14 \cdot 10^{-4}$
4	8390965	rs142001570	A	G	ACOX3	380	205	175	10	$1.32 \cdot 10^{-2}$	0.979	0.288	$7.32 \cdot 10^{-4}$

Table 14: Top variants in the GWAS_EUR invn Adjusted Age+SEX model (**bold** variants indicate previously identified associations)

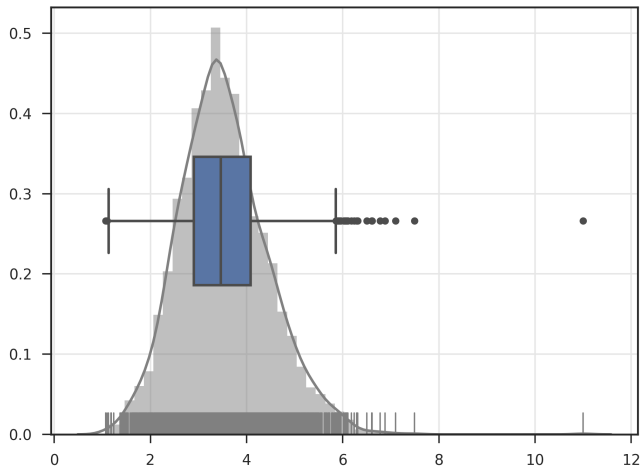
CHR	POS	ID	EA	OA	GENE _{CLOSEST}	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
17	69238807	rs9302933	G	A	AC007461	373	199	174	85	0.114	0.579	0.117	$1.05 \cdot 10^{-6}$
1	156613517	rs4233511	C	A	BCAN	373	199	174	32	0.957	0.891	0.182	$1.38 \cdot 10^{-6}$
17	30032420	rs1551355	C	T	COPRS	373	199	174	170	0.228	0.378	$8.49 \cdot 10^{-2}$	$1.15 \cdot 10^{-5}$
22	37493178	rs2160906	A	G	TMPRSS6	373	199	174	176	0.236	0.36	$8.26 \cdot 10^{-2}$	$1.76 \cdot 10^{-5}$
18	49524506	rs7240111	T	C	DCC	373	199	174	299	0.401	0.325	$7.62 \cdot 10^{-2}$	$2.53 \cdot 10^{-5}$
11	112393443	rs1945107	C	A	PLET1	369	196	173	175	0.763	0.357	$8.43 \cdot 10^{-2}$	$2.95 \cdot 10^{-5}$
11	409815	rs4074794	G	A	SIGIRR	373	199	174	106	0.142	0.454	0.108	$3.29 \cdot 10^{-5}$
12	11917397	rs7963499	T	C	ETV6	373	199	174	158	0.212	0.381	$9.08 \cdot 10^{-2}$	$3.36 \cdot 10^{-5}$
20	37310927	rs1475096	G	A	ARHGAP40	373	199	174	259	0.653	0.317	$7.61 \cdot 10^{-2}$	$3.88 \cdot 10^{-5}$
20	37323183	rs6027331	T	C	SLC32A1	373	199	174	259	0.653	0.317	$7.61 \cdot 10^{-2}$	$3.88 \cdot 10^{-5}$
3	50536273	rs752183	A	C	CACNA2D2	373	199	174	67	$8.98 \cdot 10^{-2}$	0.548	0.133	$4.71 \cdot 10^{-5}$
16	7533307	rs17143804	T	C	RBFOX1	373	199	174	85	0.114	0.475	0.116	$5.41 \cdot 10^{-5}$
4	20173391	rs4696948	G	A	SLIT2	373	199	174	282	0.622	0.313	$7.71 \cdot 10^{-2}$	$5.95 \cdot 10^{-5}$
1	38929864	rs2494441	G	A	RRAGC	373	199	174	345	0.462	0.289	$7.18 \cdot 10^{-2}$	$6.73 \cdot 10^{-5}$
4	120086883	rs11098490	A	C	MYOZ2	373	199	174	313	0.42	0.289	$7.16 \cdot 10^{-2}$	$6.78 \cdot 10^{-5}$
4	11414037	rs224463	A	G	HS3ST1	373	199	174	269	0.361	0.313	$7.78 \cdot 10^{-2}$	$6.85 \cdot 10^{-5}$
20	50466232	rs6067967	C	T	SALL4	371	198	173	343	0.538	0.293	$7.31 \cdot 10^{-2}$	$7.21 \cdot 10^{-5}$
3	53026714	rs2115779	C	A	SFMBT1	373	199	174	261	0.35	0.306	$7.67 \cdot 10^{-2}$	$8.21 \cdot 10^{-5}$
9	123166160	rs2297453	G	A	CDK5RAP2	372	199	173	214	0.712	0.32	$8.04 \cdot 10^{-2}$	$8.53 \cdot 10^{-5}$
8	74998868	rs2891355	G	A	LY96	373	199	174	56	$7.51 \cdot 10^{-2}$	0.53	0.134	$9.01 \cdot 10^{-5}$

Table 15: Top variants in the METABO_EUR invn Adjusted Age+SEX model (**bold** variants indicate previously identified associations)

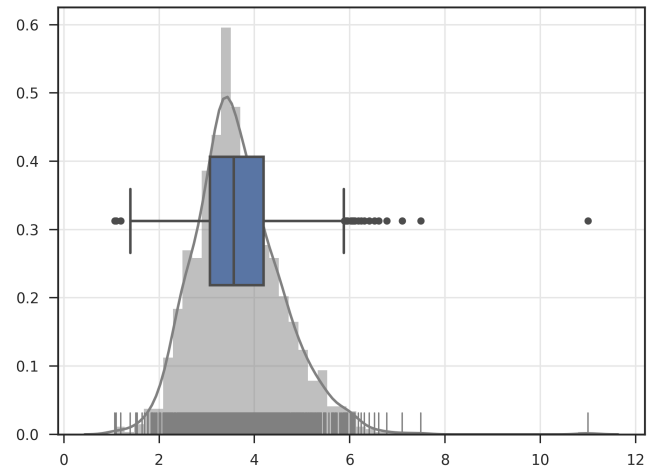
CHR	POS	ID	EA	OA	GENE _{CLOSEST}	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
1	159875455	rs10752632	A	G	AL590560	9	4	5	8	0.556	1.168	0.182	$3.59 \cdot 10^{-4}$
15	63340227	rs4075583	G	A	TPM1	9	4	5	8	0.444	1.168	0.182	$3.59 \cdot 10^{-4}$
2	16031027	rs746104	T	C	MYCN	9	4	5	8	0.444	1.168	0.182	$3.59 \cdot 10^{-4}$
3	196519878	rs7649045	C	T	PAK2	9	4	5	8	0.444	1.168	0.182	$3.59 \cdot 10^{-4}$
12	68584706	rs2870950	A	G	IL26	9	4	5	9	0.5	1.05	0.168	$4.26 \cdot 10^{-4}$
11	8264149	rs442264	G	A	LMO1	9	4	5	9	0.5	1.28	0.211	$5.06 \cdot 10^{-4}$
13	114033418	rs9577254	A	G	GRTP1	9	4	5	9	0.5	1.28	0.211	$5.06 \cdot 10^{-4}$
2	43859090	rs13412979	A	C	PLEKHH2	9	4	5	9	0.5	1.28	0.211	$5.06 \cdot 10^{-4}$
3	48556339	rs2267846	A	G	PFKFB4	9	4	5	9	0.5	1.28	0.211	$5.06 \cdot 10^{-4}$
5	106896617	rs2484103	T	C	EFNA5	9	4	5	9	0.5	1.28	0.211	$5.06 \cdot 10^{-4}$
6	119340881	rs3756939	C	T	FAM184A	9	4	5	9	0.5	1.28	0.211	$5.06 \cdot 10^{-4}$
10	94368178	rs11187094	G	A	KIF11	9	4	5	7	0.389	1.079	0.185	$6.53 \cdot 10^{-4}$
1	219588803	rs2791559	G	A	ZC3H11B	9	4	5	7	0.389	1.334	0.243	$9.26 \cdot 10^{-4}$
12	50271497	rs73116304	T	C	FAIM2	9	4	5	7	0.389	1.334	0.243	$9.26 \cdot 10^{-4}$
16	85407454	rs4783175	A	G	GSE1	9	4	5	7	0.389	1.334	0.243	$9.26 \cdot 10^{-4}$
17	2766970	rs9901515	G	A	RAP1GAP2	9	4	5	7	0.611	1.334	0.243	$9.26 \cdot 10^{-4}$
2	117342103	rs10496522	T	C	DPP10	9	4	5	7	0.389	1.334	0.243	$9.26 \cdot 10^{-4}$
2	3526603	rs10205909	A	G	ADI1	9	4	5	7	0.389	1.334	0.243	$9.26 \cdot 10^{-4}$
2	86466516	rs2278105	C	T	REEP1	9	4	5	7	0.389	1.334	0.243	$9.26 \cdot 10^{-4}$
3	48727112	rs4858798	G	A	IP6K2	9	4	5	7	0.389	1.334	0.243	$9.26 \cdot 10^{-4}$

5 LDL Cholesterol (LDL_CALCULATED)

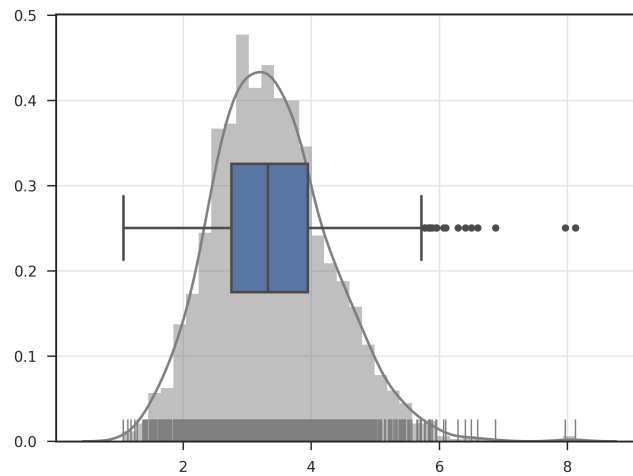
5.1 Summary



(a) EXBROAD_EUR



(b) GWAS_EUR



(c) METABO_EUR

Figure 17: Distribution of LDL_CALCULATED in cohort-level analyses

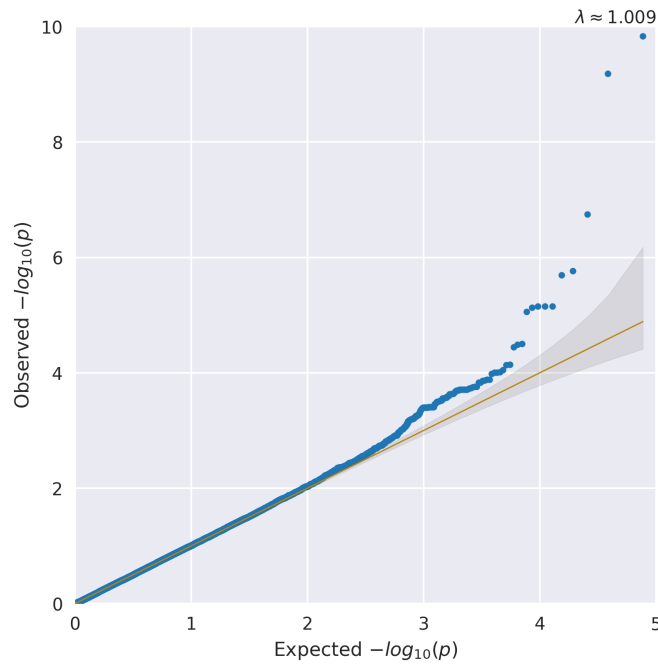
Table 16: Summary of samples removed from LDL Cholesterol analysis by cohort and model

Cohort	Array	Ancestry	Trans	Covars	Total	-SampleQc	-missObs	-Kinship	-PcOutlier
EXBROAD_EUR	EXBROAD	EUR	invn	Age+Age2+SEX+BMI	3563	36	1052	25	0
GWAS_EUR	GWAS	EUR	invn	Age+Age2+SEX+BMI	1796	19	475	92	0
METABO_EUR	METABO	EUR	invn	Age+Age2+SEX+BMI	2344	43	624	140	0

Table 17: Summary of samples remaining for LDL Cholesterol analysis by cohort and model

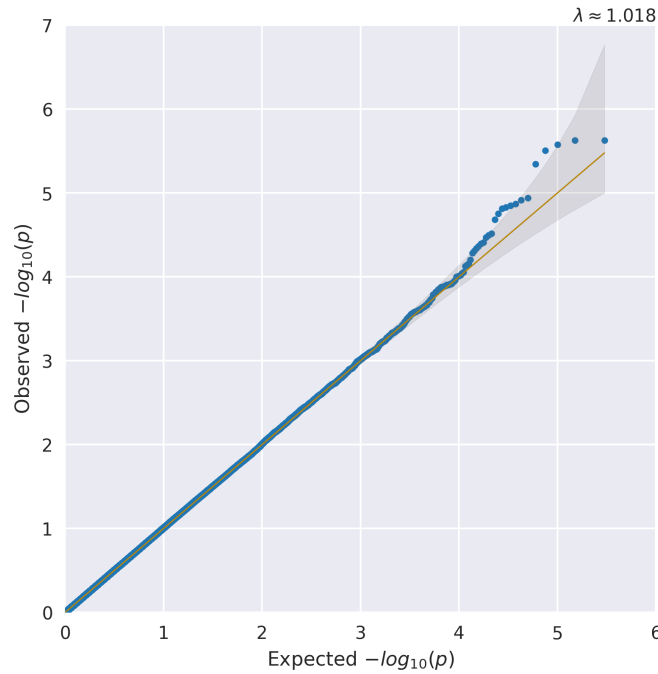
Cohort	Array	Ancestry	Trans	Covars	PCs	N	Male	Female	Max	Min	μ	\bar{x}	σ
EXBROAD_EUR	EXBROAD	EUR	invn	Age+Age2+SEX+BMI	0	2460	1362	1098	11.0	1.07	3.529	3.455	0.927
GWAS_EUR	GWAS	EUR	invn	Age+Age2+SEX+BMI	0	1213	669	544	11.0	1.07	3.673	3.57	0.923
METABO_EUR	METABO	EUR	invn	Age+Age2+SEX+BMI	1	1562	823	739	8.13	1.06	3.39	3.33	0.927

