AMP-DCC Data Analysis Report

METSIM

Phase 1

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This document was generated using Loamstream [18] and the AMP-DCC Data Analysis Pipeline [19]

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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; EX, and OMNI. 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
EX	metsim_exomechip_portal	bfile	N/A
OMNI	metsim_omniexpress_portal	bfile	N/A

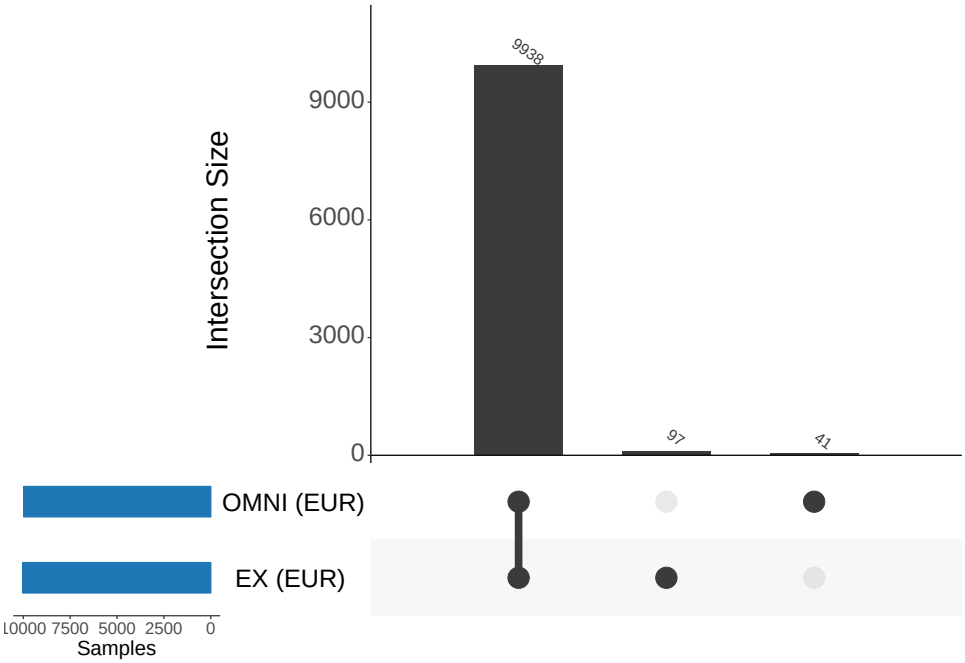


Figure 1: Samples remaining for analysis after quality control

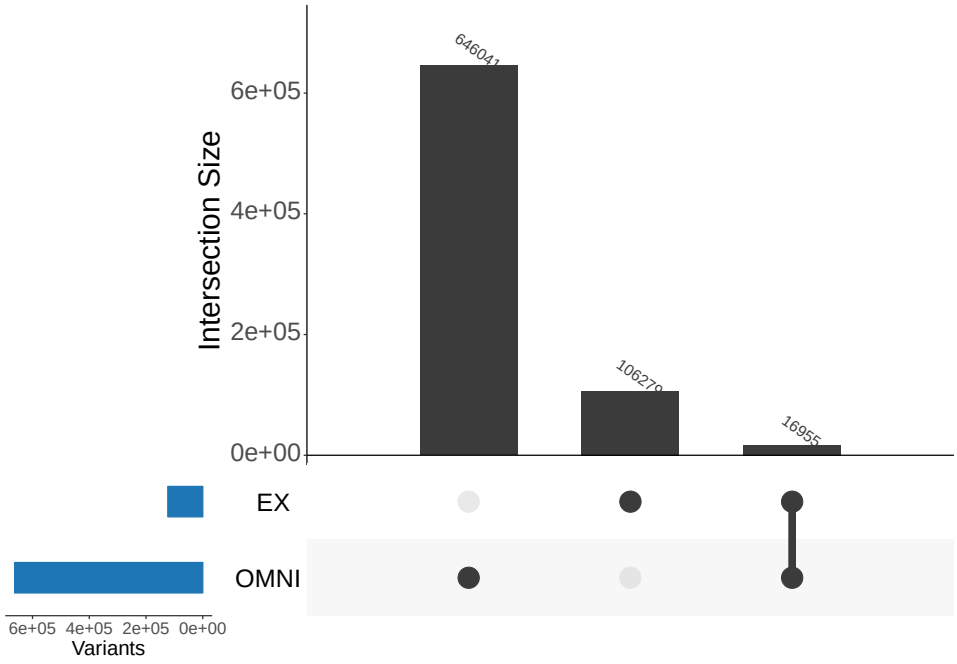


Figure 2: Variants remaining for analysis after quality control

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
EX_EUR	EX	EUR	NO
OMNI_EUR	OMNI	EUR	NO

2.1.2 Merged results

In order to present results in a comprehensive way, we identified a single reference set of results as the default and merged in results from other arrays where either the variant failed to provide a p-value or did not exist in the reference set. Table 3 describes the merges performed. The '>' symbol in the 'Cohorts/Metas' column implies the strategy used to combine the results. The left-most results set was kept as reference, while variants from the following set were merged in where applicable. This merge was repeated (ie. additively) for all sets listed from left to right.

Table 3: Merged results

ID	Cohorts/Metas	Report
MERGE	EX_EUR>OMNI_EUR	YES

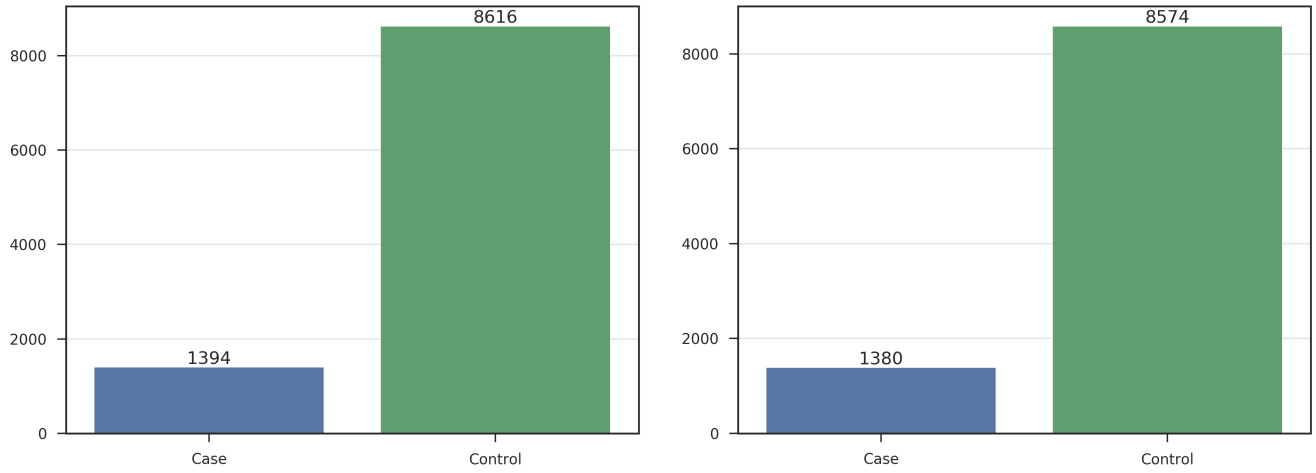
2.2 Ancestry Adjustment and Outlier Removal

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 Nth PC exhibited a statistically significant p-value ($p <= 0.05$), 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 Type 2 Diabetes (T2D_UNKNOWN)

3.1 Summary



(a) EX_EUR

(b) OMNI_EUR

Figure 3: Distribution of T2D_UNKNOWN in cohort-level analyses

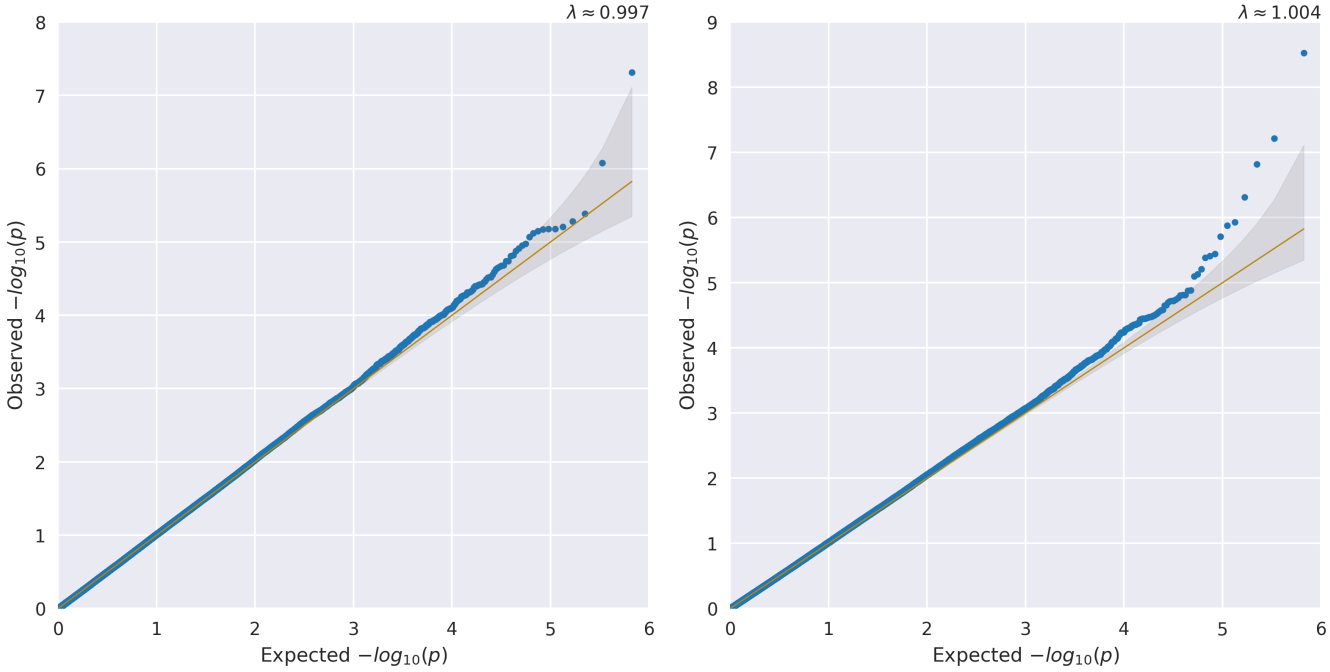
Table 4: Summary of samples removed from Type 2 Diabetes analysis by cohort and model

Cohort	Array	Ancestry	Trans	Covars	Total	-SampleQc	-missObs	-Kinship	-PcOutlier
EX_EUR	EX	EUR	-	Age+BMI	10071	36	29	1516	1
			-	Age	10071	36	25	1516	1
OMNI_EUR	OMNI	EUR	-	Age+BMI	10048	69	29	1492	1
			-	Age	10048	69	25	1494	1

Table 5: Summary of samples remaining for Type 2 Diabetes analysis by cohort and model

Cohort	Array	Ancestry	Trans	Covars	PCs	N	Male	Female	Case	Ctrl
EX_EUR	EX	EUR	-	Age+BMI	0	8489	8489	0	1193	7296
			-	Age	0	8493	8493	0	1195	7298
OMNI_EUR	OMNI	EUR	-	Age+BMI	10	8457	8457	0	1180	7277
			-	Age	10	8459	8459	0	1182	7277

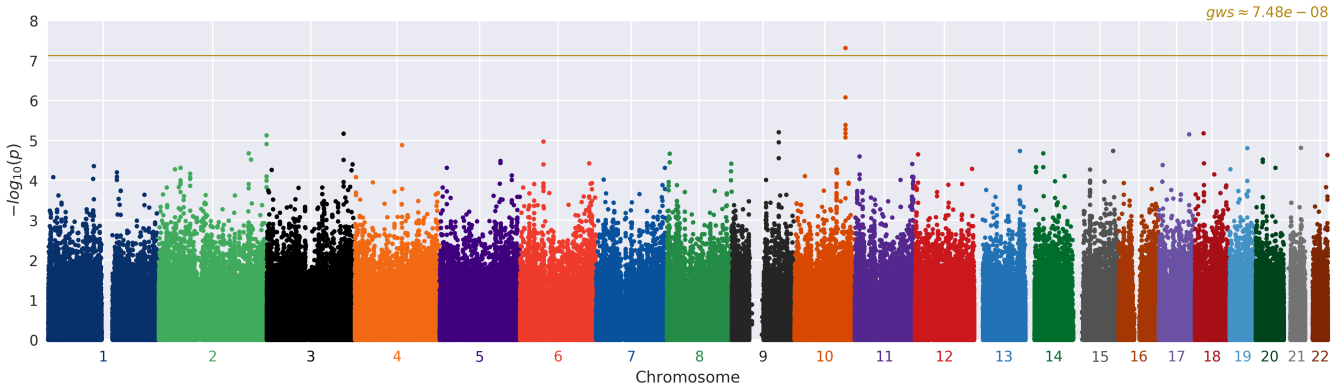
3.2 Calibration



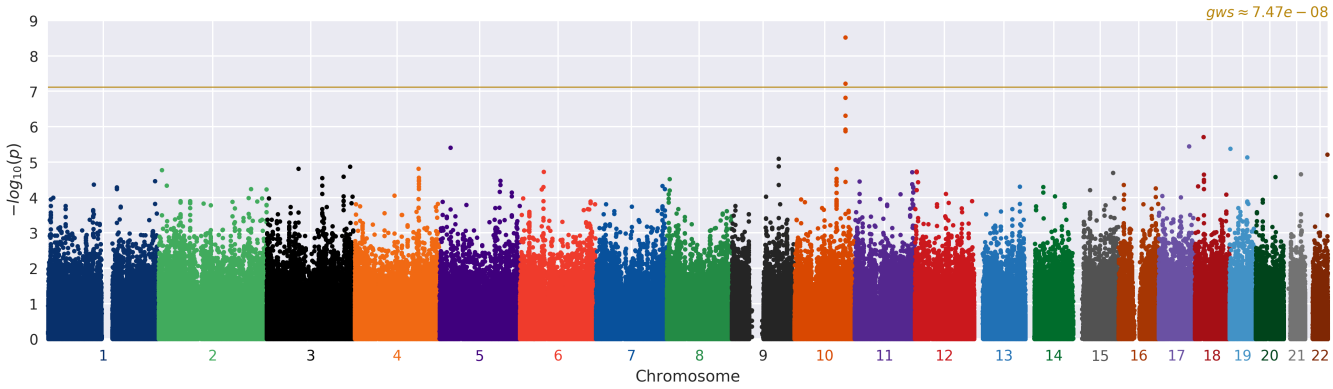
(a) Adjusted Age

(b) Adjusted Age+BMI

Figure 4: QQ plots for T2D_UNKNOWN in the MERGE analysis



(a) Adjusted Age



(b) Adjusted Age+BMI

Figure 5: Manhattan plots for T2D_UNKNOWN in the MERGE analysis

3.3 Top associations

Table 6: Top variants in the MERGE Adjusted Age model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	$\text{GENE}_{\text{CLOSEST}}$	COHORT	N	MALE	FEMALE	CASE	CTRL	MAC	FREQ	EFFECT	OR	P
10	114808902	**rs12255372**	T	G	**TCF7L2**	OMNI_EUR	8,456	8,456	0	1,182	7,274	2,612	0.154	0.325	1.384	$4.86 \cdot 10^{-8}$
9	105474758	rs1576949	A	G	CYLC2	OMNI_EUR	8,456	8,456	0	1,181	7,275	5,601	0.669	0.214	1.239	$6.24 \cdot 10^{-6}$
18	20010336	rs16967156	T	G	CTAGE1	OMNI_EUR	8,458	8,458	0	1,182	7,276	5,037	0.298	0.221	1.247	$6.62 \cdot 10^{-6}$
3	172845803	rs11929145	G	A	SPATA16	OMNI_EUR	8,456	8,456	0	1,182	7,274	3,094	0.183	0.253	1.288	$6.76 \cdot 10^{-6}$
17	68102331	rs9890060	T	C	KCNJ16	OMNI_EUR	8,457	8,457	0	1,182	7,275	6,975	0.588	0.209	1.232	$7.04 \cdot 10^{-6}$
2	242039198	rs3796093	C	T	MTERF4	EX_EUR	8,493	8,493	0	1,195	7,298	631	$3.71 \cdot 10^{-2}$	0.481	1.618	$7.54 \cdot 10^{-6}$
6	52268890	rs17591381	G	A	PAQR8	OMNI_EUR	8,459	8,459	0	1,182	7,277	3,257	0.193	0.261	1.298	$1.06 \cdot 10^{-5}$
2	242065498	rs740393	G	A	PASK	EX_EUR	8,492	8,492	0	1,195	7,297	750	$4.42 \cdot 10^{-2}$	0.436	1.546	$1.22 \cdot 10^{-5}$
4	106108902	rs17508261	C	T	TET2	OMNI_EUR	8,449	8,449	0	1,182	7,267	3,182	0.188	0.246	1.279	$1.32 \cdot 10^{-5}$
21	38499784	rs2835616	A	C	TTC3	OMNI_EUR	8,458	8,458	0	1,182	7,276	3,416	0.202	0.235	1.265	$1.52 \cdot 10^{-5}$
19	39835169	rs1368442	T	G	SAMD4B	OMNI_EUR	8,456	8,456	0	1,181	7,275	6,854	0.595	0.202	1.224	$1.55 \cdot 10^{-5}$
15	89565622	rs733952	A	C	ABHD2	OMNI_EUR	8,451	8,451	0	1,180	7,271	1,008	$5.96 \cdot 10^{-2}$	0.386	1.471	$1.82 \cdot 10^{-5}$
13	102493676	rs4772418	G	A	FGF14	OMNI_EUR	8,458	8,458	0	1,182	7,276	4,045	0.239	0.232	1.262	$1.83 \cdot 10^{-5}$
14	40032181	rs17109387	C	T	FBXO33	OMNI_EUR	8,431	8,431	0	1,178	7,253	1,570	$9.31 \cdot 10^{-2}$	0.317	1.374	$2.09 \cdot 10^{-5}$
2	202025621	rs1594	G	A	CFLAR	OMNI_EUR	8,458	8,458	0	1,182	7,276	8,299	0.491	0.192	1.212	$2.1 \cdot 10^{-5}$
8	6743108	rs7826831	C	T	DEFB1	OMNI_EUR	8,440	8,440	0	1,179	7,261	4,924	0.292	0.208	1.231	$2.16 \cdot 10^{-5}$
12	7617083	ss1388041837	C	T	CD163	OMNI_EUR	8,458	8,458	0	1,182	7,276	3,491	0.206	0.244	1.276	$2.24 \cdot 10^{-5}$
22	50347045	rs28523622	A	G	PIM3	OMNI_EUR	8,455	8,455	0	1,182	7,273	2,879	0.17	0.246	1.279	$2.35 \cdot 10^{-5}$
11	11037708	rs4910217	A	G	ZBED5	OMNI_EUR	8,455	8,455	0	1,182	7,273	7,426	0.439	0.192	1.212	$2.54 \cdot 10^{-5}$
2	207835223	rs13385857	G	A	CPO	OMNI_EUR	8,456	8,456	0	1,182	7,274	913	$5.4 \cdot 10^{-2}$	0.467	1.595	$3.02 \cdot 10^{-5}$

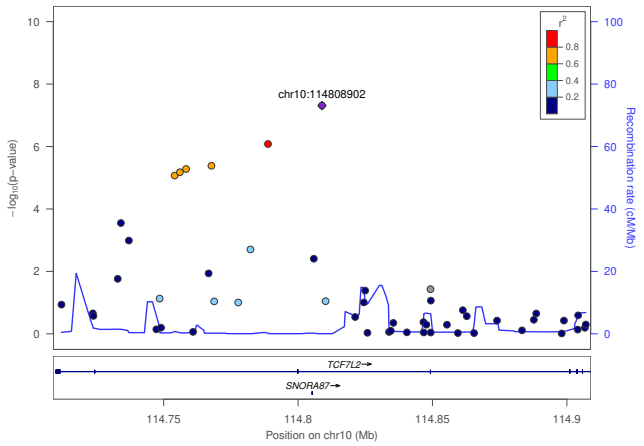


Figure 6: Regional plot for cohort MERGE model Adjusted Age: rs12255372 $\pm 100kb$

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

CHR	POS	ID	EA	OA	$GENE_{CLOSEST}$	COHORT	N	MALE	FEMALE	CASE	CTRL	MAC	FREQ	EFFECT	OR	P
10	114808902	**rs12255372**	T	G	**TCF7L2**	OMNI_EUR	8,454	8,454	0	1,180	7,274	2,613	0.155	0.37	1.448	$2.96 \cdot 10^{-9}$
18	20010336	rs16967156	T	G	CTAGE1	OMNI_EUR	8,456	8,456	0	1,180	7,276	5,036	0.298	0.245	1.278	$1.95 \cdot 10^{-6}$
17	68102331	rs9890060	T	C	KCNJ16	OMNI_EUR	8,455	8,455	0	1,180	7,275	6,977	0.587	0.226	1.254	$3.61 \cdot 10^{-6}$
5	24541782	rs10473690	T	C	CDH10	OMNI_EUR	8,449	8,449	0	1,177	7,272	629	0.963	0.643	1.902	$3.87 \cdot 10^{-6}$
19	2160529	rs3803915	A	C	DOT1L	EX_EUR	8,489	8,489	0	1,193	7,296	2,262	0.133	0.308	1.361	$4.15 \cdot 10^{-6}$
22	50347045	rs28523622	A	G	PIM3	OMNI_EUR	8,453	8,453	0	1,180	7,273	2,878	0.17	0.275	1.316	$6.15 \cdot 10^{-6}$
19	39835169	rs1368442	T	G	SAMD4B	OMNI_EUR	8,454	8,454	0	1,179	7,275	6,852	0.595	0.218	1.244	$7.4 \cdot 10^{-6}$
9	105474758	rs1576949	A	G	CYLC2	OMNI_EUR	8,454	8,454	0	1,179	7,275	5,601	0.669	0.222	1.248	$8.02 \cdot 10^{-6}$
3	187050471	rs4011965	C	T	RTP4	OMNI_EUR	8,450	8,450	0	1,178	7,272	2,863	0.169	0.283	1.327	$1.33 \cdot 10^{-5}$
4	143655174	rs986081	G	A	INPP4B	OMNI_EUR	8,454	8,454	0	1,179	7,275	727	$4.3 \cdot 10^{-2}$	0.542	1.72	$1.53 \cdot 10^{-5}$
3	71324328	rs1541903	T	C	FOXP1	OMNI_EUR	8,456	8,456	0	1,180	7,276	1,352	$7.99 \cdot 10^{-2}$	0.359	1.431	$1.54 \cdot 10^{-5}$
10	94499577	rs2488071	G	A	**HHEX**	OMNI_EUR	8,457	8,457	0	1,180	7,277	7,712	0.544	0.205	1.228	$1.57 \cdot 10^{-5}$
2	7329760	rs6706981	G	T	RNF144A	OMNI_EUR	8,456	8,456	0	1,180	7,276	7,634	0.549	0.202	1.224	$1.7 \cdot 10^{-5}$
12	4334295	rs7309743	A	G	CCND2	OMNI_EUR	8,455	8,455	0	1,180	7,275	3,860	0.228	0.248	1.281	$1.82 \cdot 10^{-5}$
6	53515130	rs6941645	G	A	KLHL31	OMNI_EUR	8,438	8,438	0	1,178	7,260	1,061	0.937	0.397	1.487	$1.89 \cdot 10^{-5}$
11	129534425	rs11221786	A	G	TMEM45B	OMNI_EUR	8,456	8,456	0	1,179	7,277	2,471	0.146	0.298	1.348	$1.91 \cdot 10^{-5}$
15	89565622	rs733952	A	C	ABHD2	OMNI_EUR	8,449	8,449	0	1,178	7,271	1,008	$5.97 \cdot 10^{-2}$	0.403	1.496	$2.01 \cdot 10^{-5}$
21	38499784	rs2835616	A	C	TTC3	OMNI_EUR	8,456	8,456	0	1,180	7,276	3,415	0.202	0.241	1.272	$2.2 \cdot 10^{-5}$
3	172845803	rs11929145	G	A	SPATA16	OMNI_EUR	8,454	8,454	0	1,180	7,274	3,093	0.183	0.247	1.28	$2.59 \cdot 10^{-5}$
20	43933188	exm1544394	A	G	MATN4	EX_EUR	8,489	8,489	0	1,193	7,296	14	$8.25 \cdot 10^{-4}$	2.43	11.357	$2.62 \cdot 10^{-5}$

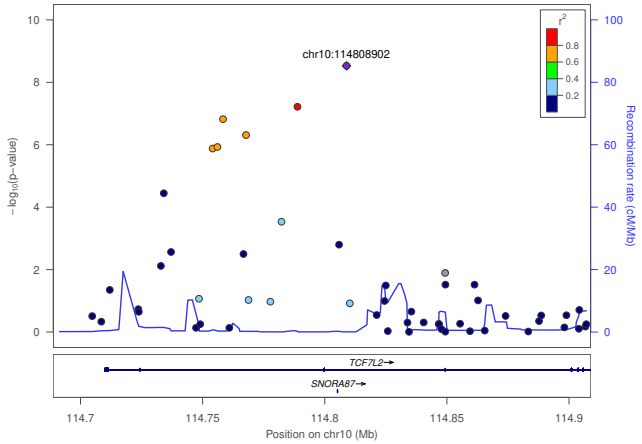


Figure 7: Regional plot for cohort MERGE model Adjusted Age+BMI: rs12255372 $\pm 100kb$

3.4 Previously identified risk loci

Table 8 shows statistics from the MERGE cohort for 48 loci that were shown to be significantly associated with Type 2 Diabetes in the 2012 Nature Genetics paper by Morris et al [7]. 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 ($\bar{R}^2 >= 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. There are 16 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 45 variants in both studies, 40 exhibit the same direction of effect with the known result (binomial test $p = 3.94e - 08$).

