

AMP-DCC Data Analysis Report

BioMe

Phase 1

07/10/2019 (15:44)

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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, ILL, and AFFY. 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	BioMe_EXOMECHIP	bfile	N/A
ILL	BioMe_ILLUMINA	bfile	N/A
AFFY	BioMe_AFFY	bfile	N/A

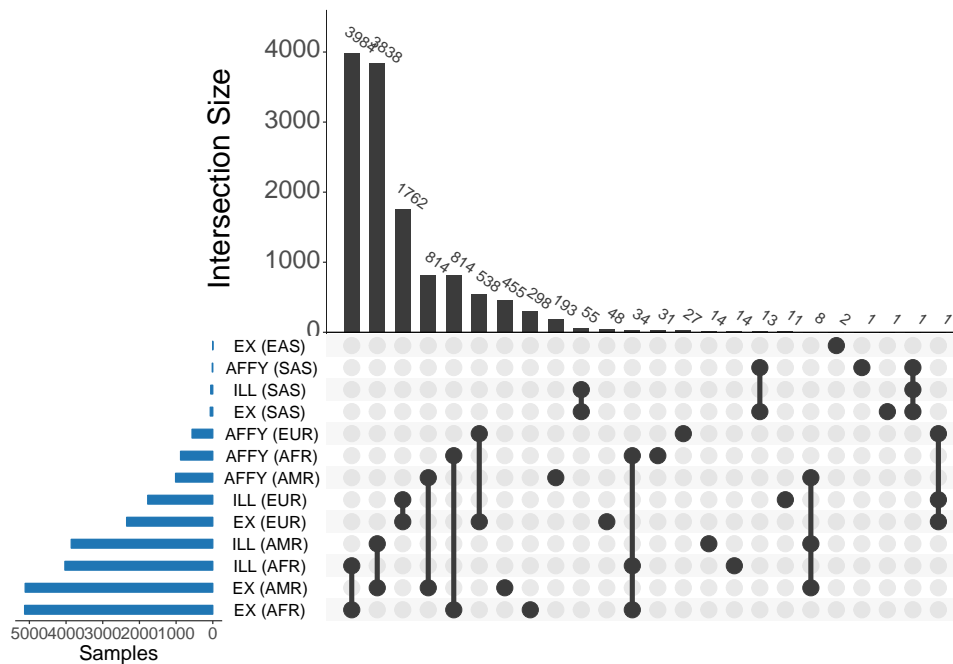


Figure 1: Samples remaining for analysis after quality control

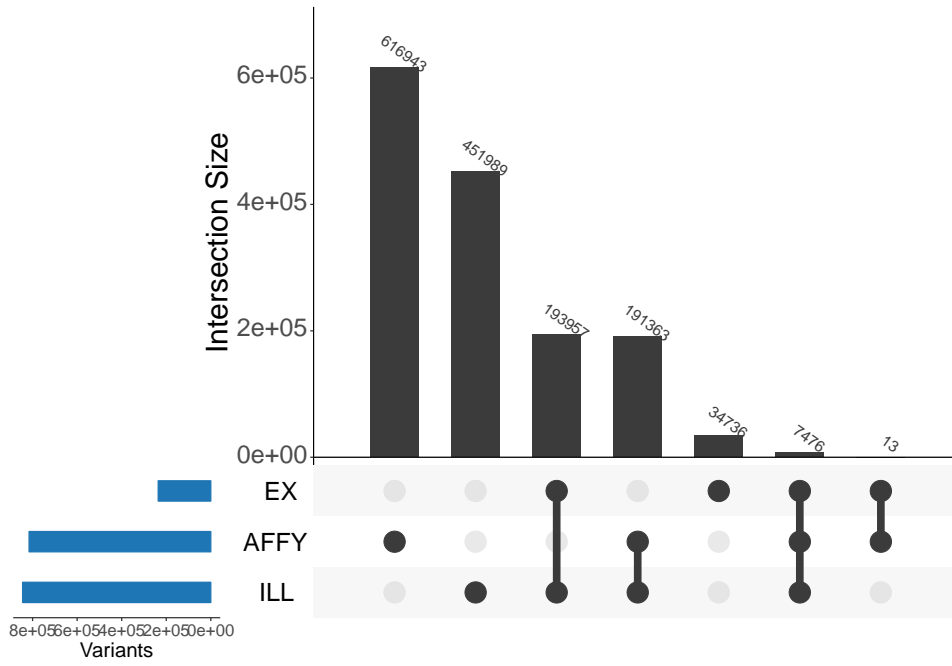


Figure 2: Variants remaining for analysis after quality control

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
EX_AFR	EX	AFR	NO
EX_AMR	EX	AMR	NO
ILL_EUR	ILL	EUR	NO
ILL_AFR	ILL	AFR	NO
ILL_AMR	ILL	AMR	NO
AFFY_EUR	AFFY	EUR	NO
AFFY_AFR	AFFY	AFR	NO
AFFY_AMR	AFFY	AMR	NO

2.1.2 Meta-analysis

Table 3 defines any meta-analyses performed on the cohorts. Each cohort that was included is detailed along with the number of samples removed prior to cohort-level association testing. In order to identify samples that needed to be removed due to relatedness across cohorts, the cohorts genotypes were first merged on common variants. Then, autosomal variants with $MAF \geq 0.01$ and $callrate \geq 0.98$ were extracted and kinship values were calculated using King [4] with the '--kinship' flag. The reference cohort, the first one listed, maintained all of its samples. Starting from the last listed cohort, any samples shown to have some relation ($kinship \geq 0.0884$) to a sample from any preceding cohort was removed. This was continued until all cohorts subsequent to the reference cohort had been processed.