5.2 Calibration



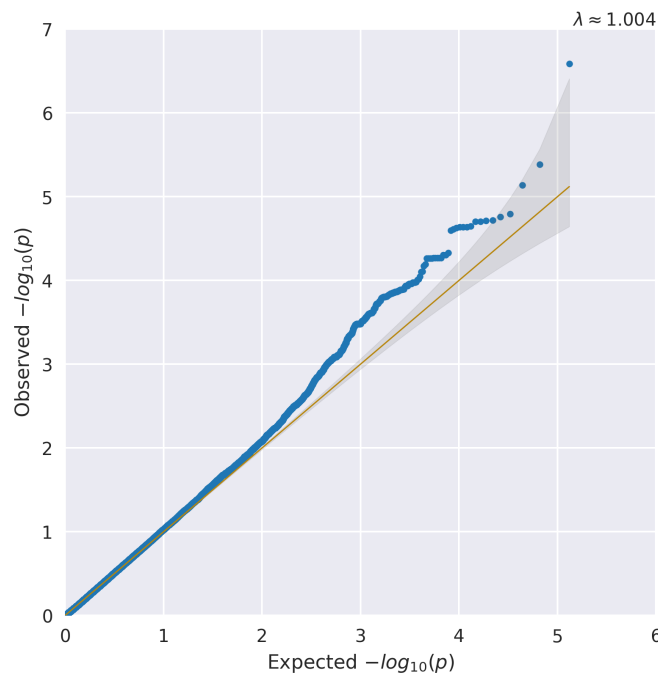
(a) invn Adjusted Age+Age2+SEX+BMI

Figure 18: QQ plots for LDL_CALCULATED in the EXBROAD_EUR analysis



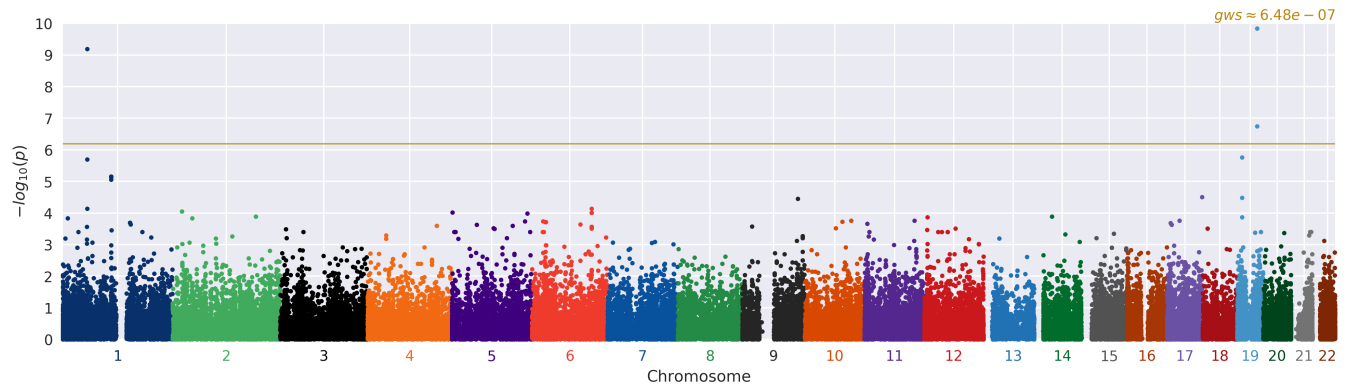
(a) invn Adjusted Age+Age2+SEX+BMI

Figure 19: QQ plots for LDL_CALCULATED in the GWAS_EUR analysis



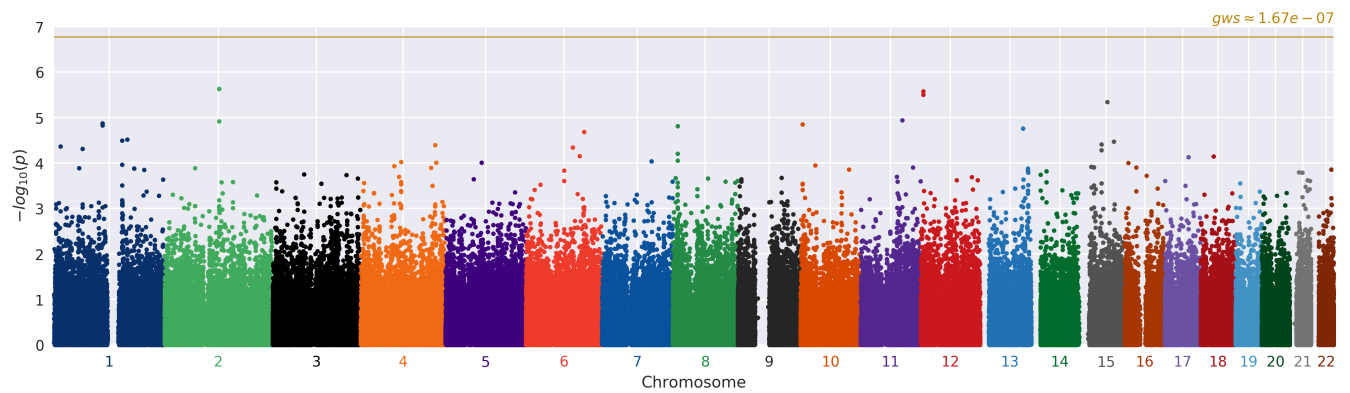
(a) invn Adjusted Age+Age2+SEX+BMI

Figure 20: QQ plots for LDL_CALCULATED in the METABO_EUR analysis



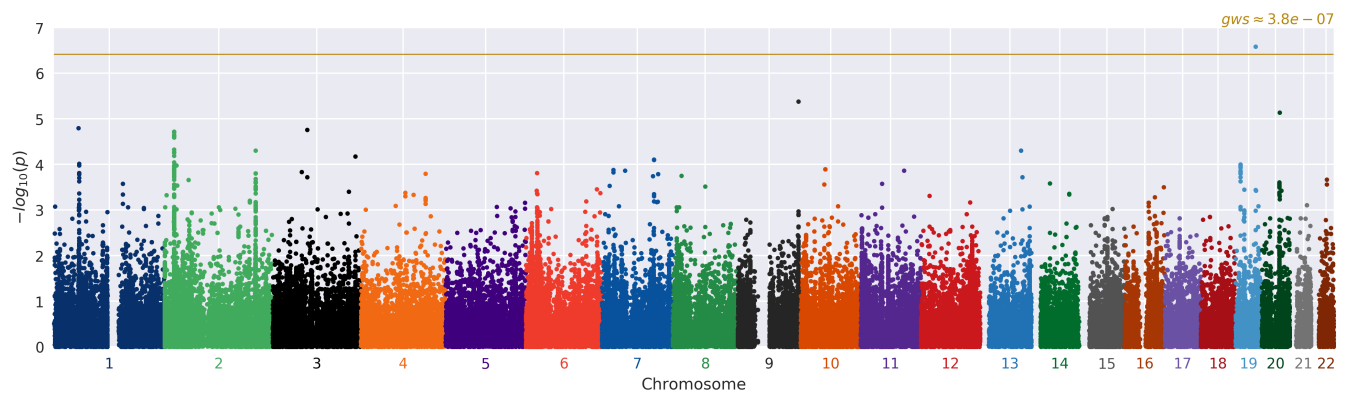
(a) invn Adjusted Age+Age2+SEX+BMI

Figure 21: Manhattan plots for LDL_CALCULATED in the EXBROAD_EUR analysis



(a) invn Adjusted Age+Age2+SEX+BMI

Figure 22: Manhattan plots for LDL_CALCULATED in the GWAS_EUR analysis



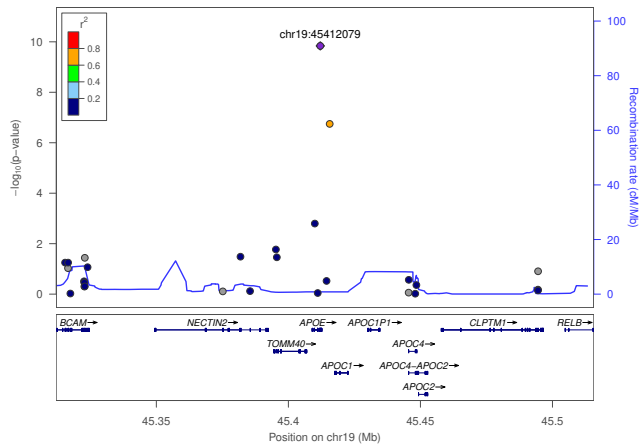
(a) invn Adjusted Age+Age2+SEX+BMI

Figure 23: Manhattan plots for LDL_CALCULATED in the METABO_EUR analysis

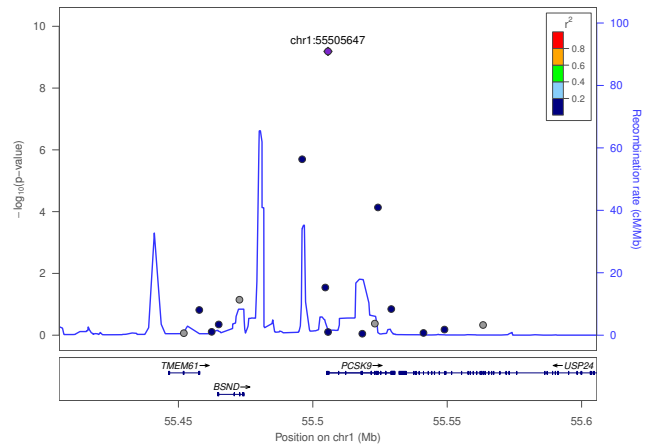
5.3 Top associations

Table 18: Top variants in the EXBROAD_EUR invn Adjusted Age+Age2+SEX+BMI model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	GENE _{CLOSEST}	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
19	45412079	rs7412	C	T	APOE	2,460	1,362	1,098	238	0.952	0.428	$6.65 \cdot 10^{-2}$	$1.45 \cdot 10^{-10}$
1	55505647	rs11591147	G	T	PCSK9	2,460	1,362	1,098	200	0.959	0.44	$7.1 \cdot 10^{-2}$	$6.5 \cdot 10^{-10}$
19	45415640	rs445925	G	A	APOC1	2,460	1,362	1,098	334	0.932	0.297	$5.68 \cdot 10^{-2}$	$1.79 \cdot 10^{-7}$
19	11202306	rs6511720	G	T	LDLR	2,460	1,362	1,098	517	0.895	0.225	$4.69 \cdot 10^{-2}$	$1.72 \cdot 10^{-6}$
1	109817590	rs12740374	G	T	CELSR2	2,460	1,362	1,098	1,097	0.777	0.156	$3.46 \cdot 10^{-2}$	$7.07 \cdot 10^{-6}$
1	109821511	rs602633	G	T	PSRC1	2,460	1,362	1,098	1,108	0.225	0.154	$3.44 \cdot 10^{-2}$	$7.41 \cdot 10^{-6}$
17	79867425	rs150714189	G	A	PCYT2	2,460	1,362	1,098	34	0.993	0.718	0.172	$3.13 \cdot 10^{-5}$
9	125281532	exm779039	C	T	OR1J4	2,460	1,362	1,098	4	0.999	2.066	0.499	$3.58 \cdot 10^{-5}$
6	135411228	rs9376090	T	C	HBS1L	2,460	1,362	1,098	1,705	0.653	0.119	$3 \cdot 10^{-2}$	$7.23 \cdot 10^{-5}$
2	20903015	rs4971516	T	C	LDAH	2,460	1,362	1,098	480	0.902	0.187	$4.78 \cdot 10^{-2}$	$8.98 \cdot 10^{-5}$
5	1335280	rs150993328	A	G	CLPTM1L	2,460	1,362	1,098	6	0.999	1.592	0.408	$9.71 \cdot 10^{-5}$
5	170648770	exm503306	A	G	RANBP17	2,460	1,362	1,098	2	1	2.743	0.706	$1.04 \cdot 10^{-4}$
2	187516795	rs147403786	C	G	ITGAV	2,460	1,362	1,098	19	0.996	0.88	0.23	$1.3 \cdot 10^{-4}$
14	39555082	rs201378245	C	T	SEC23A	2,460	1,362	1,098	7	0.999	1.447	0.378	$1.31 \cdot 10^{-4}$
12	6954864	ss1388024686	G	A	CDCA3	2,460	1,362	1,098	431	0.912	0.189	$4.94 \cdot 10^{-2}$	$1.38 \cdot 10^{-4}$
1	11788564	rs4846033	A	G	DRAXIN	2,460	1,362	1,098	15	$3.05 \cdot 10^{-3}$	0.983	0.258	$1.46 \cdot 10^{-4}$
2	43931168	rs145437024	G	A	PLEKHH2	2,460	1,362	1,098	4	0.999	1.899	0.499	$1.47 \cdot 10^{-4}$
17	28320335	exm1308553	C	A	EFCAB5	2,460	1,362	1,098	4	0.999	1.877	0.499	$1.74 \cdot 10^{-4}$
10	105218160	rs41317256	T	C	CALHM1	2,460	1,362	1,098	3	0.999	2.167	0.576	$1.75 \cdot 10^{-4}$
11	112456221	rs7105881	C	T	PLET1	2,460	1,362	1,098	1,629	0.331	0.114	$3.04 \cdot 10^{-2}$	$1.77 \cdot 10^{-4}$



(a) rs7412 ±100kb



(b) rs11591147 ±100kb

Figure 24: Regional plots for cohort EXBROAD_EUR model invn Adjusted Age+Age2+SEX+BMI

Table 19: Top variants in the GWAS_EUR invn Adjusted Age+Age2+SEX+BMI model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	GENE _{CLOSEST}	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
2	122734147	rs1517712	T	C	TSN	1,213	669	544	841	0.653	0.194	$4.1 \cdot 10^{-2}$	$2.35 \cdot 10^{-6}$
12	5676977	rs3782582	G	T	ANO2	1,213	669	544	984	0.406	0.191	$4.04 \cdot 10^{-2}$	$2.65 \cdot 10^{-6}$
15	63282106	rs4405494	T	C	TPM1	1,213	669	544	52	0.979	0.647	0.14	$4.53 \cdot 10^{-6}$
11	93552855	rs585768	C	T	VSTM5	1,212	669	543	345	0.142	0.257	$5.84 \cdot 10^{-2}$	$1.15 \cdot 10^{-5}$
1	109815252	rs611917	A	G	CELSR2	1,213	669	544	817	0.337	0.182	$4.17 \cdot 10^{-2}$	$1.34 \cdot 10^{-5}$
10	4464252	rs1751284	C	A	AKR1E2	1,213	669	544	315	0.13	0.262	$6.02 \cdot 10^{-2}$	$1.42 \cdot 10^{-5}$
8	11266131	rs7003840	C	T	FAM167A	1,213	669	544	1,133	0.533	0.174	$4 \cdot 10^{-2}$	$1.54 \cdot 10^{-5}$
13	96374386	rs9302083	T	C	DNAJC3	1,213	669	544	1,169	0.518	0.172	$3.98 \cdot 10^{-2}$	$1.76 \cdot 10^{-5}$
6	130832922	rs17059166	C	T	TMEM200A	1,213	669	544	343	0.141	0.25	$5.85 \cdot 10^{-2}$	$2.08 \cdot 10^{-5}$
1	165190876	rs6686960	T	C	LMX1A	1,210	667	543	377	0.844	0.235	$5.6 \cdot 10^{-2}$	$3.03 \cdot 10^{-5}$
1	153642909	rs11265625	A	G	ILF2	1,213	669	544	1,073	0.442	0.166	$3.97 \cdot 10^{-2}$	$3.18 \cdot 10^{-5}$
15	78497593	rs1554377	T	C	ACSBG1	1,210	668	542	1,131	0.467	0.169	$4.07 \cdot 10^{-2}$	$3.39 \cdot 10^{-5}$
15	50221346	rs2413979	G	T	ATP8B4	1,213	669	544	148	$6.1 \cdot 10^{-2}$	0.339	$8.22 \cdot 10^{-2}$	$3.91 \cdot 10^{-5}$
4	167244207	rs1373557	G	T	TLL1	1,213	669	544	216	$8.9 \cdot 10^{-2}$	0.291	$7.06 \cdot 10^{-2}$	$4.02 \cdot 10^{-5}$
1	15197909	rs2803396	T	C	KAZN	1,213	669	544	476	0.804	0.208	$5.07 \cdot 10^{-2}$	$4.32 \cdot 10^{-5}$
6	105751550	rs6571225	A	G	PREP	1,210	667	543	109	$4.5 \cdot 10^{-2}$	0.389	$9.5 \cdot 10^{-2}$	$4.56 \cdot 10^{-5}$
1	64699594	rs4915953	T	G	UBE2U	1,213	669	544	437	0.18	0.213	$5.24 \cdot 10^{-2}$	$4.88 \cdot 10^{-5}$
6	121106523	rs2817936	A	C	TBC1D32	1,213	669	544	48	$1.98 \cdot 10^{-2}$	0.571	0.143	$6.99 \cdot 10^{-5}$
18	29273129	rs10438933	A	G	B4GALT6	1,213	669	544	319	0.131	0.242	$6.08 \cdot 10^{-2}$	$7.17 \cdot 10^{-5}$
17	53455706	rs4794574	T	C	MMD	1,213	669	544	177	$7.3 \cdot 10^{-2}$	0.305	$7.68 \cdot 10^{-2}$	$7.45 \cdot 10^{-5}$

Table 20: Top variants in the METABO_EUR invn Adjusted Age+Age2+SEX+BMI model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	GENE _{CLOSEST}	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
19	45412079	rs7412	C	T	APOE	1,561	823	738	140	0.955	0.448	$8.66 \cdot 10^{-2}$	$2.59 \cdot 10^{-7}$
9	136145425	rs9411378	A	C	ABO	1,541	810	731	867	0.719	0.187	$4.06 \cdot 10^{-2}$	$4.14 \cdot 10^{-6}$
20	40116207	rs3092194	G	A	CHD6	1,562	823	739	562	0.82	0.208	$4.61 \cdot 10^{-2}$	$7.29 \cdot 10^{-6}$
1	55505647	rs11591147	G	T	PCSK9	1,562	823	739	112	0.964	0.415	$9.58 \cdot 10^{-2}$	$1.61 \cdot 10^{-5}$
3	77667044	rs1523768	A	G	ROBO2	1,559	820	739	1,000	0.321	0.163	$3.77 \cdot 10^{-2}$	$1.74 \cdot 10^{-5}$
2	21273490	rs7575840	T	G	APOB	1,562	823	739	922	0.705	0.167	$3.9 \cdot 10^{-2}$	$1.91 \cdot 10^{-5}$
13	91995570	rs17556509	T	C	GPC5	1,562	823	739	244	0.922	0.271	$6.66 \cdot 10^{-2}$	$4.97 \cdot 10^{-5}$
2	204366776	rs16839858	G	A	RAPH1	1,562	823	739	800	0.744	0.164	$4.03 \cdot 10^{-2}$	$4.99 \cdot 10^{-5}$
2	21311691	rs754523	G	A	TDRD15	1,562	823	739	871	0.721	0.163	$4.02 \cdot 10^{-2}$	$5.37 \cdot 10^{-5}$
3	185769644	rs75136052	A	G	ETV5	1,562	823	739	61	0.98	0.521	0.13	$6.73 \cdot 10^{-5}$
7	117064625	rs10249651	T	C	ASZ1	1,561	823	738	1,283	0.589	0.142	$3.6 \cdot 10^{-2}$	$7.8 \cdot 10^{-5}$
7	116954785	rs39312	A	C	WNT2	1,562	823	739	1,288	0.588	0.143	$3.6 \cdot 10^{-2}$	$7.95 \cdot 10^{-5}$
2	21121656	rs34504815	G	T	LDAH	1,562	823	739	244	0.922	0.266	$6.77 \cdot 10^{-2}$	$8.97 \cdot 10^{-5}$
1	56968477	rs4912314	T	C	PLPP3	1,561	823	738	686	0.78	0.169	$4.32 \cdot 10^{-2}$	$9.61 \cdot 10^{-5}$
19	11188247	rs56289821	G	A	LDLR	1,561	823	738	291	0.907	0.243	$6.22 \cdot 10^{-2}$	$9.91 \cdot 10^{-5}$
2	26636390	rs6710942	A	G	DRC1	1,562	823	739	1,161	0.628	0.144	$3.7 \cdot 10^{-2}$	$1.05 \cdot 10^{-4}$
10	56004457	rs7910314	G	T	PCDH15	1,562	823	739	38	0.988	0.628	0.164	$1.28 \cdot 10^{-4}$
7	25919798	rs4722534	G	A	NFE2L3	1,562	823	739	322	0.103	0.229	$5.97 \cdot 10^{-2}$	$1.31 \cdot 10^{-4}$
11	97487929	rs11211967	G	A	JRKL	1,562	823	739	505	0.838	0.188	$4.92 \cdot 10^{-2}$	$1.36 \cdot 10^{-4}$
7	52008579	rs450297	T	C	COBL	1,562	823	739	18	$5.76 \cdot 10^{-3}$	0.904	0.236	$1.36 \cdot 10^{-4}$