Table 8: Top known loci in MERGE model Adjusted Age (**bold** variants indicate matching direction of effect)

CHR	POS	ID	EA	OA	N	CASE	CTRL	FREQ	OR	P	COHORT	$GENE_{CLOSEST}$	R^2	ID_{KNOWN}	N_{KNOWN}	$CASE_{KNOWN}$	$CTRL_{KNOWN}$	OR_{KNOWN}	P_{KNOWN}
10	114758349	**rs7903146**	T	C	8,495	1,191	7,304	0.818	1.288	$5.69 \cdot 10^{-6}$	EX_EUR	TCF7L2	1	rs7903146	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.389	$1.2 \cdot 10^{-139}$
6	20679709	**rs7756992**	G	A	8,495	1,191	7,304	0.652	1.155	$2.18 \cdot 10^{-3}$	EX_EUR	CDKAL1	1	rs7756992	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.167	$6.95 \cdot 10^{-35}$
9	22132076	**rs2383208**	A	G	8,495	1,191	7,304	0.849	1.119	$8.11 \cdot 10^{-2}$	EX_EUR	CDKN2B	1	rs2383208	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.178	$6.73 \cdot 10^{-26}$
3	185511687	**rs4402960**	T	G	8,495	1,191	7,304	0.678	1.122	$1.46 \cdot 10^{-2}$	EX_EUR	IGF2BP2	1	rs4402960	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.131	$2.39 \cdot 10^{-23}$
16	53819169	**rs9936385**	C	T	8,457	1,182	7,275	0.597	1.038	0.425	OMNI_EUR	FTO	1	rs9936385	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.129	$2.61 \cdot 10^{-23}$
8	118185025	**rs3802177**	G	A	8,494	1,191	7,303	0.607	1.099	$4.08 \cdot 10^{-2}$	EX_EUR	SLC30A8	1	rs3802177	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.136	$1.26 \cdot 10^{-21}$
10	94466495	**rs10882102**	G	C	8,438	1,181	7,257	0.535	1.169	$5.56 \cdot 10^{-4}$	OMNI_EUR	HHEX	1	rs10882102	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.117	$6.46 \cdot 10^{-19}$
7	28180556	**rs864745**	T	C	8,493	1,190	7,303	0.519	1.065	0.16	EX_EUR	JAZF1	1	rs864745	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.099	$2.28 \cdot 10^{-16}$
4	6289986	**rs4458523**	G	T	8,459	1,182	7,277	0.442	1.101	$3.45 \cdot 10^{-2}$	OMNI_EUR	WFS1	1	rs4458523	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.098	$2.02 \cdot 10^{-15}$
10	94209939	**rs6583813**	C	T	8,456	1,181	7,275	0.616	1.16	$1.51 \cdot 10^{-3}$	OMNI_EUR	IDE	1	rs6583813	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.098	$6.45 \cdot 10^{-14}$
3	123065778	**rs11708067**	A	G	8,492	1,191	7,301	0.842	1.204	$2.98 \cdot 10^{-3}$	EX_EUR	ADCY5	1	rs11708067	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.113	$7.19 \cdot 10^{-14}$
10	94354204	**rs3824735**	T	G	8,451	1,181	7,270	0.613	1.184	$2.9 \cdot 10^{-4}$	OMNI_EUR	KIF11	1	rs3824735	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.097	$7.43 \cdot 10^{-13}$
2	227100698	**rs2972146**	T	G	8,495	1,191	7,304	0.376	1.061	0.205	EX_EUR	IRS1	1	rs2972146	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.092	$8.97 \cdot 10^{-13}$
3	12393125	**rs1801282**	C	G	8,449	1,180	7,269	0.849	1.092	0.168	OMNI_EUR	PPARG	1	rs1801282	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.13	$1.05 \cdot 10^{-12}$
11	2847069	**rs163184**	G	T	8,451	1,182	7,269	0.372	1.022	0.636	OMNI_EUR	KCNQ1	1	rs163184	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.086	$1.18 \cdot 10^{-11}$
11	92673828	**rs1387153**	T	C	8,495	1,191	7,304	0.635	1.021	0.656	EX_EUR	MTNR1B	1	rs1387153	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.093	$1.59 \cdot 10^{-11}$
4	6315954	**rs10804976**	T	G	8,451	1,180	7,271	0.508	1.085	$7.17 \cdot 10^{-2}$	OMNI_EUR	PPP2R2C	1	rs10804976	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.085	$3.77 \cdot 10^{-11}$
2	43566146	**rs4372955**	A	G	8,447	1,181	7,266	0.938	1.047	0.631	OMNI_EUR	THADA	1	rs4372955	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.135	$5.26 \cdot 10^{-11}$
7	14898282	**rs17168486**	T	C	8,459	1,182	7,277	0.803	1.122	$4.07 \cdot 10^{-2}$	OMNI_EUR	DGKB	1	rs17168486	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.105	$5.94 \cdot 10^{-11}$
3	64705365	**rs6795735**	C	T	8,495	1,191	7,304	0.64	1.071	0.147	EX_EUR	ADAMTS9	1	rs6795735	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.08	$7.39 \cdot 10^{-11}$
10	80942631	**rs12571751**	A	G	8,495	1,191	7,304	0.524	1.09	$5.55 \cdot 10^{-2}$	EX_EUR	ZMIZ1	1	rs12571751	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.078	$1.02 \cdot 10^{-10}$
5	76425867	rs7708285	A	G	8,443	1,179	7,264	0.213	1.043	0.448	OMNI_EUR	ZBED3	1	rs7708285	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	0.913	$1.45 \cdot 10^{-10}$
11	72433098	**rs1552224**	A	C	8,494	1,191	7,303	0.752	1.161	$5.26 \cdot 10^{-3}$	EX_EUR	ARAP1	1	rs1552224	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.107	$1.79 \cdot 10^{-10}$
17	36099840	**rs11651755**	C	T	8,459	1,182	7,277	0.37	1.138	$5.07 \cdot 10^{-3}$	OMNI_EUR	HNF1B	1	rs11651755	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.098	$1.84 \cdot 10^{-10}$
8	41519248	**rs516946**	C	T	8,495	1,191	7,304	0.196	1.132	$2.92 \cdot 10^{-2}$	EX_EUR	ANK1	1	rs516946	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.091	$2.49 \cdot 10^{-10}$
2	227020653	**rs7578326**	A	G	8,494	1,191	7,303	0.647	1.04	0.401	EX_EUR	NYAP2	1	rs7578326	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.083	$3.81 \cdot 10^{-10}$
12	27965150	**rs10842994**	C	T	8,495	1,191	7,304	0.828	1.12	$5.97 \cdot 10^{-2}$	EX_EUR	KLHL42	1	rs10842994	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.096	$6.08 \cdot 10^{-10}$
11	17408630	rs5215	T	C	8,494	1,191	7,303	0.467	1.08	$8.7 \cdot 10^{-2}$	EX_EUR	KCNJ11	1	rs5215	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	0.93	$8.5 \cdot 10^{-10}$
12	66212318	**rs2261181**	T	C	8,458	1,182	7,276	0.932	1.032	0.724	OMNI_EUR	HMGA2	1	rs2261181	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.126	$1.16 \cdot 10^{-9}$
3	23454790	**rs1496653**	A	G	8,459	1,182	7,277	0.653	1.038	0.431	OMNI_EUR	UBE2E2	1	rs1496653	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.085	$3.56 \cdot 10^{-9}$
15	77832762	**rs7177055**	A	G	8,495	1,191	7,304	0.339	1.064	0.196	EX_EUR	HMG20A	1	rs7177055	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.077	$4.6 \cdot 10^{-9}$
11	17418477	rs757110	A	C	8,494	1,191	7,303	0.465	1.09	$5.62 \cdot 10^{-2}$	EX_EUR	ABCC8	1	rs757110	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	0.931	$5 \cdot 10^{-9}$
9	84308948	**rs2796441**	G	A	8,495	1,191	7,304	0.579	1.019	0.68	EX_EUR	TLE1	1	rs2796441	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.074	$5.39 \cdot 10^{-9}$
5	55806751	**rs459193**	G	A	8,495	1,191	7,304	0.336	1.072	0.147	EX_EUR	AC022431.2	1	rs459193	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.081	$5.99 \cdot 10^{-9}$
15	91544076	**rs12899811**	G	A	8,456	1,182	7,274	0.651	1.073	0.132	OMNI_EUR	VPS33B	1	rs12899811	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.076	$6.34 \cdot 10^{-9}$
19	19407718	**rs10401969**	C	T	8,495	1,191	7,304	0.943	1.076	0.447	EX_EUR	SUGP1	1	rs10401969	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.135	$7.04 \cdot 10^{-9}$
2	165528876	**rs13389219**	C	T	8,495	1,191	7,304	0.685	1.134	$9.84 \cdot 10^{-3}$	EX_EUR	COBLL1	1	rs13389219	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.073	$1 \cdot 10^{-8}$
19	19658472	**rs16996148**	T	G	8,495	1,191	7,304	0.941	1.081	0.403	EX_EUR	CILP2	1	rs16996148	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.124	$1.12 \cdot 10^{-8}$
18	57884750	rs12970134	G	A	8,495	1,191	7,304	0.825	1.005	0.927	EX_EUR	MC4R	1	rs12970134	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	0.927	$1.19 \cdot 10^{-8}$
13	80717156	**rs1359790**	G	A	8,495	1,191	7,304	0.711	1.058	0.259	EX_EUR	SPRY2	1	rs1359790	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.077	$1.39 \cdot 10^{-8}$
11	72669777	**rs11605166**	T	C	8,456	1,182	7,274	0.696	1.119	$2.34 \cdot 10^{-2}$	OMNI_EUR	FCHSD2	1	rs11605166	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.089	$1.86 \cdot 10^{-8}$
2	60573870	**rs243083**	G	A	8,458	1,182	7,276	0.552	1.034	0.458	OMNI_EUR	BCL11A	1	rs243083	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.069	$2.17 \cdot 10^{-8}$
16	75247245	**rs7202877**	T	G	8,494	1,191	7,303	0.861	1.082	0.232	EX_EUR	CTRB1	1	rs7202877	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.117	$3.5 \cdot 10^{-8}$
4	153520475	rs6813195	T	C	8,495	1,191	7,304	0.658	1.055	0.262	EX_EUR	TMEM154	1	rs6813195	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	0.932	$5.26 \cdot 10^{-8}$
2	43841269	**rs7576643**	C	T	8,457	1,181	7,276	0.927	1.092	0.318	OMNI_EUR	PLEKHH2	1	rs17031133	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.106	$2.69 \cdot 10^{-8}$
12	71405206	rs1877527	T	C	8,441	1,179	7,262	0.354	1.016	0.743	OMNI_EUR	CTD-2021H9.3	0.934	rs7955901	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	0.933	$6.51 \cdot 10^{-9}$
19	19379549	**rs58542926**	T	C	8,494	1,191	7,303	0.943	1.064	0.518	EX_EUR	HAPLN4	0.879	rs72999033	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.172	$2.6 \cdot 10^{-8}$
11	72669777	**rs11605166**	T	C	8,456	1,182	7,274	0.696	1.119	$2.34 \cdot 10^{-2}$	OMNI_EUR	STARD10	0.851	rs613937	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.099	$8.64 \cdot 10^{-10}$

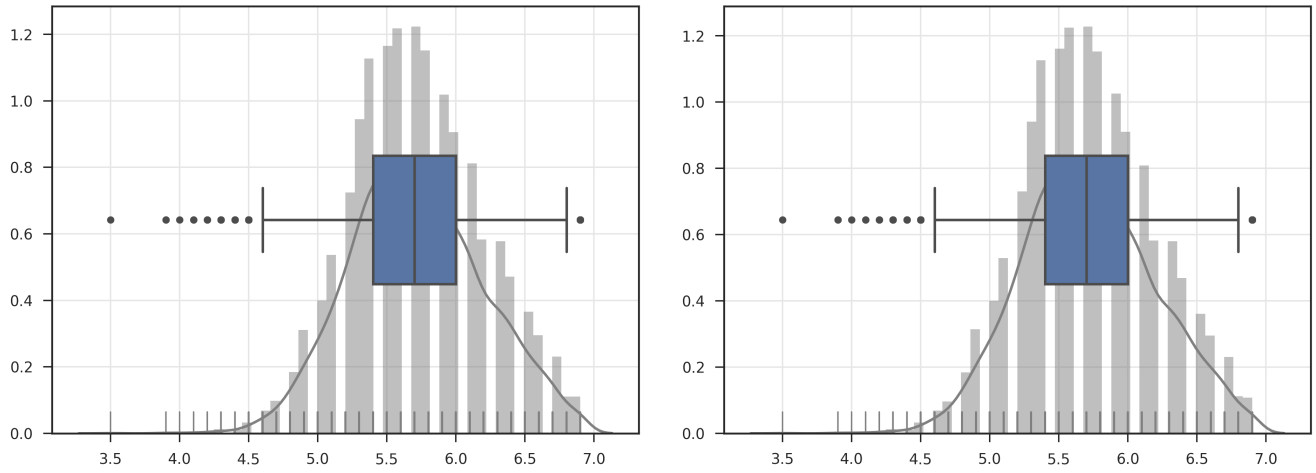
Table 9 shows statistics from the MERGE cohort for 48 loci that were shown to be significantly associated with Type 2 Diabetes in the 2012 Nature Genetics paper by Morris et al [7]. Where a previously reported variant was not genotyped in the study (indicated by $\bar{R^2} < 1$), if available, a tagging variant in LD with the reported variant ($\bar{R^2} >= 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. There are 18 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 45 variants in both studies, 39 exhibit the same direction of effect with the known result (binomial test $p = 2.71e - 07$).

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

CHR	POS	ID	EA	OA	N	CASE	CTRL	FREQ	OR	P	COHORT	$GENE_{CLOSEST}$	R^2	ID_{KNOWN}	N_{KNOWN}	$CASE_{KNOWN}$	$CTRL_{KNOWN}$	OR_{KNOWN}	P_{KNOWN}
10	114758349	**rs7903146**	T	C	8,490	1,193	7,297	0.182	1.354	$2.04 \cdot 10^{-7}$	EX_EUR	TCF7L2	1	rs7903146	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.389	$1.2 \cdot 10^{-139}$
6	20679709	**rs7756992**	G	A	8,490	1,193	7,297	0.347	1.198	$2.24 \cdot 10^{-4}$	EX_EUR	CDKAL1	1	rs7756992	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.167	$6.95 \cdot 10^{-35}$
9	22132076	**rs2383208**	A	G	8,490	1,193	7,297	0.151	1.14	$5.35 \cdot 10^{-2}$	EX_EUR	CDKN2B	1	rs2383208	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.178	$6.73 \cdot 10^{-26}$
3	185511687	**rs4402960**	T	G	8,490	1,193	7,297	0.322	1.147	$5.64 \cdot 10^{-3}$	EX_EUR	IGF2BP2	1	rs4402960	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.131	$2.39 \cdot 10^{-23}$
16	53819169	rs9936385	T	C	8,455	1,181	7,274	0.403	1.028	0.573	OMNI_EUR	FTO	1	rs9936385	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	0.886	$2.61 \cdot 10^{-23}$
8	118185025	**rs3802177**	G	A	8,489	1,193	7,296	0.393	1.131	$1.06 \cdot 10^{-2}$	EX_EUR	SLC30A8	1	rs3802177	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.136	$1.26 \cdot 10^{-21}$
10	94466495	**rs10882102**	G	C	8,436	1,180	7,256	0.465	1.196	$1.54 \cdot 10^{-4}$	OMNI_EUR	HHEX	1	rs10882102	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.117	$6.46 \cdot 10^{-19}$
7	28180556	**rs864745**	T	C	8,488	1,192	7,296	0.482	1.084	$8.6 \cdot 10^{-2}$	EX_EUR	JAZF1	1	rs864745	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.099	$2.28 \cdot 10^{-16}$
4	6289986	**rs4458523**	G	T	8,457	1,181	7,276	0.558	1.11	$2.9 \cdot 10^{-2}$	OMNI_EUR	WFS1	1	rs4458523	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.098	$2.02 \cdot 10^{-15}$
10	94209939	**rs6583813**	C	T	8,454	1,180	7,274	0.385	1.182	$6.51 \cdot 10^{-4}$	OMNI_EUR	IDE	1	rs6583813	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.098	$6.45 \cdot 10^{-14}$
3	123065778	**rs11708067**	A	G	8,487	1,193	7,294	0.158	1.217	$2.72 \cdot 10^{-3}$	EX_EUR	ADCY5	1	rs11708067	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.113	$7.19 \cdot 10^{-14}$
10	94354204	**rs3824735**	T	G	8,449	1,180	7,269	0.387	1.21	$1.02 \cdot 10^{-4}$	OMNI_EUR	KIF11	1	rs3824735	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.097	$7.43 \cdot 10^{-13}$
2	227100698	**rs2972146**	T	G	8,490	1,193	7,297	0.624	1.114	$2.75 \cdot 10^{-2}$	EX_EUR	IRS1	1	rs2972146	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.092	$8.97 \cdot 10^{-13}$
3	12393125	**rs1801282**	C	G	8,447	1,179	7,268	0.151	1.115	0.107	OMNI_EUR	PPARG	1	rs1801282	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.13	$1.05 \cdot 10^{-12}$
11	2847069	**rs163184**	G	T	8,449	1,181	7,268	0.628	1.021	0.666	OMNI_EUR	KCNQ1	1	rs163184	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.086	$1.18 \cdot 10^{-11}$
11	92673828	**rs1387153**	T	C	8,490	1,193	7,297	0.365	1.048	0.339	EX_EUR	MTNR1B	1	rs1387153	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.093	$1.59 \cdot 10^{-11}$
4	6315954	**rs10804976**	T	G	8,449	1,179	7,270	0.492	1.103	$3.85 \cdot 10^{-2}$	OMNI_EUR	PPP2R2C	1	rs10804976	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.085	$3.77 \cdot 10^{-11}$
2	43566146	**rs4372955**	A	G	8,445	1,180	7,265	$6.25 \cdot 10^{-2}$	1.071	0.486	OMNI_EUR	THADA	1	rs4372955	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.135	$5.26 \cdot 10^{-11}$
7	14898282	**rs17168486**	T	C	8,457	1,181	7,276	0.197	1.159	$1.19 \cdot 10^{-2}$	OMNI_EUR	DGKB	1	rs17168486	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.105	$5.94 \cdot 10^{-11}$
3	64705365	**rs6795735**	C	T	8,490	1,193	7,297	0.361	1.09	$7.81 \cdot 10^{-2}$	EX_EUR	ADAMTS9	1	rs6795735	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.08	$7.39 \cdot 10^{-11}$
10	80942631	**rs12571751**	A	G	8,490	1,193	7,297	0.476	1.1	$4.12 \cdot 10^{-2}$	EX_EUR	ZMIZ1	1	rs12571751	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.078	$1.02 \cdot 10^{-10}$
5	76425867	rs7708285	A	G	8,441	1,178	7,263	0.786	1.017	0.764	OMNI_EUR	ZBED3	1	rs7708285	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	0.913	$1.45 \cdot 10^{-10}$
11	72433098	**rs1552224**	A	C	8,489	1,193	7,296	0.248	1.237	$1.62 \cdot 10^{-4}$	EX_EUR	ARAP1	1	rs1552224	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.107	$1.79 \cdot 10^{-10}$
17	36099840	**rs11651755**	C	T	8,457	1,181	7,276	0.63	1.159	$2.31 \cdot 10^{-3}$	OMNI_EUR	HNF1B	1	rs11651755	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.098	$1.84 \cdot 10^{-10}$
8	41519248	**rs516946**	C	T	8,490	1,193	7,297	0.804	1.1	0.109	EX_EUR	ANK1	1	rs516946	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.091	$2.49 \cdot 10^{-10}$
2	227020653	**rs7578326**	A	G	8,489	1,193	7,296	0.353	1.094	$6.73 \cdot 10^{-2}$	EX_EUR	NYAP2	1	rs7578326	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.083	$3.81 \cdot 10^{-10}$
12	27965150	**rs10842994**	C	T	8,490	1,193	7,297	0.172	1.13	$5.1 \cdot 10^{-2}$	EX_EUR	KLHL42	1	rs10842994	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.096	$6.08 \cdot 10^{-10}$
11	17408630	rs5215	T	C	8,489	1,193	7,296	0.533	1.074	0.128	EX_EUR	KCNJ11	1	rs5215	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	0.93	$8.5 \cdot 10^{-10}$
12	66212318	**rs2261181**	T	C	8,456	1,181	7,275	$6.85 \cdot 10^{-2}$	1.04	0.674	OMNI_EUR	HMGA2	1	rs2261181	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.126	$1.16 \cdot 10^{-9}$
3	23454790	**rs1496653**	A	G	8,457	1,181	7,276	0.347	1.027	0.595	OMNI_EUR	UBE2E2	1	rs1496653	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.085	$3.56 \cdot 10^{-9}$
15	77832762	**rs7177055**	A	G	8,490	1,193	7,297	0.66	1.044	0.392	EX_EUR	HMG20A	1	rs7177055	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.077	$4.6 \cdot 10^{-9}$
11	17418477	rs757110	A	C	8,489	1,193	7,296	0.535	1.087	$7.68 \cdot 10^{-2}$	EX_EUR	ABCC8	1	rs757110	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	0.931	$5 \cdot 10^{-9}$
9	84308948	**rs2796441**	G	A	8,490	1,193	7,297	0.421	1.051	0.293	EX_EUR	TLE1	1	rs2796441	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.074	$5.39 \cdot 10^{-9}$
5	55806751	**rs459193**	G	A	8,490	1,193	7,297	0.664	1.074	0.154	EX_EUR	AC022431.2	1	rs459193	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.081	$5.99 \cdot 10^{-9}$
15	91544076	**rs12899811**	G	A	8,454	1,181	7,273	0.349	1.1	$5.29 \cdot 10^{-2}$	OMNI_EUR	VPS33B	1	rs12899811	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.076	$6.34 \cdot 10^{-9}$
19	19407718	**rs10401969**	C	T	8,490	1,193	7,297	$5.67 \cdot 10^{-2}$	1.06	0.56	EX_EUR	SUGP1	1	rs10401969	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.135	$7.04 \cdot 10^{-9}$
2	165528876	**rs13389219**	C	T	8,490	1,193	7,297	0.315	1.201	$3.3 \cdot 10^{-4}$	EX_EUR	COBLL1	1	rs13389219	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.073	$1 \cdot 10^{-8}$
19	19658472	**rs16996148**	T	G	8,490	1,193	7,297	$5.95 \cdot 10^{-2}$	1.065	0.516	EX_EUR	CILP2	1	rs16996148	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.124	$1.12 \cdot 10^{-8}$
18	57884750	rs12970134	G	A	8,490	1,193	7,297	0.175	1.051	0.417	EX_EUR	MC4R	1	rs12970134	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	0.927	$1.19 \cdot 10^{-8}$
13	80717156	**rs1359790**	G	A	8,490	1,193	7,297	0.289	1.088	0.105	EX_EUR	SPRY2	1	rs1359790	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.077	$1.39 \cdot 10^{-8}$
11	72669777	**rs11605166**	T	C	8,454	1,181	7,273	0.304	1.177	$1.67 \cdot 10^{-3}$	OMNI_EUR	FCHSD2	1	rs11605166	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.089	$1.86 \cdot 10^{-8}$
2	60573870	**rs243083**	G	A	8,456	1,181	7,275	0.448	1.046	0.343	OMNI_EUR	BCL11A	1	rs243083	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.069	$2.17 \cdot 10^{-8}$
16	75247245	**rs7202877**	T	G	8,489	1,193	7,296	0.139	1.088	0.221	EX_EUR	CTRB1	1	rs7202877	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.117	$3.5 \cdot 10^{-8}$
4	153520475	rs6813195	T	C	8,490	1,193	7,297	0.341	1.046	0.365	EX_EUR	TMEM154	1	rs6813195	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	0.932	$5.26 \cdot 10^{-8}$
2	43841269	**rs7576643**	C	T	8,455	1,180	7,275	$7.36 \cdot 10^{-2}$	1.084	0.379	OMNI_EUR	PLEKHH2	1	rs17031133	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.106	$2.69 \cdot 10^{-8}$
12	71405206	rs1877527	T	C	8,439	1,178	7,261	0.646	1.041	0.423	OMNI_EUR	CTD-2021H9.3	0.934	rs7955901	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	0.933	$6.51 \cdot 10^{-9}$
19	19379549	**rs58542926**	T	C	8,489	1,193	7,296	$5.71 \cdot 10^{-2}$	1.055	0.591	EX_EUR	HAPLN4	0.879	rs72999033	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.172	$2.6 \cdot 10^{-8}$
11	72669777	**rs11605166**	T	C	8,454	1,181	7,273	0.304	1.177	$1.67 \cdot 10^{-3}$	OMNI_EUR	STARD10	0.851	rs613937	$1.5 \cdot 10^5$	34,840	$1.15 \cdot 10^5$	1.099	$8.64 \cdot 10^{-10}$