Table 3: Meta-analysis

ID	Cohort	KinshipRemove	Report
META_EX			NO
	EX_EUR	0	
	EX_AFR	0	
	EX_AMR	57	
META_GWAS			NO
	ILL_EUR	0	
	ILL_AFR	0	
	ILL_AMR	0	
	AFFY_EUR	8	
	AFFY_AFR	154	
	AFFY_AMR	177	

2.1.3 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 4 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 4: Merged results

ID	Cohorts/Metas	Report
MERGE	META_EX>META_GWAS	YES

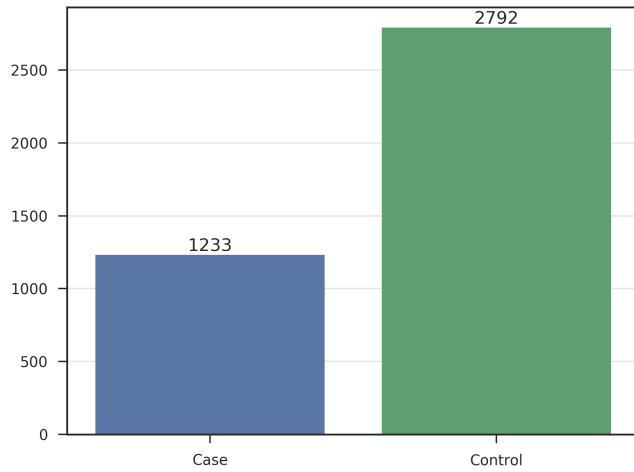
2.2 Ancestry Adjustment and Outlier Removal

Adjusting the statistical models for underlying ancestry is often crucial to reduce or eliminate Type 1 error. Often analysts include principal components of ancestry as covariates in their models as a matter of convention. In our case, we undertook a more nuanced approach. First, the top 10 PC's were calculated for each cohort using the PC-AiR method [3]. Then, the phenotype of interest was regressed on the covariates to be used in the model

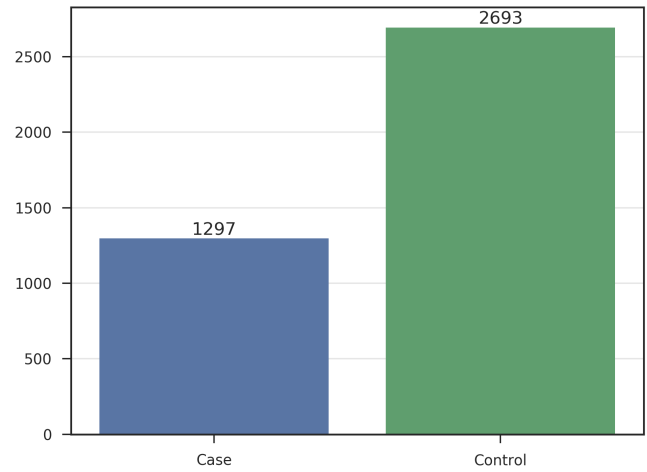
and all of the PC's. If the N th PC exhibited a statistically significant p -value ($p \leq 0.05$), we selected PC's $1 - N$ to be included in association testing. Once determined, any sample lying outside 6 standard deviations from the mean on any of the N PC's was marked as an outlier and removed from the sample set. This process was repeated up to a maximum of ten times until no outliers were found, resulting in more homogeneous sample sets for each particular analysis. For this project, a hard minimum of 0 PC's to be included in analysis was set by the analyst.