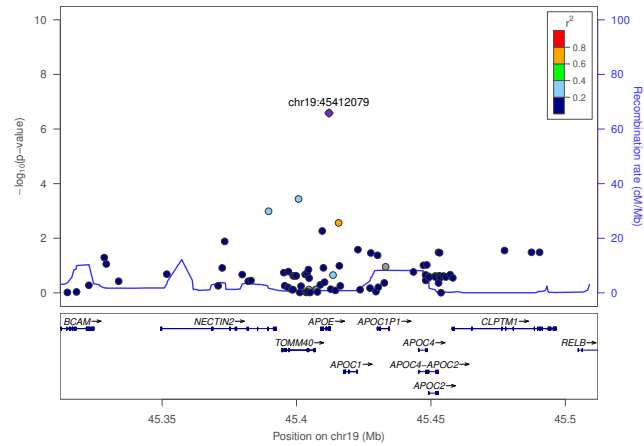


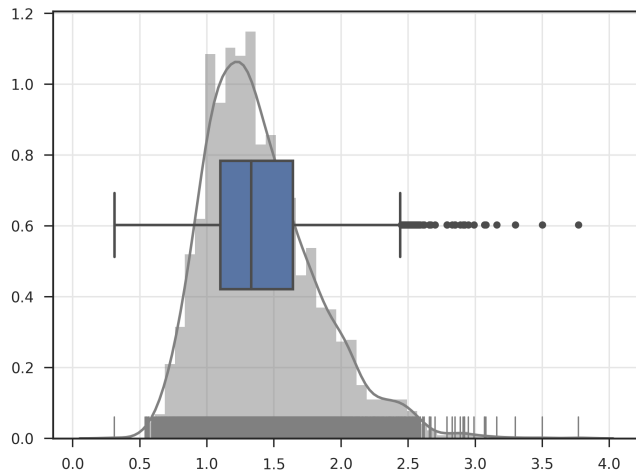
Figure 25: Regional plot for cohort METABO_EUR model invn Adjusted Age+Age2+SEX+BMI: rs7412 ±100kb

5.4 Previously identified risk loci

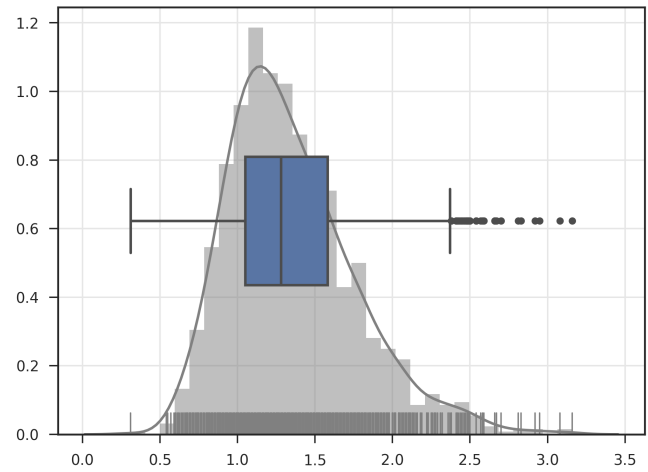
Table 21 shows statistics from the EXBROAD_EUR cohort for 50 loci that were shown to be significantly associated with LDL Cholesterol in the 2013 Nature Genetics paper by Willer et al [12]. Where a previously reported variant was not genotyped in the study (indicated by $\bar{R}^2 < 1$), if available, a tagging variant in LD with the reported variant ($\bar{R}^2 \geq 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. There are 20 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 50 variants in both studies, 43 exhibit the same direction of effect with the known result (binomial test $p = 1.05e - 07$).

6 HDL Cholesterol (HDL)

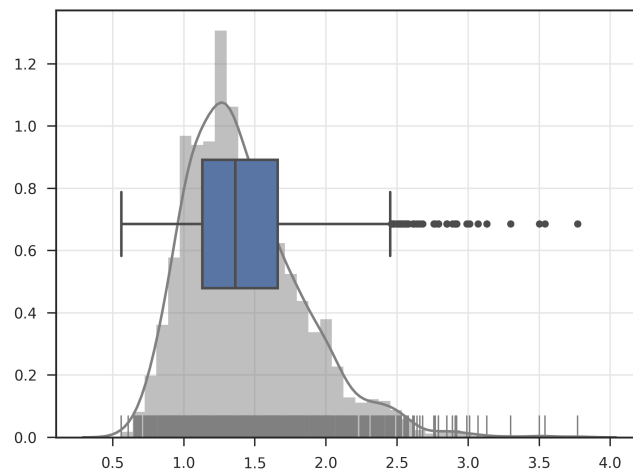
6.1 Summary



(a) EXBROAD_EUR



(b) GWAS_EUR



(c) METABO_EUR

Figure 26: Distribution of HDL in cohort-level analyses

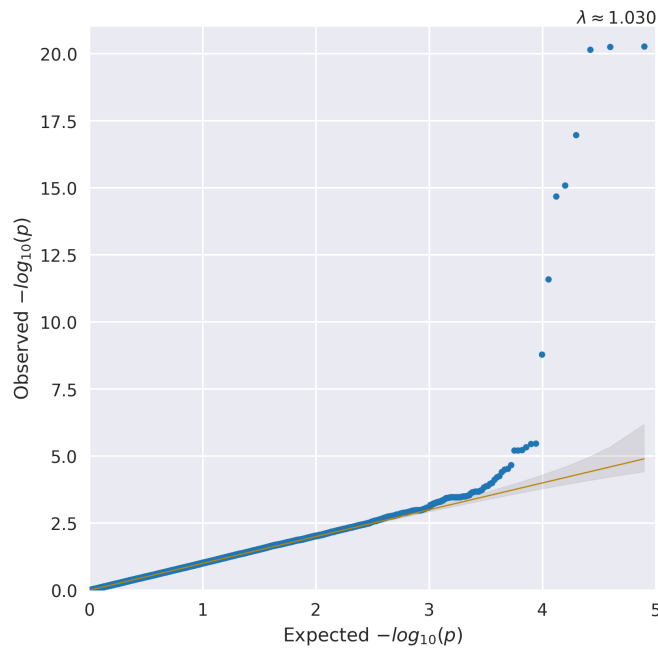
Table 24: Summary of samples removed from HDL Cholesterol analysis by cohort and model

Cohort	Array	Ancestry	Trans	Covars	Total	-SampleQc	-missObs	-Kinship	-PcOutlier
EXBROAD_EUR	EXBROAD	EUR	invn	Age+Age2+SEX+BMI	3563	36	635	34	0
GWAS_EUR	GWAS	EUR	invn	Age+Age2+SEX+BMI	1796	19	443	93	0
METABO_EUR	METABO	EUR	invn	Age+Age2+SEX+BMI	2344	43	224	146	15

Table 25: Summary of samples remaining for HDL Cholesterol analysis by cohort and model

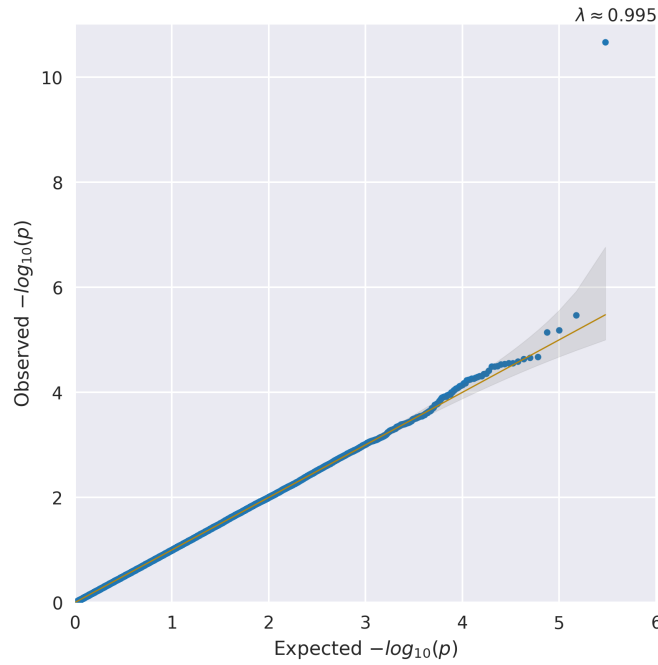
Cohort	Array	Ancestry	Trans	Covars	PCs	N	Male	Female	Max	Min	μ	\tilde{x}	σ
EXBROAD_EUR	EXBROAD	EUR	invn	Age+Age2+SEX+BMI	0	2865	1654	1211	3.77	0.31	1.402	1.33	0.42
GWAS_EUR	GWAS	EUR	invn	Age+Age2+SEX+BMI	3	1244	693	551	3.16	0.31	1.356	1.29	0.414
METABO_EUR	METABO	EUR	invn	Age+Age2+SEX+BMI	0	1917	1073	844	3.77	0.56	1.435	1.36	0.418