4 Fasting Glucose (GLU_FAST)

4.1 Summary



(a) EX_EUR (b) OMNI_EUR

Figure 8: Distribution of GLU_FAST in cohort-level analyses

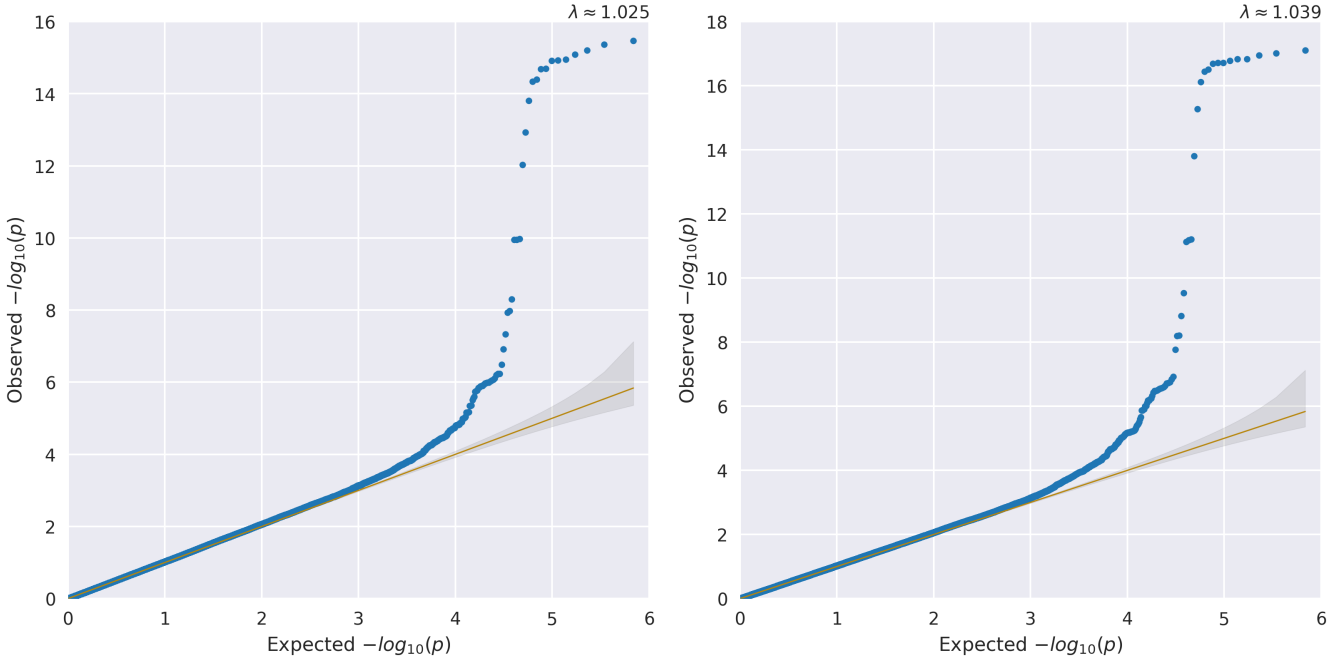
Table 10: Summary of samples removed from Fasting Glucose analysis by cohort and model

Cohort	Array	Ancestry	Trans	Covars	Total	-SampleQc	-missObs	-Kinship	-PcOutlier
EX_EUR	EX	EUR	invn	Age+BMI	10071	36	1438	1312	2
			invn	Age	10071	36	1435	1311	3
OMNI_EUR	OMNI	EUR	invn	Age+BMI	10048	69	1428	1291	0
			invn	Age	10048	69	1425	1292	1

Table 11: Summary of samples remaining for Fasting Glucose analysis by cohort and model

Cohort	Array	Ancestry	Trans	Covars	PCs	N	Male	Female	Max	Min	μ	$\tilde{x}$	σ
EX_EUR	EX	EUR	invn	Age+BMI	5	7290	7290	0	6.9	3.5	5.717	5.7	0.483
			invn	Age	5	7293	7293	0	6.9	3.5	5.717	5.7	0.482
OMNI_EUR	OMNI	EUR	invn	Age+BMI	2	7270	7270	0	6.9	3.5	5.719	5.7	0.482
			invn	Age	5	7271	7271	0	6.9	3.5	5.719	5.7	0.482

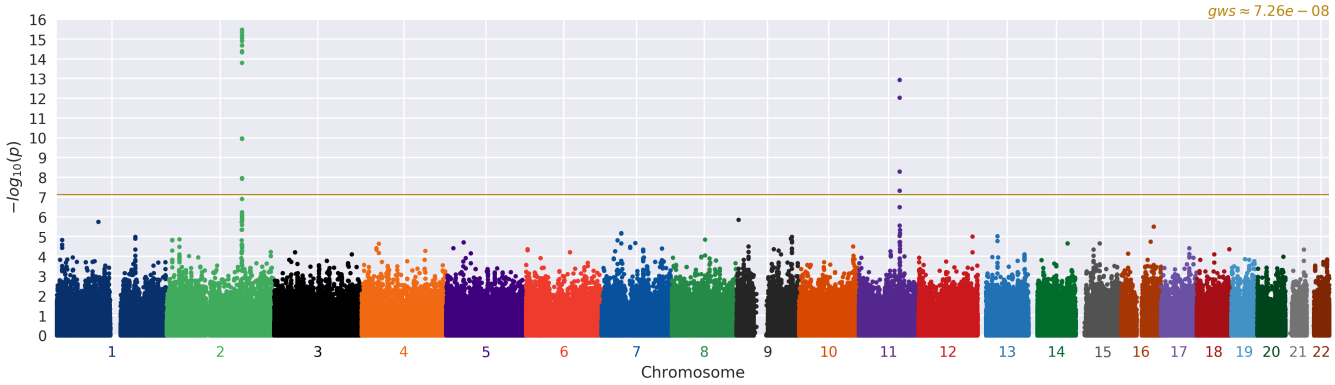
4.2 Calibration



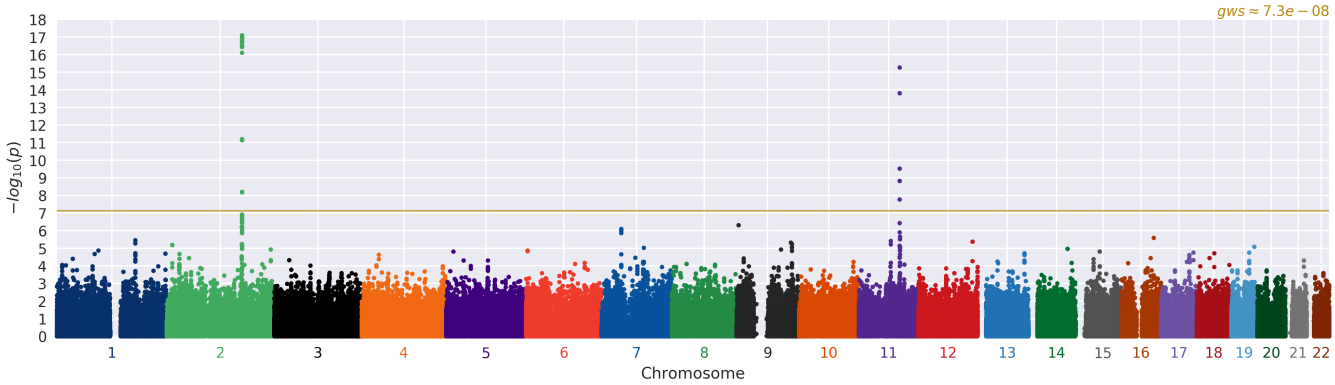
(a) invn Adjusted Age

(b) invn Adjusted Age+BMI

Figure 9: QQ plots for GLU_FAST in the MERGE analysis



(a) invn Adjusted Age



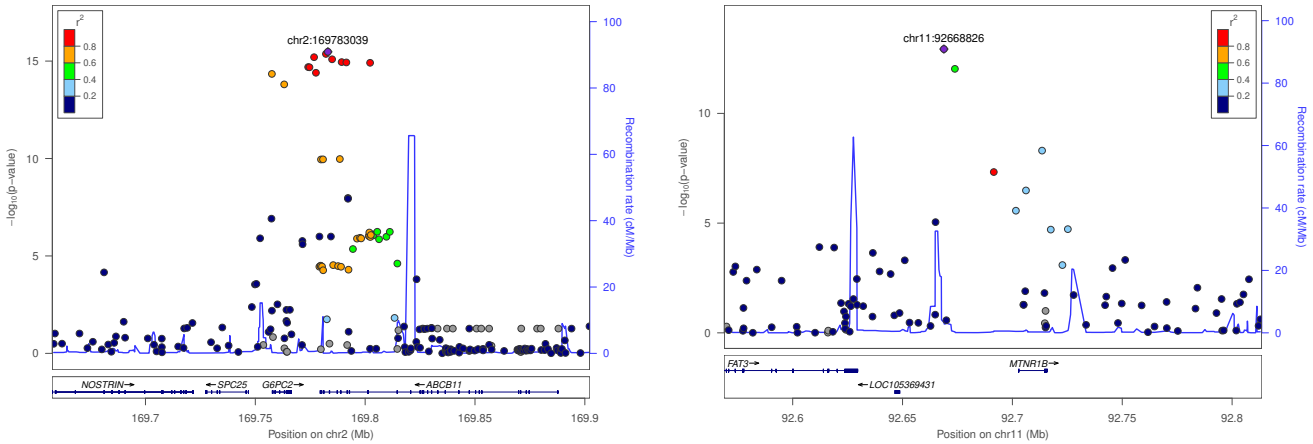
(b) invn Adjusted Age+BMI

Figure 10: Manhattan plots for GLU_FAST in the MERGE analysis

4.3 Top associations

Table 12: Top variants in the MERGE invn Adjusted Age model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	$\text{GENE}_{\text{CLOSEST}}$	COHORT	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
2	169783039	**rs579060**	T	G	**ABCB11**	OMNI_EUR	7,253	7,253	0	4,688	0.677	0.143	$1.75 \cdot 10^{-2}$	$3.34 \cdot 10^{-16}$
2	169757541	**rs573225**	A	G	**G6PC2**	OMNI_EUR	7,266	7,266	0	4,148	0.715	0.143	$1.82 \cdot 10^{-2}$	$4.55 \cdot 10^{-15}$
11	92668826	**rs3847554**	T	C	**MTNR1B**	EX_EUR	7,293	7,293	0	7,276	0.501	0.123	$1.66 \cdot 10^{-2}$	$1.17 \cdot 10^{-13}$
2	169752190	**rs16856115**	A	G	**SPC25**	OMNI_EUR	7,270	7,270	0	767	$5.28 \cdot 10^{-2}$	0.18	$3.72 \cdot 10^{-2}$	$1.24 \cdot 10^{-6}$
9	4291928	rs10974438	C	A	**GLIS3**	OMNI_EUR	7,269	7,269	0	5,580	0.384	$8.15 \cdot 10^{-2}$	$1.69 \cdot 10^{-2}$	$1.42 \cdot 10^{-6}$
1	94342061	rs41292661	C	T	DNTTIP2	EX_EUR	7,293	7,293	0	433	$2.97 \cdot 10^{-2}$	0.234	$4.89 \cdot 10^{-2}$	$1.75 \cdot 10^{-6}$
2	169352260	**rs10174987**	G	A	**CERS6**	OMNI_EUR	7,271	7,271	0	1,685	0.884	0.124	$2.59 \cdot 10^{-2}$	$1.82 \cdot 10^{-6}$
16	73823696	rs17329095	G	A	PSMD7	OMNI_EUR	7,270	7,270	0	2,167	0.149	0.109	$2.33 \cdot 10^{-2}$	$3.12 \cdot 10^{-6}$
11	93216751	rs2658801	G	A	SMCO4	OMNI_EUR	7,270	7,270	0	3,889	0.267	$8.55 \cdot 10^{-2}$	$1.86 \cdot 10^{-2}$	$4.52 \cdot 10^{-6}$
7	44211337	**rs2971671**	C	T	**GCK**	OMNI_EUR	7,271	7,271	0	4,377	0.301	$8.08 \cdot 10^{-2}$	$1.79 \cdot 10^{-2}$	$6.66 \cdot 10^{-6}$
11	92665020	rs4526739	C	T	**FAT3**	OMNI_EUR	7,269	7,269	0	5,307	0.365	$7.63 \cdot 10^{-2}$	$1.72 \cdot 10^{-2}$	$9.01 \cdot 10^{-6}$
13	44880783	rs1998659	G	A	SERP2	OMNI_EUR	7,270	7,270	0	3,153	0.217	$8.89 \cdot 10^{-2}$	$2.01 \cdot 10^{-2}$	$9.46 \cdot 10^{-6}$
12	122478728	rs7316212	G	A	BCL7A	OMNI_EUR	7,267	7,267	0	718	$4.94 \cdot 10^{-2}$	0.167	$3.77 \cdot 10^{-2}$	$9.77 \cdot 10^{-6}$
1	177621201	rs1572511	T	C	SEC16B	OMNI_EUR	7,270	7,270	0	6,802	0.468	$7.32 \cdot 10^{-2}$	$1.66 \cdot 10^{-2}$	$1.03 \cdot 10^{-5}$
9	125384197	rs10124314	T	C	OR1Q1	OMNI_EUR	7,271	7,271	0	2,449	0.168	$9.66 \cdot 10^{-2}$	$2.19 \cdot 10^{-2}$	$1.04 \cdot 10^{-5}$
9	123041996	rs759125	A	G	CDK5RAP2	OMNI_EUR	7,270	7,270	0	1,163	0.92	0.131	$3 \cdot 10^{-2}$	$1.27 \cdot 10^{-5}$
2	28645120	rs7589485	C	A	FOSL2	EX_EUR	7,293	7,293	0	6,549	0.551	$7.21 \cdot 10^{-2}$	$1.65 \cdot 10^{-2}$	$1.34 \cdot 10^{-5}$
8	75339134	rs9650249	T	C	GDAP1	OMNI_EUR	7,271	7,271	0	6,255	0.57	$7.29 \cdot 10^{-2}$	$1.68 \cdot 10^{-2}$	$1.39 \cdot 10^{-5}$
1	12336147	rs7546794	C	T	VPS13D	EX_EUR	7,293	7,293	0	357	$2.45 \cdot 10^{-2}$	0.233	$5.37 \cdot 10^{-2}$	$1.48 \cdot 10^{-5}$
2	12366908	rs1453488	T	C	LPIN1	OMNI_EUR	7,270	7,270	0	2,382	0.836	$9.73 \cdot 10^{-2}$	$2.24 \cdot 10^{-2}$	$1.49 \cdot 10^{-5}$

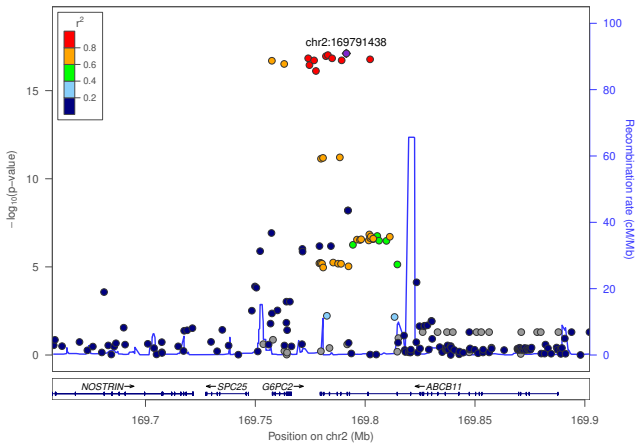


(a) rs579060 $\pm 100kb$ (b) rs3847554 $\pm 100kb$

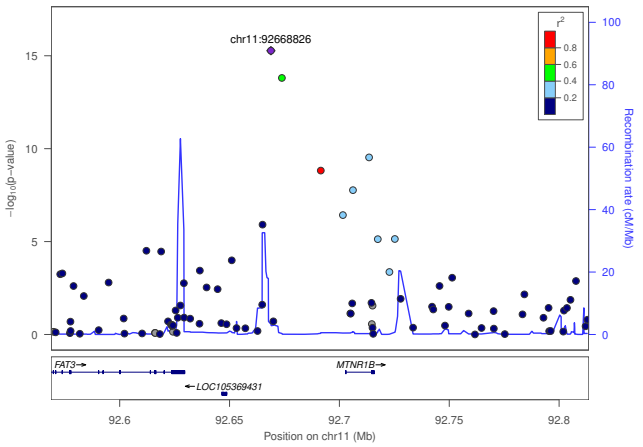
Figure 11: Regional plots for cohort MERGE model invn Adjusted Age

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

CHR	POS	ID	EA	OA	$\text{GENE}_{\text{CLOSEST}}$	COHORT	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
2	169791438	**rs552976**	G	A	**ABCB11**	EX_EUR	7,290	7,290	0	4,693	0.678	0.152	$1.76 \cdot 10^{-2}$	$7.78 \cdot 10^{-18}$
2	169757541	**rs573225**	A	G	**G6PC2**	OMNI_EUR	7,265	7,265	0	4,147	0.715	0.155	$1.82 \cdot 10^{-2}$	$2.02 \cdot 10^{-17}$
11	92668826	**rs3847554**	T	C	**MTNR1B**	EX_EUR	7,290	7,290	0	7,274	0.501	0.135	$1.66 \cdot 10^{-2}$	$5.34 \cdot 10^{-16}$
9	4291928	rs10974438	C	A	**GLIS3**	OMNI_EUR	7,268	7,268	0	5,577	0.384	$8.52 \cdot 10^{-2}$	$1.69 \cdot 10^{-2}$	$4.74 \cdot 10^{-7}$
2	169352260	**rs10174987**	G	A	**CERS6**	OMNI_EUR	7,270	7,270	0	1,684	0.884	0.13	$2.59 \cdot 10^{-2}$	$5.93 \cdot 10^{-7}$
7	44231216	**rs3757840**	T	G	**GCK**	OMNI_EUR	7,267	7,267	0	6,642	0.543	$8.26 \cdot 10^{-2}$	$1.67 \cdot 10^{-2}$	$7.8 \cdot 10^{-7}$
11	92665020	rs4526739	C	T	**FAT3**	OMNI_EUR	7,268	7,268	0	5,308	0.365	$8.34 \cdot 10^{-2}$	$1.72 \cdot 10^{-2}$	$1.22 \cdot 10^{-6}$
2	169752190	**rs16856115**	A	G	**SPC25**	OMNI_EUR	7,269	7,269	0	766	$5.27 \cdot 10^{-2}$	0.18	$3.72 \cdot 10^{-2}$	$1.28 \cdot 10^{-6}$
11	93216751	rs2658801	G	A	SMCO4	OMNI_EUR	7,269	7,269	0	3,886	0.267	$8.83 \cdot 10^{-2}$	$1.86 \cdot 10^{-2}$	$2.19 \cdot 10^{-6}$
16	73823696	rs17329095	G	A	PSMD7	OMNI_EUR	7,269	7,269	0	2,168	0.149	0.11	$2.33 \cdot 10^{-2}$	$2.55 \cdot 10^{-6}$
1	177621201	rs1572511	T	C	SEC16B	OMNI_EUR	7,269	7,269	0	6,801	0.468	$7.7 \cdot 10^{-2}$	$1.66 \cdot 10^{-2}$	$3.52 \cdot 10^{-6}$
11	72237045	rs341093	T	G	PDE2A	OMNI_EUR	7,270	7,270	0	1,101	0.924	0.143	$3.09 \cdot 10^{-2}$	$3.78 \cdot 10^{-6}$
12	122478728	rs7316212	G	A	BCL7A	OMNI_EUR	7,266	7,266	0	717	$4.93 \cdot 10^{-2}$	0.174	$3.78 \cdot 10^{-2}$	$4.12 \cdot 10^{-6}$
9	123041996	rs759125	A	G	CDK5RAP2	OMNI_EUR	7,269	7,269	0	1,163	0.92	0.138	$3 \cdot 10^{-2}$	$4.71 \cdot 10^{-6}$
9	125384197	rs10124314	T	C	OR1Q1	OMNI_EUR	7,270	7,270	0	2,449	0.168	$9.92 \cdot 10^{-2}$	$2.19 \cdot 10^{-2}$	$5.74 \cdot 10^{-6}$
2	169182294	rs13421263	C	T	STK39	OMNI_EUR	7,270	7,270	0	1,372	$9.44 \cdot 10^{-2}$	0.128	$2.83 \cdot 10^{-2}$	$6.08 \cdot 10^{-6}$
2	12369870	rs4669834	A	G	LPIN1	OMNI_EUR	7,269	7,269	0	2,387	0.164	0.101	$2.24 \cdot 10^{-2}$	$6.48 \cdot 10^{-6}$
2	12566495	rs11680047	T	C	TRIB2	OMNI_EUR	7,268	7,268	0	620	$4.27 \cdot 10^{-2}$	0.185	$4.11 \cdot 10^{-2}$	$6.54 \cdot 10^{-6}$
19	51583616	rs867191	C	T	KLK14	OMNI_EUR	7,269	7,269	0	1,939	0.133	0.108	$2.42 \cdot 10^{-2}$	$8.35 \cdot 10^{-6}$
11	93166368	rs2658781	C	T	CCDC67	OMNI_EUR	7,269	7,269	0	1,987	0.863	0.107	$2.39 \cdot 10^{-2}$	$8.41 \cdot 10^{-6}$



(a) rs552976 $\pm 100kb$



(b) rs3847554 $\pm 100kb$

Figure 12: Regional plots for cohort MERGE model invn Adjusted Age+BMI

4.4 Previously identified risk loci

Table 14 shows statistics from the MERGE cohort for 50 loci that were shown to be significantly associated with Fasting Glucose in the 2012 Nature Genetics paper by Scott 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 ($\bar{R}^2 >= 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. There are 24

variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 50 variants in both studies, 47 exhibit the same direction of effect with the known result (binomial test $p = 1.85e - 11$).