3 Type 2 Diabetes (T2D_OTHER)

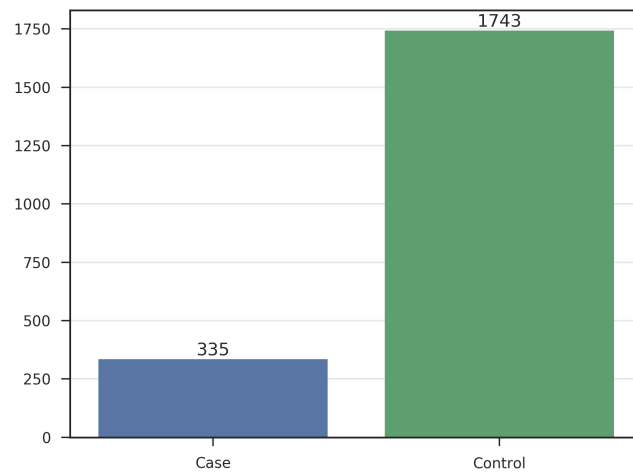
3.1 Summary



(a) EX_AFR

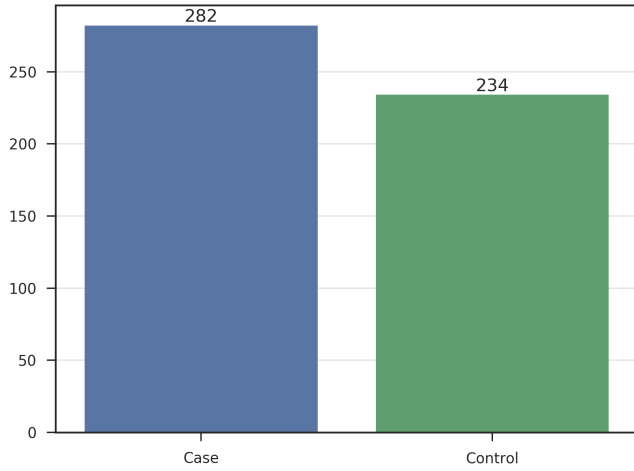


(b) EX_AMR

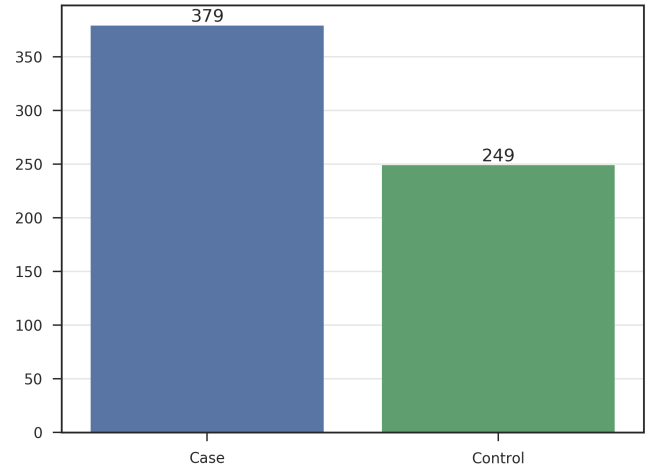


(c) EX_EUR

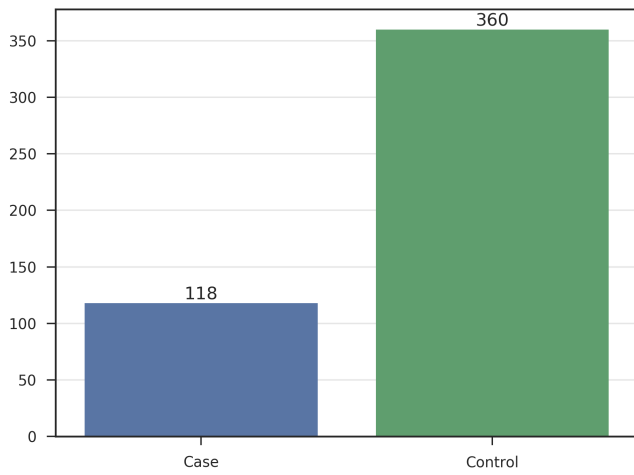
Figure 3: Distribution of T2D_OTHER in META_EX by cohort



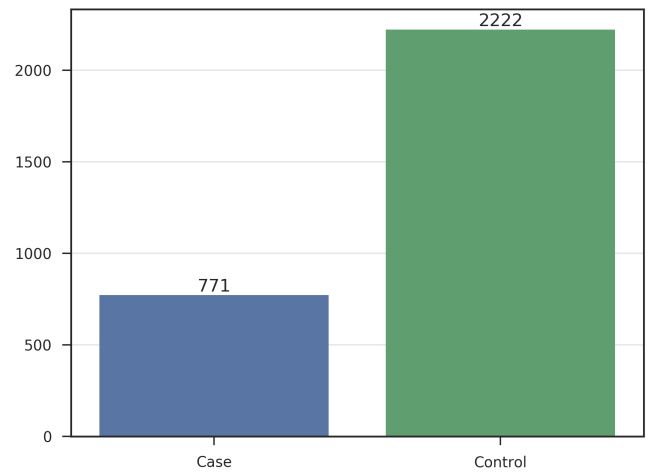
(a) AFFY_AFR



(b) AFFY_AMR



(c) AFFY_EUR



(d) ILL_AFR

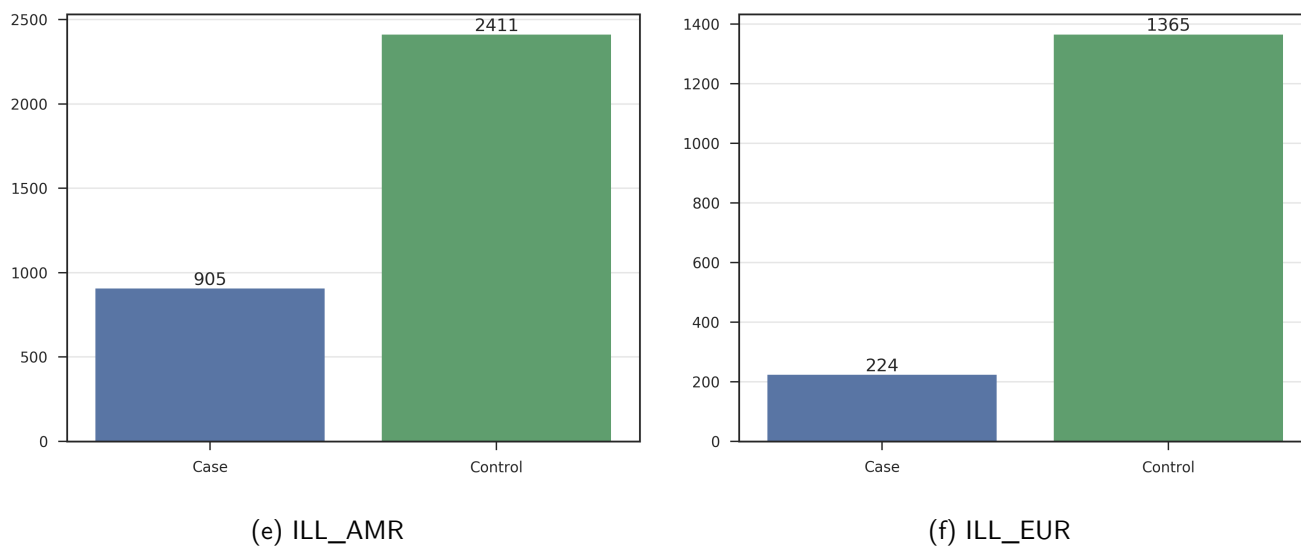


Figure 4: Distribution of T2D_OTHER in META_GWAS by cohort

Table 5: Summary of samples removed from Type 2 Diabetes analysis by cohort and model