6.2 Calibration



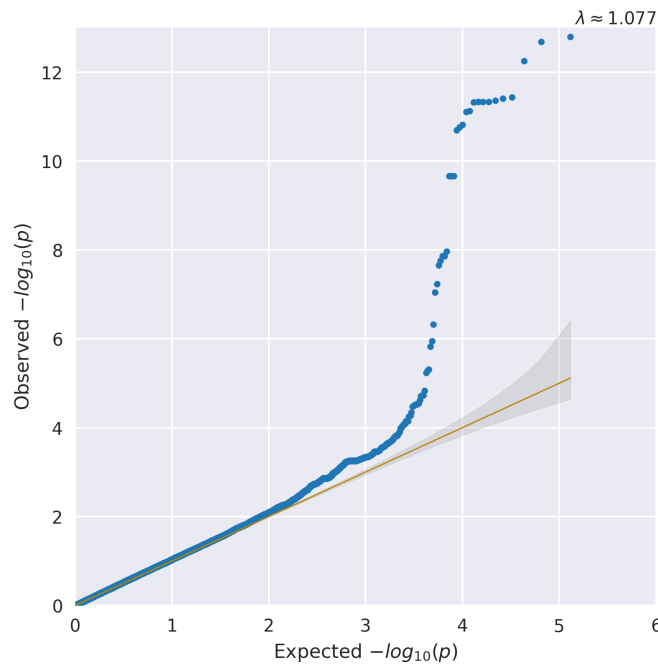
(a) invn Adjusted Age+Age2+SEX+BMI

Figure 27: QQ plots for HDL in the EXBROAD_EUR analysis



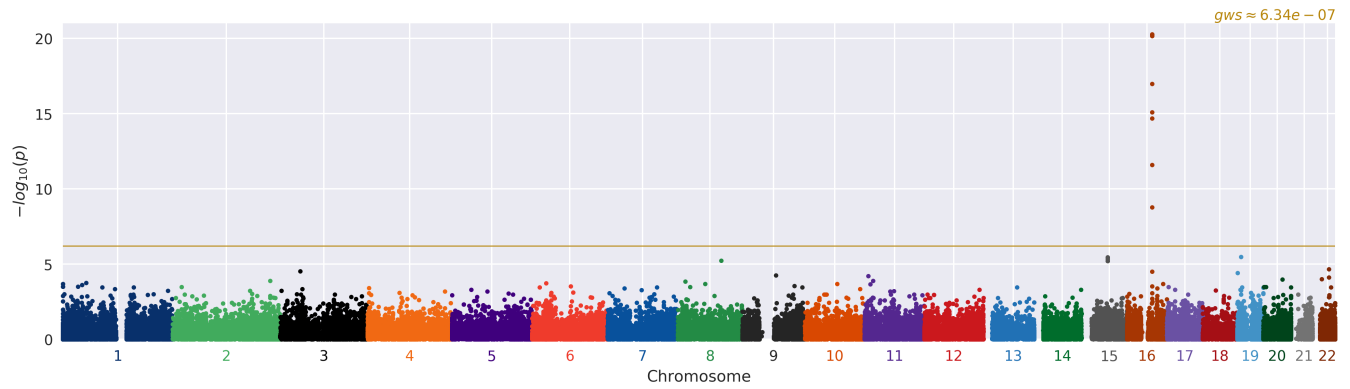
(a) invn Adjusted Age+Age2+SEX+BMI

Figure 28: QQ plots for HDL in the GWAS_EUR analysis



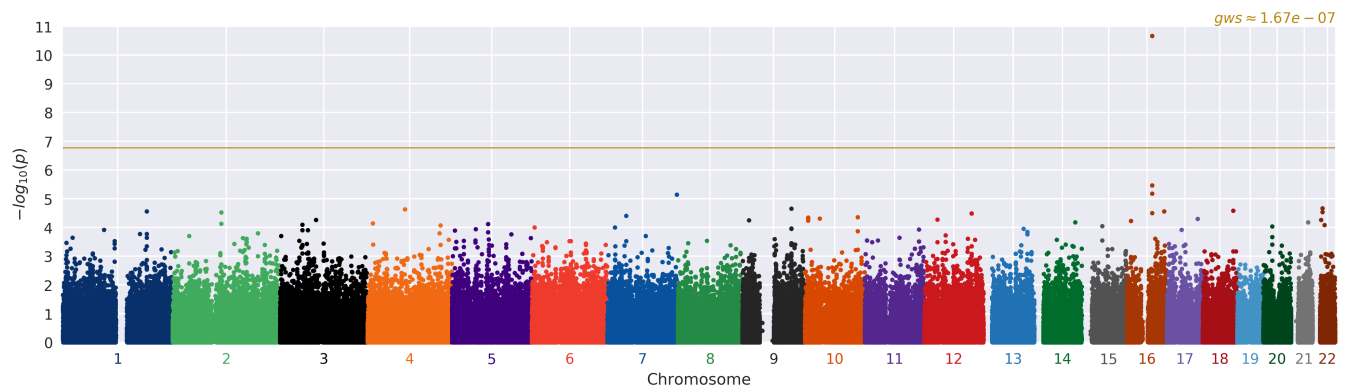
(a) invn Adjusted Age+Age2+SEX+BMI

Figure 29: QQ plots for HDL in the METABO_EUR analysis



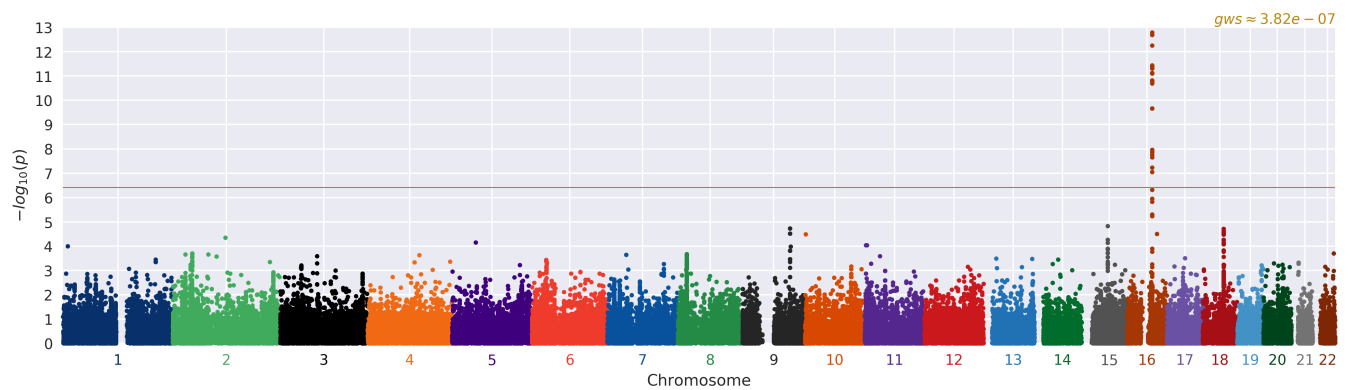
(a) invn Adjusted Age+Age2+SEX+BMI

Figure 30: Manhattan plots for HDL in the EXBROAD_EUR analysis



(a) invn Adjusted Age+Age2+SEX+BMI

Figure 31: Manhattan plots for HDL in the GWAS_EUR analysis



(a) invn Adjusted Age+Age2+SEX+BMI

Figure 32: Manhattan plots for HDL in the METABO_EUR analysis

6.3 Top associations

Table 26: Top variants in the EXBROAD_EUR invn Adjusted Age+Age2+SEX+BMI model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	GENE _{CLOSEST}	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
16	56989590	rs247616	T	C	CETP	2,865	1,654	1,211	1,549	0.27	0.278	$2.93 \cdot 10^{-2}$	$5.22 \cdot 10^{-21}$
16	56985139	rs9989419	G	A	HERPUD1	2,865	1,654	1,211	2,263	0.605	0.161	$2.67 \cdot 10^{-2}$	$1.63 \cdot 10^{-9}$
19	8429323	rs116843064	A	G	ANGPTL4	2,865	1,654	1,211	138	$2.41 \cdot 10^{-2}$	0.396	$8.5 \cdot 10^{-2}$	$3.32 \cdot 10^{-6}$
15	58678512	rs10468017	T	C	LIPC	2,865	1,654	1,211	1,904	0.332	0.129	$2.78 \cdot 10^{-2}$	$3.48 \cdot 10^{-6}$
8	98289238	rs151015596	C	T	TSPYL5	2,865	1,654	1,211	12	$2.09 \cdot 10^{-3}$	1.308	0.288	$5.96 \cdot 10^{-6}$
22	37467392	rs5756506	C	G	TMPRSS6	2,865	1,654	1,211	2,339	0.408	0.115	$2.71 \cdot 10^{-2}$	$2.13 \cdot 10^{-5}$
3	45942554	rs45530037	G	A	CCR9	2,865	1,654	1,211	43	$7.5 \cdot 10^{-3}$	0.626	0.15	$2.94 \cdot 10^{-5}$
19	740436	rs149788617	G	A	PALM	2,865	1,654	1,211	4	$6.98 \cdot 10^{-4}$	2.056	0.499	$3.89 \cdot 10^{-5}$
9	75764565	rs3758354	C	A	ANXA1	2,865	1,654	1,211	210	$3.66 \cdot 10^{-2}$	0.283	$7.01 \cdot 10^{-2}$	$5.45 \cdot 10^{-5}$
11	7960232	rs138046496	G	A	OR10A3	2,865	1,654	1,211	5	$8.73 \cdot 10^{-4}$	1.791	0.446	$6.14 \cdot 10^{-5}$
22	21354970	exm1588273	G	C	THAP7	2,864	1,653	1,211	773	0.865	0.151	$3.88 \cdot 10^{-2}$	$9.99 \cdot 10^{-5}$
20	43042364	rs1800961	C	T	HNF4A	2,865	1,654	1,211	256	$4.47 \cdot 10^{-2}$	0.244	$6.29 \cdot 10^{-2}$	$1.07 \cdot 10^{-4}$
11	19251491	exm895635	C	G	E2F8	2,865	1,654	1,211	2	$3.49 \cdot 10^{-4}$	2.709	0.706	$1.26 \cdot 10^{-4}$
2	220494849	exm270030	T	C	SLC4A3	2,865	1,654	1,211	9	$1.57 \cdot 10^{-3}$	1.276	0.333	$1.3 \cdot 10^{-4}$
8	17406339	rs142593316	T	C	SLC7A2	2,865	1,654	1,211	2	$3.49 \cdot 10^{-4}$	2.686	0.706	$1.44 \cdot 10^{-4}$
1	53681725	rs113278028	C	T	C1orf123	2,865	1,654	1,211	148	$2.58 \cdot 10^{-2}$	0.307	$8.19 \cdot 10^{-2}$	$1.78 \cdot 10^{-4}$
6	32097421	rs35580488	G	C	FKBPL	2,865	1,654	1,211	106	$1.85 \cdot 10^{-2}$	0.369	$9.87 \cdot 10^{-2}$	$1.9 \cdot 10^{-4}$
1	976963	rs150359724	G	A	AGRN	2,865	1,654	1,211	7	$1.22 \cdot 10^{-3}$	1.402	0.378	$2.08 \cdot 10^{-4}$
8	61955772	rs2882217	C	T	CHD7	2,865	1,654	1,211	2,271	0.396	$9.82 \cdot 10^{-2}$	$2.65 \cdot 10^{-2}$	$2.1 \cdot 10^{-4}$
10	73563128	rs202052174	A	G	CDH23	2,865	1,654	1,211	3	$5.24 \cdot 10^{-4}$	2.139	0.576	$2.1 \cdot 10^{-4}$

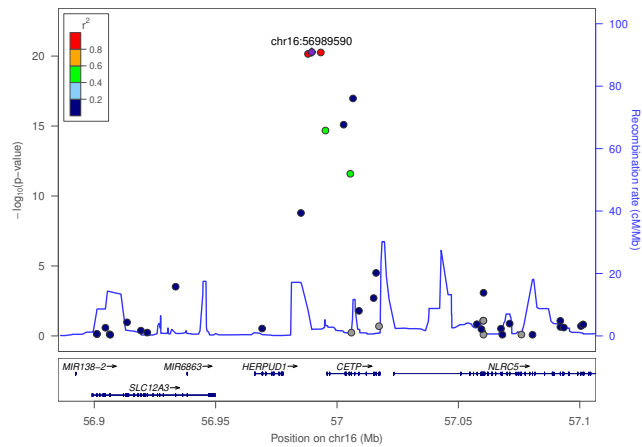


Figure 33: Regional plot for cohort EXBROAD_EUR model invn Adjusted Age+Age2+SEX+BMI: rs247616 ±100kb

Table 27: Top variants in the GWAS_EUR invn Adjusted Age+Age2+SEX+BMI model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	GENE _{CLOSEST}	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
16	56993324	rs3764261	A	C	CETP	1,244	693	551	673	0.73	0.3	$4.43 \cdot 10^{-2}$	$2.16 \cdot 10^{-11}$
7	157216093	rs2286842	T	C	DNAJB6	1,244	693	551	959	0.615	0.187	$4.14 \cdot 10^{-2}$	$7.18 \cdot 10^{-6}$
22	22430952	rs928901	G	A	TOP3B	1,241	692	549	1,193	0.481	0.174	$4.09 \cdot 10^{-2}$	$2.12 \cdot 10^{-5}$
9	111008699	rs4644328	C	T	AL162389	1,244	693	551	718	0.289	0.187	$4.39 \cdot 10^{-2}$	$2.18 \cdot 10^{-5}$
4	84189869	rs4693596	C	T	COQ2	1,244	693	551	705	0.283	0.187	$4.4 \cdot 10^{-2}$	$2.3 \cdot 10^{-5}$
18	68714195	rs1942204	T	C	SOCS6	1,244	693	551	375	0.849	0.236	$5.58 \cdot 10^{-2}$	$2.57 \cdot 10^{-5}$
16	83967469	rs9923900	A	G	MLYCD	1,244	693	551	847	0.66	0.177	$4.2 \cdot 10^{-2}$	$2.76 \cdot 10^{-5}$
1	190389741	rs6678713	A	G	BRINP3	1,244	693	551	1,049	0.578	0.168	$3.99 \cdot 10^{-2}$	$2.77 \cdot 10^{-5}$
2	110270250	rs10221803	T	C	SH3RF3	1,241	690	551	1,050	0.423	0.167	$3.98 \cdot 10^{-2}$	$2.94 \cdot 10^{-5}$
16	56985139	rs9989419	G	A	HERPUD1	1,243	693	550	967	0.389	0.171	$4.1 \cdot 10^{-2}$	$3.15 \cdot 10^{-5}$
12	106704974	rs4964460	A	G	TCP11L2	1,244	693	551	796	0.32	0.177	$4.24 \cdot 10^{-2}$	$3.2 \cdot 10^{-5}$
7	42745578	rs2583893	G	A	C7orf25	1,244	693	551	892	0.359	0.171	$4.15 \cdot 10^{-2}$	$3.88 \cdot 10^{-5}$
10	119473576	rs2182096	T	C	EMX2	1,243	693	550	970	0.61	0.167	$4.07 \cdot 10^{-2}$	$4.37 \cdot 10^{-5}$
10	7601084	rs3814696	C	T	ITIH5	1,244	693	551	229	0.908	0.278	$6.79 \cdot 10^{-2}$	$4.47 \cdot 10^{-5}$
10	33511047	rs2273466	C	T	NRP1	1,244	693	551	496	0.801	0.208	$5.1 \cdot 10^{-2}$	$4.89 \cdot 10^{-5}$
17	69538917	rs4793358	G	A	AC007461	1,244	693	551	587	0.236	0.189	$4.64 \cdot 10^{-2}$	$5.03 \cdot 10^{-5}$
12	29237140	rs1498795	T	C	FAR2	1,244	693	551	425	0.829	0.216	$5.31 \cdot 10^{-2}$	$5.23 \cdot 10^{-5}$
22	19924021	rs6518591	A	G	TXNRD2	1,243	692	551	363	0.854	0.223	$5.5 \cdot 10^{-2}$	$5.43 \cdot 10^{-5}$
3	81349843	rs11714085	A	G	GBE1	1,244	693	551	206	0.917	0.287	$7.09 \cdot 10^{-2}$	$5.45 \cdot 10^{-5}$
9	14434284	rs958957	G	A	NFIB	1,244	693	551	1,126	0.547	0.16	$3.97 \cdot 10^{-2}$	$5.63 \cdot 10^{-5}$

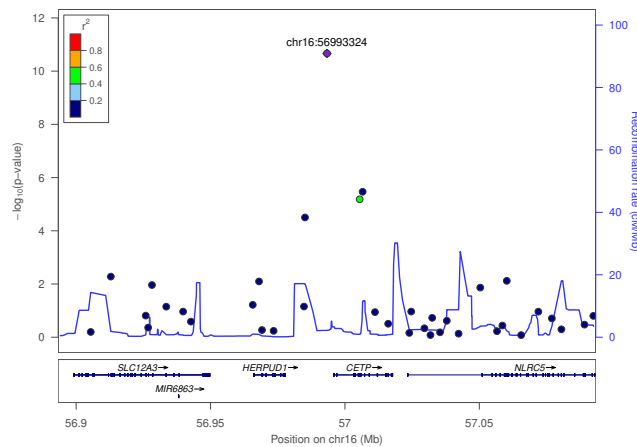


Figure 34: Regional plot for cohort GWAS_EUR model invn Adjusted Age+Age2+SEX+BMI: rs3764261 ±100kb

Table 28: Top variants in the METABO_EUR invn Adjusted Age+Age2+SEX+BMI model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	GENE _{CLOSEST}	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
16	57006590	rs7499892	C	T	CETP	1,915	1,072	843	683	0.178	0.311	$4.18 \cdot 10^{-2}$	$1.61 \cdot 10^{-13}$
16	56987015	rs12446515	T	C	HERPUD1	1,917	1,073	844	1,045	0.273	0.25	$3.58 \cdot 10^{-2}$	$3.88 \cdot 10^{-12}$
15	58723479	rs1077834	C	T	LIPC	1,917	1,073	844	970	0.253	0.162	$3.72 \cdot 10^{-2}$	$1.48 \cdot 10^{-5}$
9	107651526	rs2275545	A	G	ABCA1	1,917	1,073	844	490	0.128	0.207	$4.83 \cdot 10^{-2}$	$1.86 \cdot 10^{-5}$
18	47162207	rs7228412	G	A	LIPG	1,917	1,073	844	898	0.234	0.159	$3.71 \cdot 10^{-2}$	$1.94 \cdot 10^{-5}$
18	47258695	rs4939890	G	A	ACAA2	1,917	1,073	844	408	0.894	0.223	$5.26 \cdot 10^{-2}$	$2.37 \cdot 10^{-5}$
16	67837004	rs76398233	C	T	RANBP10	1,917	1,073	844	6	$1.56 \cdot 10^{-3}$	1.702	0.408	$3.15 \cdot 10^{-5}$
10	1581875	rs2813462	C	T	ADARB2	1,917	1,073	844	723	0.811	0.173	$4.15 \cdot 10^{-2}$	$3.24 \cdot 10^{-5}$
2	118827119	rs17527212	C	T	INSIG2	1,917	1,073	844	174	$4.54 \cdot 10^{-2}$	0.315	$7.7 \cdot 10^{-2}$	$4.53 \cdot 10^{-5}$
5	53441597	rs26608	T	C	ARL15	1,916	1,073	843	976	0.255	0.146	$3.66 \cdot 10^{-2}$	$7.06 \cdot 10^{-5}$
18	47385799	rs488191	G	A	MYO5B	1,917	1,073	844	404	0.895	0.209	$5.28 \cdot 10^{-2}$	$8.12 \cdot 10^{-5}$
11	2918639	rs379781	A	G	SLC22A18AS	1,917	1,073	844	1,256	0.328	0.135	$3.45 \cdot 10^{-2}$	$9.1 \cdot 10^{-5}$
11	4659085	rs16923484	T	G	OR51D1	1,917	1,073	844	258	$6.73 \cdot 10^{-2}$	0.252	$6.43 \cdot 10^{-2}$	$9.2 \cdot 10^{-5}$
1	11908146	rs41300100	C	G	NPPA	1,917	1,073	844	8	$2.09 \cdot 10^{-3}$	1.379	0.354	$1 \cdot 10^{-4}$
9	109150127	rs7035112	T	A	ZNF462	1,917	1,073	844	328	$8.56 \cdot 10^{-2}$	0.224	$5.77 \cdot 10^{-2}$	$1.03 \cdot 10^{-4}$
2	43765010	rs12019156	T	C	THADA	1,917	1,073	844	60	$1.56 \cdot 10^{-2}$	0.488	0.131	$1.98 \cdot 10^{-4}$
22	48280506	rs2064804	C	T	FAM19A5	1,917	1,073	844	1,387	0.638	0.124	$3.32 \cdot 10^{-2}$	$2.01 \cdot 10^{-4}$
8	19819439	rs326	G	A	LPL	1,917	1,073	844	989	0.258	0.135	$3.64 \cdot 10^{-2}$	$2.08 \cdot 10^{-4}$
2	43851430	rs66994860	T	C	PLEKHH2	1,917	1,073	844	967	0.252	0.136	$3.67 \cdot 10^{-2}$	$2.09 \cdot 10^{-4}$
2	79970191	rs17786853	C	A	CTNNA2	1,917	1,073	844	23	$6 \cdot 10^{-3}$	0.744	0.201	$2.17 \cdot 10^{-4}$

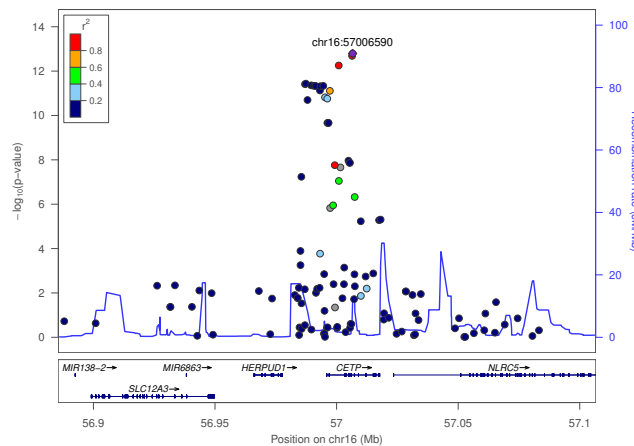


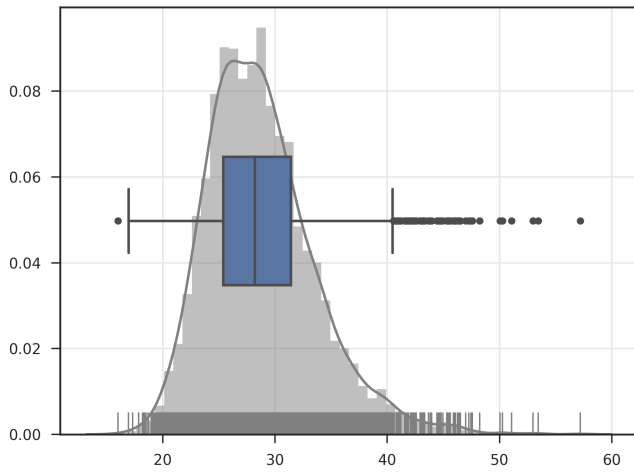
Figure 35: Regional plot for cohort METABO_EUR model invn Adjusted Age+Age2+SEX+BMI: rs7499892 $\pm 100kb$

6.4 Previously identified risk loci

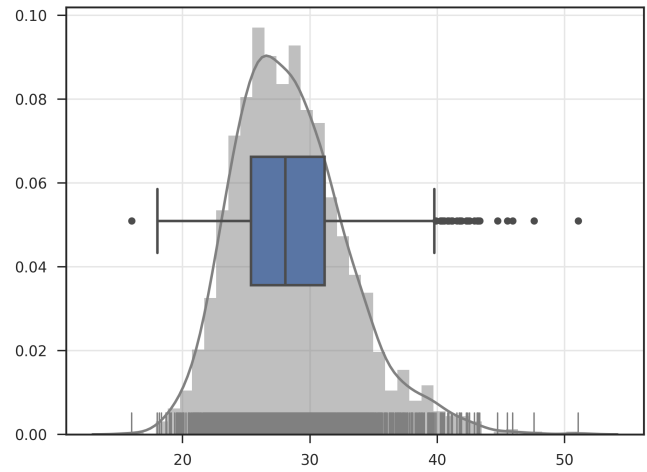
Table 29 shows statistics from the EXBROAD_EUR cohort for 50 loci that were shown to be significantly associated with HDL Cholesterol in the 2013 Nature Genetics paper by Willer et al [10]. Where a previously reported variant was not genotyped in the study (indicated by $\bar{R}^2 < 1$), if available, a tagging variant in LD with