Table 14: Top known loci in MERGE model invn Adjusted Age (**bold** variants indicate matching direction of effect)

CHR	POS	ID	EA	OA	N	FREQ	EFFECT	STDERR	P	COHORT	$GENE_{CLOSEST}$	R^2	ID_{KNOWN}	N_{KNOWN}	$EFFECT_{KNOWN}$	$STDERR_{KNOWN}$	P_{KNOWN}
2	169763148	**rs560887**	C	T	7,293	0.28	0.143	$1.84 \cdot 10^{-2}$	$7.85 \cdot 10^{-15}$	EX_EUR	G6PC2	1	rs560887	$1.33 \cdot 10^{5}$	$7.1 \cdot 10^{-2}$	$2.5 \cdot 10^{-3}$	$1.4 \cdot 10^{-178}$
2	169802252	**rs853787**	T	G	7,273	0.32	0.141	$1.76 \cdot 10^{-2}$	$1.37 \cdot 10^{-15}$	OMNI_EUR	ABCB11	1	rs853787	$1.33 \cdot 10^{5}$	$6.1 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$5.51 \cdot 10^{-166}$
11	92673828	**rs1387153**	T	C	7,293	0.635	0.123	$1.71 \cdot 10^{-2}$	$7.61 \cdot 10^{-13}$	EX_EUR	MTNR1B	1	rs1387153	$1.33 \cdot 10^{5}$	$6.1 \cdot 10^{-2}$	$2.4 \cdot 10^{-3}$	$3.91 \cdot 10^{-143}$
7	44231886	**rs6975024**	C	T	7,288	0.9	0.105	$2.76 \cdot 10^{-2}$	$1.33 \cdot 10^{-4}$	EX_EUR	GCK	1	rs6975024	$1.33 \cdot 10^{5}$	$6.1 \cdot 10^{-2}$	$2.9 \cdot 10^{-3}$	$2.88 \cdot 10^{-99}$
2	169750483	**rs477224**	C	T	7,264	0.172	$7.89 \cdot 10^{-2}$	$2.17 \cdot 10^{-2}$	$2.73 \cdot 10^{-4}$	OMNI_EUR	SPC25	1	rs477224	$1.33 \cdot 10^{5}$	$3.6 \cdot 10^{-2}$	$2.3 \cdot 10^{-3}$	$6.02 \cdot 10^{-57}$
7	15064309	**rs2191349**	T	G	7,293	0.572	$4.63 \cdot 10^{-2}$	$1.66 \cdot 10^{-2}$	$5.37 \cdot 10^{-3}$	EX_EUR	DGKB	1	rs2191349	$1.33 \cdot 10^{5}$	$2.9 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$1.28 \cdot 10^{-42}$
2	27730940	**rs1260326**	C	T	7,292	0.372	$5.44 \cdot 10^{-2}$	$1.71 \cdot 10^{-2}$	$1.44 \cdot 10^{-3}$	EX_EUR	GCKR	1	rs1260326	$1.33 \cdot 10^{5}$	$2.9 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$2.17 \cdot 10^{-41}$
8	118185733	**rs11558471**	A	G	7,293	0.603	$4.9 \cdot 10^{-2}$	$1.68 \cdot 10^{-2}$	$3.54 \cdot 10^{-3}$	EX_EUR	SLC30A8	1	rs11558471	$1.33 \cdot 10^{5}$	$2.9 \cdot 10^{-2}$	$2.3 \cdot 10^{-3}$	$7.8 \cdot 10^{-37}$
15	62383155	**rs4502156**	T	C	7,293	0.436	$4.9 \cdot 10^{-2}$	$1.66 \cdot 10^{-2}$	$3.08 \cdot 10^{-3}$	EX_EUR	C2CD4A	1	rs4502156	$1.33 \cdot 10^{5}$	$2.2 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$1.38 \cdot 10^{-25}$
10	114758349	**rs7903146**	T	C	7,293	0.823	$6.05 \cdot 10^{-2}$	$2.15 \cdot 10^{-2}$	$4.95 \cdot 10^{-3}$	EX_EUR	TCF7L2	1	rs7903146	$1.33 \cdot 10^{5}$	$2.2 \cdot 10^{-2}$	$2.4 \cdot 10^{-3}$	$2.71 \cdot 10^{-20}$
11	45873091	**rs11605924**	A	C	7,285	0.528	$4.44 \cdot 10^{-2}$	$1.67 \cdot 10^{-2}$	$7.72 \cdot 10^{-3}$	EX_EUR	CRY2	1	rs11605924	$1.33 \cdot 10^{5}$	$2 \cdot 10^{-2}$	$2.3 \cdot 10^{-3}$	$3.93 \cdot 10^{-19}$
11	61603510	**rs174576**	C	A	7,273	0.576	$3.8 \cdot 10^{-2}$	$1.69 \cdot 10^{-2}$	$2.41 \cdot 10^{-2}$	OMNI_EUR	FADS2	1	rs174576	$1.33 \cdot 10^{5}$	$2 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$1.18 \cdot 10^{-18}$
3	123065778	**rs11708067**	A	G	7,290	0.838	$6.39 \cdot 10^{-2}$	$2.23 \cdot 10^{-2}$	$4.25 \cdot 10^{-3}$	EX_EUR	ADCY5	1	rs11708067	$1.33 \cdot 10^{5}$	$2.3 \cdot 10^{-2}$	$2.6 \cdot 10^{-3}$	$1.3 \cdot 10^{-18}$
3	170717996	**rs11924648**	A	G	7,272	0.867	$4.33 \cdot 10^{-2}$	$2.43 \cdot 10^{-2}$	$7.54 \cdot 10^{-2}$	OMNI_EUR	SLC2A2	1	rs11924648	$1.33 \cdot 10^{5}$	$2.6 \cdot 10^{-2}$	$3.1 \cdot 10^{-3}$	$1.02 \cdot 10^{-17}$
11	61571348	rs174548	C	G	7,262	0.598	$2.92 \cdot 10^{-2}$	$1.7 \cdot 10^{-2}$	$8.51 \cdot 10^{-2}$	OMNI_EUR	FADS1	1	rs174548	$1.33 \cdot 10^{5}$	$-1.9 \cdot 10^{-2}$	$2.3 \cdot 10^{-3}$	$1.02 \cdot 10^{-17}$
9	22132076	**rs2383208**	A	G	7,293	0.847	$6.41 \cdot 10^{-2}$	$2.31 \cdot 10^{-2}$	$5.5 \cdot 10^{-3}$	EX_EUR	CDKN2B	1	rs2383208	$1.33 \cdot 10^{5}$	$2.3 \cdot 10^{-2}$	$2.7 \cdot 10^{-3}$	$2.16 \cdot 10^{-17}$
11	61551356	**rs174535**	T	C	7,273	0.576	$3.5 \cdot 10^{-2}$	$1.69 \cdot 10^{-2}$	$3.79 \cdot 10^{-2}$	OMNI_EUR	MYRF	1	rs174535	$1.33 \cdot 10^{5}$	$1.9 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$2.38 \cdot 10^{-17}$
11	61557803	**rs102275**	T	C	7,293	0.576	$4.65 \cdot 10^{-2}$	$1.68 \cdot 10^{-2}$	$5.73 \cdot 10^{-3}$	EX_EUR	TMEM258	1	rs102275	$1.33 \cdot 10^{5}$	$1.9 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$4.97 \cdot 10^{-17}$
10	113042093	**rs10885122**	G	T	7,293	0.154	$2.42 \cdot 10^{-2}$	$2.31 \cdot 10^{-2}$	0.296	EX_EUR	ADRA2A	1	rs10885122	$1.33 \cdot 10^{5}$	$2.7 \cdot 10^{-2}$	$3.3 \cdot 10^{-3}$	$6.32 \cdot 10^{-17}$
5	95539448	**rs4869272**	T	C	7,293	0.32	$2.4 \cdot 10^{-2}$	$1.78 \cdot 10^{-2}$	0.178	EX_EUR	PCSK1	1	rs4869272	$1.33 \cdot 10^{5}$	$1.8 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$1.02 \cdot 10^{-15}$
13	28487599	**rs11619319**	G	A	7,292	0.745	$2.89 \cdot 10^{-2}$	$1.9 \cdot 10^{-2}$	0.129	EX_EUR	PDX1	1	rs11619319	$1.33 \cdot 10^{5}$	$2 \cdot 10^{-2}$	$2.4 \cdot 10^{-3}$	$1.33 \cdot 10^{-15}$
11	47318157	**rs749067**	T	C	7,273	0.696	$1.88 \cdot 10^{-2}$	$1.8 \cdot 10^{-2}$	0.297	OMNI_EUR	MADD	1	rs749067	$1.33 \cdot 10^{5}$	$1.7 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$6.12 \cdot 10^{-15}$
8	9177732	**rs983309**	T	G	7,271	0.202	$7.53 \cdot 10^{-2}$	$2.08 \cdot 10^{-2}$	$3.03 \cdot 10^{-4}$	OMNI_EUR	RP11-10A14.4	1	rs983309	$1.33 \cdot 10^{5}$	$2.6 \cdot 10^{-2}$	$3.3 \cdot 10^{-3}$	$6.29 \cdot 10^{-15}$
11	47659135	**rs7118178**	G	A	7,271	0.813	$4.9 \cdot 10^{-2}$	$2.11 \cdot 10^{-2}$	$2.03 \cdot 10^{-2}$	OMNI_EUR	MTCH2	1	rs7118178	$1.33 \cdot 10^{5}$	$1.8 \cdot 10^{-2}$	$2.4 \cdot 10^{-3}$	$3.84 \cdot 10^{-14}$
11	47600438	**rs2280231**	C	T	7,272	0.813	$4.74 \cdot 10^{-2}$	$2.11 \cdot 10^{-2}$	$2.5 \cdot 10^{-2}$	OMNI_EUR	KBTBD4	1	rs2280231	$1.33 \cdot 10^{5}$	$1.8 \cdot 10^{-2}$	$2.4 \cdot 10^{-3}$	$1.67 \cdot 10^{-13}$
2	27975394	**rs6547796**	T	C	7,273	0.264	$3.37 \cdot 10^{-2}$	$1.87 \cdot 10^{-2}$	$7.19 \cdot 10^{-2}$	OMNI_EUR	MRPL33	1	rs6547796	$1.33 \cdot 10^{5}$	$1.7 \cdot 10^{-2}$	$2.4 \cdot 10^{-3}$	$3.13 \cdot 10^{-13}$
2	169605967	**rs2390732**	A	G	7,273	0.341	$3.16 \cdot 10^{-2}$	$1.76 \cdot 10^{-2}$	$7.26 \cdot 10^{-2}$	OMNI_EUR	CERS6	1	rs2390732	$1.33 \cdot 10^{5}$	$1.5 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$7.1 \cdot 10^{-13}$
9	4292083	**rs10758593**	A	G	7,293	0.576	$5.95 \cdot 10^{-2}$	$1.67 \cdot 10^{-2}$	$3.75 \cdot 10^{-4}$	EX_EUR	GLIS3	1	rs10758593	$1.33 \cdot 10^{5}$	$1.6 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$1.17 \cdot 10^{-12}$
7	50791579	**rs6943153**	T	C	7,292	0.515	$3.99 \cdot 10^{-2}$	$1.66 \cdot 10^{-2}$	$1.6 \cdot 10^{-2}$	EX_EUR	GRB10	1	rs6943153	$1.33 \cdot 10^{5}$	$1.5 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$1.63 \cdot 10^{-12}$
2	27860258	**rs2141371**	G	A	7,261	0.332	$2.12 \cdot 10^{-2}$	$1.76 \cdot 10^{-2}$	0.229	OMNI_EUR	GPN1	1	rs2141371	$1.33 \cdot 10^{5}$	$1.7 \cdot 10^{-2}$	$2.5 \cdot 10^{-3}$	$6.59 \cdot 10^{-12}$
2	169721377	**rs479661**	G	A	7,293	0.107	$6 \cdot 10^{-2}$	$2.67 \cdot 10^{-2}$	$2.47 \cdot 10^{-2}$	EX_EUR	NOSTRIN	1	rs479661	$1.33 \cdot 10^{5}$	$1.9 \cdot 10^{-2}$	$2.8 \cdot 10^{-3}$	$8.56 \cdot 10^{-12}$
11	72432985	**rs11603334**	G	A	7,293	0.748	$6.29 \cdot 10^{-2}$	$1.93 \cdot 10^{-2}$	$1.1 \cdot 10^{-3}$	EX_EUR	ARAP1	1	rs11603334	$1.33 \cdot 10^{5}$	$1.9 \cdot 10^{-2}$	$2.8 \cdot 10^{-3}$	$1.12 \cdot 10^{-11}$
2	27951658	**rs867282**	T	C	7,273	0.244	$2.68 \cdot 10^{-2}$	$1.91 \cdot 10^{-2}$	0.161	OMNI_EUR	AC074091.13	1	rs867282	$1.33 \cdot 10^{5}$	$1.7 \cdot 10^{-2}$	$2.5 \cdot 10^{-3}$	$1.76 \cdot 10^{-11}$
7	44162355	**rs2979422**	C	T	7,271	0.847	$4.07 \cdot 10^{-2}$	$2.3 \cdot 10^{-2}$	$7.76 \cdot 10^{-2}$	OMNI_EUR	POLD2	1	rs2979422	$1.33 \cdot 10^{5}$	$2 \cdot 10^{-2}$	$3 \cdot 10^{-3}$	$1.78 \cdot 10^{-11}$
20	22557099	**rs6113722**	G	A	7,293	0.966	$6.35 \cdot 10^{-2}$	$4.57 \cdot 10^{-2}$	0.165	EX_EUR	FOXA2	1	rs6113722	$1.33 \cdot 10^{5}$	$3.5 \cdot 10^{-2}$	$5.3 \cdot 10^{-3}$	$2.49 \cdot 10^{-11}$
9	111680359	**rs16913693**	T	G	7,293	0.975	$9.74 \cdot 10^{-2}$	$5.28 \cdot 10^{-2}$	$6.54 \cdot 10^{-2}$	EX_EUR	IKBKAP	1	rs16913693	$1.33 \cdot 10^{5}$	$4.3 \cdot 10^{-2}$	$6.6 \cdot 10^{-3}$	$3.51 \cdot 10^{-11}$
1	214145706	**rs340883**	T	C	7,273	0.651	$1.37 \cdot 10^{-2}$	$1.73 \cdot 10^{-2}$	0.427	OMNI_EUR	PROX1	1	rs340883	$1.33 \cdot 10^{5}$	$1.4 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$4.08 \cdot 10^{-11}$
2	27152874	**rs1371614**	T	C	7,273	0.801	$2.49 \cdot 10^{-2}$	$2.09 \cdot 10^{-2}$	0.233	OMNI_EUR	DPYSL5	1	rs1371614	$1.33 \cdot 10^{5}$	$1.6 \cdot 10^{-2}$	$2.4 \cdot 10^{-3}$	$7.09 \cdot 10^{-11}$
11	47275064	rs10838681	G	A	7,271	0.612	$2.22 \cdot 10^{-3}$	$1.71 \cdot 10^{-2}$	0.897	OMNI_EUR	NR1H3	1	rs10838681	$1.33 \cdot 10^{5}$	$-1.5 \cdot 10^{-2}$	$2.4 \cdot 10^{-3}$	$8.84 \cdot 10^{-11}$
11	48009074	**rs11039482**	C	T	7,293	0.894	$3.65 \cdot 10^{-3}$	$2.68 \cdot 10^{-2}$	0.892	EX_EUR	PTPRJ	1	rs11039482	$1.33 \cdot 10^{5}$	$2 \cdot 10^{-2}$	$3 \cdot 10^{-3}$	$9.36 \cdot 10^{-11}$
15	62424649	**rs4775471**	C	T	7,271	0.802	$2.86 \cdot 10^{-2}$	$2.1 \cdot 10^{-2}$	0.173	OMNI_EUR	C2CD4B	1	rs4775471	$1.33 \cdot 10^{5}$	$1.6 \cdot 10^{-2}$	$2.5 \cdot 10^{-3}$	$9.73 \cdot 10^{-11}$
9	139256766	**rs3829109**	G	A	7,293	0.647	$9.56 \cdot 10^{-3}$	$1.72 \cdot 10^{-2}$	0.577	EX_EUR	DNLZ	1	rs3829109	$1.33 \cdot 10^{5}$	$1.7 \cdot 10^{-2}$	$2.7 \cdot 10^{-3}$	$1.13 \cdot 10^{-10}$
14	100839261	rs3783347	T	G	7,293	0.807	$9.44 \cdot 10^{-3}$	$2.13 \cdot 10^{-2}$	0.658	EX_EUR	WARS	1	rs3783347	$1.33 \cdot 10^{5}$	$-1.7 \cdot 10^{-2}$	$2.6 \cdot 10^{-3}$	$1.32 \cdot 10^{-10}$
3	170670279	**rs16855567**	C	T	7,265	0.915	$4.79 \cdot 10^{-2}$	$2.94 \cdot 10^{-2}$	0.104	OMNI_EUR	EIF5A2	1	rs16855567	$1.33 \cdot 10^{5}$	$2.7 \cdot 10^{-2}$	$4.1 \cdot 10^{-3}$	$1.57 \cdot 10^{-10}$
11	47929846	**rs6485795**	G	A	7,272	0.783	$1.68 \cdot 10^{-2}$	$2 \cdot 10^{-2}$	0.402	OMNI_EUR	NUP160	1	rs6485795	$1.33 \cdot 10^{5}$	$1.5 \cdot 10^{-2}$	$2.3 \cdot 10^{-3}$	$1.81 \cdot 10^{-10}$
11	47065072	**rs10838651**	G	A	7,271	0.902	$4.12 \cdot 10^{-2}$	$2.77 \cdot 10^{-2}$	0.137	OMNI_EUR	C11orf49	1	rs10838651	$1.33 \cdot 10^{5}$	$2.1 \cdot 10^{-2}$	$3.3 \cdot 10^{-3}$	$1.9 \cdot 10^{-10}$
2	28301540	**rs937813**	T	C	7,273	0.889	$7.3 \cdot 10^{-2}$	$2.62 \cdot 10^{-2}$	$5.42 \cdot 10^{-3}$	OMNI_EUR	BRE	1	rs937813	$1.33 \cdot 10^{5}$	$2.1 \cdot 10^{-2}$	$3.4 \cdot 10^{-3}$	$9.87 \cdot 10^{-10}$
2	27895073	**rs2178198**	C	T	7,264	0.88	$2.48 \cdot 10^{-2}$	$2.54 \cdot 10^{-2}$	0.329	OMNI_EUR	SLC4A1AP	1	rs2178198	$1.33 \cdot 10^{5}$	$2 \cdot 10^{-2}$	$3.3 \cdot 10^{-3}$	$1.02 \cdot 10^{-9}$
11	92818649	**rs9804472**	T	C	7,272	0.193	$1.67 \cdot 10^{-2}$	$2.1 \cdot 10^{-2}$	0.427	OMNI_EUR	SLC36A4	1	rs9804472	$1.33 \cdot 10^{5}$	$1.6 \cdot 10^{-2}$	$2.5 \cdot 10^{-3}$	$1.18 \cdot 10^{-9}$
11	48333360	**rs1483121**	G	A	7,292	0.887	$9.69 \cdot 10^{-3}$	$2.61 \cdot 10^{-2}$	0.711	EX_EUR	OR4S1	1	rs1483121	$1.33 \cdot 10^{5}$	$1.8 \cdot 10^{-2}$	$3.1 \cdot 10^{-3}$	$1.7 \cdot 10^{-9}$

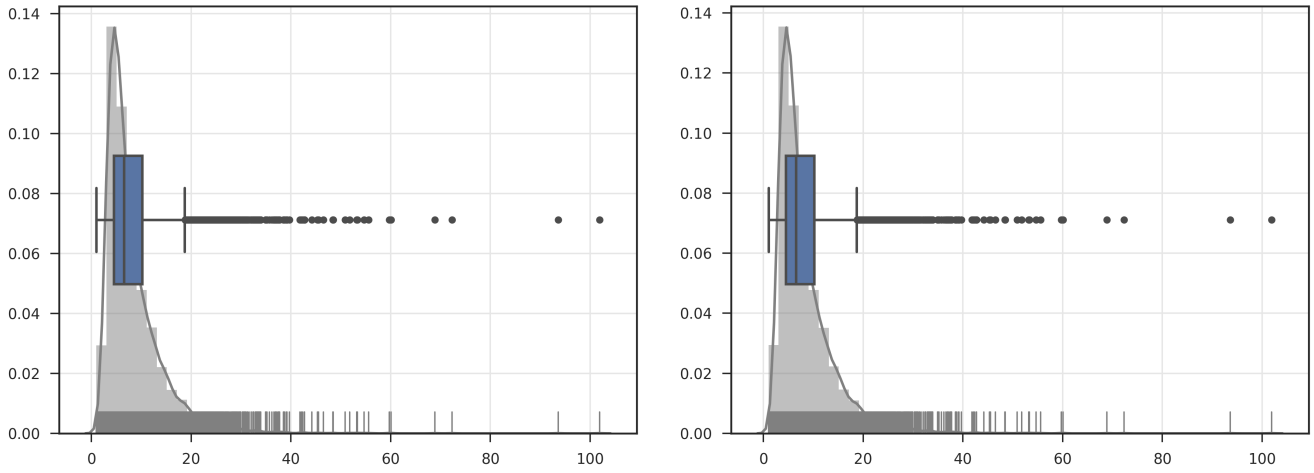
Table 15 shows statistics from the MERGE cohort for 50 loci that were shown to be significantly associated with Fasting Glucose in the 2012 Nature Genetics paper by Scott et al [9]. Where a previously reported variant was not genotyped in the study (indicated by $\bar{R^2} < 1$), if available, a tagging variant in LD with the reported variant ($\bar{R^2} >= 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. There are 29 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 50 variants in both studies, 47 exhibit the same direction of effect with the known result (binomial test $p = 1.85e - 11$).