Cohort	Array	Ancestry	Trans	Covars	Total	-SampleQc	-missObs	-Kinship	-PcOutlier
META_EX EX_AFR	EX	AFR	-	AGE_T2D_OTHER+SEX+BMI	5172	44	2015	218	0
			-	AGE_T2D_OTHER+SEX	5172	44	1154	270	0
META_EX EX_AMR	EX	AMR	-	AGE_T2D_OTHER+SEX+BMI	5144	32	2038	313	0
			-	AGE_T2D_OTHER+SEX	5144	32	1131	391	0
META_EX EX_EUR	EX	EUR	-	AGE_T2D_OTHER+SEX	2379	30	292	8	0
			-	AGE_T2D_OTHER+SEX+BMI	2379	30	811	6	0
META_GWAS AFFY_AFR	AFFY	AFR	-	AGE_T2D_OTHER+SEX+BMI	897	18	409	85	14
			-	AGE_T2D_OTHER+SEX	897	18	243	111	16
META_GWAS AFFY_AMR	AFFY	AMR	-	AGE_T2D_OTHER+SEX	1035	20	278	138	0
			-	AGE_T2D_OTHER+SEX+BMI	1035	20	480	105	7
META_GWAS AFFY_EUR	AFFY	EUR	-	AGE_T2D_OTHER+SEX	578	12	104	7	0
			-	AGE_T2D_OTHER+SEX+BMI	578	12	250	7	0
META_GWAS ILL_AFR	ILL	AFR	-	AGE_T2D_OTHER+SEX+BMI	4077	46	1546	4	0
			-	AGE_T2D_OTHER+SEX	4077	46	875	3	49
META_GWAS ILL_AMR	ILL	AMR	-	AGE_T2D_OTHER+SEX	3884	26	814	0	0
			-	AGE_T2D_OTHER+SEX+BMI	3884	26	1489	2	0
META_GWAS ILL_EUR	ILL	EUR	-	AGE_T2D_OTHER+SEX	1797	23	184	0	0
			-	AGE_T2D_OTHER+SEX+BMI	1797	23	562	1	0

Table 6: Summary of samples remaining for Type 2 Diabetes analysis by cohort and model

Cohort	Array	Ancestry	Trans	Covars	PCs	N	Male	Female	Case	Ctrl
META_EX EX_AFR	EX	AFR	-	AGE_T2D_OTHER+SEX+BMI	0	2916	1087	1829	840	2076
			-	AGE_T2D_OTHER+SEX	0	3716	1427	2289	1138	2578
META_EX EX_AMR	EX	AMR	-	AGE_T2D_OTHER+SEX+BMI	3	2772	1131	1641	842	1930
			-	AGE_T2D_OTHER+SEX	3	3594	1562	2032	1181	2413
META_EX EX_EUR	EX	EUR	-	AGE_T2D_OTHER+SEX	2	2051	1369	682	335	1716
			-	AGE_T2D_OTHER+SEX+BMI	5	1541	1011	530	216	1325
META_GWAS AFFY_AFR	AFFY	AFR	-	AGE_T2D_OTHER+SEX+BMI	5	383	174	209	202	181
			-	AGE_T2D_OTHER+SEX	9	519	234	285	285	234
META_GWAS AFFY_AMR	AFFY	AMR	-	AGE_T2D_OTHER+SEX	0	606	275	331	369	237
			-	AGE_T2D_OTHER+SEX+BMI	0	431	185	246	250	181
META_GWAS AFFY_EUR	AFFY	EUR	-	AGE_T2D_OTHER+SEX	2	456	373	83	107	349
			-	AGE_T2D_OTHER+SEX+BMI	0	315	258	57	62	253
META_GWAS ILL_AFR	ILL	AFR	-	AGE_T2D_OTHER+SEX+BMI	0	2504	912	1592	616	1888
			-	AGE_T2D_OTHER+SEX	10	3123	1181	1942	822	2301
META_GWAS ILL_AMR	ILL	AMR	-	AGE_T2D_OTHER+SEX	5	3048	1302	1746	841	2207
			-	AGE_T2D_OTHER+SEX+BMI	5	2377	967	1410	616	1761
META_GWAS ILL_EUR	ILL	EUR	-	AGE_T2D_OTHER+SEX	2	1591	992	599	229	1362
			-	AGE_T2D_OTHER+SEX+BMI	2	1219	748	471	154	1065