7 Body Mass Index (BMI)

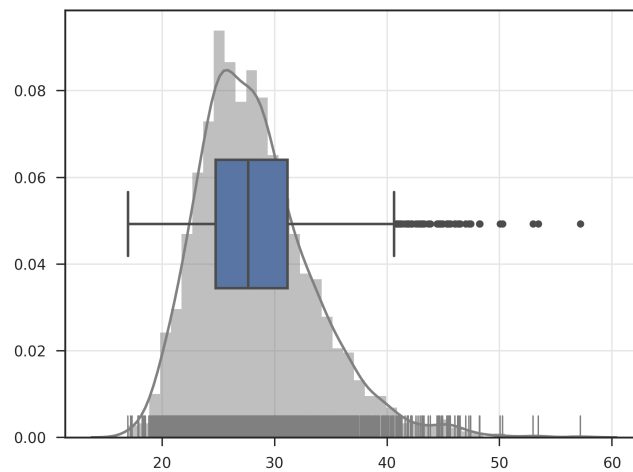
7.1 Summary



(a) EXBROAD_EUR



(b) GWAS_EUR



(c) METABO_EUR

Figure 36: Distribution of BMI in cohort-level analyses

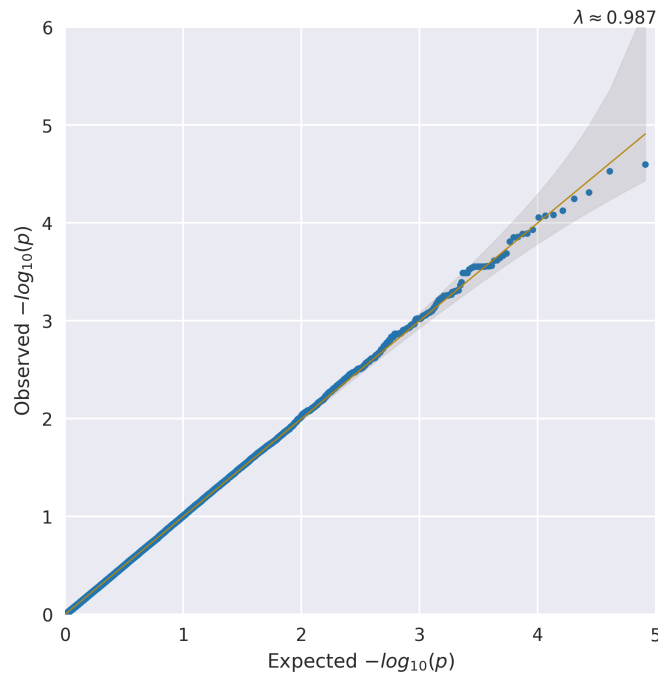
Table 32: Summary of samples removed from Body Mass Index analysis by cohort and model

Cohort	Array	Ancestry	Trans	Covars	Total	-SampleQc	-missObs	-Kinship	-PcOutlier
EXBROAD_EUR	EXBROAD	EUR	invn	Age+Age2+SEX	3563	36	70	38	47
GWAS_EUR	GWAS	EUR	invn	Age+Age2+SEX	1796	19	61	103	0
METABO_EUR	METABO	EUR	invn	Age+Age2+SEX	2344	43	11	153	0

Table 33: Summary of samples remaining for Body Mass Index analysis by cohort and model

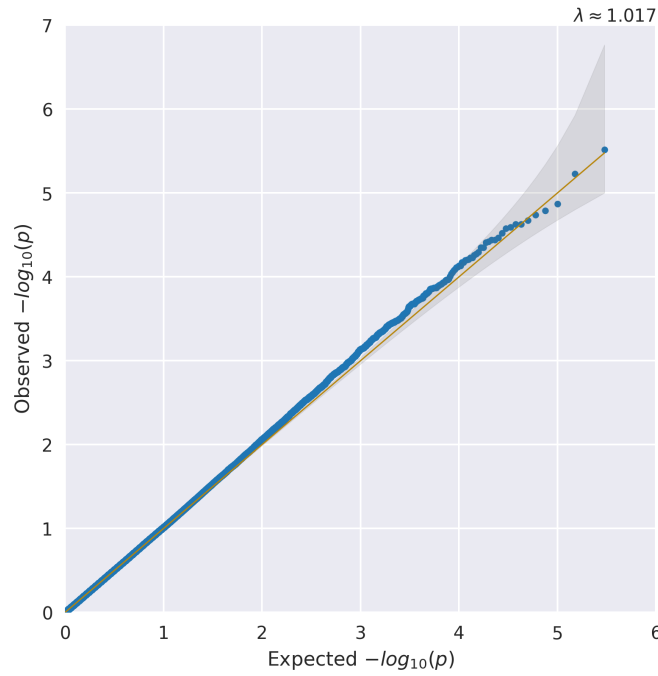
Cohort	Array	Ancestry	Trans	Covars	PCs	N	Male	Female	Max	Min	μ	\bar{x}	σ
EXBROAD_EUR	EXBROAD	EUR	invn	Age+Age2+SEX	2	3373	1907	1466	57.183	16.0	28.787	28.22	4.87
GWAS_EUR	GWAS	EUR	invn	Age+Age2+SEX	0	1614	875	739	51.075	16.0	28.623	28.145	4.531
METABO_EUR	METABO	EUR	invn	Age+Age2+SEX	2	2137	1188	949	57.183	16.937	28.405	27.751	5.19

7.2 Calibration



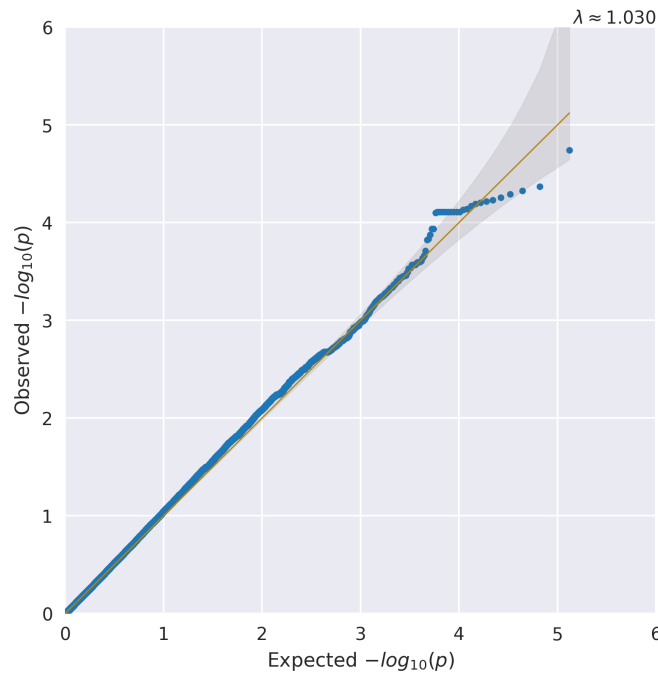
(a) invn Adjusted Age+Age2+SEX

Figure 37: QQ plots for BMI in the EXBROAD_EUR analysis



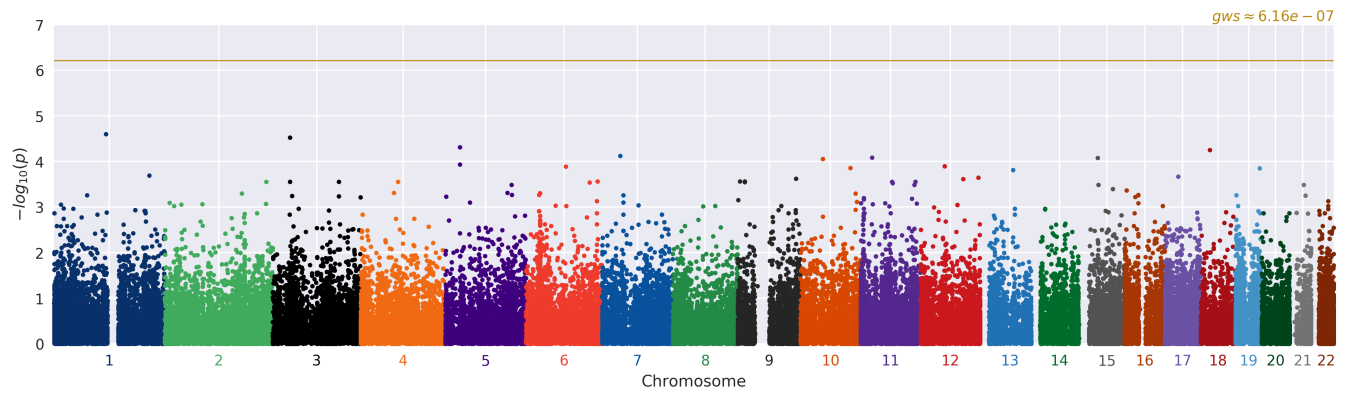
(a) invn Adjusted Age+Age2+SEX

Figure 38: QQ plots for BMI in the GWAS_EUR analysis



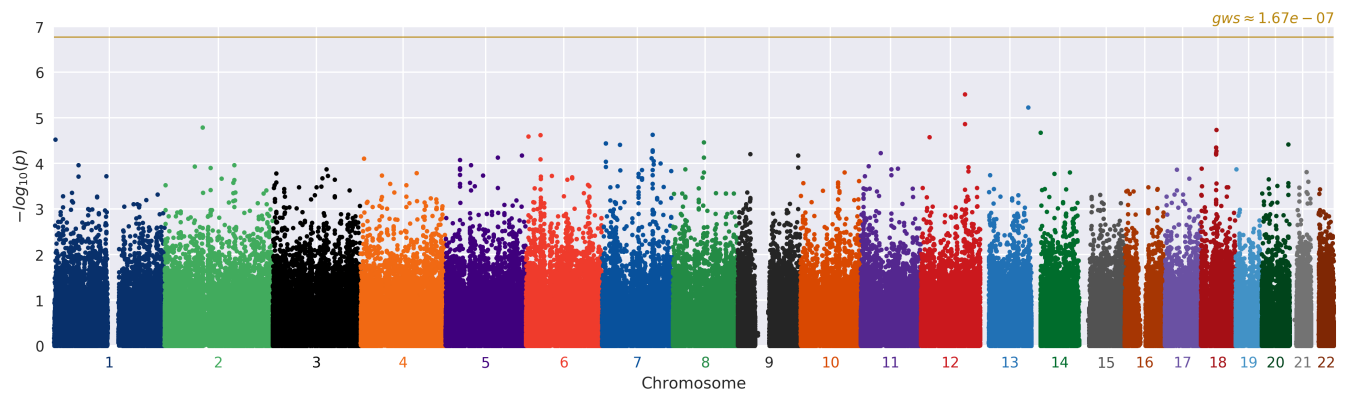
(a) invn Adjusted Age+Age2+SEX

Figure 39: QQ plots for BMI in the METABO_EUR analysis



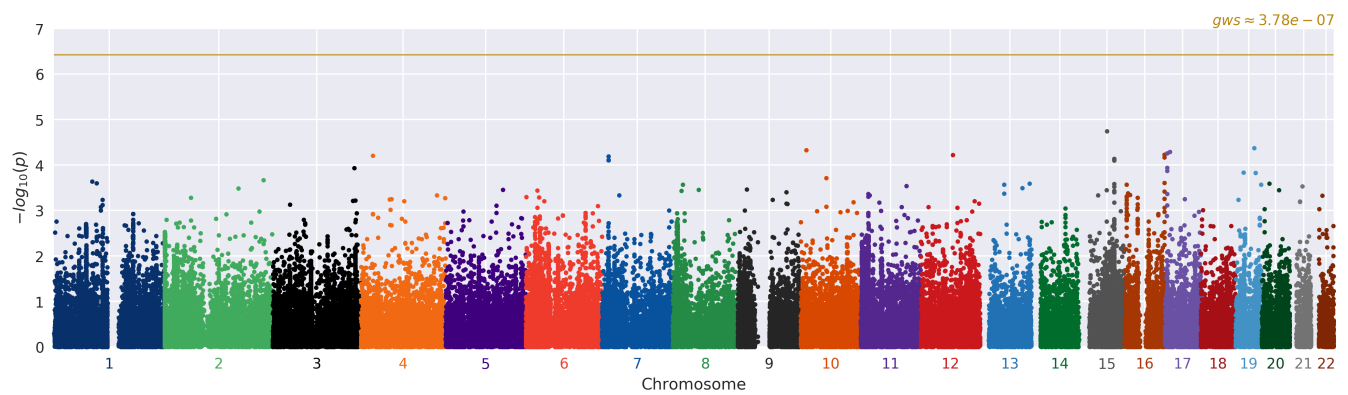
(a) invn Adjusted Age+Age2+SEX

Figure 40: Manhattan plots for BMI in the EXBROAD_EUR analysis



(a) invn Adjusted Age+Age2+SEX

Figure 41: Manhattan plots for BMI in the GWAS_EUR analysis



(a) invn Adjusted Age+Age2+SEX

Figure 42: Manhattan plots for BMI in the METABO_EUR analysis

7.3 Top associations

Table 34: Top variants in the EXBROAD_EUR invn Adjusted Age+Age2+SEX model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	GENE _{CLOSEST}	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
1	117504129	rs185563430	T	A	PTGFRN	3,373	1,907	1,466	77	0.989	0.483	0.114	$2.52 \cdot 10^{-5}$
3	38766760	rs73062575	G	T	SCN10A	3,373	1,907	1,466	81	0.988	0.467	0.112	$2.97 \cdot 10^{-5}$
5	32286948	rs11959574	C	T	MTMR12	3,373	1,907	1,466	2,507	0.628	0.101	$2.48 \cdot 10^{-2}$	$4.85 \cdot 10^{-5}$
18	20602153	rs140196819	G	A	RBBP8	3,373	1,907	1,466	2	1	2.83	0.702	$5.64 \cdot 10^{-5}$
7	41417008	rs12701888	G	T	INHBA	3,373	1,907	1,466	1,645	0.244	0.113	$2.85 \cdot 10^{-2}$	$7.5 \cdot 10^{-5}$
11	25929959	rs1441519	A	C	ANO3	3,373	1,907	1,466	2,629	0.39	$9.69 \cdot 10^{-2}$	$2.46 \cdot 10^{-2}$	$8.25 \cdot 10^{-5}$
15	41853422	exm2223257	G	C	TYRO3	3,373	1,907	1,466	4	0.999	1.954	0.496	$8.41 \cdot 10^{-5}$
10	50157552	rs2663028	T	C	LRRC18	3,373	1,907	1,466	3,249	0.482	$9.58 \cdot 10^{-2}$	$2.44 \cdot 10^{-2}$	$8.81 \cdot 10^{-5}$
5	32400266	rs1051489	G	A	ZFR	3,373	1,907	1,466	1,860	0.724	0.103	$2.68 \cdot 10^{-2}$	$1.18 \cdot 10^{-4}$
12	54107594	rs34229062	A	C	CALCOCO1	3,373	1,907	1,466	103	0.985	0.378	$9.84 \cdot 10^{-2}$	$1.27 \cdot 10^{-4}$
6	89967498	rs282129	A	G	GABRR2	3,373	1,907	1,466	2,053	0.696	0.102	$2.66 \cdot 10^{-2}$	$1.3 \cdot 10^{-4}$
10	112344129	rs142524280	G	A	SMC3	3,373	1,907	1,466	21	0.997	0.793	0.208	$1.39 \cdot 10^{-4}$
19	54676763	rs641738	T	C	TMC4	3,373	1,907	1,466	2,569	0.619	$9.54 \cdot 10^{-2}$	$2.5 \cdot 10^{-2}$	$1.41 \cdot 10^{-4}$
13	73883426	rs1411328	G	A	KLF5	3,373	1,907	1,466	2,375	0.352	$9.53 \cdot 10^{-2}$	$2.52 \cdot 10^{-2}$	$1.55 \cdot 10^{-4}$
1	214819818	rs79923436	G	A	CENPF	3,373	1,907	1,466	76	0.989	0.423	0.114	$2.05 \cdot 10^{-4}$
17	30222002	rs3760454	T	C	UTP6	3,373	1,907	1,466	2,993	0.556	$9.08 \cdot 10^{-2}$	$2.45 \cdot 10^{-2}$	$2.15 \cdot 10^{-4}$
12	129566566	rs144217964	T	C	TMEM132D	3,373	1,907	1,466	53	0.992	0.507	0.137	$2.27 \cdot 10^{-4}$
9	131217494	rs149189122	C	T	ODF2	3,373	1,907	1,466	17	0.997	0.888	0.242	$2.39 \cdot 10^{-4}$
12	95676206	rs192620355	T	C	VEZT	3,373	1,907	1,466	57	0.992	0.471	0.128	$2.42 \cdot 10^{-4}$
9	5213687	rs10975003	T	C	INSL4	3,373	1,907	1,466	2,512	0.628	$9.1 \cdot 10^{-2}$	$2.5 \cdot 10^{-2}$	$2.73 \cdot 10^{-4}$

Table 35: Top variants in the GWAS_EUR invn Adjusted Age+Age2+SEX model (**bold** variants indicate previously identified associations)