Table 15: Top known loci in MERGE model invn Adjusted Age+BMI (**bold** variants indicate matching direction of effect)

CHR	POS	ID	EA	OA	N	FREQ	EFFECT	STDERR	P	COHORT	$GENE_{CLOSEST}$	R^2	ID_{KNOWN}	N_{KNOWN}	$EFFECT_{KNOWN}$	$STDERR_{KNOWN}$	P_{KNOWN}
2	169763148	**rs560887**	C	T	7,292	0.28	0.157	$1.83 \cdot 10^{-2}$	$1.67 \cdot 10^{-17}$	EX_EUR	G6PC2	1	rs560887	$1.33 \cdot 10^{5}$	$7.1 \cdot 10^{-2}$	$2.5 \cdot 10^{-3}$	$1.4 \cdot 10^{-178}$
2	169802252	**rs853787**	T	G	7,268	0.32	0.151	$1.76 \cdot 10^{-2}$	$1.06 \cdot 10^{-17}$	OMNI_EUR	ABCB11	1	rs853787	$1.33 \cdot 10^{5}$	$6.1 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$5.51 \cdot 10^{-166}$
11	92673828	**rs1387153**	T	C	7,292	0.635	0.131	$1.71 \cdot 10^{-2}$	$2.84 \cdot 10^{-14}$	EX_EUR	MTNR1B	1	rs1387153	$1.33 \cdot 10^{5}$	$6.1 \cdot 10^{-2}$	$2.4 \cdot 10^{-3}$	$3.91 \cdot 10^{-143}$
7	44231886	**rs6975024**	C	T	7,287	0.9	0.106	$2.76 \cdot 10^{-2}$	$1.16 \cdot 10^{-4}$	EX_EUR	GCK	1	rs6975024	$1.33 \cdot 10^{5}$	$6.1 \cdot 10^{-2}$	$2.9 \cdot 10^{-3}$	$2.88 \cdot 10^{-99}$
2	169750483	**rs477224**	C	T	7,259	0.172	$8.27 \cdot 10^{-2}$	$2.17 \cdot 10^{-2}$	$1.38 \cdot 10^{-4}$	OMNI_EUR	SPC25	1	rs477224	$1.33 \cdot 10^{5}$	$3.6 \cdot 10^{-2}$	$2.3 \cdot 10^{-3}$	$6.02 \cdot 10^{-57}$
7	15064309	**rs2191349**	T	G	7,292	0.572	$5.26 \cdot 10^{-2}$	$1.66 \cdot 10^{-2}$	$1.58 \cdot 10^{-3}$	EX_EUR	DGKB	1	rs2191349	$1.33 \cdot 10^{5}$	$2.9 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$1.28 \cdot 10^{-42}$
2	27730940	**rs1260326**	C	T	7,291	0.372	$5.11 \cdot 10^{-2}$	$1.71 \cdot 10^{-2}$	$2.73 \cdot 10^{-3}$	EX_EUR	GCKR	1	rs1260326	$1.33 \cdot 10^{5}$	$2.9 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$2.17 \cdot 10^{-41}$
8	118185733	**rs11558471**	A	G	7,292	0.603	$5.8 \cdot 10^{-2}$	$1.68 \cdot 10^{-2}$	$5.5 \cdot 10^{-4}$	EX_EUR	SLC30A8	1	rs11558471	$1.33 \cdot 10^{5}$	$2.9 \cdot 10^{-2}$	$2.3 \cdot 10^{-3}$	$7.8 \cdot 10^{-37}$
15	62383155	**rs4502156**	T	C	7,292	0.435	$4.88 \cdot 10^{-2}$	$1.66 \cdot 10^{-2}$	$3.22 \cdot 10^{-3}$	EX_EUR	C2CD4A	1	rs4502156	$1.33 \cdot 10^{5}$	$2.2 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$1.38 \cdot 10^{-25}$
10	114758349	**rs7903146**	T	C	7,292	0.823	$7.15 \cdot 10^{-2}$	$2.15 \cdot 10^{-2}$	$9 \cdot 10^{-4}$	EX_EUR	TCF7L2	1	rs7903146	$1.33 \cdot 10^{5}$	$2.2 \cdot 10^{-2}$	$2.4 \cdot 10^{-3}$	$2.71 \cdot 10^{-20}$
11	45873091	**rs11605924**	A	C	7,284	0.528	$3.89 \cdot 10^{-2}$	$1.67 \cdot 10^{-2}$	$1.95 \cdot 10^{-2}$	EX_EUR	CRY2	1	rs11605924	$1.33 \cdot 10^{5}$	$2 \cdot 10^{-2}$	$2.3 \cdot 10^{-3}$	$3.93 \cdot 10^{-19}$
11	61603510	**rs174576**	C	A	7,268	0.576	$4.4 \cdot 10^{-2}$	$1.69 \cdot 10^{-2}$	$9.21 \cdot 10^{-3}$	OMNI_EUR	FADS2	1	rs174576	$1.33 \cdot 10^{5}$	$2 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$1.18 \cdot 10^{-18}$
3	123065778	**rs11708067**	A	G	7,289	0.838	$6.24 \cdot 10^{-2}$	$2.23 \cdot 10^{-2}$	$5.21 \cdot 10^{-3}$	EX_EUR	ADCY5	1	rs11708067	$1.33 \cdot 10^{5}$	$2.3 \cdot 10^{-2}$	$2.6 \cdot 10^{-3}$	$1.3 \cdot 10^{-18}$
3	170717996	**rs11924648**	A	G	7,267	0.866	$4.23 \cdot 10^{-2}$	$2.44 \cdot 10^{-2}$	$8.23 \cdot 10^{-2}$	OMNI_EUR	SLC2A2	1	rs11924648	$1.33 \cdot 10^{5}$	$2.6 \cdot 10^{-2}$	$3.1 \cdot 10^{-3}$	$1.02 \cdot 10^{-17}$
11	61571348	rs174548	C	G	7,257	0.598	$3.51 \cdot 10^{-2}$	$1.7 \cdot 10^{-2}$	$3.88 \cdot 10^{-2}$	OMNI_EUR	FADS1	1	rs174548	$1.33 \cdot 10^{5}$	$-1.9 \cdot 10^{-2}$	$2.3 \cdot 10^{-3}$	$1.02 \cdot 10^{-17}$
9	22132076	**rs2383208**	A	G	7,292	0.847	$6.8 \cdot 10^{-2}$	$2.31 \cdot 10^{-2}$	$3.24 \cdot 10^{-3}$	EX_EUR	CDKN2B	1	rs2383208	$1.33 \cdot 10^{5}$	$2.3 \cdot 10^{-2}$	$2.7 \cdot 10^{-3}$	$2.16 \cdot 10^{-17}$
11	61551356	**rs174535**	T	C	7,268	0.576	$4.08 \cdot 10^{-2}$	$1.69 \cdot 10^{-2}$	$1.56 \cdot 10^{-2}$	OMNI_EUR	MYRF	1	rs174535	$1.33 \cdot 10^{5}$	$1.9 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$2.38 \cdot 10^{-17}$
11	61557803	**rs102275**	T	C	7,292	0.576	$5.14 \cdot 10^{-2}$	$1.68 \cdot 10^{-2}$	$2.27 \cdot 10^{-3}$	EX_EUR	TMEM258	1	rs102275	$1.33 \cdot 10^{5}$	$1.9 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$4.97 \cdot 10^{-17}$
10	113042093	**rs10885122**	G	T	7,292	0.154	$2.33 \cdot 10^{-2}$	$2.31 \cdot 10^{-2}$	0.313	EX_EUR	ADRA2A	1	rs10885122	$1.33 \cdot 10^{5}$	$2.7 \cdot 10^{-2}$	$3.3 \cdot 10^{-3}$	$6.32 \cdot 10^{-17}$
5	95539448	**rs4869272**	T	C	7,292	0.32	$3.8 \cdot 10^{-2}$	$1.78 \cdot 10^{-2}$	$3.24 \cdot 10^{-2}$	EX_EUR	PCSK1	1	rs4869272	$1.33 \cdot 10^{5}$	$1.8 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$1.02 \cdot 10^{-15}$
13	28487599	**rs11619319**	G	A	7,291	0.745	$3.57 \cdot 10^{-2}$	$1.9 \cdot 10^{-2}$	$6.08 \cdot 10^{-2}$	EX_EUR	PDX1	1	rs11619319	$1.33 \cdot 10^{5}$	$2 \cdot 10^{-2}$	$2.4 \cdot 10^{-3}$	$1.33 \cdot 10^{-15}$
11	47318157	**rs749067**	T	C	7,268	0.696	$1.75 \cdot 10^{-2}$	$1.81 \cdot 10^{-2}$	0.331	OMNI_EUR	MADD	1	rs749067	$1.33 \cdot 10^{5}$	$1.7 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$6.12 \cdot 10^{-15}$
8	9177732	**rs983309**	T	G	7,266	0.202	$7.83 \cdot 10^{-2}$	$2.09 \cdot 10^{-2}$	$1.73 \cdot 10^{-4}$	OMNI_EUR	RP11-10A14.4	1	rs983309	$1.33 \cdot 10^{5}$	$2.6 \cdot 10^{-2}$	$3.3 \cdot 10^{-3}$	$6.29 \cdot 10^{-15}$
11	47659135	**rs7118178**	G	A	7,266	0.813	$4.9 \cdot 10^{-2}$	$2.12 \cdot 10^{-2}$	$2.07 \cdot 10^{-2}$	OMNI_EUR	MTCH2	1	rs7118178	$1.33 \cdot 10^{5}$	$1.8 \cdot 10^{-2}$	$2.4 \cdot 10^{-3}$	$3.84 \cdot 10^{-14}$
11	47600438	**rs2280231**	C	T	7,267	0.813	$4.72 \cdot 10^{-2}$	$2.12 \cdot 10^{-2}$	$2.58 \cdot 10^{-2}$	OMNI_EUR	KBTBD4	1	rs2280231	$1.33 \cdot 10^{5}$	$1.8 \cdot 10^{-2}$	$2.4 \cdot 10^{-3}$	$1.67 \cdot 10^{-13}$
2	27975394	**rs6547796**	T	C	7,268	0.263	$3.83 \cdot 10^{-2}$	$1.87 \cdot 10^{-2}$	$4.1 \cdot 10^{-2}$	OMNI_EUR	MRPL33	1	rs6547796	$1.33 \cdot 10^{5}$	$1.7 \cdot 10^{-2}$	$2.4 \cdot 10^{-3}$	$3.13 \cdot 10^{-13}$
2	169605967	**rs2390732**	A	G	7,268	0.341	$3.85 \cdot 10^{-2}$	$1.76 \cdot 10^{-2}$	$2.9 \cdot 10^{-2}$	OMNI_EUR	CERS6	1	rs2390732	$1.33 \cdot 10^{5}$	$1.5 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$7.1 \cdot 10^{-13}$
9	4292083	**rs10758593**	A	G	7,292	0.577	$5.33 \cdot 10^{-2}$	$1.67 \cdot 10^{-2}$	$1.46 \cdot 10^{-3}$	EX_EUR	GLIS3	1	rs10758593	$1.33 \cdot 10^{5}$	$1.6 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$1.17 \cdot 10^{-12}$
7	50791579	**rs6943153**	T	C	7,291	0.515	$3.76 \cdot 10^{-2}$	$1.66 \cdot 10^{-2}$	$2.3 \cdot 10^{-2}$	EX_EUR	GRB10	1	rs6943153	$1.33 \cdot 10^{5}$	$1.5 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$1.63 \cdot 10^{-12}$
2	27860258	**rs2141371**	G	A	7,256	0.333	$2.12 \cdot 10^{-2}$	$1.76 \cdot 10^{-2}$	0.229	OMNI_EUR	GPN1	1	rs2141371	$1.33 \cdot 10^{5}$	$1.7 \cdot 10^{-2}$	$2.5 \cdot 10^{-3}$	$6.59 \cdot 10^{-12}$
2	169721377	**rs479661**	G	A	7,292	0.107	$6.21 \cdot 10^{-2}$	$2.67 \cdot 10^{-2}$	$2.01 \cdot 10^{-2}$	EX_EUR	NOSTRIN	1	rs479661	$1.33 \cdot 10^{5}$	$1.9 \cdot 10^{-2}$	$2.8 \cdot 10^{-3}$	$8.56 \cdot 10^{-12}$
11	72432985	**rs11603334**	G	A	7,292	0.748	$7.63 \cdot 10^{-2}$	$1.93 \cdot 10^{-2}$	$7.5 \cdot 10^{-5}$	EX_EUR	ARAP1	1	rs11603334	$1.33 \cdot 10^{5}$	$1.9 \cdot 10^{-2}$	$2.8 \cdot 10^{-3}$	$1.12 \cdot 10^{-11}$
2	27951658	**rs867282**	T	C	7,268	0.244	$2.96 \cdot 10^{-2}$	$1.91 \cdot 10^{-2}$	0.122	OMNI_EUR	AC074091.13	1	rs867282	$1.33 \cdot 10^{5}$	$1.7 \cdot 10^{-2}$	$2.5 \cdot 10^{-3}$	$1.76 \cdot 10^{-11}$
7	44162355	**rs2979422**	C	T	7,266	0.847	$3.33 \cdot 10^{-2}$	$2.31 \cdot 10^{-2}$	0.15	OMNI_EUR	POLD2	1	rs2979422	$1.33 \cdot 10^{5}$	$2 \cdot 10^{-2}$	$3 \cdot 10^{-3}$	$1.78 \cdot 10^{-11}$
20	22557099	**rs6113722**	G	A	7,292	0.966	$7.49 \cdot 10^{-2}$	$4.56 \cdot 10^{-2}$	0.101	EX_EUR	FOXA2	1	rs6113722	$1.33 \cdot 10^{5}$	$3.5 \cdot 10^{-2}$	$5.3 \cdot 10^{-3}$	$2.49 \cdot 10^{-11}$
9	111680359	**rs16913693**	T	G	7,292	0.975	0.113	$5.28 \cdot 10^{-2}$	$3.23 \cdot 10^{-2}$	EX_EUR	IKBKAP	1	rs16913693	$1.33 \cdot 10^{5}$	$4.3 \cdot 10^{-2}$	$6.6 \cdot 10^{-3}$	$3.51 \cdot 10^{-11}$
1	214145706	**rs340883**	T	C	7,268	0.651	$1.28 \cdot 10^{-2}$	$1.73 \cdot 10^{-2}$	0.46	OMNI_EUR	PROX1	1	rs340883	$1.33 \cdot 10^{5}$	$1.4 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$4.08 \cdot 10^{-11}$
2	27152874	**rs1371614**	T	C	7,268	0.801	$2.64 \cdot 10^{-2}$	$2.09 \cdot 10^{-2}$	0.206	OMNI_EUR	DPYSL5	1	rs1371614	$1.33 \cdot 10^{5}$	$1.6 \cdot 10^{-2}$	$2.4 \cdot 10^{-3}$	$7.09 \cdot 10^{-11}$
11	47275064	rs10838681	G	A	7,266	0.612	$3.37 \cdot 10^{-4}$	$1.71 \cdot 10^{-2}$	0.984	OMNI_EUR	NR1H3	1	rs10838681	$1.33 \cdot 10^{5}$	$-1.5 \cdot 10^{-2}$	$2.4 \cdot 10^{-3}$	$8.84 \cdot 10^{-11}$
11	48009074	**rs11039482**	C	T	7,292	0.894	$7.74 \cdot 10^{-3}$	$2.68 \cdot 10^{-2}$	0.773	EX_EUR	PTPRJ	1	rs11039482	$1.33 \cdot 10^{5}$	$2 \cdot 10^{-2}$	$3 \cdot 10^{-3}$	$9.36 \cdot 10^{-11}$
15	62424649	**rs4775471**	C	T	7,266	0.802	$3.76 \cdot 10^{-2}$	$2.1 \cdot 10^{-2}$	$7.32 \cdot 10^{-2}$	OMNI_EUR	C2CD4B	1	rs4775471	$1.33 \cdot 10^{5}$	$1.6 \cdot 10^{-2}$	$2.5 \cdot 10^{-3}$	$9.73 \cdot 10^{-11}$
9	139256766	**rs3829109**	G	A	7,292	0.647	$1.62 \cdot 10^{-2}$	$1.71 \cdot 10^{-2}$	0.344	EX_EUR	DNLZ	1	rs3829109	$1.33 \cdot 10^{5}$	$1.7 \cdot 10^{-2}$	$2.7 \cdot 10^{-3}$	$1.13 \cdot 10^{-10}$
14	100839261	rs3783347	T	G	7,292	0.807	$8.25 \cdot 10^{-3}$	$2.13 \cdot 10^{-2}$	0.699	EX_EUR	WARS	1	rs3783347	$1.33 \cdot 10^{5}$	$-1.7 \cdot 10^{-2}$	$2.6 \cdot 10^{-3}$	$1.32 \cdot 10^{-10}$
3	170670279	**rs16855567**	C	T	7,260	0.915	$4.97 \cdot 10^{-2}$	$2.94 \cdot 10^{-2}$	$9.11 \cdot 10^{-2}$	OMNI_EUR	EIF5A2	1	rs16855567	$1.33 \cdot 10^{5}$	$2.7 \cdot 10^{-2}$	$4.1 \cdot 10^{-3}$	$1.57 \cdot 10^{-10}$
11	47929846	**rs6485795**	G	A	7,267	0.783	$1.52 \cdot 10^{-2}$	$2 \cdot 10^{-2}$	0.447	OMNI_EUR	NUP160	1	rs6485795	$1.33 \cdot 10^{5}$	$1.5 \cdot 10^{-2}$	$2.3 \cdot 10^{-3}$	$1.81 \cdot 10^{-10}$
11	47065072	**rs10838651**	G	A	7,266	0.902	$3.71 \cdot 10^{-2}$	$2.77 \cdot 10^{-2}$	0.181	OMNI_EUR	C11orf49	1	rs10838651	$1.33 \cdot 10^{5}$	$2.1 \cdot 10^{-2}$	$3.3 \cdot 10^{-3}$	$1.9 \cdot 10^{-10}$
2	28301540	**rs937813**	T	C	7,268	0.89	$8.08 \cdot 10^{-2}$	$2.63 \cdot 10^{-2}$	$2.12 \cdot 10^{-3}$	OMNI_EUR	BRE	1	rs937813	$1.33 \cdot 10^{5}$	$2.1 \cdot 10^{-2}$	$3.4 \cdot 10^{-3}$	$9.87 \cdot 10^{-10}$
2	27895073	**rs2178198**	C	T	7,259	0.88	$1.8 \cdot 10^{-2}$	$2.55 \cdot 10^{-2}$	0.481	OMNI_EUR	SLC4A1AP	1	rs2178198	$1.33 \cdot 10^{5}$	$2 \cdot 10^{-2}$	$3.3 \cdot 10^{-3}$	$1.02 \cdot 10^{-9}$
11	92818649	**rs9804472**	T	C	7,267	0.193	$1.65 \cdot 10^{-2}$	$2.1 \cdot 10^{-2}$	0.433	OMNI_EUR	SLC36A4	1	rs9804472	$1.33 \cdot 10^{5}$	$1.6 \cdot 10^{-2}$	$2.5 \cdot 10^{-3}$	$1.18 \cdot 10^{-9}$
11	48333360	**rs1483121**	G	A	7,291	0.887	$1.6 \cdot 10^{-2}$	$2.61 \cdot 10^{-2}$	0.541	EX_EUR	OR4S1	1	rs1483121	$1.33 \cdot 10^{5}$	$1.8 \cdot 10^{-2}$	$3.1 \cdot 10^{-3}$	$1.7 \cdot 10^{-9}$

5 Fasting Insulin (INS_FAST)

5.1 Summary



(a) EX_EUR (b) OMNI_EUR

Figure 13: Distribution of INS_FAST in cohort-level analyses

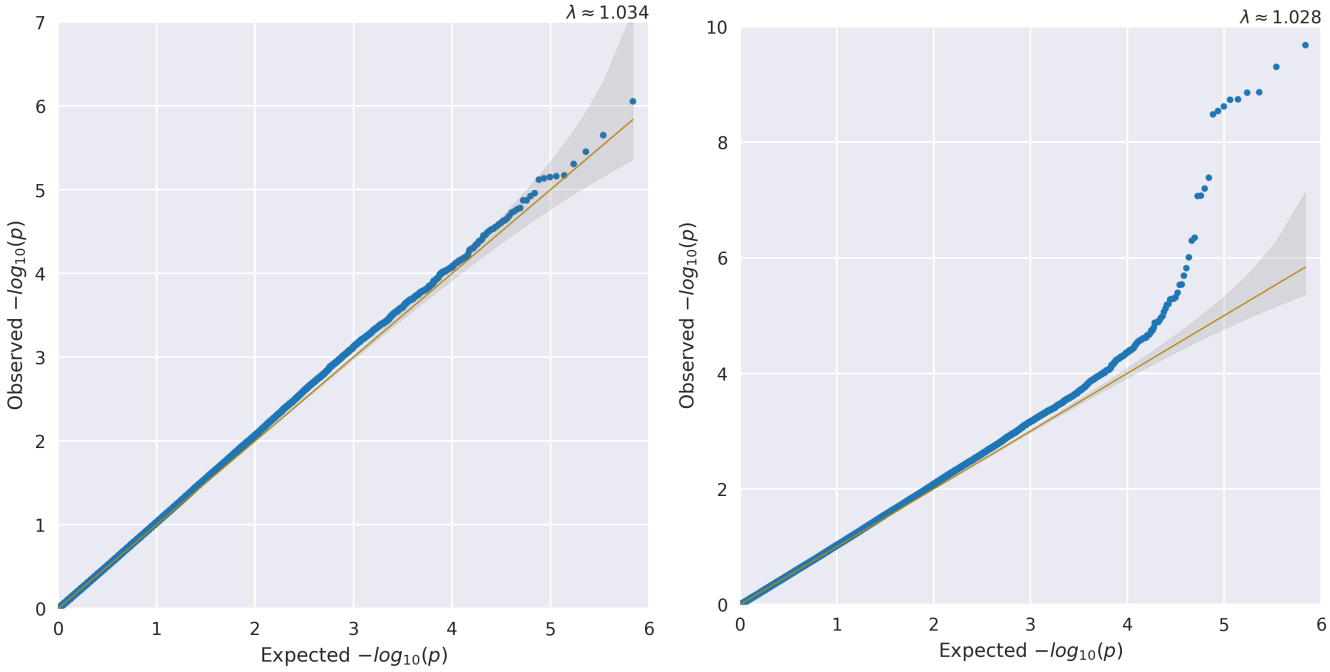
Table 16: Summary of samples removed from Fasting Insulin analysis by cohort and model

Cohort	Array	Ancestry	Trans	Covars	Total	-SampleQc	-missObs	-Kinship	-PcOutlier
EX_EUR	EX	EUR	invn	Age	10071	36	1439	1309	1
			invn	Age+BMI	10071	36	1442	1312	1
OMNI_EUR	OMNI	EUR	invn	Age+BMI	10048	69	1432	1292	0
			invn	Age	10048	69	1429	1293	1

Table 17: Summary of samples remaining for Fasting Insulin analysis by cohort and model

Cohort	Array	Ancestry	Trans	Covars	PCs	N	Male	Female	Max	Min	μ	$\tilde{x}$	σ
EX_EUR	EX	EUR	invn	Age	6	7292	7292	0	101.9	1.0	8.336	6.5	6.005
			invn	Age+BMI	4	7286	7286	0	101.9	1.0	8.329	6.5	6.003
OMNI_EUR	OMNI	EUR	invn	Age+BMI	4	7265	7265	0	101.9	1.1	8.328	6.5	5.983
			invn	Age	9	7266	7266	0	101.9	1.1	8.327	6.5	5.982