3.2 Calibration

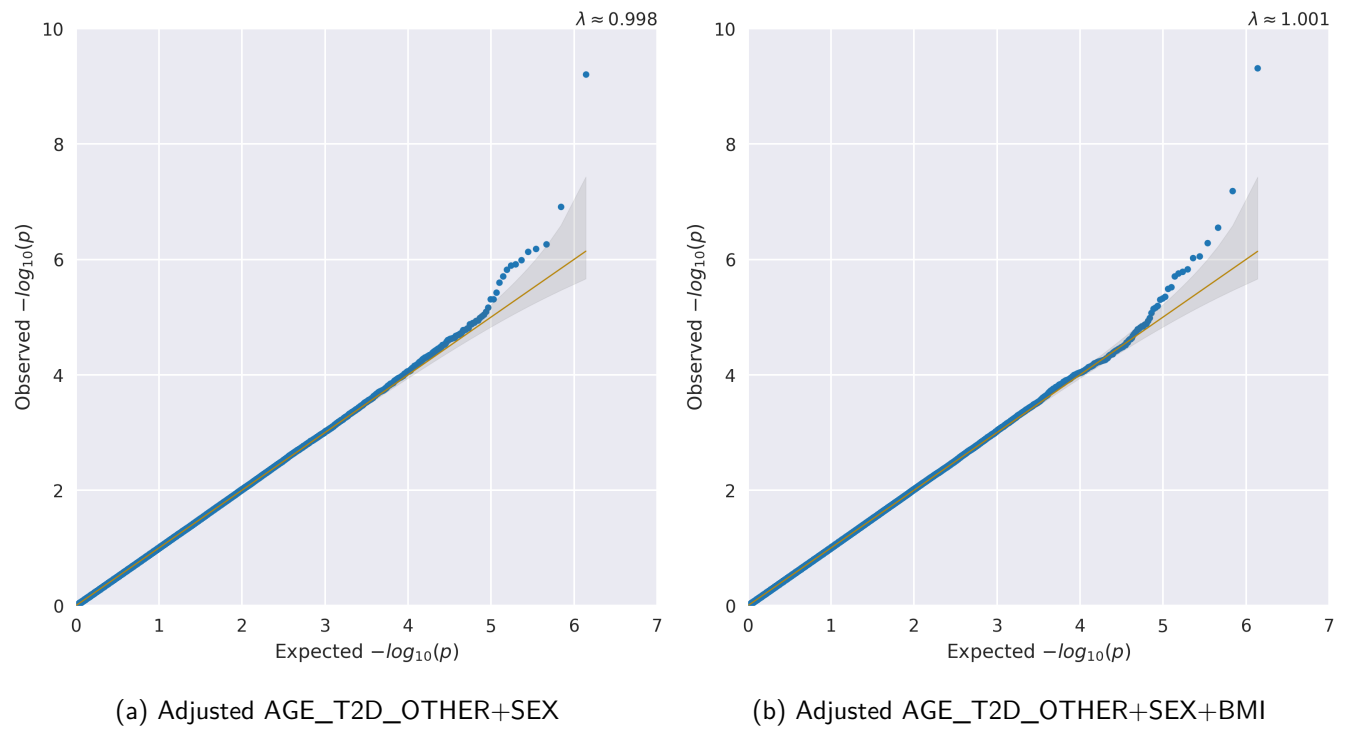
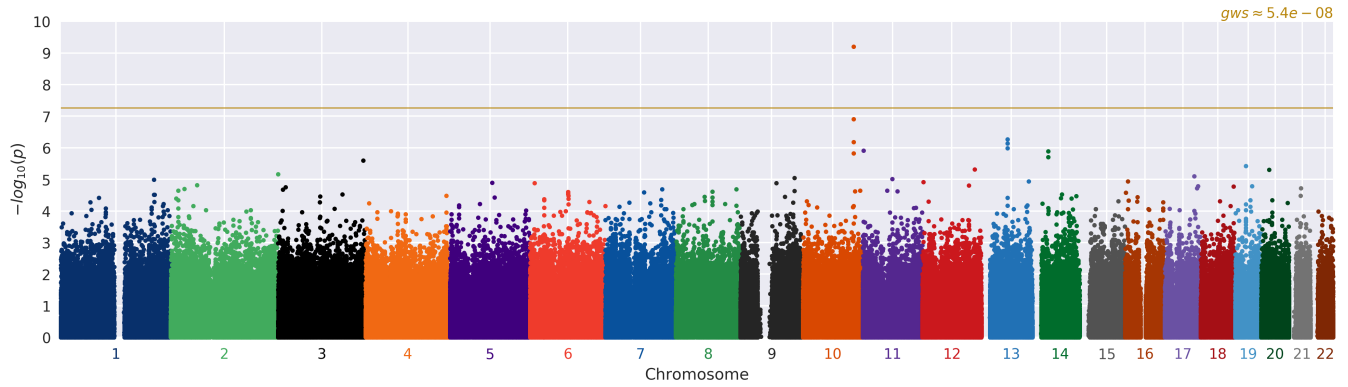
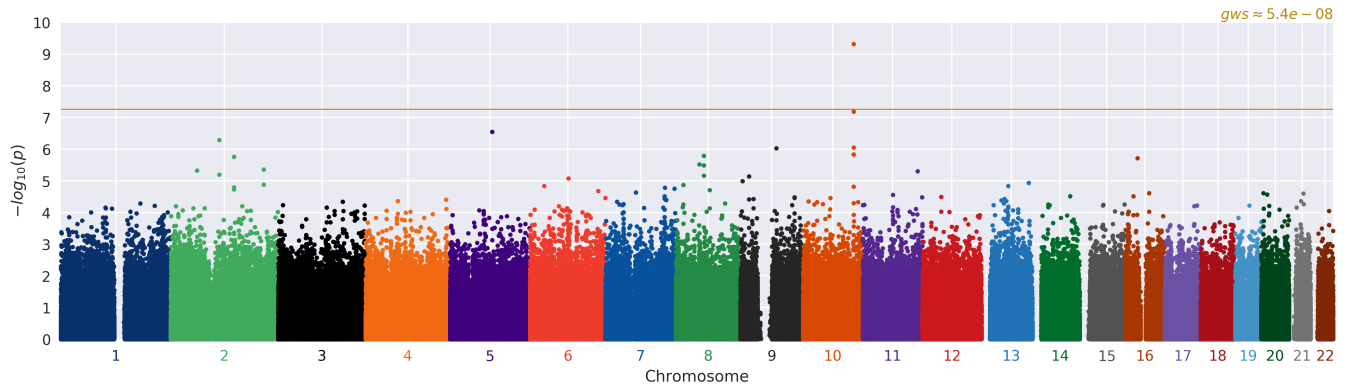