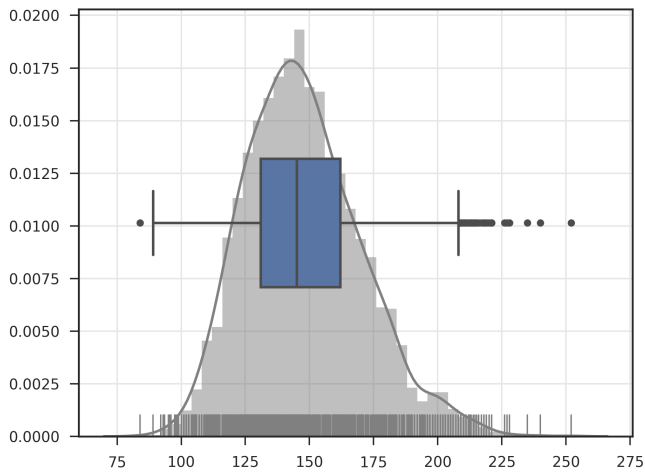
CHR	POS	ID	EA	OA	GENE _{CLOSEST}	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
12	99326756	rs621284	G	T	ANKS1B	1,614	875	739	585	0.819	0.208	$4.45 \cdot 10^{-2}$	$3.05 \cdot 10^{-6}$
13	108227879	rs9301233	G	A	FAM155A	1,614	875	739	1,278	0.396	0.161	$3.55 \cdot 10^{-2}$	$5.89 \cdot 10^{-6}$
2	85738944	rs2044475	T	C	MAT2A	1,613	875	738	696	0.216	0.183	$4.24 \cdot 10^{-2}$	$1.63 \cdot 10^{-5}$
18	34803165	rs3747899	G	A	KIAA1328	1,611	873	738	561	0.174	0.197	$4.59 \cdot 10^{-2}$	$1.83 \cdot 10^{-5}$
14	20930038	rs1760941	A	C	TMEM55B	1,614	875	739	643	0.199	0.188	$4.42 \cdot 10^{-2}$	$2.13 \cdot 10^{-5}$
7	114229139	rs1229758	G	A	FOXP2	1,608	871	737	1,464	0.545	0.148	$3.49 \cdot 10^{-2}$	$2.36 \cdot 10^{-5}$
6	33045558	rs3135021	G	A	HLA-DPB1	1,614	875	739	1,157	0.358	0.152	$3.58 \cdot 10^{-2}$	$2.37 \cdot 10^{-5}$
6	5958615	rs11759185	C	T	NRN1	1,614	875	739	521	0.161	0.202	$4.78 \cdot 10^{-2}$	$2.56 \cdot 10^{-5}$
12	20030738	rs7971571	G	A	AEBP2	1,614	875	739	764	0.237	0.173	$4.12 \cdot 10^{-2}$	$2.66 \cdot 10^{-5}$
1	3411413	rs2821038	C	T	MEGF6	1,594	861	733	190	$5.96 \cdot 10^{-2}$	0.313	$7.47 \cdot 10^{-2}$	$3.01 \cdot 10^{-5}$
8	70449375	rs10957496	C	A	SULF1	1,614	875	739	810	0.251	0.168	$4.05 \cdot 10^{-2}$	$3.44 \cdot 10^{-5}$
7	8595389	rs6963644	G	A	NXP1	1,614	875	739	126	$3.9 \cdot 10^{-2}$	0.373	$9.01 \cdot 10^{-2}$	$3.65 \cdot 10^{-5}$
20	59844577	rs4812289	A	G	CDH4	1,614	875	739	474	0.853	0.204	$4.95 \cdot 10^{-2}$	$3.79 \cdot 10^{-5}$
7	40826041	rs7807596	C	T	SUGCT	1,614	875	739	1,274	0.395	0.15	$3.62 \cdot 10^{-2}$	$3.9 \cdot 10^{-5}$
11	45050849	rs2129677	G	A	PRDM11	1,614	875	739	391	0.121	0.217	$5.38 \cdot 10^{-2}$	$5.91 \cdot 10^{-5}$
9	27864330	rs6476020	C	T	LINGO2	1,614	875	739	434	0.134	0.205	$5.1 \cdot 10^{-2}$	$6.19 \cdot 10^{-5}$
5	171930378	rs7704936	G	A	SH3PXD2B	1,614	875	739	911	0.282	0.151	$3.79 \cdot 10^{-2}$	$6.7 \cdot 10^{-5}$
9	135602727	rs1999121	T	C	AK8	1,614	875	739	567	0.824	0.181	$4.52 \cdot 10^{-2}$	$6.72 \cdot 10^{-5}$
5	117711064	rs7704260	A	G	DTWD2	1,614	875	739	1,438	0.445	0.139	$3.5 \cdot 10^{-2}$	$7.41 \cdot 10^{-5}$
7	111661836	rs2522217	T	G	DOCK4	1,614	875	739	506	0.157	0.194	$4.89 \cdot 10^{-2}$	$7.68 \cdot 10^{-5}$

Table 36: Top variants in the METABO_EUR invn Adjusted Age+Age2+SEX model (**bold** variants indicate previously identified associations)

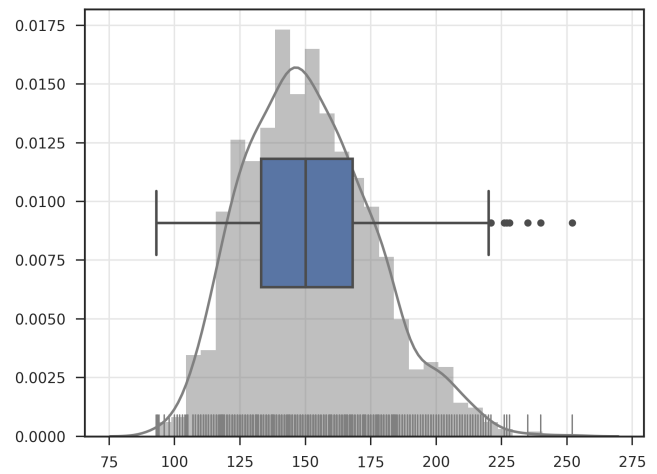
CHR	POS	ID	EA	OA	GENE _{CLOSEST}	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
15	62434977	rs117251325	A	C	C2CD4B	2,137	1,188	949	38	0.991	0.697	0.162	$1.81 \cdot 10^{-5}$
19	42130776	rs929502	A	G	CEACAM4	2,137	1,188	949	1,080	0.253	0.141	$3.44 \cdot 10^{-2}$	$4.27 \cdot 10^{-5}$
10	13255201	rs11258252	C	T	MCM10	2,137	1,188	949	1,179	0.724	0.136	$3.34 \cdot 10^{-2}$	$4.74 \cdot 10^{-5}$
17	11935026	rs17613899	C	T	MAP2K4	2,137	1,188	949	113	0.974	0.385	$9.49 \cdot 10^{-2}$	$5.13 \cdot 10^{-5}$
17	5280440	rs3026101	C	T	RABEP1	2,137	1,188	949	1,845	0.568	0.124	$3.08 \cdot 10^{-2}$	$5.56 \cdot 10^{-5}$
16	89560178	rs4329923	C	T	ANKRD11	2,137	1,188	949	2,108	0.493	0.122	$3.04 \cdot 10^{-2}$	$5.88 \cdot 10^{-5}$
12	72009051	rs17109991	C	T	ZFC3H1	2,137	1,188	949	116	0.973	0.375	$9.32 \cdot 10^{-2}$	$6.04 \cdot 10^{-5}$
4	27209559	rs1488268	G	T	STIM2	2,137	1,188	949	1,216	0.715	0.136	$3.39 \cdot 10^{-2}$	$6.22 \cdot 10^{-5}$
7	15003258	rs59827390	A	G	DGKB	2,137	1,188	949	15	0.996	1.028	0.257	$6.46 \cdot 10^{-5}$
15	79080798	rs3743058	T	C	ADAMTS7	2,135	1,187	948	1,604	0.624	0.125	$3.13 \cdot 10^{-2}$	$7.23 \cdot 10^{-5}$
3	183633574	rs2872250	T	C	ABCC5	2,137	1,188	949	288	0.933	0.236	$6.11 \cdot 10^{-2}$	$1.16 \cdot 10^{-4}$
17	5415623	rs9911319	T	C	NLRP1	2,137	1,188	949	1,794	0.42	0.119	$3.12 \cdot 10^{-2}$	$1.33 \cdot 10^{-4}$
19	17910639	rs36689	G	A	B3GNT3	2,135	1,187	948	1,491	0.349	0.121	$3.19 \cdot 10^{-2}$	$1.47 \cdot 10^{-4}$
19	45245015	rs2965174	G	A	BCL3	2,137	1,188	949	1,976	0.538	0.116	$3.06 \cdot 10^{-2}$	$1.5 \cdot 10^{-4}$
10	57795407	rs12250597	A	G	ZWINT	2,137	1,188	949	820	0.808	0.144	$3.86 \cdot 10^{-2}$	$1.94 \cdot 10^{-4}$
2	222313432	rs16862677	C	T	EPHA4	2,137	1,188	949	255	0.94	0.234	$6.31 \cdot 10^{-2}$	$2.17 \cdot 10^{-4}$
1	85972024	rs10493768	G	A	DDAH1	2,137	1,188	949	1,633	0.382	0.115	$3.12 \cdot 10^{-2}$	$2.31 \cdot 10^{-4}$
16	89602006	rs11640186	G	C	SPG7	2,137	1,188	949	1,979	0.463	0.114	$3.1 \cdot 10^{-2}$	$2.48 \cdot 10^{-4}$
1	96595179	rs1222069	A	C	PTBP2	2,137	1,188	949	1,746	0.591	0.111	$3.03 \cdot 10^{-2}$	$2.53 \cdot 10^{-4}$
13	110990833	rs117505015	A	G	COL4A2	2,137	1,188	949	122	0.971	0.337	$9.19 \cdot 10^{-2}$	$2.55 \cdot 10^{-4}$

8 Systolic Blood Pressure (SBP15)

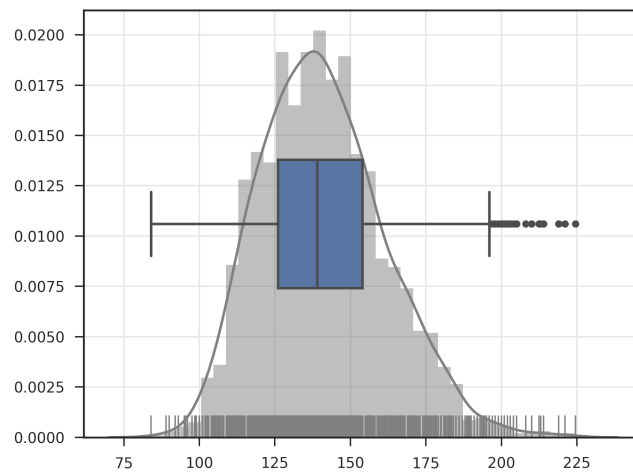
8.1 Summary



(a) EXBROAD_EUR



(b) GWAS_EUR



(c) METABO_EUR

Figure 43: Distribution of SBP15 in cohort-level analyses

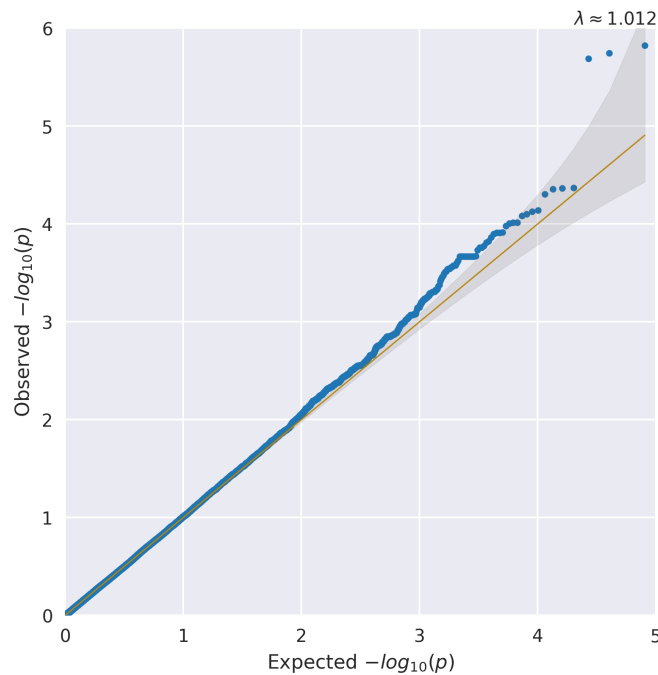
Table 40: Summary of samples removed from Systolic Blood Pressure analysis by cohort and model

Cohort	Array	Ancestry	Trans	Covars	Total	-SampleQc	-missObs	-Kinship	-PcOutlier
EXBROAD_EUR	EXBROAD	EUR	invn	Age+Age2+SEX+BMI	3563	36	74	38	82
GWAS_EUR	GWAS	EUR	invn	Age+Age2+SEX+BMI	1796	19	61	103	0
METABO_EUR	METABO	EUR	invn	Age+Age2+SEX+BMI	2344	43	16	152	9

Table 41: Summary of samples remaining for Systolic Blood Pressure analysis by cohort and model

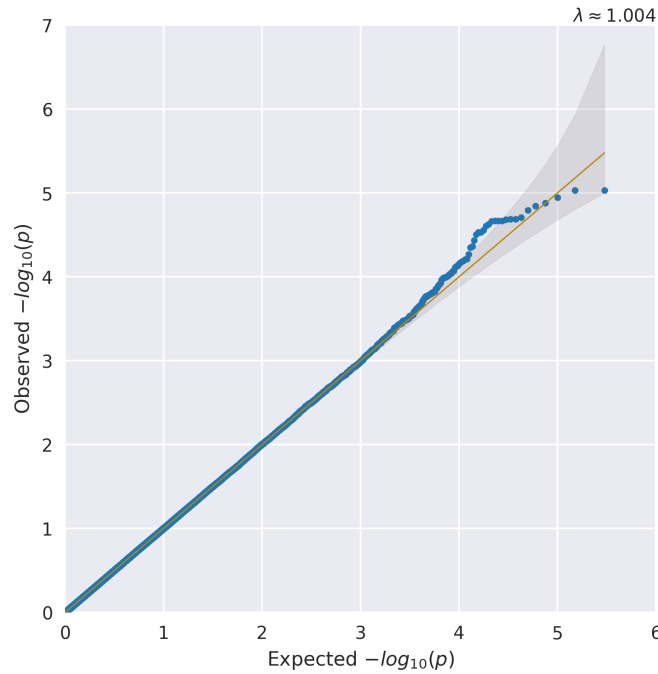
Cohort	Array	Ancestry	Trans	Covars	PCs	N	Male	Female	Max	Min	μ	\bar{x}	σ
EXBROAD_EUR	EXBROAD	EUR	invn	Age+Age2+SEX+BMI	9	3335	1882	1453	252.0	84.0	147.8	145.5	22.807
GWAS_EUR	GWAS	EUR	invn	Age+Age2+SEX+BMI	0	1614	875	739	252.0	93.0	152.702	151.0	24.452
METABO_EUR	METABO	EUR	invn	Age+Age2+SEX+BMI	6	2124	1181	943	224.5	84.0	141.386	140.0	20.478