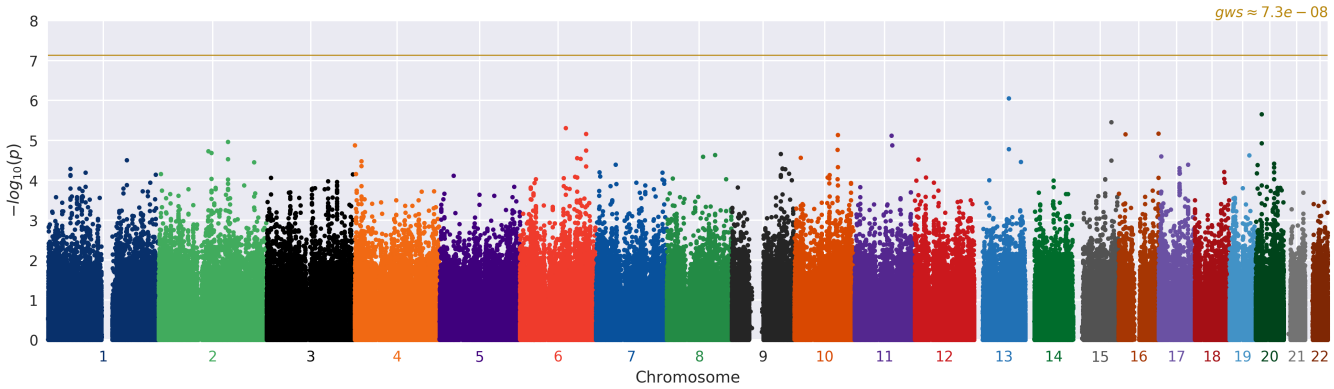
5.2 Calibration



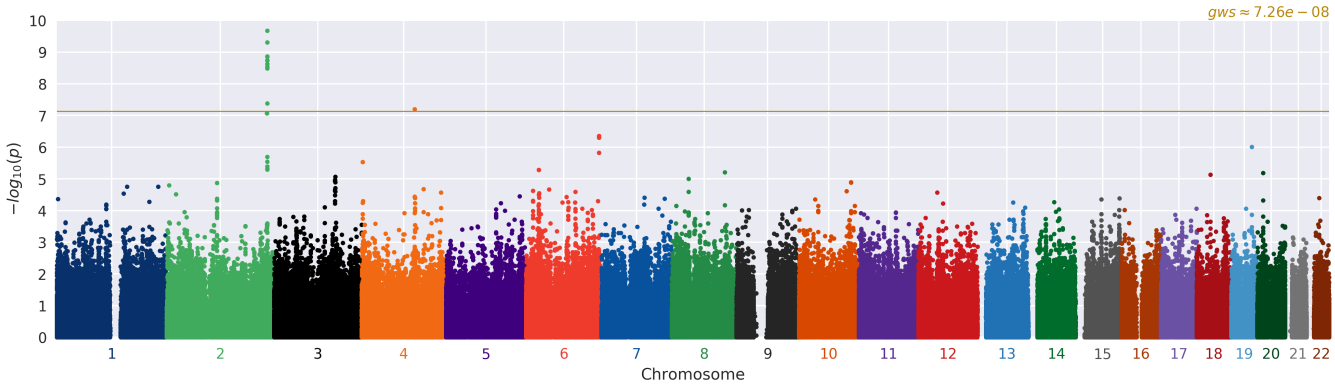
(a) invn Adjusted Age

(b) invn Adjusted Age+BMI

Figure 14: QQ plots for INS_FAST in the MERGE analysis



(a) invn Adjusted Age



(b) invn Adjusted Age+BMI

Figure 15: Manhattan plots for INS_FAST in the MERGE analysis

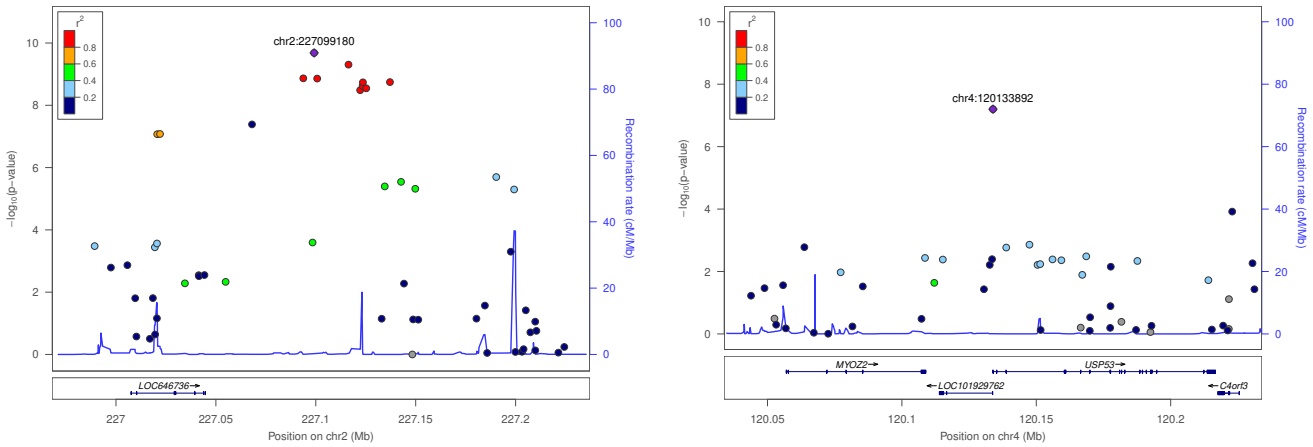
5.3 Top associations

Table 18: Top variants in the MERGE invn Adjusted Age model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	$GENE_{CLOSEST}$	COHORT	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
13	78136392	rs17067931	A	G	SCEL	OMNI_EUR	7,262	7,262	0	968	$6.66 \cdot 10^{-2}$	0.163	$3.32 \cdot 10^{-2}$	$8.77 \cdot 10^{-7}$
20	13151531	rs6041937	A	G	SPTLC3	OMNI_EUR	7,266	7,266	0	6,496	0.447	$7.8 \cdot 10^{-2}$	$1.65 \cdot 10^{-2}$	$2.23 \cdot 10^{-6}$
15	86052670	rs756426	G	T	AKAP13	OMNI_EUR	7,196	7,196	0	3,269	0.227	$9.13 \cdot 10^{-2}$	$1.97 \cdot 10^{-2}$	$3.52 \cdot 10^{-6}$
6	102635841	rs7750307	A	G	GRIK2	OMNI_EUR	7,266	7,266	0	4,104	0.282	$8.38 \cdot 10^{-2}$	$1.83 \cdot 10^{-2}$	$4.9 \cdot 10^{-6}$
16	89570635	rs4347628	T	C	SPG7	OMNI_EUR	7,266	7,266	0	6,216	0.572	$7.53 \cdot 10^{-2}$	$1.67 \cdot 10^{-2}$	$6.72 \cdot 10^{-6}$
6	148781825	rs9399650	T	C	SASH1	OMNI_EUR	7,266	7,266	0	4,657	0.32	$8.02 \cdot 10^{-2}$	$1.78 \cdot 10^{-2}$	$6.9 \cdot 10^{-6}$
16	15148646	rs11075253	C	A	NTAN1	OMNI_EUR	7,266	7,266	0	3,968	0.273	$8.27 \cdot 10^{-2}$	$1.84 \cdot 10^{-2}$	$7.08 \cdot 10^{-6}$
10	97158713	rs2274489	G	A	SORBS1	OMNI_EUR	7,266	7,266	0	5,854	0.403	$7.56 \cdot 10^{-2}$	$1.68 \cdot 10^{-2}$	$7.29 \cdot 10^{-6}$
11	82381787	rs10898021	A	G	FAM181B	OMNI_EUR	7,261	7,261	0	4,784	0.671	$7.89 \cdot 10^{-2}$	$1.76 \cdot 10^{-2}$	$7.57 \cdot 10^{-6}$
2	155450180	rs808935	A	G	KCNJ3	OMNI_EUR	7,264	7,264	0	5,164	0.355	$7.64 \cdot 10^{-2}$	$1.74 \cdot 10^{-2}$	$1.09 \cdot 10^{-5}$
4	515503	rs115766555	G	C	PIGG	EX_EUR	7,291	7,291	0	25	$1.71 \cdot 10^{-3}$	0.872	0.2	$1.33 \cdot 10^{-5}$
11	84053382	rs4944487	A	G	DLG2	OMNI_EUR	7,264	7,264	0	1,719	0.118	0.113	$2.59 \cdot 10^{-2}$	$1.34 \cdot 10^{-5}$
2	111794388	rs3789085	G	A	ACOXL	OMNI_EUR	7,265	7,265	0	6,538	0.45	$7.15 \cdot 10^{-2}$	$1.67 \cdot 10^{-2}$	$1.88 \cdot 10^{-5}$
2	118872427	rs3849327	T	C	INSIG2	OMNI_EUR	7,213	7,213	0	2,676	0.186	$9.06 \cdot 10^{-2}$	$2.12 \cdot 10^{-2}$	$2.05 \cdot 10^{-5}$
9	110008143	rs10978769	A	G	RAD23B	OMNI_EUR	7,266	7,266	0	5,698	0.392	$7.15 \cdot 10^{-2}$	$1.69 \cdot 10^{-2}$	$2.21 \cdot 10^{-5}$
8	108759874	rs9297399	T	C	RSPO2	OMNI_EUR	7,147	7,147	0	1,434	0.1	0.118	$2.78 \cdot 10^{-2}$	$2.31 \cdot 10^{-5}$
19	44198526	rs8111293	T	G	IRGC	OMNI_EUR	7,264	7,264	0	6,437	0.557	$7.01 \cdot 10^{-2}$	$1.66 \cdot 10^{-2}$	$2.37 \cdot 10^{-5}$
17	5326089	rs1071648	T	C	RPAIN	EX_EUR	7,292	7,292	0	6,141	0.421	$7.17 \cdot 10^{-2}$	$1.7 \cdot 10^{-2}$	$2.51 \cdot 10^{-5}$
8	81430806	rs190969114	G	T	ZBTB10	EX_EUR	7,291	7,291	0	218	$1.5 \cdot 10^{-2}$	0.285	$6.77 \cdot 10^{-2}$	$2.56 \cdot 10^{-5}$
10	13817944	rs2049745	A	G	FRMD4A	OMNI_EUR	7,254	7,254	0	4,721	0.675	$7.42 \cdot 10^{-2}$	$1.77 \cdot 10^{-2}$	$2.71 \cdot 10^{-5}$

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

CHR	POS	ID	EA	OA	$GENE_{CLOSEST}$	COHORT	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
2	227099180	**rs2943645**	T	C	**IRS1**	OMNI_EUR	7,260	7,260	0	5,502	0.621	0.109	$1.71 \cdot 10^{-2}$	$2.08 \cdot 10^{-10}$
4	120133892	rs6833072	C	T	USP53	OMNI_EUR	7,256	7,256	0	6,076	0.419	$9.07 \cdot 10^{-2}$	$1.67 \cdot 10^{-2}$	$6.31 \cdot 10^{-8}$
2	227022036	**rs13405357**	T	C	**NYAP2**	OMNI_EUR	7,261	7,261	0	5,163	0.356	$9.26 \cdot 10^{-2}$	$1.73 \cdot 10^{-2}$	$8.32 \cdot 10^{-8}$
6	164956384	rs9355479	G	A	C6orf118	OMNI_EUR	7,264	7,264	0	1,025	0.929	0.163	$3.23 \cdot 10^{-2}$	$4.44 \cdot 10^{-7}$
19	46800433	rs3826795	G	A	HIF3A	OMNI_EUR	7,265	7,265	0	2,144	0.148	0.115	$2.35 \cdot 10^{-2}$	$9.74 \cdot 10^{-7}$
4	2471974	rs4974695	T	C	RNF4	OMNI_EUR	7,265	7,265	0	6,168	0.425	$7.88 \cdot 10^{-2}$	$1.68 \cdot 10^{-2}$	$2.91 \cdot 10^{-6}$
6	29257967	rs1033568	A	G	OR14J1	OMNI_EUR	7,265	7,265	0	3,972	0.727	$8.51 \cdot 10^{-2}$	$1.87 \cdot 10^{-2}$	$5.17 \cdot 10^{-6}$
8	119856209	rs3134086	G	A	TNFRSF11B	OMNI_EUR	7,262	7,262	0	4,895	0.663	$7.95 \cdot 10^{-2}$	$1.76 \cdot 10^{-2}$	$6.23 \cdot 10^{-6}$
20	13151531	rs6041937	A	G	SPTLC3	OMNI_EUR	7,265	7,265	0	6,491	0.447	$7.43 \cdot 10^{-2}$	$1.65 \cdot 10^{-2}$	$6.51 \cdot 10^{-6}$
18	30847180	rs58448816	C	T	CCDC178	EX_EUR	7,286	7,286	0	442	$3.03 \cdot 10^{-2}$	0.215	$4.8 \cdot 10^{-2}$	$7.47 \cdot 10^{-6}$
3	138096097	rs12695685	C	A	MRAS	OMNI_EUR	7,263	7,263	0	1,455	0.1	0.123	$2.75 \cdot 10^{-2}$	$8.61 \cdot 10^{-6}$
8	37750289	rs7812866	C	A	RAB11FIP1	OMNI_EUR	7,265	7,265	0	6,681	0.46	$7.37 \cdot 10^{-2}$	$1.67 \cdot 10^{-2}$	$1.01 \cdot 10^{-5}$
3	137882949	rs2724712	T	C	DBR1	OMNI_EUR	7,263	7,263	0	4,823	0.668	$7.64 \cdot 10^{-2}$	$1.73 \cdot 10^{-2}$	$1.08 \cdot 10^{-5}$
10	118221256	rs1897515	G	T	PNLIPRP3	OMNI_EUR	7,264	7,264	0	2,959	0.796	$8.93 \cdot 10^{-2}$	$2.05 \cdot 10^{-2}$	$1.29 \cdot 10^{-5}$
2	113591275	rs3136558	G	A	IL1B	OMNI_EUR	7,264	7,264	0	3,788	0.261	$8.25 \cdot 10^{-2}$	$1.89 \cdot 10^{-2}$	$1.33 \cdot 10^{-5}$
2	5288644	rs4668488	T	G	SOX11	OMNI_EUR	7,265	7,265	0	5,743	0.395	$7.38 \cdot 10^{-2}$	$1.71 \cdot 10^{-2}$	$1.59 \cdot 10^{-5}$
1	229772141	exm157618	T	A	URB2	EX_EUR	7,286	7,286	0	7	$4.8 \cdot 10^{-4}$	1.621	0.377	$1.78 \cdot 10^{-5}$
1	159117690	rs3026935	T	C	CADM3	OMNI_EUR	7,236	7,236	0	1,233	$8.52 \cdot 10^{-2}$	0.128	$2.99 \cdot 10^{-2}$	$1.78 \cdot 10^{-5}$
4	139908503	rs4309784	A	G	NOCT	OMNI_EUR	7,257	7,257	0	6,666	0.459	$7.15 \cdot 10^{-2}$	$1.68 \cdot 10^{-2}$	$2.12 \cdot 10^{-5}$
6	52319050	rs1570624	A	G	EFHC1	EX_EUR	7,283	7,283	0	635	$4.36 \cdot 10^{-2}$	0.173	$4.07 \cdot 10^{-2}$	$2.16 \cdot 10^{-5}$



(a) rs2943645 $\pm 100kb$ (b) rs6833072 $\pm 100kb$

Figure 16: Regional plots for cohort MERGE model invn Adjusted Age+BMI

5.4 Previously identified risk loci

Table 20 shows statistics from the MERGE cohort for 18 loci that were shown to be significantly associated with Fasting Insulin in the 2012 Nature Genetics paper by Scott et al [15]. 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 ($\bar{R}^2 >= 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. There are 6 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 15 variants in both studies, 12 exhibit the same direction of effect with the known result (binomial test $p = 0.0176$).

Table 20: Top known loci in MERGE model invn Adjusted Age (**bold** variants indicate matching direction of effect)

CHR	POS	ID	EA	OA	N	FREQ	EFFECT	STDERR	P	COHORT	$GENE_{CLOSEST}$	R^2	ID_{KNOWN}	N_{KNOWN}	$EFFECT_{KNOWN}$	$STDERR_{KNOWN}$	P_{KNOWN}
2	27730940	**rs1260326**	C	T	7,286	0.628	$4.94 \cdot 10^{-2}$	$1.71 \cdot 10^{-2}$	$3.78 \cdot 10^{-3}$	EX_EUR	GCKR	1	rs1260326	$1.33 \cdot 10^{5}$	$2.1 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$2.74 \cdot 10^{-22}$
2	227099180	**rs2943645**	T	C	7,260	0.621	$3.47 \cdot 10^{-2}$	$1.72 \cdot 10^{-2}$	$4.35 \cdot 10^{-2}$	OMNI_EUR	IRS1	1	rs2943645	$1.33 \cdot 10^{5}$	$1.9 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$2.26 \cdot 10^{-19}$
2	165513091	rs10195252	C	T	7,287	0.332	$4.32 \cdot 10^{-3}$	$1.76 \cdot 10^{-2}$	0.806	EX_EUR	COBLL1	1	rs10195252	$1.33 \cdot 10^{5}$	$-1.7 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$1.26 \cdot 10^{-16}$
2	227020653	**rs7578326**	A	G	7,286	0.354	$3.18 \cdot 10^{-2}$	$1.73 \cdot 10^{-2}$	$6.67 \cdot 10^{-2}$	EX_EUR	NYAP2	1	rs7578326	$1.33 \cdot 10^{5}$	$1.8 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$2.25 \cdot 10^{-16}$
8	9185146	**rs2126259**	T	C	7,287	0.817	$5.77 \cdot 10^{-2}$	$2.15 \cdot 10^{-2}$	$7.38 \cdot 10^{-3}$	EX_EUR	RP11-10A14.4	1	rs2126259	$1.33 \cdot 10^{5}$	$2.4 \cdot 10^{-2}$	$3.3 \cdot 10^{-3}$	$3.3 \cdot 10^{-13}$
5	53272664	**rs4865796**	A	G	7,265	0.648	$2.81 \cdot 10^{-2}$	$1.74 \cdot 10^{-2}$	0.107	OMNI_EUR	ARL15	1	rs4865796	$1.33 \cdot 10^{5}$	$1.5 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$2.16 \cdot 10^{-12}$
3	12390484	**rs17036328**	T	C	7,262	0.152	$3.75 \cdot 10^{-2}$	$2.31 \cdot 10^{-2}$	0.105	OMNI_EUR	PPARG	1	rs17036328	$1.33 \cdot 10^{5}$	$2.1 \cdot 10^{-2}$	$3 \cdot 10^{-3}$	$3.59 \cdot 10^{-12}$
19	33899065	**rs731839**	G	A	7,287	0.664	$1.35 \cdot 10^{-2}$	$1.74 \cdot 10^{-2}$	0.438	EX_EUR	PEPD	1	rs731839	$1.33 \cdot 10^{5}$	$1.5 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$5.13 \cdot 10^{-12}$
4	106071064	rs974801	A	G	7,263	0.386	$7.5 \cdot 10^{-3}$	$1.7 \cdot 10^{-2}$	0.66	OMNI_EUR	TET2	1	rs974801	$1.33 \cdot 10^{5}$	$-1.4 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$3.27 \cdot 10^{-11}$
5	55806751	**rs459193**	G	A	7,287	0.662	$3.72 \cdot 10^{-2}$	$1.74 \cdot 10^{-2}$	$3.28 \cdot 10^{-2}$	EX_EUR	AC022431.2	1	rs459193	$1.33 \cdot 10^{5}$	$1.5 \cdot 10^{-2}$	$2.3 \cdot 10^{-3}$	$1.15 \cdot 10^{-10}$
4	157683685	**rs1425486**	C	T	7,252	0.259	$1.47 \cdot 10^{-2}$	$1.88 \cdot 10^{-2}$	0.434	OMNI_EUR	PDGFC	1	rs1425486	$1.33 \cdot 10^{5}$	$1.4 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$2.84 \cdot 10^{-10}$
1	219652033	**rs2791552**	C	A	7,287	0.677	$4.61 \cdot 10^{-2}$	$1.78 \cdot 10^{-2}$	$9.68 \cdot 10^{-3}$	EX_EUR	LYPLAL1	1	rs2791552	$1.33 \cdot 10^{5}$	$1.3 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$2.57 \cdot 10^{-9}$
1	219750717	**rs4846567**	G	T	7,285	0.283	$1.33 \cdot 10^{-2}$	$1.84 \cdot 10^{-2}$	0.469	EX_EUR	SLC30A10	1	rs4846567	$1.33 \cdot 10^{5}$	$1.3 \cdot 10^{-2}$	$2.3 \cdot 10^{-3}$	$9.61 \cdot 10^{-9}$
3	12159294	**rs160208**	G	A	7,263	0.91	$5.42 \cdot 10^{-2}$	$2.91 \cdot 10^{-2}$	$6.22 \cdot 10^{-2}$	OMNI_EUR	TIMP4	1	rs308971	$1.33 \cdot 10^{5}$	$2.1 \cdot 10^{-2}$	$3.1 \cdot 10^{-3}$	$2.97 \cdot 10^{-11}$
4	157615583	rs1996770	T	C	7,261	0.292	$1.25 \cdot 10^{-2}$	$1.82 \cdot 10^{-2}$	0.493	OMNI_EUR	RP11-171N4.2	1	rs1464454	$1.33 \cdot 10^{5}$	$-1.2 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$5.11 \cdot 10^{-8}$
12	102908297	rs855213	G	A	7,265	0.786	$6.09 \cdot 10^{-2}$	$2.02 \cdot 10^{-2}$	$2.59 \cdot 10^{-3}$	OMNI_EUR	IGF1	0.993	rs860598	$1.33 \cdot 10^{5}$	$-1.5 \cdot 10^{-2}$	$2.7 \cdot 10^{-3}$	$1.46 \cdot 10^{-8}$
4	89740128	rs13133548	G	A	7,287	0.531	$5.92 \cdot 10^{-3}$	$1.67 \cdot 10^{-2}$	0.723	EX_EUR	FAM13A	0.98	rs3822072	$1.33 \cdot 10^{5}$	$-1.2 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$1.8 \cdot 10^{-8}$
2	27783801	**rs4665382**	T	C	7,265	0.298	$2.45 \cdot 10^{-2}$	$1.81 \cdot 10^{-2}$	0.175	OMNI_EUR	ZNF512	0.913	rs2068834	$1.33 \cdot 10^{5}$	$1.4 \cdot 10^{-2}$	$2.3 \cdot 10^{-3}$	$1.24 \cdot 10^{-9}$

Table 21 shows statistics from the MERGE cohort for 18 loci that were shown to be significantly associated with Fasting Insulin in the 2012 Nature Genetics paper by Scott et al [15]. Where a previously reported variant

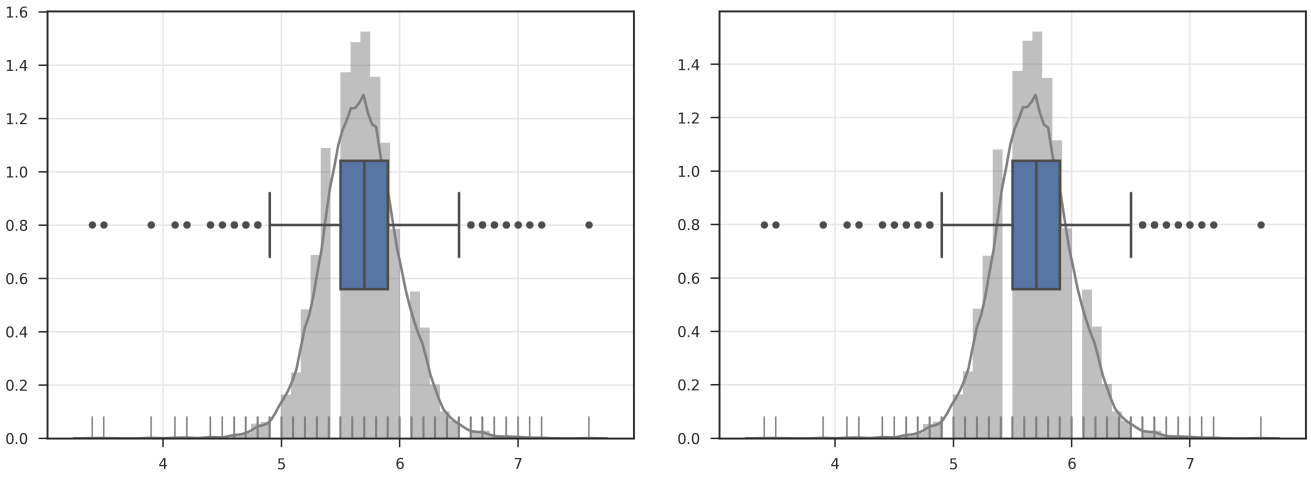
was not genotyped in the study (indicated by $\bar{R^2} < 1$), if available, a tagging variant in LD with the reported variant ($\bar{R^2} >= 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. There are 9 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 15 variants in both studies, 13 exhibit the same direction of effect with the known result (binomial test $p = 0.00369$).