Figure 5: QQ plots for T2D_OTHER in the MERGE analysis



(a) Adjusted AGE_T2D_OTHER+SEX



(b) Adjusted AGE_T2D_OTHER+SEX+BMI

Figure 6: Manhattan plots for T2D_OTHER in the MERGE analysis

3.3 Top associations

Table 7: Top variants in the MERGE Adjusted AGE_T2D_OTHER+SEX model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	GENE_CLOSEST	COHORT	DIR	N	MALE	FEMALE	CASE	CTRL	FREQ_AVG	FREQ_MIN	FREQ_MAX	EFFECT	STDERR	OR	ZSCORE	P
10	114758349	rs7903146	T	C	TCF7L2	META_EX	+++	9,358	4,357	5,001	2,653	6,705	0.292	0.285	0.298	0.235	$3.81 \cdot 10^{-2}$	1.265	6.185	$6.22 \cdot 10^{-10}$
13	59279856	rs9563637	C	T	DIAPH3	META_GWAS	+++xxx	7,762	3,475	4,287	1,892	5,870	0.216	0.132	0.294	0.254	$5.08 \cdot 10^{-2}$	1.29	-5.009	$5.46 \cdot 10^{-7}$
11	2193840	rs10770141	A	G	TH	META_GWAS	+++xxx	7,759	3,475	4,284	1,891	5,868	0.514	0.399	0.631	0.197	$4.06 \cdot 10^{-2}$	1.218	-4.853	$1.22 \cdot 10^{-6}$
14	35822265	rs4982263	T	C	PSMA6	META_GWAS	xxx+++	1,581	882	699	761	820	0.833	0.758	0.907	0.52	0.107	1.682	-4.844	$1.28 \cdot 10^{-6}$
3	192390777	rs1505453	T	C	FGF12	META_GWAS	xxx+++	1,576	880	696	759	817	0.726	0.668	0.841	0.414	$8.8 \cdot 10^{-2}$	1.513	-4.708	$2.5 \cdot 10^{-6}$
19	24356260	rs17687371	C	T	ZNF254	META_GWAS	xxx+++	1,580	881	699	760	820	$8.29 \cdot 10^{-2}$	$1.83 \cdot 10^{-2}$	0.147	0.696	0.15	2.006	-4.626	$3.72 \cdot 10^{-6}$
12	118087822	rs41459444	G	A	KSR2	META_GWAS	xxx+++	1,581	882	699	761	820	$9.2 \cdot 10^{-2}$	$9.87 \cdot 10^{-3}$	0.198	0.646	0.141	1.908	4.57	$4.88 \cdot 10^{-6}$
20	17707401	rs2182948	T	C	BANF2	META_GWAS	+++++	9,339	4,354	4,985	2,652	6,687	0.206	0.151	0.251	0.204	$4.45 \cdot 10^{-2}$	1.226	-4.569	$4.91 \cdot 10^{-6}$
2	243020723	rs4973686	A	G	AC131097	META_GWAS	+++xxx	7,761	3,474	4,287	1,892	5,869	0.302	0.189	0.438	0.199	$4.42 \cdot 10^{-2}$	1.22	4.499	$6.84 \cdot 10^{-6}$
17	66711309	rs8067692	T	C	FAM20A	META_GWAS	+++xxx	7,760	3,474	4,286	1,892	5,868	0.539	0.462	0.612	0.178	$3.99 \cdot 10^{-2}$	1.195	-4.464	$8.03 \cdot 10^{-6}$
9	122140786	rs2025501	G	A	BRINP1	META_GWAS	+++++	9,330	4,348	4,982	2,648	6,682	0.329	0.198	0.459	0.176	$3.97 \cdot 10^{-2}$	1.193	-4.439	$9.04 \cdot 10^{-6}$
11	67294198	rs4930430	T	C	CABP2	META_GWAS	+++++	9,339	4,355	4,984	2,652	6,687	0.582	0.38	0.753	0.166	$3.76 \cdot 10^{-2}$	1.181	4.426	$9.62 \cdot 10^{-6}$
1	211517202	rs2280079	G	A	TRAF5	META_GWAS	xxx+++	1,580	882	698	760	820	0.107	$7.53 \cdot 10^{-2}$	0.164	0.58	0.132	1.786	-4.41	$1.03 \cdot 10^{-5}$
16	6759606	rs2110342	T	C	RBFOX1	META_GWAS	+++xxx	7,762	3,475	4,287	1,892	5,870	0.358	0.144	0.262	0.205	$4.66 \cdot 10^{-2}$	1.227	-4.388	$1.14 \cdot 10^{-5}$
13	106831286	rs4995008	A	G	EFNB2	META_GWAS	+++xxx	7,762	3,475	4,287	1,892	5,870	0.237	0.177	0.267	0.202	$4.6 \cdot 10^{-2}$	1.223	4.387	$1.15 \cdot 10^{-5}$
12	2438328	rs2238063	C	T	CACNA1C	META_GWAS	+++xxx	7,756	3,473	4,283	1,889	5,867	0.113	$9.57 \cdot 10^{-2}$	0.131	0.282	$6.45 \cdot 10^{-2}$	1.326	-4.373	$1.23 \cdot 10^{-5}$
5	95554857	rs4594875	T	C	PCSK1	META_GWAS	xxxx+	1,123	509	614	652	471	$5.16 \cdot 10^{-2}$	$2.32 \cdot 10^{-2}$	$8.48 \cdot 10^{-2}$	0.969	0.222	2.634	4.366	$1.27 \cdot 10^{-5}$
6	10315275	rs8180539	G	A	TFAP2A	META_GWAS	+++++	9,332	4,347	4,985	2,648	6,684	0.468	0.328	0.573	0.16	$3.66 \cdot 10^{-2}$	1.173	-4.358	$1.31 \cdot 10^{-5}$
9	81226596	rs7856547	T	C	PSAT1	META_GWAS	+++xxx	7,761	3,475	4,286	1,892	5,869	0.323	0.254	0.4	0.188	$4.32 \cdot 10^{-2}$	1.207	-4.358	$1.32 \cdot 10^{-5}$
2	59794014	rs17050238	A	G	BCL11A	META_GWAS	xxx+x+	1,062	648	414	476	586	$1.18 \cdot 10^{-2}$	$6.58 \cdot 10^{-3}$	$1.57 \cdot 10^{-2}$	2.238	0.517	9.371	4.325	$1.53 \cdot 10^{-5}$