8.2 Calibration



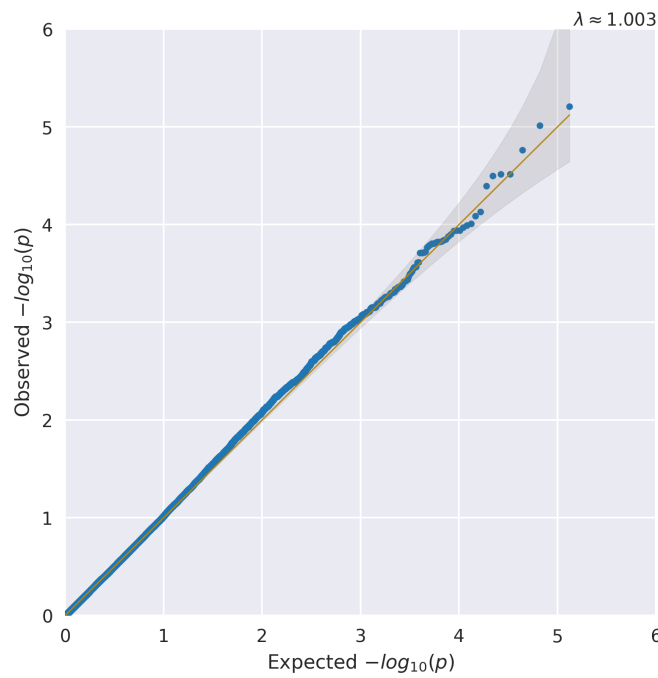
(a) invn Adjusted Age+Age2+SEX+BMI

Figure 44: QQ plots for SBP15 in the EXBROAD_EUR analysis



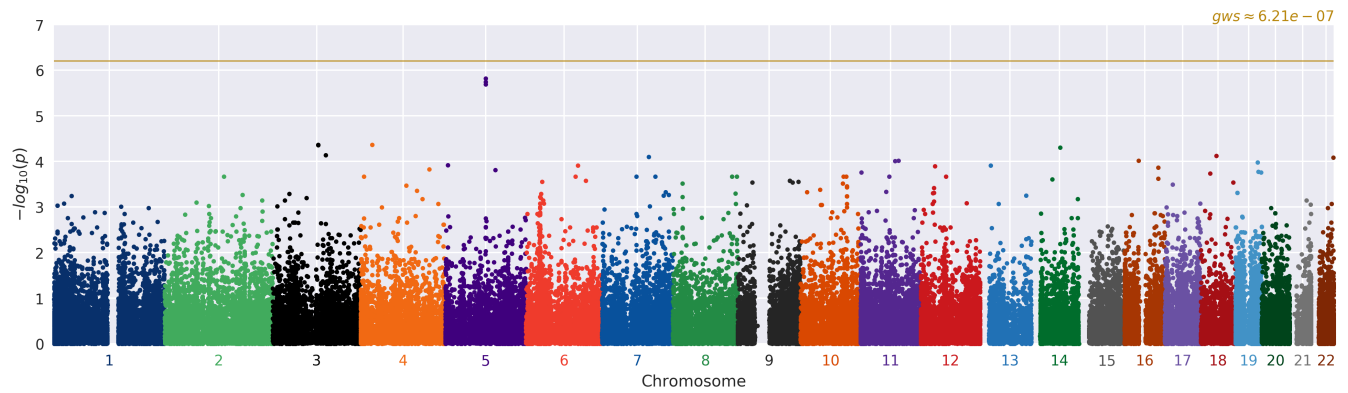
(a) invn Adjusted Age+Age2+SEX+BMI

Figure 45: QQ plots for SBP15 in the GWAS_EUR analysis



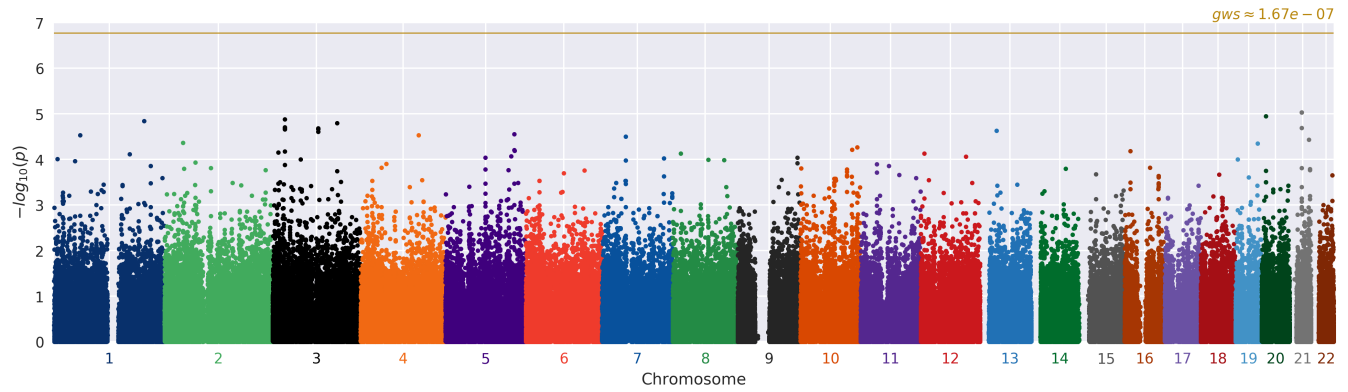
(a) invn Adjusted Age+Age2+SEX+BMI

Figure 46: QQ plots for SBP15 in the METABO_EUR analysis



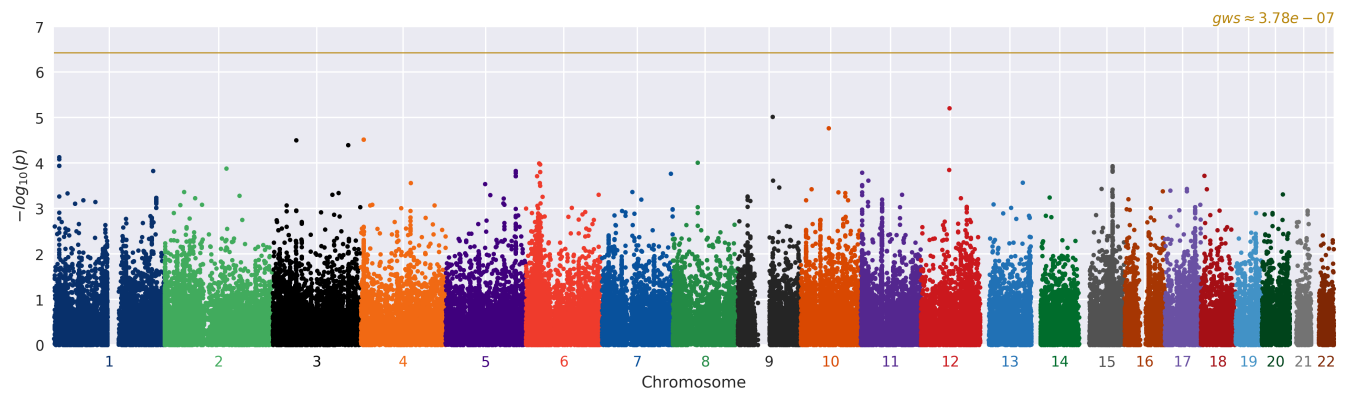
(a) invn Adjusted Age+Age2+SEX+BMI

Figure 47: Manhattan plots for SBP15 in the EXBROAD_EUR analysis



(a) invn Adjusted Age+Age2+SEX+BMI

Figure 48: Manhattan plots for SBP15 in the GWAS_EUR analysis



(a) invn Adjusted Age+Age2+SEX+BMI

Figure 49: Manhattan plots for SBP15 in the METABO_EUR analysis

8.3 Top associations

Table 42: Top variants in the EXBROAD_EUR invn Adjusted Age+Age2+SEX+BMI model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	GENE _{CLOSEST}	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
5	89943571	rs2366777	T	G	ADGRV1	3,335	1,882	1,453	2,247	0.663	0.125	$2.59 \cdot 10^{-2}$	$1.51 \cdot 10^{-6}$
4	25749303	rs7701	C	A	SEL1L3	3,335	1,882	1,453	2,668	0.4	0.101	$2.48 \cdot 10^{-2}$	$4.29 \cdot 10^{-5}$
3	102181131	rs12054046	G	A	ZPLD1	3,335	1,882	1,453	798	0.12	0.151	$3.69 \cdot 10^{-2}$	$4.33 \cdot 10^{-5}$
14	65253667	exm1108600	C	T	SPTB	3,335	1,882	1,453	10	$1.5 \cdot 10^{-3}$	1.283	0.316	$4.95 \cdot 10^{-5}$
3	118945760	rs138372481	C	T	B4GALT4	3,335	1,882	1,453	127	$1.9 \cdot 10^{-2}$	0.354	$8.91 \cdot 10^{-2}$	$7.29 \cdot 10^{-5}$
18	34740290	rs140424487	A	C	KIAA1328	3,335	1,882	1,453	61	$9.15 \cdot 10^{-3}$	0.512	0.129	$7.5 \cdot 10^{-5}$
7	105665004	rs117406926	A	C	CDHR3	3,335	1,882	1,453	31	$4.65 \cdot 10^{-3}$	0.691	0.175	$7.97 \cdot 10^{-5}$
22	50436143	exm1620216	T	C	IL17REL	3,335	1,882	1,453	8	$1.2 \cdot 10^{-3}$	1.389	0.352	$8.27 \cdot 10^{-5}$
11	84822734	rs201189173	C	G	DLG2	3,335	1,882	1,453	4	$6 \cdot 10^{-4}$	1.946	0.498	$9.68 \cdot 10^{-5}$
16	31382513	exm1236418	T	C	ITGAX	3,335	1,882	1,453	6	$9 \cdot 10^{-4}$	1.589	0.407	$9.71 \cdot 10^{-5}$
11	77386177	exm943663	C	T	RSF1	3,335	1,882	1,453	3	$4.5 \cdot 10^{-4}$	2.245	0.576	$9.84 \cdot 10^{-5}$
19	50000009	rs2280401	A	G	RPS11	3,335	1,882	1,453	1,235	0.185	0.123	$3.16 \cdot 10^{-2}$	$1.05 \cdot 10^{-4}$
5	5209219	exm442886	A	C	ADAMTS16	3,335	1,882	1,453	13	$1.95 \cdot 10^{-3}$	1.081	0.281	$1.22 \cdot 10^{-4}$
6	116879222	rs145628712	C	T	FAM26D	3,335	1,882	1,453	6	$9 \cdot 10^{-4}$	1.566	0.407	$1.23 \cdot 10^{-4}$
13	23908464	rs200453385	C	T	SACS	3,335	1,882	1,453	5	$7.5 \cdot 10^{-4}$	1.716	0.447	$1.23 \cdot 10^{-4}$
12	32134638	rs2166807	T	C	KIAA1551	3,335	1,882	1,453	1,294	0.806	0.119	$3.11 \cdot 10^{-2}$	$1.27 \cdot 10^{-4}$
16	75301838	rs148519476	G	C	BCAR1	3,335	1,882	1,453	120	$1.8 \cdot 10^{-2}$	0.351	$9.21 \cdot 10^{-2}$	$1.38 \cdot 10^{-4}$
4	154644537	rs10517577	C	T	RNF175	3,335	1,882	1,453	1,693	0.254	0.106	$2.78 \cdot 10^{-2}$	$1.5 \cdot 10^{-4}$
5	112242968	rs469727	T	C	REEP5	3,335	1,882	1,453	2,282	0.342	$9.71 \cdot 10^{-2}$	$2.56 \cdot 10^{-2}$	$1.54 \cdot 10^{-4}$
19	51535330	rs61910728	A	G	KLK12	3,335	1,882	1,453	3	$4.5 \cdot 10^{-4}$	2.171	0.576	$1.68 \cdot 10^{-4}$

Table 43: Top variants in the GWAS_EUR invn Adjusted Age+Age2+SEX+BMI model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	GENE _{CLOSEST}	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
21	26940815	rs1893650	T	C	MRPL39	1,614	875	739	942	0.708	0.171	$3.85 \cdot 10^{-2}$	$9.34 \cdot 10^{-6}$
20	9349033	rs725941	G	A	PLCB4	1,614	875	739	1,219	0.378	0.159	$3.6 \cdot 10^{-2}$	$1.14 \cdot 10^{-5}$
3	27472936	rs3755652	T	C	SLC4A7	1,614	875	739	575	0.178	0.199	$4.56 \cdot 10^{-2}$	$1.33 \cdot 10^{-5}$
1	203245214	rs2494302	G	A	BTG2	1,614	875	739	202	$6.26 \cdot 10^{-2}$	0.32	$7.36 \cdot 10^{-2}$	$1.43 \cdot 10^{-5}$
3	144949453	rs6800639	C	T	AC107021	1,614	875	739	651	0.798	0.187	$4.32 \cdot 10^{-2}$	$1.61 \cdot 10^{-5}$
3	27361432	rs533175	A	G	NEK10	1,614	875	739	807	0.25	0.167	$3.91 \cdot 10^{-2}$	$1.95 \cdot 10^{-5}$
3	102157417	rs6784389	G	A	ZPLD1	1,614	875	739	386	0.12	0.223	$5.23 \cdot 10^{-2}$	$2.07 \cdot 10^{-5}$
13	37209815	rs2759295	A	C	SERTM1	1,613	874	739	63	0.98	0.542	0.128	$2.36 \cdot 10^{-5}$
5	154856170	rs267015	A	G	SGCD	1,614	875	739	560	0.827	0.195	$4.64 \cdot 10^{-2}$	$2.79 \cdot 10^{-5}$
4	130230383	rs4355401	A	C	C4orf33	1,614	875	739	1,292	0.6	0.145	$3.46 \cdot 10^{-2}$	$2.93 \cdot 10^{-5}$
1	59368947	rs927743	T	G	JUN	1,613	874	739	1,440	0.446	0.148	$3.53 \cdot 10^{-2}$	$2.95 \cdot 10^{-5}$
7	53258694	rs1525575	A	G	POM121L12	1,614	875	739	899	0.279	0.16	$3.83 \cdot 10^{-2}$	$3.13 \cdot 10^{-5}$
21	43291997	rs2276232	A	C	PRDM15	1,594	864	730	1,564	0.491	0.144	$3.48 \cdot 10^{-2}$	$3.67 \cdot 10^{-5}$
2	41540966	rs7602964	G	T	C2orf91	1,613	875	738	763	0.763	0.168	$4.11 \cdot 10^{-2}$	$4.34 \cdot 10^{-5}$
19	50000009	rs2280401	A	G	RPS11	1,614	875	739	585	0.181	0.186	$4.55 \cdot 10^{-2}$	$4.5 \cdot 10^{-5}$
10	127744829	rs1710293	A	C	ADAM12	1,614	875	739	1,182	0.634	0.146	$3.62 \cdot 10^{-2}$	$5.38 \cdot 10^{-5}$
10	116175677	rs4752697	A	G	AFAP1L2	1,614	875	739	1,189	0.368	0.146	$3.63 \cdot 10^{-2}$	$6.12 \cdot 10^{-5}$
16	13174595	rs276604	T	C	SHISA9	1,612	874	738	895	0.722	0.155	$3.88 \cdot 10^{-2}$	$6.58 \cdot 10^{-5}$
3	12402601	rs1373640	G	A	PPARG	1,614	875	739	1,141	0.647	0.146	$3.65 \cdot 10^{-2}$	$7.02 \cdot 10^{-5}$
8	18535156	rs2220352	C	T	PSD3	1,613	875	738	1,133	0.351	0.145	$3.65 \cdot 10^{-2}$	$7.37 \cdot 10^{-5}$

Table 44: Top variants in the METABO_EUR invn Adjusted Age+Age2+SEX+BMI model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	GENE _{CLOSEST}	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
12	64325654	rs11175211	G	A	SRGAP1	2,124	1,181	943	644	0.152	0.189	$4.17 \cdot 10^{-2}$	$6.19 \cdot 10^{-6}$
9	78642228	rs12342299	C	T	PCSK5	2,124	1,181	943	336	$7.91 \cdot 10^{-2}$	0.244	$5.51 \cdot 10^{-2}$	$9.7 \cdot 10^{-6}$
10	63551607	rs117695533	C	T	C10orf107	2,124	1,181	943	5	$1.18 \cdot 10^{-3}$	1.903	0.442	$1.72 \cdot 10^{-5}$
4	6280822	rs73795939	A	G	WFS1	2,124	1,181	943	9	$2.12 \cdot 10^{-3}$	1.377	0.33	$3.06 \cdot 10^{-5}$
3	52465186	rs661777	G	A	SEMA3G	2,124	1,181	943	99	$2.33 \cdot 10^{-2}$	0.421	0.101	$3.17 \cdot 10^{-5}$
3	169528523	rs9831661	G	T	LRRC34	2,124	1,181	943	1,217	0.286	0.14	$3.39 \cdot 10^{-2}$	$4.04 \cdot 10^{-5}$
1	11801023	rs17875920	T	C	AGTRAP	2,122	1,180	942	1,006	0.237	0.141	$3.55 \cdot 10^{-2}$	$7.39 \cdot 10^{-5}$
8	56282834	rs4738099	T	G	XKR4	2,124	1,181	943	1,726	0.406	0.12	$3.08 \cdot 10^{-2}$	$9.8 \cdot 10^{-5}$
6	29735693	rs1737046	G	A	HLA-F	2,121	1,180	941	1,690	0.602	0.118	$3.04 \cdot 10^{-2}$	$1.02 \cdot 10^{-4}$
6	31508069	rs12665501	G	T	DDX39B	2,124	1,181	943	163	$3.84 \cdot 10^{-2}$	0.309	$7.96 \cdot 10^{-2}$	$1.07 \cdot 10^{-4}$
15	75308837	rs4886648	G	A	SCAMP5	2,124	1,181	943	1,441	0.339	0.122	$3.15 \cdot 10^{-2}$	$1.16 \cdot 10^{-4}$
2	138853971	rs16840302	C	T	HNMT	2,124	1,181	943	728	0.171	0.157	$4.09 \cdot 10^{-2}$	$1.31 \cdot 10^{-4}$
12	63921978	rs4763089	A	G	DPY19L2	2,124	1,181	943	1,112	0.262	0.132	$3.47 \cdot 10^{-2}$	$1.41 \cdot 10^{-4}$
15	75330159	rs4886417	T	G	PPCDC	2,124	1,181	943	1,439	0.339	0.12	$3.15 \cdot 10^{-2}$	$1.44 \cdot 10^{-4}$
5	157898103	rs2419911	T	G	EBF1	2,123	1,181	942	916	0.784	0.141	$3.72 \cdot 10^{-2}$	$1.5 \cdot 10^{-4}$
1	223444263	rs17161988	A	G	SUSD4	2,124	1,181	943	1,809	0.426	0.117	$3.07 \cdot 10^{-2}$	$1.5 \cdot 10^{-4}$
6	31629499	rs707974	G	A	GPANK1	2,124	1,181	943	349	$8.22 \cdot 10^{-2}$	0.207	$5.46 \cdot 10^{-2}$	$1.57 \cdot 10^{-4}$
6	31669496	rs1266071	T	C	ABHD16A	2,124	1,181	943	349	$8.22 \cdot 10^{-2}$	0.207	$5.46 \cdot 10^{-2}$	$1.57 \cdot 10^{-4}$
11	2919292	rs10832878	G	A	SLC22A18AS	2,124	1,181	943	498	0.117	0.176	$4.65 \cdot 10^{-2}$	$1.61 \cdot 10^{-4}$
7	154664510	rs2293356	T	C	DPP6	2,124	1,181	943	790	0.186	0.147	$3.91 \cdot 10^{-2}$	$1.72 \cdot 10^{-4}$

8.4 Previously identified risk loci

Table 45 shows statistics from the EXBROAD_EUR cohort for 19 loci that were shown to be significantly associated with Systolic Blood Pressure in the 2011 Nature paper by Ehret et al [14]. Where a previously reported variant was not genotyped in the study (indicated by $\bar{R}^2 < 1$), if available, a tagging variant in LD with the reported variant ($\bar{R}^2 \geq 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. There are 5 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 14 variants in both studies, 8 exhibit the same direction of effect with the known result (binomial test $p = 0.395$).