Table 21: Top known loci in MERGE model invn Adjusted Age+BMI (**bold** variants indicate matching direction of effect)

CHR	POS	ID	EA	OA	N	FREQ	EFFECT	STDERR	P	COHORT	$GENE_{CLOSEST}$	R^2	ID_{KNOWN}	N_{KNOWN}	$EFFECT_{KNOWN}$	$STDERR_{KNOWN}$	P_{KNOWN}
2	27730940	**rs1260326**	C	T	7,286	0.372	$3.82 \cdot 10^{-2}$	$1.71 \cdot 10^{-2}$	$2.51 \cdot 10^{-2}$	EX_EUR	GCKR	1	rs1260326	$1.33 \cdot 10^{5}$	$2.1 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$2.74 \cdot 10^{-22}$
2	227099180	**rs2943645**	T	C	7,261	0.379	0.108	$1.71 \cdot 10^{-2}$	$3.37 \cdot 10^{-10}$	OMNI_EUR	IRS1	1	rs2943645	$1.33 \cdot 10^{5}$	$1.9 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$2.26 \cdot 10^{-19}$
2	165513091	**rs10195252**	T	C	7,287	0.668	$2.85 \cdot 10^{-2}$	$1.76 \cdot 10^{-2}$	0.104	EX_EUR	COBLL1	1	rs10195252	$1.33 \cdot 10^{5}$	$1.7 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$1.26 \cdot 10^{-16}$
2	227020653	**rs7578326**	A	G	7,286	0.646	$9.13 \cdot 10^{-2}$	$1.73 \cdot 10^{-2}$	$1.35 \cdot 10^{-7}$	EX_EUR	NYAP2	1	rs7578326	$1.33 \cdot 10^{5}$	$1.8 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$2.25 \cdot 10^{-16}$
8	9185146	**rs2126259**	T	C	7,287	0.183	$4.46 \cdot 10^{-2}$	$2.15 \cdot 10^{-2}$	$3.82 \cdot 10^{-2}$	EX_EUR	RP11-10A14.4	1	rs2126259	$1.33 \cdot 10^{5}$	$2.4 \cdot 10^{-2}$	$3.3 \cdot 10^{-3}$	$3.3 \cdot 10^{-13}$
5	53272664	**rs4865796**	A	G	7,266	0.352	$3.89 \cdot 10^{-2}$	$1.74 \cdot 10^{-2}$	$2.55 \cdot 10^{-2}$	OMNI_EUR	ARL15	1	rs4865796	$1.33 \cdot 10^{5}$	$1.5 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$2.16 \cdot 10^{-12}$
3	12390484	**rs17036328**	T	C	7,263	0.848	$8.4 \cdot 10^{-2}$	$2.31 \cdot 10^{-2}$	$2.76 \cdot 10^{-4}$	OMNI_EUR	PPARG	1	rs17036328	$1.33 \cdot 10^{5}$	$2.1 \cdot 10^{-2}$	$3 \cdot 10^{-3}$	$3.59 \cdot 10^{-12}$
19	33899065	**rs731839**	G	A	7,287	0.336	$2.86 \cdot 10^{-2}$	$1.74 \cdot 10^{-2}$	0.101	EX_EUR	PEPD	1	rs731839	$1.33 \cdot 10^{5}$	$1.5 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$5.13 \cdot 10^{-12}$
4	106071064	**rs974801**	G	A	7,264	0.614	$2.18 \cdot 10^{-2}$	$1.7 \cdot 10^{-2}$	0.2	OMNI_EUR	TET2	1	rs974801	$1.33 \cdot 10^{5}$	$1.4 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$3.27 \cdot 10^{-11}$
5	55806751	**rs459193**	G	A	7,287	0.338	$3.61 \cdot 10^{-2}$	$1.74 \cdot 10^{-2}$	$3.83 \cdot 10^{-2}$	EX_EUR	AC022431.2	1	rs459193	$1.33 \cdot 10^{5}$	$1.5 \cdot 10^{-2}$	$2.3 \cdot 10^{-3}$	$1.15 \cdot 10^{-10}$
4	157683685	**rs1425486**	C	T	7,253	0.741	$3.09 \cdot 10^{-2}$	$1.87 \cdot 10^{-2}$	$9.95 \cdot 10^{-2}$	OMNI_EUR	PDGFC	1	rs1425486	$1.33 \cdot 10^{5}$	$1.4 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$2.84 \cdot 10^{-10}$
1	219652033	**rs2791552**	C	A	7,287	0.322	$4.18 \cdot 10^{-2}$	$1.78 \cdot 10^{-2}$	$1.9 \cdot 10^{-2}$	EX_EUR	LYPLAL1	1	rs2791552	$1.33 \cdot 10^{5}$	$1.3 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$2.57 \cdot 10^{-9}$
1	219750717	rs4846567	T	G	7,285	0.718	$1.19 \cdot 10^{-2}$	$1.84 \cdot 10^{-2}$	0.518	EX_EUR	SLC30A10	1	rs4846567	$1.33 \cdot 10^{5}$	$-1.3 \cdot 10^{-2}$	$2.3 \cdot 10^{-3}$	$9.61 \cdot 10^{-9}$
3	12159294	**rs160208**	G	A	7,264	$8.95 \cdot 10^{-2}$	$5.3 \cdot 10^{-2}$	$2.91 \cdot 10^{-2}$	$6.85 \cdot 10^{-2}$	OMNI_EUR	TIMP4	1	rs308971	$1.33 \cdot 10^{5}$	$2.1 \cdot 10^{-2}$	$3.1 \cdot 10^{-3}$	$2.97 \cdot 10^{-11}$
4	157615583	rs1996770	T	C	7,262	0.708	$2.9 \cdot 10^{-2}$	$1.82 \cdot 10^{-2}$	0.111	OMNI_EUR	RP11-171N4.2	1	rs1464454	$1.33 \cdot 10^{5}$	$-1.2 \cdot 10^{-2}$	$2.2 \cdot 10^{-3}$	$5.11 \cdot 10^{-8}$
12	102908297	rs855213	G	A	7,266	0.214	$6.19 \cdot 10^{-2}$	$2.02 \cdot 10^{-2}$	$2.19 \cdot 10^{-3}$	OMNI_EUR	IGF1	0.993	rs860598	$1.33 \cdot 10^{5}$	$-1.5 \cdot 10^{-2}$	$2.7 \cdot 10^{-3}$	$1.46 \cdot 10^{-8}$
4	89740128	**rs13133548**	A	G	7,287	0.47	$2.52 \cdot 10^{-2}$	$1.67 \cdot 10^{-2}$	0.131	EX_EUR	FAM13A	0.98	rs3822072	$1.33 \cdot 10^{5}$	$1.2 \cdot 10^{-2}$	$2.1 \cdot 10^{-3}$	$1.8 \cdot 10^{-8}$
2	27783801	**rs4665382**	T	C	7,266	0.701	$3.42 \cdot 10^{-2}$	$1.81 \cdot 10^{-2}$	$5.83 \cdot 10^{-2}$	OMNI_EUR	ZNF512	0.913	rs2068834	$1.33 \cdot 10^{5}$	$1.4 \cdot 10^{-2}$	$2.3 \cdot 10^{-3}$	$1.24 \cdot 10^{-9}$

6 Hemoglobin A1c (HBA1C_PCT)

6.1 Summary



(a) EX_EUR (b) OMNI_EUR

Figure 17: Distribution of HBA1C_PCT in cohort-level analyses

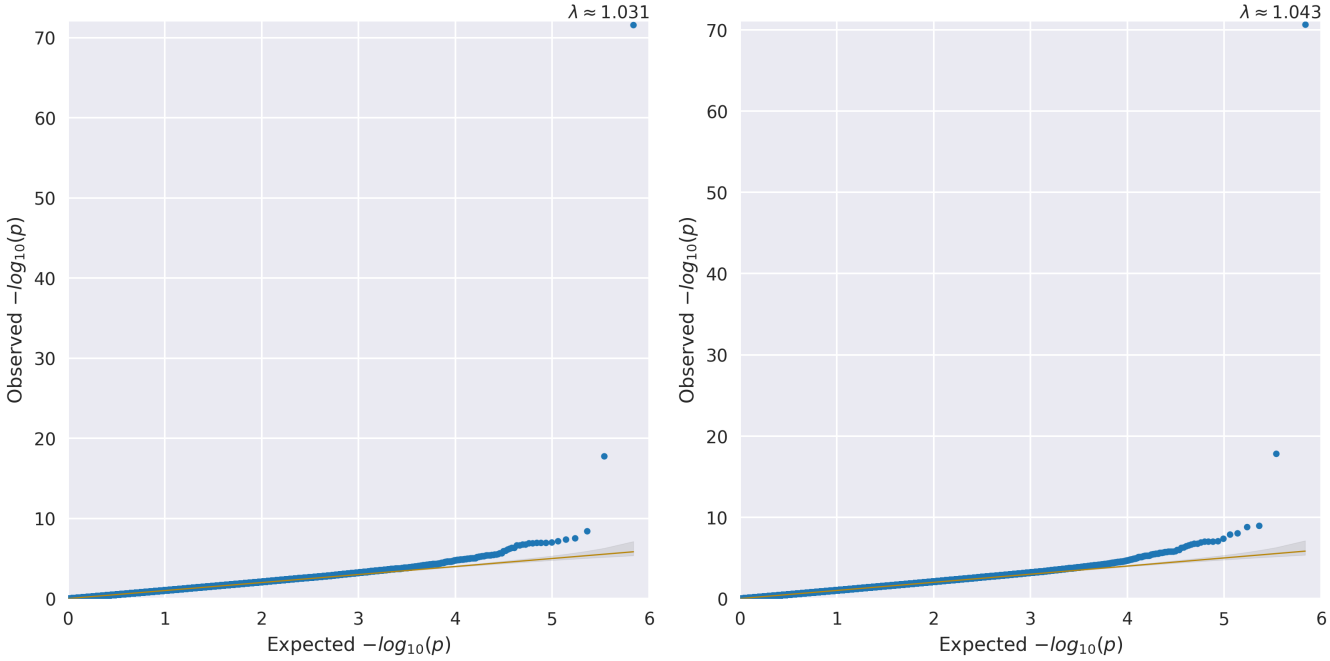
Table 22: Summary of samples removed from Hemoglobin A1c analysis by cohort and model

Cohort	Array	Ancestry	Trans	Covars	Total	-SampleQc	-missObs	-Kinship	-PcOutlier
EX_EUR	EX	EUR	invn	Age	10071	36	1435	1308	2
			invn	Age+BMI	10071	36	1438	1310	2
OMNI_EUR	OMNI	EUR	invn	Age+BMI	10048	69	1428	1294	0
			invn	Age	10048	69	1425	1292	1

Table 23: Summary of samples remaining for Hemoglobin A1c analysis by cohort and model

Cohort	Array	Ancestry	Trans	Covars	PCs	N	Male	Female	Max	Min	μ	$\tilde{x}$	σ
EX_EUR	EX	EUR	invn	Age	3	7297	7297	0	7.6	3.4	5.67	5.7	0.335
			invn	Age+BMI	3	7291	7291	0	7.6	3.4	5.67	5.7	0.335
OMNI_EUR	OMNI	EUR	invn	Age+BMI	3	7267	7267	0	7.6	3.4	5.671	5.7	0.334
			invn	Age	3	7271	7271	0	7.6	3.4	5.671	5.7	0.334

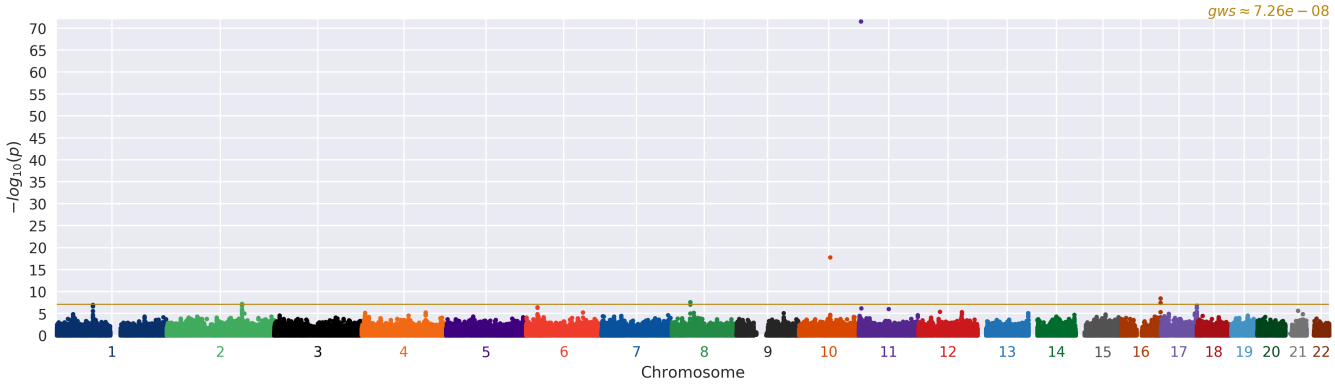
6.2 Calibration



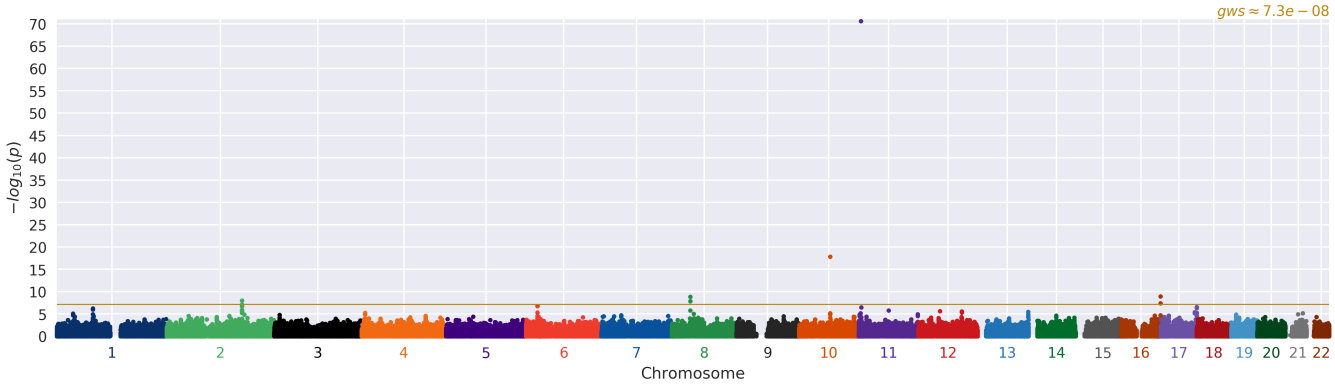
(a) invn Adjusted Age

(b) invn Adjusted Age+BMI

Figure 18: QQ plots for HBA1C_PCT in the MERGE analysis



(a) invn Adjusted Age



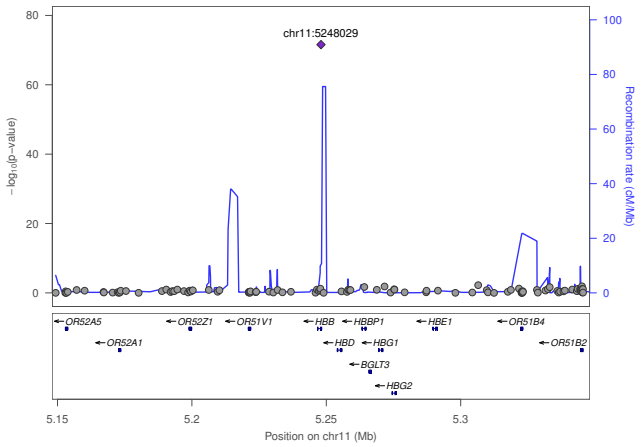
(b) invn Adjusted Age+BMI

Figure 19: Manhattan plots for HBA1C_PCT in the MERGE analysis

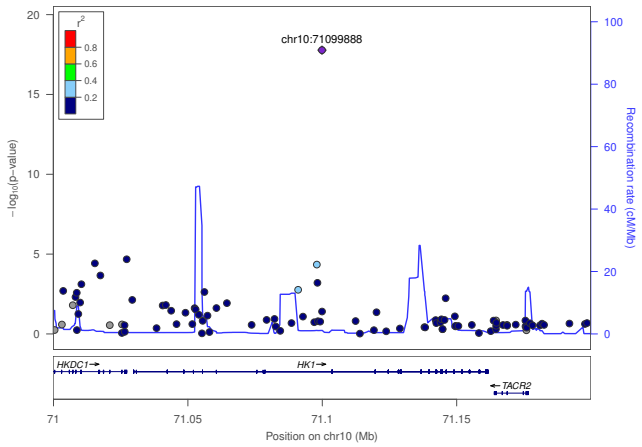
6.3 Top associations

Table 24: Top variants in the MERGE invn Adjusted Age model (**bold** variants indicate previously identified associations)

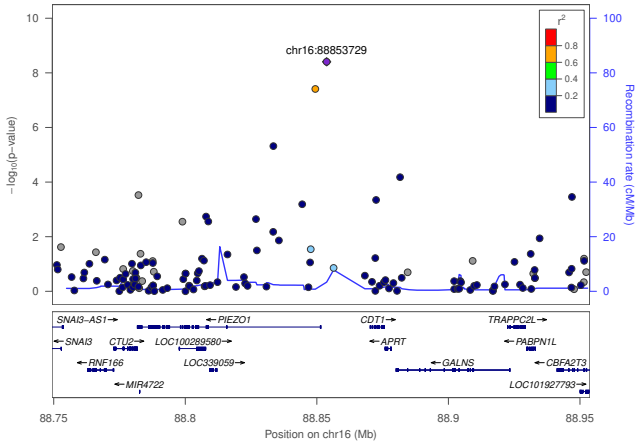
CHR	POS	ID	EA	OA	$GENE_{CLOSEST}$	COHORT	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
11	5248029	rs1135071	A	C	HBB	EX_EUR	7,296	7,296	0	64	$4.39 \cdot 10^{-3}$	2.229	0.123	$2.64 \cdot 10^{-72}$
10	71099888	**rs10159477**	G	A	**HK1**	OMNI_EUR	7,270	7,270	0	1,074	$7.39 \cdot 10^{-2}$	0.276	$3.14 \cdot 10^{-2}$	$1.68 \cdot 10^{-18}$
16	88853729	rs837763	T	C	PIEZO1	EX_EUR	7,296	7,296	0	6,762	0.537	$9.71 \cdot 10^{-2}$	$1.65 \cdot 10^{-2}$	$3.93 \cdot 10^{-9}$
8	41630405	**rs4737009**	A	G	**ANK1**	EX_EUR	7,253	7,253	0	3,812	0.263	0.104	$1.87 \cdot 10^{-2}$	$2.88 \cdot 10^{-8}$
2	169757541	**rs573225**	A	G	**G6PC2**	OMNI_EUR	7,266	7,266	0	4,150	0.714	$9.84 \cdot 10^{-2}$	$1.82 \cdot 10^{-2}$	$6.6 \cdot 10^{-8}$
2	169779205	rs4148804	T	C	**ABCB11**	OMNI_EUR	7,271	7,271	0	744	$5.12 \cdot 10^{-2}$	0.201	$3.77 \cdot 10^{-2}$	$1.05 \cdot 10^{-7}$
1	82056068	rs1359308	A	G	ADGRL2	OMNI_EUR	7,270	7,270	0	5,888	0.405	$8.96 \cdot 10^{-2}$	$1.69 \cdot 10^{-2}$	$1.17 \cdot 10^{-7}$
17	80685426	**rs1046875**	A	G	**FN3KRP**	OMNI_EUR	7,270	7,270	0	3,608	0.752	$9.93 \cdot 10^{-2}$	$1.9 \cdot 10^{-2}$	$1.73 \cdot 10^{-7}$
2	169752190	rs16856115	A	G	**SPC25**	OMNI_EUR	7,270	7,270	0	767	$5.28 \cdot 10^{-2}$	0.194	$3.71 \cdot 10^{-2}$	$1.83 \cdot 10^{-7}$
6	26091179	rs1799945	C	G	**HFE**	EX_EUR	7,297	7,297	0	1,461	0.1	0.139	$2.75 \cdot 10^{-2}$	$4.3 \cdot 10^{-7}$
6	26107463	rs198846	G	A	HIST1H1T	EX_EUR	7,297	7,297	0	1,465	0.9	0.139	$2.74 \cdot 10^{-2}$	$4.47 \cdot 10^{-7}$
11	5652608	rs904376	G	T	TRIM34	OMNI_EUR	7,269	7,269	0	1,020	0.93	0.161	$3.24 \cdot 10^{-2}$	$7.41 \cdot 10^{-7}$
11	67288594	rs2276118	C	T	CABP2	EX_EUR	7,297	7,297	0	6,652	0.544	$8.07 \cdot 10^{-2}$	$1.65 \cdot 10^{-2}$	$1.04 \cdot 10^{-6}$
21	28839569	rs2830960	G	T	ADAMTS5	OMNI_EUR	7,265	7,265	0	1,222	$8.41 \cdot 10^{-2}$	0.141	$2.98 \cdot 10^{-2}$	$2.19 \cdot 10^{-6}$
12	48531571	exm998138	T	C	PFKM	EX_EUR	7,297	7,297	0	146	$1 \cdot 10^{-2}$	0.386	$8.33 \cdot 10^{-2}$	$3.73 \cdot 10^{-6}$
17	80690632	**rs2459703**	C	T	**FN3K**	OMNI_EUR	7,271	7,271	0	5,381	0.63	$7.94 \cdot 10^{-2}$	$1.72 \cdot 10^{-2}$	$3.74 \cdot 10^{-6}$
12	98181636	rs11109212	C	T	TMPO	OMNI_EUR	7,263	7,263	0	4,069	0.28	$8.4 \cdot 10^{-2}$	$1.84 \cdot 10^{-2}$	$4.84 \cdot 10^{-6}$
4	144616366	rs7676614	G	A	FREM3	OMNI_EUR	7,269	7,269	0	4,844	0.333	$7.99 \cdot 10^{-2}$	$1.76 \cdot 10^{-2}$	$5.38 \cdot 10^{-6}$
6	129190200	rs10457510	A	G	LAMA2	OMNI_EUR	7,267	7,267	0	819	$5.64 \cdot 10^{-2}$	0.161	$3.56 \cdot 10^{-2}$	$6.15 \cdot 10^{-6}$
4	8056846	rs7661897	C	T	ABLIM2	OMNI_EUR	7,263	7,263	0	2,671	0.184	$9.56 \cdot 10^{-2}$	$2.12 \cdot 10^{-2}$	$6.64 \cdot 10^{-6}$



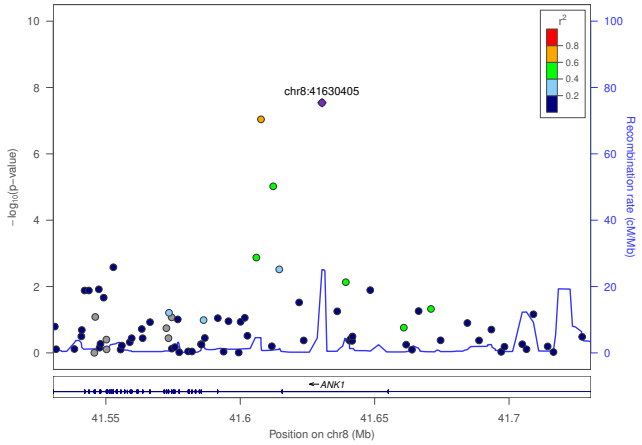
(a) rs1135071 $\pm 100kb$



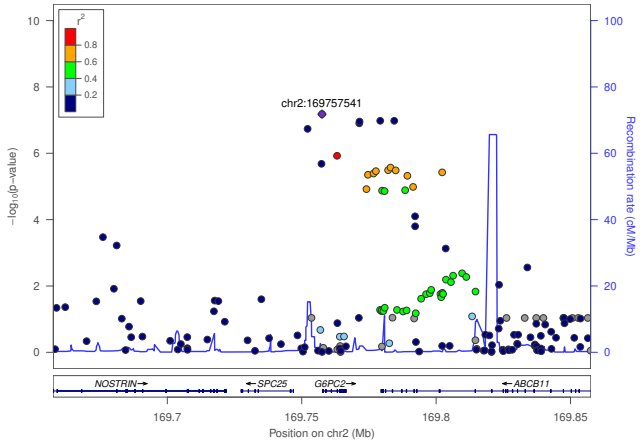
(b) rs10159477 $\pm 100kb$



(c) rs837763 $\pm 100kb$



(d) rs4737009 $\pm 100kb$

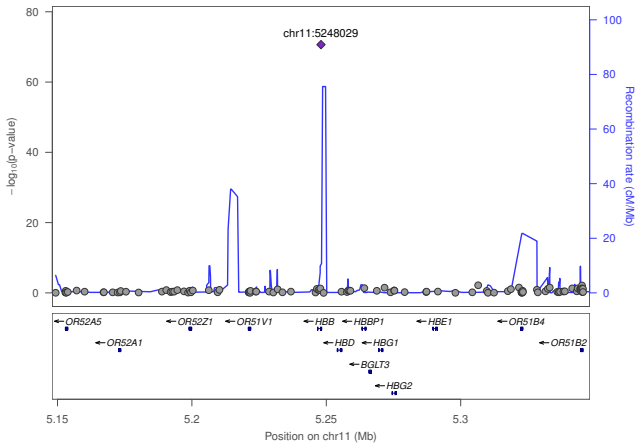


(e) rs573225 $\pm 100kb$

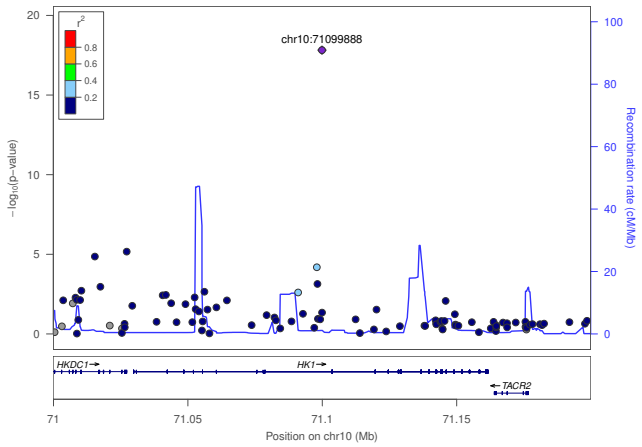
Figure 20: Regional plots for cohort MERGE model invn Adjusted Age