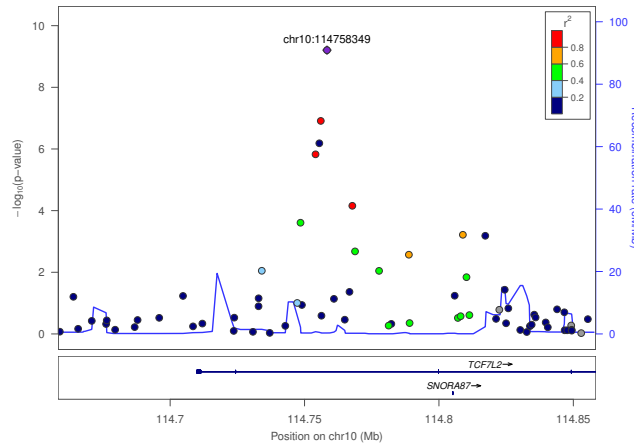


Figure 7: Regional plot for cohort MERGE model Adjusted AGE_T2D_OTHER+SEX: rs7903146 ±100kb

Table 8: Top variants in the MERGE Adjusted AGE_T2D_OTHER+SEX+BMI model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	GENE_CLOSEST	COHORT	DIR	N	MALE	FEMALE	CASE	CTRL	FREQ_AVG	FREQ_MIN	FREQ_MAX	EFFECT	STDERR	OR	ZSCORE	P
10	114758349	rs7903146	T	C	TCF7L2	META_EX	+++	7,227	3,228	3,999	1,897	5,330	0.289	0.282	0.296	0.279	4.49 · 10 ⁻²	1.322	6.225	4.81 · 10 ⁻¹⁰
5	95554857	rs4594875	T	C	PCSK1	META_GWAS	xxxx++	812	359	453	450	362	5.48 · 10 ⁻²	2.68 · 10 ⁻²	8.62 · 10 ⁻²	1.323	0.257	3.754	5.137	2.79 · 10 ⁻⁷
2	109917069	rs7597710	G	T	SH3RF3	META_GWAS	+++++	7,227	3,244	3,983	1,899	5,328	0.186	8.09 · 10 ⁻²	0.315	0.284	5.65 · 10 ⁻²	1.328	-5.02	5.16 · 10 ⁻⁷
9	81226596	rs7856547	T	C	PSAT1	META_GWAS	+++xxx	6,099	2,627	3,472	1,386	4,713	0.324	0.256	0.396	0.248	5.05 · 10 ⁻²	1.281	-4.904	9.4 · 10 ⁻⁷
8	63719844	rs4416814	C	A	NKAIN3	META_GWAS	xxx+++	1,129	617	512	514	615	6.64 · 10 ⁻²	5.92 · 10 ⁻²	7.94 · 10 ⁻²	0.986	0.205	2.679	-4.796	1.62 · 10 ⁻⁶
2	142716216	rs16847729	T	C	LRP1B	META_GWAS	+++xxx	6,094	2,626	3,468	1,385	4,709	0.152	8.82 · 10 ⁻²	0.226	0.33	6.89 · 10 ⁻²	1.39	-4.782	1.74 · 10 ⁻⁶
16	28003858	rs7188624	A	G	GSG1L	META_GWAS	+++xxx	6,100	2,627	3,473	1,386	4,714	0.596	0.438	0.731	0.235	4.94 · 10 ⁻²	1.265	4.759	1.95 · 10 ⁻⁶
8	53111074	rs17220174	G	A	ST18	META_GWAS	xxx+++	1,129	617	512	514	615	0.128	2.48 · 10 ⁻²	0.222	0.722	0.155	2.059	-4.67	3.02 · 10 ⁻⁶
2	210024301	rs16842496	A	C	MAP2	META_GWAS	+++xxx	6,098	2,627	3,471	1,386	4,712	0.339	0.32	0.347	0.224	4.89 · 10 ⁻²	1.252	4.59	4.42 · 10 ⁻⁶
2	59794014	rs17050238	A	G	BCL11A	META_GWAS	xxx+++	746	443	303	312	434	1.14 · 10 ⁻²	7.94 · 10 ⁻³	1.39 · 10 ⁻²	2.938	0.642	18.872	4.577	4.72 · 10 ⁻⁶
11	124310110	rs147220624	A	C	OR8B8	META_EX	x+x	2,915	1,087	1,828	839	2,076	1.54 · 10 ⁻³	1.54 · 10 ⁻³	1.54 · 10 ⁻³	4.25	0.93	70.084	4.568	4.92 · 10 ⁻⁶
9	19234830	rs4977291	T	G	DENND4C	META_GWAS	+++xxx	6,074	2,614	3,460	1,381	4,693	0.866	0.849	0.883	0.304	6.77 · 10 ⁻²	1.355	-4.488	7.19 · 10 ⁻⁶
6	86866457	rs9294342	T	C	SYNCRIP	META_GWAS	xxx+++	1,129	617	512	514	615	0.189	8.41 · 10 ⁻²	0.319	0.533	0.12	1.704	4.455	8.41 · 10 ⁻⁶
9	4487575	rs10974573	G	T	SLC1A1	META_GWAS	xxx++	1,128	616	512	514	614	0.21	0.19	0.232	0.532	0.121	1.703	4.412	1.02 · 10 ⁻⁵
13	106831286	rs4995008	A	G	EFNB2	META_GWAS	+++xxx	6,100	2,627	3,473	1,386	4,714	0.239	0.18	0.269	0.234	5.33 · 10 ⁻²	1.263	4.386	1.15 · 10 ⁻⁵
8	16931954	rs11787157	T	C	MICU3	META_GWAS	+++xxx	6,096	2,625	3,471	1,385	4,711	0.195	0.119	0.248	0.257	5.9 · 10 ⁻²	1.293	4.354	1.33 · 10 ⁻⁵
13	60251770	rs9538496	T	A	DIAPH3	META_GWAS	xxx+++	1,129	617	512	514	615	0.182	7.05 · 10 ⁻²	0.279	0.569	0.131	1.766	-4.338	1.44 · 10 ⁻⁵
6	31802684	rs9368700	C	A	C6orf48	META_GWAS	x+++xx	4,879	1,879	3,000	1,231	3,648	1.08 · 10 ⁻²	9.39 · 10 ⁻³	1.22 · 10 ⁻²	0.964	0.222	2.622	4.337	1.45 · 10 ⁻⁵
7	134512943	rs17168076	G	A	CALD1	META_GWAS	xxxx++	813	359	454	452	361	5.54 · 10 ⁻²	2.67 · 10 ⁻²	8.75 · 10 ⁻²	1.025	0.238	2.787	4.311	1.62 · 10 ⁻⁵
7	155815950	rs6976474	G	A	SHH	META_GWAS	xxx+++	1,128	617	511	513	615	0.637	0.362	0.843	0.468	0.109	1.596	-4.293	1.77 · 10 ⁻⁵