Table 45: Top known loci in EXBROAD_EUR model invn Adjusted Age+Age2+SEX+BMI (**bold** variants indicate matching direction of effect)

CHR	POS	ID	EA	OA	N	FREQ	EFFECT	STDERR	P	GENE _{CLOSEST}	R ²	ID _{KNOWN}	N _{KNOWN}	EFFECT _{KNOWN}	STDERR _{KNOWN}	P _{KNOWN}
12	90060586	rs17249754	G	A	3,334	$7.87 \cdot 10^{-2}$	$5.31 \cdot 10^{-2}$	$4.57 \cdot 10^{-2}$	0.245	ATP2B1	1	rs17249754	$2 \cdot 10^5$	0.955	0.134	$9.73 \cdot 10^{-13}$
1	11862778	rs17367504	A	G	3,334	0.141	$4.46 \cdot 10^{-2}$	$3.47 \cdot 10^{-2}$	0.199	MTHFR	1	rs17367504	$2 \cdot 10^5$	-0.861	0.136	$2.11 \cdot 10^{-10}$
15	75077367	rs1378942	C	A	3,334	0.548	$3.96 \cdot 10^{-2}$	$2.48 \cdot 10^{-2}$	0.111	CSK	1	rs1378942	$2 \cdot 10^5$	0.632	0.101	$3.43 \cdot 10^{-10}$
10	104846178	rs11191548	T	C	3,334	$7.86 \cdot 10^{-2}$	0.154	$4.57 \cdot 10^{-2}$	$7.87 \cdot 10^{-4}$	CNNM2	1	rs11191548	$2 \cdot 10^5$	1.083	0.174	$5.03 \cdot 10^{-10}$
10	104594507	rs1004467	A	G	3,334	$9.33 \cdot 10^{-2}$	0.152	$4.22 \cdot 10^{-2}$	$3.25 \cdot 10^{-4}$	CYP17A1	1	rs1004467	$2 \cdot 10^5$	-1.01	0.164	$6.61 \cdot 10^{-10}$
10	104906211	rs11191580	T	C	3,334	$7.87 \cdot 10^{-2}$	0.151	$4.57 \cdot 10^{-2}$	$9.32 \cdot 10^{-4}$	NT5C2	1	rs11191580	$2 \cdot 10^5$	1.058	0.173	$9.16 \cdot 10^{-10}$
12	112007756	rs653178	C	T	3,334	0.583	$1.94 \cdot 10^{-2}$	$2.48 \cdot 10^{-2}$	0.435	ATXN2	1	rs653178	$2 \cdot 10^5$	-0.605	$9.88 \cdot 10^{-2}$	$9.3 \cdot 10^{-10}$
10	104660004	rs11191454	A	G	3,334	$7.96 \cdot 10^{-2}$	0.157	$4.53 \cdot 10^{-2}$	$5.39 \cdot 10^{-4}$	BORCS7-ASMT	1	rs11191454	$2 \cdot 10^5$	-1.043	0.171	$1.12 \cdot 10^{-9}$
12	111884608	rs3184504	T	C	3,334	0.59	$1.71 \cdot 10^{-2}$	$2.49 \cdot 10^{-2}$	0.493	SH2B3	1	rs3184504	$2 \cdot 10^5$	0.598	$9.93 \cdot 10^{-2}$	$1.69 \cdot 10^{-9}$
12	112072424	rs11065987	G	A	3,334	0.387	$2.7 \cdot 10^{-2}$	$2.5 \cdot 10^{-2}$	0.28	BRAP	1	rs11065987	$2 \cdot 10^5$	0.57	0.102	$2.12 \cdot 10^{-8}$
11	16917219	rs11024074	C	T	3,334	0.263	$9.51 \cdot 10^{-3}$	$2.82 \cdot 10^{-2}$	0.736	PLEKHA7	1	rs11024074	$2 \cdot 10^5$	-0.591	0.107	$3.13 \cdot 10^{-8}$
12	112486818	rs17696736	G	A	3,334	0.403	$3.84 \cdot 10^{-2}$	$2.47 \cdot 10^{-2}$	0.121	NAA25	1	rs17696736	$2 \cdot 10^5$	0.549	$9.96 \cdot 10^{-2}$	$3.43 \cdot 10^{-8}$
12	112871372	rs11066301	G	A	3,333	0.403	$3.51 \cdot 10^{-2}$	$2.47 \cdot 10^{-2}$	0.155	PTPN11	1	rs11066301	$2 \cdot 10^5$	0.544	$9.98 \cdot 10^{-2}$	$4.94 \cdot 10^{-8}$
10	104652323	rs11191447	C	T	3,334	$7.96 \cdot 10^{-2}$	0.157	$4.53 \cdot 10^{-2}$	$5.39 \cdot 10^{-4}$	AS3MT	1	rs3740390	$2 \cdot 10^5$	-1.005	0.172	$4.61 \cdot 10^{-9}$
1	11862778	rs17367504	A	G	3,334	0.141	$4.46 \cdot 10^{-2}$	$3.47 \cdot 10^{-2}$	0.199	CLCN6	0.976	rs12567136	$2 \cdot 10^5$	0.847	0.135	$3.41 \cdot 10^{-10}$
12	112486818	rs17696736	G	A	3,334	0.403	$3.84 \cdot 10^{-2}$	$2.47 \cdot 10^{-2}$	0.121	TRAFD1	0.922	rs17630235	$2 \cdot 10^5$	0.569	0.1	$1.45 \cdot 10^{-8}$
12	112486818	rs17696736	G	A	3,334	0.403	$3.84 \cdot 10^{-2}$	$2.47 \cdot 10^{-2}$	0.121	HECTD4	0.913	rs11066188	$2 \cdot 10^5$	0.567	0.101	$1.72 \cdot 10^{-8}$
12	90060586	rs17249754	G	A	3,334	$7.87 \cdot 10^{-2}$	$5.31 \cdot 10^{-2}$	$4.57 \cdot 10^{-2}$	0.245	POC1B-GALNT4	0.904	rs11105328	$2 \cdot 10^5$	0.838	0.137	$1.08 \cdot 10^{-9}$
15	75033400	rs2472299	A	G	3,334	0.679	$1.58 \cdot 10^{-2}$	$2.66 \cdot 10^{-2}$	0.553	LMAN1L	0.778	rs7162232	$2 \cdot 10^5$	-0.606	0.109	$2.33 \cdot 10^{-8}$

Table 46 shows statistics from the GWAS_EUR cohort for 17 loci that were shown to be significantly associated with Systolic Blood Pressure in the 2011 Nature paper by Ehret et al [14]. Where a previously reported variant was not genotyped in the study (indicated by $\bar{R}^2 < 1$), if available, a tagging variant in LD with the reported variant ($\bar{R}^2 \geq 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. There are 7 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 11 variants in both studies, 6 exhibit the same direction of effect with the known result (binomial test $p = 0.5$).

Table 46: Top known loci in GWAS_EUR model invn Adjusted Age+Age2+SEX+BMI (**bold** variants indicate matching direction of effect)

CHR	POS	ID	EA	OA	N	FREQ	EFFECT	STDERR	P	GENE _{CLOSEST}	R ²	ID _{KNOWN}	N _{KNOWN}	EFFECT _{KNOWN}	STDERR _{KNOWN}	P _{KNOWN}
12	90008959	rs2681472	A	G	1,614	0.919	0.168	6.44 · 10 ⁻²	9.4 · 10 ⁻³	ATP2B1	1	rs2681472	2 · 10 ⁵	-0.946	0.133	1.32 · 10 ⁻¹²
1	11862778	rs17367504	A	G	1,614	0.856	6.33 · 10 ⁻²	5.03 · 10 ⁻²	0.208	MTHFR	1	rs17367504	2 · 10 ⁵	-0.861	0.136	2.11 · 10 ⁻¹⁰
15	75077367	rs1378942	C	A	1,609	0.452	6.72 · 10 ⁻³	3.59 · 10 ⁻²	0.852	CSK	1	rs1378942	2 · 10 ⁵	0.632	0.101	3.43 · 10 ⁻¹⁰
12	112007756	rs653178	C	T	1,614	0.41	4.58 · 10 ⁻²	3.52 · 10 ⁻²	0.194	ATXN2	1	rs653178	2 · 10 ⁵	-0.605	9.88 · 10 ⁻²	9.3 · 10 ⁻¹⁰
10	104616663	rs4409766	T	C	1,614	0.911	0.236	6.24 · 10 ⁻²	1.66 · 10 ⁻⁴	BORCS7-ASMT	1	rs4409766	2 · 10 ⁵	0.983	0.163	1.57 · 10 ⁻⁹
12	111884608	rs3184504	T	C	1,606	0.4	4.14 · 10 ⁻²	3.54 · 10 ⁻²	0.243	SH2B3	1	rs3184504	2 · 10 ⁵	0.598	9.93 · 10 ⁻²	1.69 · 10 ⁻⁹
10	104719096	rs12413409	G	A	1,614	0.922	0.244	6.59 · 10 ⁻²	2.21 · 10 ⁻⁴	CNNM2	1	rs12413409	2 · 10 ⁵	1.034	0.172	2 · 10 ⁻⁹
4	81164723	rs1458038	T	C	1,613	0.651	5.58 · 10 ⁻²	3.64 · 10 ⁻²	0.125	FGF5	1	rs1458038	2 · 10 ⁵	0.662	0.111	2.12 · 10 ⁻⁹
10	104554529	rs284844	G	A	1,614	0.11	0.195	5.61 · 10 ⁻²	5.15 · 10 ⁻⁴	WBP1L	1	rs284844	2 · 10 ⁵	0.888	0.155	1.02 · 10 ⁻⁸
15	75057203	rs4886406	G	T	1,614	0.296	1.38 · 10 ⁻²	3.94 · 10 ⁻²	0.727	CYP1A2	1	rs4886406	2 · 10 ⁵	-0.599	0.108	3.06 · 10 ⁻⁸
12	112906415	rs11066320	A	G	1,614	0.39	5.5 · 10 ⁻²	3.55 · 10 ⁻²	0.121	PTPN11	1	rs11066320	2 · 10 ⁵	-0.544	9.96 · 10 ⁻²	4.56 · 10 ⁻⁸
10	104616663	rs4409766	T	C	1,614	0.911	0.236	6.24 · 10 ⁻²	1.66 · 10 ⁻⁴	CYP17A1	0.989	rs1004467	2 · 10 ⁵	-1.01	0.164	6.61 · 10 ⁻¹⁰
10	104685299	rs12411886	C	A	1,612	0.922	0.244	6.61 · 10 ⁻²	2.33 · 10 ⁻⁴	NT5C2	0.988	rs17094683	2 · 10 ⁵	-1.067	0.174	8.42 · 10 ⁻¹⁰
1	11862778	rs17367504	A	G	1,614	0.856	6.33 · 10 ⁻²	5.03 · 10 ⁻²	0.208	CLCN6	0.976	rs12567136	2 · 10 ⁵	0.847	0.135	3.41 · 10 ⁻¹⁰
15	75092384	rs2301249	T	C	1,614	0.315	9.65 · 10 ⁻³	3.87 · 10 ⁻²	0.803	LMAN1L	0.966	rs7162232	2 · 10 ⁵	-0.606	0.109	2.33 · 10 ⁻⁸
12	90008959	rs2681472	A	G	1,614	0.919	0.168	6.44 · 10 ⁻²	9.4 · 10 ⁻³	POC1B-GALNT4	0.897	rs11105328	2 · 10 ⁵	-0.838	0.137	1.08 · 10 ⁻⁹
12	112007756	rs653178	C	T	1,614	0.41	4.58 · 10 ⁻²	3.52 · 10 ⁻²	0.194	BRAP	0.811	rs11065987	2 · 10 ⁵	0.57	0.102	2.12 · 10 ⁻⁸

Table 47 shows statistics from the METABO_EUR cohort for 22 loci that were shown to be significantly associated with Systolic Blood Pressure in the 2011 Nature paper by Ehret et al [14]. Where a previously reported variant was not genotyped in the study (indicated by $\bar{R}^2 < 1$), if available, a tagging variant in LD with the reported variant ($\bar{R}^2 \geq 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. There are 3 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 21 variants in both studies, 9 exhibit the same direction of effect with the known result (binomial test $p = 0.808$).

Table 47: Top known loci in METABO_EUR model invn Adjusted Age+Age2+SEX+BMI (**bold** variants indicate matching direction of effect)

CHR	POS	ID	EA	OA	N	FREQ	EFFECT	STDERR	P	GENE _{CLOSEST}	R ²	ID _{KNOWN}	N _{KNOWN}	EFFECT _{KNOWN}	STDERR _{KNOWN}	P _{KNOWN}
12	90008959	rs2681472	G	A	2,124	0.925	2.18 · 10 ⁻³	5.82 · 10 ⁻²	0.97	ATP2B1	1	rs2681472	2 · 10 ⁵	0.946	0.133	1.32 · 10 ⁻¹²
1	11862778	rs17367504	A	G	2,124	0.861	3.27 · 10 ⁻²	4.31 · 10 ⁻²	0.449	MTHFR	1	rs17367504	2 · 10 ⁵	-0.861	0.136	2.11 · 10 ⁻¹⁰
1	11883731	rs12567136	C	T	2,124	0.862	3.1 · 10 ⁻²	4.31 · 10 ⁻²	0.473	CLCN6	1	rs12567136	2 · 10 ⁵	-0.847	0.135	3.41 · 10 ⁻¹⁰
15	75077367	rs1378942	C	A	2,124	0.444	6.03 · 10 ⁻²	3.05 · 10 ⁻²	4.79 · 10 ⁻²	CSK	1	rs1378942	2 · 10 ⁵	0.632	0.101	3.43 · 10 ⁻¹⁰
10	104846178	rs11191548	T	C	2,123	0.923	4.94 · 10 ⁻²	5.68 · 10 ⁻²	0.384	CNNM2	1	rs11191548	2 · 10 ⁵	1.083	0.174	5.03 · 10 ⁻¹⁰
10	104851889	rs12217501	T	C	2,124	0.923	5.26 · 10 ⁻²	5.68 · 10 ⁻²	0.354	NT5C2	1	rs12217501	2 · 10 ⁵	1.077	0.174	5.89 · 10 ⁻¹⁰
10	104594507	rs1004467	A	G	2,124	0.909	6.25 · 10 ⁻²	5.24 · 10 ⁻²	0.233	CYP17A1	1	rs1004467	2 · 10 ⁵	-1.01	0.164	6.61 · 10 ⁻¹⁰
12	112007756	rs653178	C	T	2,124	0.412	3.89 · 10 ⁻²	3.12 · 10 ⁻²	0.214	ATXN2	1	rs653178	2 · 10 ⁵	-0.605	9.88 · 10 ⁻²	9.3 · 10 ⁻¹⁰
10	104614350	rs3824754	C	T	2,124	0.909	6.25 · 10 ⁻²	5.24 · 10 ⁻²	0.233	BORCS7-ASMT	1	rs3824754	2 · 10 ⁵	-0.997	0.163	9.75 · 10 ⁻¹⁰
12	111884608	rs3184504	T	C	2,124	0.406	3.55 · 10 ⁻²	3.12 · 10 ⁻²	0.255	SH2B3	1	rs3184504	2 · 10 ⁵	0.598	9.93 · 10 ⁻²	1.69 · 10 ⁻⁹
4	81164723	rs1458038	T	C	2,120	0.646	7.2 · 10 ⁻²	3.27 · 10 ⁻²	2.81 · 10 ⁻²	FGF5	1	rs1458038	2 · 10 ⁵	0.662	0.111	2.12 · 10 ⁻⁹
11	16902268	rs381815	T	C	2,116	0.747	4.95 · 10 ⁻³	3.61 · 10 ⁻²	0.891	PLEKHA7	1	rs381815	2 · 10 ⁵	0.655	0.11	2.45 · 10 ⁻⁹
10	104638480	rs3740390	C	T	2,124	0.922	5.26 · 10 ⁻²	5.62 · 10 ⁻²	0.35	AS3MT	1	rs3740390	2 · 10 ⁵	-1.005	0.172	4.61 · 10 ⁻⁹
10	104556054	rs176185	C	G	2,122	0.113	7.5 · 10 ⁻²	4.88 · 10 ⁻²	0.124	WBP1L	1	rs176185	2 · 10 ⁵	-0.889	0.155	9.99 · 10 ⁻⁹
12	112591686	rs17630235	A	G	2,124	0.616	3.63 · 10 ⁻²	3.14 · 10 ⁻²	0.248	TRAFD1	1	rs17630235	2 · 10 ⁵	-0.569	0.1	1.45 · 10 ⁻⁸
12	112610714	rs11066188	A	G	2,124	0.616	3.63 · 10 ⁻²	3.14 · 10 ⁻²	0.248	HECTD4	1	rs11066188	2 · 10 ⁵	-0.567	0.101	1.72 · 10 ⁻⁸
15	75107880	rs7176022	A	C	2,123	0.333	6.97 · 10 ⁻²	3.21 · 10 ⁻²	3.02 · 10 ⁻²	LMAN1L	1	rs7176022	2 · 10 ⁵	-0.602	0.107	2.11 · 10 ⁻⁸
12	112072424	rs11065987	G	A	2,124	0.615	3.24 · 10 ⁻²	3.14 · 10 ⁻²	0.302	BRAP	1	rs11065987	2 · 10 ⁵	0.57	0.102	2.12 · 10 ⁻⁸
12	112486818	rs17696736	G	A	2,124	0.596	4.33 · 10 ⁻²	3.13 · 10 ⁻²	0.167	NAA25	1	rs17696736	2 · 10 ⁵	0.549	9.96 · 10 ⁻²	3.43 · 10 ⁻⁸
12	112906415	rs11066320	A	G	2,124	0.403	4.4 · 10 ⁻²	3.13 · 10 ⁻²	0.16	PTPN11	1	rs11066320	2 · 10 ⁵	-0.544	9.96 · 10 ⁻²	4.56 · 10 ⁻⁸
11	100593538	rs633185	C	G	2,122	0.288	2.88 · 10 ⁻³	3.32 · 10 ⁻²	0.931	ARHGAP42	1	rs633185	2 · 10 ⁵	-0.584	0.107	5.23 · 10 ⁻⁸
12	90026523	rs11105354	G	A	2,124	0.924	3.21 · 10 ⁻³	5.8 · 10 ⁻²	0.956	POC1B-GALNT4	0.904	rs11105328	2 · 10 ⁵	0.838	0.137	1.08 · 10 ⁻⁹

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