Table 25: Top variants in the MERGE invn Adjusted Age+BMI model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	$GENE_{CLOSEST}$	COHORT	N	MALE	FEMALE	MAC	FREQ	EFFECT	STDERR	P
11	5248029	rs1135071	A	C	HBB	EX_EUR	7,290	7,290	0	64	0.996	2.214	0.123	$2.25 \cdot 10^{-71}$
10	71099888	**rs10159477**	G	A	**HK1**	OMNI_EUR	7,266	7,266	0	1,071	0.926	0.277	$3.15 \cdot 10^{-2}$	$1.51 \cdot 10^{-18}$
16	88853729	rs837763	T	C	PIEZO1	EX_EUR	7,290	7,290	0	6,760	0.464	0.1	$1.65 \cdot 10^{-2}$	$1.11 \cdot 10^{-9}$
8	41630405	**rs4737009**	A	G	**ANK1**	EX_EUR	7,247	7,247	0	3,809	0.737	0.113	$1.87 \cdot 10^{-2}$	$1.44 \cdot 10^{-9}$
2	169757541	**rs573225**	A	G	**G6PC2**	OMNI_EUR	7,262	7,262	0	4,146	0.285	0.105	$1.82 \cdot 10^{-2}$	$9.17 \cdot 10^{-9}$
2	169779205	rs4148804	T	C	**ABCB11**	OMNI_EUR	7,267	7,267	0	742	0.949	0.202	$3.77 \cdot 10^{-2}$	$9.01 \cdot 10^{-8}$
6	26091179	rs1799945	C	G	**HFE**	EX_EUR	7,291	7,291	0	1,460	0.9	0.144	$2.75 \cdot 10^{-2}$	$1.69 \cdot 10^{-7}$
6	26107463	rs198846	G	A	HIST1H1T	EX_EUR	7,291	7,291	0	1,464	0.1	0.143	$2.74 \cdot 10^{-2}$	$1.77 \cdot 10^{-7}$
2	169752190	rs16856115	A	G	**SPC25**	OMNI_EUR	7,266	7,266	0	765	0.947	0.193	$3.72 \cdot 10^{-2}$	$2.1 \cdot 10^{-7}$
17	80685533	**rs1046896**	T	C	**FN3KRP**	EX_EUR	7,291	7,291	0	3,606	0.753	$9.75 \cdot 10^{-2}$	$1.9 \cdot 10^{-2}$	$2.78 \cdot 10^{-7}$
11	5652608	rs904376	G	T	TRIM34	OMNI_EUR	7,265	7,265	0	1,020	$7.02 \cdot 10^{-2}$	0.165	$3.24 \cdot 10^{-2}$	$3.5 \cdot 10^{-7}$
1	82056068	rs1359308	A	G	ADGRL2	OMNI_EUR	7,266	7,266	0	5,884	0.595	$8.49 \cdot 10^{-2}$	$1.69 \cdot 10^{-2}$	$5.31 \cdot 10^{-7}$
11	67288594	rs2276118	C	T	CABP2	EX_EUR	7,291	7,291	0	6,649	0.456	$7.94 \cdot 10^{-2}$	$1.65 \cdot 10^{-2}$	$1.55 \cdot 10^{-6}$
12	48531571	exm998138	T	C	PFKM	EX_EUR	7,291	7,291	0	146	0.99	0.393	$8.33 \cdot 10^{-2}$	$2.41 \cdot 10^{-6}$
12	98181636	rs11109212	C	T	TMPO	OMNI_EUR	7,259	7,259	0	4,066	0.72	$8.58 \cdot 10^{-2}$	$1.84 \cdot 10^{-2}$	$2.98 \cdot 10^{-6}$
13	114930229	rs389862	A	C	RP11-569D9	OMNI_EUR	7,267	7,267	0	1,265	0.913	0.136	$2.92 \cdot 10^{-2}$	$3.24 \cdot 10^{-6}$
17	76126204	rs429216	G	T	TMC6	OMNI_EUR	7,265	7,265	0	2,219	0.847	0.106	$2.29 \cdot 10^{-2}$	$3.73 \cdot 10^{-6}$
6	26125342	rs129128	T	C	HIST1H2AC	OMNI_EUR	7,255	7,255	0	1,129	$7.78 \cdot 10^{-2}$	0.142	$3.09 \cdot 10^{-2}$	$4.56 \cdot 10^{-6}$
17	80887206	**rs729124**	G	A	**TBCD**	OMNI_EUR	7,266	7,266	0	4,365	0.7	$8.14 \cdot 10^{-2}$	$1.79 \cdot 10^{-2}$	$5.3 \cdot 10^{-6}$
4	8056846	rs7661897	C	T	ABLIM2	OMNI_EUR	7,259	7,259	0	2,671	0.816	$9.64 \cdot 10^{-2}$	$2.12 \cdot 10^{-2}$	$5.61 \cdot 10^{-6}$



(a) rs1135071 $\pm 100kb$



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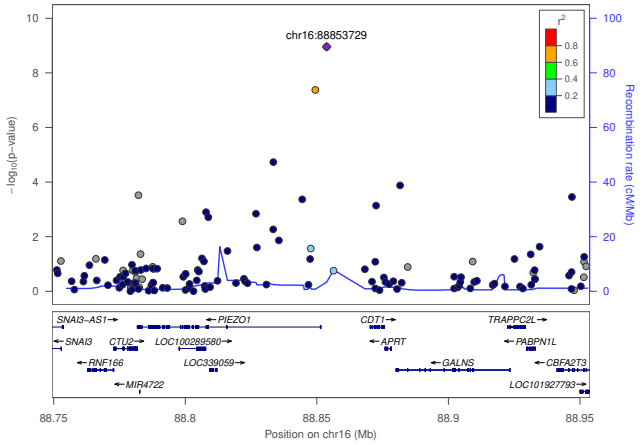
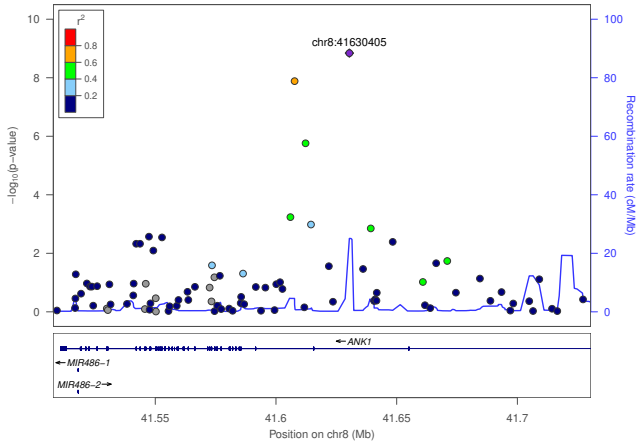
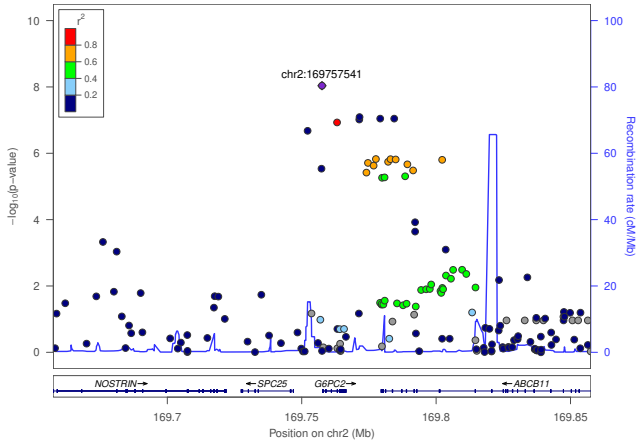


(c) rs837763 $\pm 100kb$



(d) rs4737009 $\pm 100kb$



(e) rs573225 $\pm 100kb$

Figure 21: Regional plots for cohort MERGE model invn Adjusted Age+BMI

6.4 Previously identified risk loci

Table 26 shows statistics from the MERGE cohort for 19 loci that were shown to be significantly associated with Hemoglobin A1c in the 2010 Diabetes paper by Soranzo et al [16]. 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 ($\bar{R}^2 >= 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. There are 17 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 18 variants in both studies, 17 exhibit the same direction of effect with the known result (binomial test $p = 7.25e-05$).

Table 26: Top known loci in MERGE model invn Adjusted Age (**bold** variants indicate matching direction of effect)

CHR	POS	ID	EA	OA	N	FREQ	EFFECT	STDERR	P	COHORT	$GENE_{CLOSEST}$	R^2	ID_{KNOWN}	N_{KNOWN}	$EFFECT_{KNOWN}$	$STDERR_{KNOWN}$	P_{KNOWN}
17	80685533	**rs1046896**	T	C	7,294	0.753	$9.37 \cdot 10^{-2}$	$1.9 \cdot 10^{-2}$	$8.17 \cdot 10^{-7}$	EX_EUR	FN3KRP	1	rs1046896	46,368	$3.46 \cdot 10^{-2}$	$3.2 \cdot 10^{-3}$	$1.58 \cdot 10^{-26}$
10	71099888	**rs10159477**	G	A	7,270	0.926	0.273	$3.14 \cdot 10^{-2}$	$4.75 \cdot 10^{-18}$	OMNI_EUR	HK1	1	rs10159477	46,368	$5.86 \cdot 10^{-2}$	$5.6 \cdot 10^{-3}$	$3.19 \cdot 10^{-25}$
7	44229068	**rs1799884**	T	C	7,294	0.9	$6.38 \cdot 10^{-2}$	$2.75 \cdot 10^{-2}$	$2.04 \cdot 10^{-2}$	EX_EUR	GCK	1	rs1799884	46,368	$3.8 \cdot 10^{-2}$	$4.1 \cdot 10^{-3}$	$1.45 \cdot 10^{-20}$
6	26093141	**rs1800562**	G	A	7,294	0.967	0.166	$4.63 \cdot 10^{-2}$	$3.38 \cdot 10^{-4}$	EX_EUR	HFE	1	rs1800562	46,368	$6.36 \cdot 10^{-2}$	$6.9 \cdot 10^{-3}$	$2.59 \cdot 10^{-20}$
17	80791469	**rs9906115**	A	G	7,271	0.788	$6.55 \cdot 10^{-2}$	$2 \cdot 10^{-2}$	$1.08 \cdot 10^{-3}$	OMNI_EUR	ZNF750	1	rs9906115	46,368	$3.54 \cdot 10^{-2}$	$3.8 \cdot 10^{-3}$	$2.65 \cdot 10^{-20}$
17	80873067	**rs9912684**	T	C	7,266	0.777	$8.29 \cdot 10^{-2}$	$1.97 \cdot 10^{-2}$	$2.68 \cdot 10^{-5}$	OMNI_EUR	TBCD	1	rs9912684	46,368	$3.48 \cdot 10^{-2}$	$3.9 \cdot 10^{-3}$	$3.07 \cdot 10^{-19}$
7	44235668	**rs4607517**	A	G	7,294	0.9	$6.38 \cdot 10^{-2}$	$2.75 \cdot 10^{-2}$	$2.04 \cdot 10^{-2}$	EX_EUR	YKT6	1	rs4607517	46,368	$4.05 \cdot 10^{-2}$	$4.6 \cdot 10^{-3}$	$6.3 \cdot 10^{-19}$
2	169791438	**rs552976**	G	A	7,294	0.321	$7.7 \cdot 10^{-2}$	$1.76 \cdot 10^{-2}$	$1.28 \cdot 10^{-5}$	EX_EUR	ABCB11	1	rs552976	46,368	$2.9 \cdot 10^{-2}$	$3.4 \cdot 10^{-3}$	$8.16 \cdot 10^{-18}$
2	169763148	**rs560887**	C	T	7,294	0.279	$8.96 \cdot 10^{-2}$	$1.83 \cdot 10^{-2}$	$1.07 \cdot 10^{-6}$	EX_EUR	G6PC2	1	rs560887	46,368	$3.18 \cdot 10^{-2}$	$3.7 \cdot 10^{-3}$	$1.04 \cdot 10^{-17}$
22	37462936	**rs855791**	A	G	7,294	0.349	$4.86 \cdot 10^{-2}$	$1.72 \cdot 10^{-2}$	$4.82 \cdot 10^{-3}$	EX_EUR	TMPRSS6	1	rs855791	46,368	$2.71 \cdot 10^{-2}$	$3.6 \cdot 10^{-3}$	$2.74 \cdot 10^{-14}$
6	25842951	**rs1408272**	T	G	7,294	0.968	0.193	$4.66 \cdot 10^{-2}$	$3.47 \cdot 10^{-5}$	EX_EUR	SLC17A3	1	rs1408272	46,368	$6.05 \cdot 10^{-2}$	$8.4 \cdot 10^{-3}$	$6.29 \cdot 10^{-13}$
6	25821770	**rs17342717**	C	T	7,293	0.925	0.109	$3.17 \cdot 10^{-2}$	$5.96 \cdot 10^{-4}$	EX_EUR	SLC17A1	1	rs17342717	46,368	$4.49 \cdot 10^{-2}$	$6.3 \cdot 10^{-3}$	$1.26 \cdot 10^{-12}$
8	41630405	**rs4737009**	A	G	7,250	0.737	0.106	$1.87 \cdot 10^{-2}$	$1.82 \cdot 10^{-8}$	EX_EUR	ANK1	1	rs4737009	46,368	$2.69 \cdot 10^{-2}$	$3.9 \cdot 10^{-3}$	$6.12 \cdot 10^{-12}$
11	92673828	rs1387153	C	T	7,294	0.635	$1.27 \cdot 10^{-3}$	$1.72 \cdot 10^{-2}$	0.941	EX_EUR	MTNR1B	1	rs1387153	46,368	$-2.58 \cdot 10^{-2}$	$3.9 \cdot 10^{-3}$	$3.96 \cdot 10^{-11}$
2	169750483	**rs477224**	C	T	7,262	0.172	$9.76 \cdot 10^{-4}$	$2.17 \cdot 10^{-2}$	0.964	OMNI_EUR	SPC25	1	rs477224	46,368	$2.36 \cdot 10^{-2}$	$3.7 \cdot 10^{-3}$	$2.05 \cdot 10^{-10}$
13	113331868	**rs7998202**	G	A	7,293	0.871	$5.81 \cdot 10^{-2}$	$2.47 \cdot 10^{-2}$	$1.9 \cdot 10^{-2}$	EX_EUR	ATP11A	1	rs7998202	46,368	$3.07 \cdot 10^{-2}$	$5.3 \cdot 10^{-3}$	$5.24 \cdot 10^{-9}$
1	158618455	**rs2246434**	A	G	7,269	0.669	$4.76 \cdot 10^{-2}$	$1.77 \cdot 10^{-2}$	$7.16 \cdot 10^{-3}$	OMNI_EUR	SPTA1	1	rs2246434	46,368	$2.27 \cdot 10^{-2}$	$3.9 \cdot 10^{-3}$	$6.04 \cdot 10^{-9}$
17	80908501	**rs12949939**	C	T	7,269	0.642	$5.76 \cdot 10^{-2}$	$1.71 \cdot 10^{-2}$	$7.77 \cdot 10^{-4}$	OMNI_EUR	B3GNTL1	1	rs12949939	46,368	$2.03 \cdot 10^{-2}$	$3.7 \cdot 10^{-3}$	$3.19 \cdot 10^{-8}$
17	80690632	rs2459703	C	T	7,271	0.37	$7.91 \cdot 10^{-2}$	$1.72 \cdot 10^{-2}$	$4.06 \cdot 10^{-6}$	OMNI_EUR	FN3K	0.993	rs3848403	46,368	$-3.84 \cdot 10^{-2}$	$5.7 \cdot 10^{-3}$	$1.88 \cdot 10^{-11}$

Table 27 shows statistics from the MERGE cohort for 19 loci that were shown to be significantly associated with Hemoglobin A1c in the 2010 Diabetes paper by Soranzo et al [16]. 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 ($\bar{R}^2 >= 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. There are 17 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 18 variants in both studies, 18 exhibit the same direction of effect with the known result (binomial test $p = 3.81e-06$).

Table 27: Top known loci in MERGE model invn Adjusted Age+BMI (**bold** variants indicate matching direction of effect)

CHR	POS	ID	EA	OA	N	FREQ	EFFECT	STDERR	P	COHORT	$GENE_{CLOSEST}$	R^2	ID_{KNOWN}	N_{KNOWN}	$EFFECT_{KNOWN}$	$STDERR_{KNOWN}$	P_{KNOWN}
17	80685533	**rs1046896**	T	C	7,294	0.247	$9.41 \cdot 10^{-2}$	$1.9 \cdot 10^{-2}$	$7.31 \cdot 10^{-7}$	EX_EUR	FN3KRP	1	rs1046896	46,368	$3.46 \cdot 10^{-2}$	$3.2 \cdot 10^{-3}$	$1.58 \cdot 10^{-26}$
10	71099888	**rs10159477**	G	A	7,269	$7.37 \cdot 10^{-2}$	0.277	$3.15 \cdot 10^{-2}$	$1.73 \cdot 10^{-18}$	OMNI_EUR	HK1	1	rs10159477	46,368	$5.86 \cdot 10^{-2}$	$5.6 \cdot 10^{-3}$	$3.19 \cdot 10^{-25}$
7	44229068	**rs1799884**	T	C	7,294	$9.99 \cdot 10^{-2}$	$6.62 \cdot 10^{-2}$	$2.75 \cdot 10^{-2}$	$1.61 \cdot 10^{-2}$	EX_EUR	GCK	1	rs1799884	46,368	$3.8 \cdot 10^{-2}$	$4.1 \cdot 10^{-3}$	$1.45 \cdot 10^{-20}$
6	26093141	**rs1800562**	G	A	7,294	$3.28 \cdot 10^{-2}$	0.167	$4.63 \cdot 10^{-2}$	$3.03 \cdot 10^{-4}$	EX_EUR	HFE	1	rs1800562	46,368	$6.36 \cdot 10^{-2}$	$6.9 \cdot 10^{-3}$	$2.59 \cdot 10^{-20}$
17	80791469	**rs9906115**	A	G	7,270	0.213	$6.61 \cdot 10^{-2}$	$2 \cdot 10^{-2}$	$9.7 \cdot 10^{-4}$	OMNI_EUR	ZNF750	1	rs9906115	46,368	$3.54 \cdot 10^{-2}$	$3.8 \cdot 10^{-3}$	$2.65 \cdot 10^{-20}$
17	80873067	**rs9912684**	T	C	7,265	0.223	$8.27 \cdot 10^{-2}$	$1.97 \cdot 10^{-2}$	$2.79 \cdot 10^{-5}$	OMNI_EUR	TBCD	1	rs9912684	46,368	$3.48 \cdot 10^{-2}$	$3.9 \cdot 10^{-3}$	$3.07 \cdot 10^{-19}$
7	44235668	**rs4607517**	A	G	7,294	$9.99 \cdot 10^{-2}$	$6.62 \cdot 10^{-2}$	$2.75 \cdot 10^{-2}$	$1.61 \cdot 10^{-2}$	EX_EUR	YKT6	1	rs4607517	46,368	$4.05 \cdot 10^{-2}$	$4.6 \cdot 10^{-3}$	$6.3 \cdot 10^{-19}$
2	169791438	**rs552976**	G	A	7,294	0.679	$8.12 \cdot 10^{-2}$	$1.76 \cdot 10^{-2}$	$4.25 \cdot 10^{-6}$	EX_EUR	ABCB11	1	rs552976	46,368	$2.9 \cdot 10^{-2}$	$3.4 \cdot 10^{-3}$	$8.16 \cdot 10^{-18}$
2	169763148	**rs560887**	C	T	7,294	0.721	$9.7 \cdot 10^{-2}$	$1.83 \cdot 10^{-2}$	$1.29 \cdot 10^{-7}$	EX_EUR	G6PC2	1	rs560887	46,368	$3.18 \cdot 10^{-2}$	$3.7 \cdot 10^{-3}$	$1.04 \cdot 10^{-17}$
22	37462936	**rs855791**	A	G	7,294	0.651	$5.43 \cdot 10^{-2}$	$1.72 \cdot 10^{-2}$	$1.66 \cdot 10^{-3}$	EX_EUR	TMPRSS6	1	rs855791	46,368	$2.71 \cdot 10^{-2}$	$3.6 \cdot 10^{-3}$	$2.74 \cdot 10^{-14}$
6	25842951	**rs1408272**	T	G	7,294	$3.24 \cdot 10^{-2}$	0.194	$4.66 \cdot 10^{-2}$	$3 \cdot 10^{-5}$	EX_EUR	SLC17A3	1	rs1408272	46,368	$6.05 \cdot 10^{-2}$	$8.4 \cdot 10^{-3}$	$6.29 \cdot 10^{-13}$
6	25821770	**rs17342717**	C	T	7,293	$7.47 \cdot 10^{-2}$	0.1	$3.17 \cdot 10^{-2}$	$1.56 \cdot 10^{-3}$	EX_EUR	SLC17A1	1	rs17342717	46,368	$4.49 \cdot 10^{-2}$	$6.3 \cdot 10^{-3}$	$1.26 \cdot 10^{-12}$
8	41630405	**rs4737009**	A	G	7,250	0.263	0.112	$1.87 \cdot 10^{-2}$	$1.97 \cdot 10^{-9}$	EX_EUR	ANK1	1	rs4737009	46,368	$2.69 \cdot 10^{-2}$	$3.9 \cdot 10^{-3}$	$6.12 \cdot 10^{-12}$
11	92673828	**rs1387153**	T	C	7,294	0.365	$3.76 \cdot 10^{-3}$	$1.72 \cdot 10^{-2}$	0.827	EX_EUR	MTNR1B	1	rs1387153	46,368	$2.58 \cdot 10^{-2}$	$3.9 \cdot 10^{-3}$	$3.96 \cdot 10^{-11}$
2	169750483	**rs477224**	C	T	7,261	0.828	$2.11 \cdot 10^{-3}$	$2.17 \cdot 10^{-2}$	0.922	OMNI_EUR	SPC25	1	rs477224	46,368	$2.36 \cdot 10^{-2}$	$3.7 \cdot 10^{-3}$	$2.05 \cdot 10^{-10}$
13	113331868	**rs7998202**	G	A	7,293	0.129	$5.92 \cdot 10^{-2}$	$2.47 \cdot 10^{-2}$	$1.68 \cdot 10^{-2}$	EX_EUR	ATP11A	1	rs7998202	46,368	$3.07 \cdot 10^{-2}$	$5.3 \cdot 10^{-3}$	$5.24 \cdot 10^{-9}$
1	158618455	**rs2246434**	A	G	7,268	0.331	$4.91 \cdot 10^{-2}$	$1.77 \cdot 10^{-2}$	$5.5 \cdot 10^{-3}$	OMNI_EUR	SPTA1	1	rs2246434	46,368	$2.27 \cdot 10^{-2}$	$3.9 \cdot 10^{-3}$	$6.04 \cdot 10^{-9}$
17	80908501	**rs12949939**	C	T	7,268	0.358	$5.86 \cdot 10^{-2}$	$1.71 \cdot 10^{-2}$	$6.39 \cdot 10^{-4}$	OMNI_EUR	B3GNTL1	1	rs12949939	46,368	$2.03 \cdot 10^{-2}$	$3.7 \cdot 10^{-3}$	$3.19 \cdot 10^{-8}$
17	80690632	rs2459703	C	T	7,270	0.63	$7.85 \cdot 10^{-2}$	$1.72 \cdot 10^{-2}$	$4.79 \cdot 10^{-6}$	OMNI_EUR	FN3K	0.993	rs3848403	46,368	$-3.84 \cdot 10^{-2}$	$5.7 \cdot 10^{-3}$	$1.88 \cdot 10^{-11}$

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