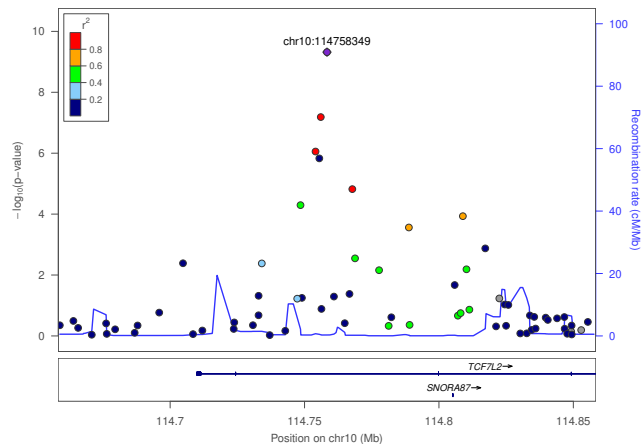


Figure 8: Regional plot for cohort MERGE model Adjusted AGE_T2D_OTHER+SEX+BMI: rs7903146 $\pm 100kb$

3.4 Previously identified risk loci

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 ($\bar{R}^2 \geq 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. There are 7 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 45 variants in both studies, 41 exhibit the same direction of effect with the known result (binomial test $p = 4.67e - 09$).

Table 9: Top known loci in MERGE model Adjusted AGE_T2D_OTHER+SEX (**bold** variants indicate matching direction of effect)

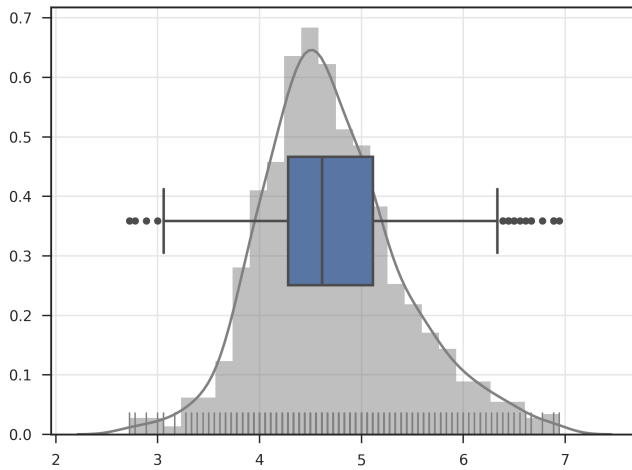
CHR	POS	ID	EA	OA	N	CASE	CTRL	FREQ _{AVG}	FREQ _{MIN}	FREQ _{MAX}	OR	P	DIR	COHORT	GENE _{CLOSEST}	R ²	ID _{KNOWN}	N _{KNOWN}	CASE _{KNOWN}	CTRL _{KNOWN}	OR _{KNOWN}	P _{KNOWN}
10	114758349	rs7903146	T	C	9,356	2,652	6,704	0.292	0.284	0.298	1.269	3.85 · 10 ⁻¹⁰	+++	META_EX	TCF7L2	1	rs7903146	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.389	1.2 · 10 ⁻¹⁰
6	20679709	rs7756992	G	A	9,359	2,653	6,706	0.43	0.302	0.568	1.044	0.234	---	META_EX	CDKAL1	1	rs7756992	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.167	6.95 · 10 ⁻³⁵
9	22134094	rs10811661	T	C	1,581	761	820	0.139	7.32 · 10 ⁻²	0.194	1.11	0.359	xxxx++	META_GWAS	CDKN2B	1	rs10811661	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.185	3.72 · 10 ⁻²⁷
3	185611687	rs4402960	T	G	9,359	2,653	6,706	0.403	0.312	0.516	1.097	1.05 · 10 ⁻²	+++	META_EX	IGF2BP2	1	rs4402960	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.131	2.39 · 10 ⁻²³
16	53819169	rs9936385	C	T	7,761	1,892	5,869	0.428	0.363	0.478	1.036	0.384	+++xxx	META_GWAS	FTO	1	rs9936385	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.129	2.61 · 10 ⁻²³
8	118185025	rs3802177	G	A	9,359	2,653	6,706	0.193	9.23 · 10 ⁻²	0.291	1.078	0.103	+++	META_EX	SLC30A8	1	rs3802177	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.136	1.26 · 10 ⁻²¹
10	94462882	rs1111875	C	T	1,580	760	820	0.313	0.241	0.387	1.115	0.207	xxxx+++	META_GWAS	HHEX	1	rs1111875	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.111	1.98 · 10 ⁻¹⁹
4	28180556	rs864745	T	C	9,343	2,647	6,696	0.366	0.252	0.51	1.057	0.139	+++	META_EX	JAZF1	1	rs864745	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.099	2.28 · 10 ⁻¹⁶
4	6289986	rs4458523	G	T	9,343	2,653	6,690	0.612	0.563	0.643	1.08	3.42 · 10 ⁻²	+++++	META_GWAS	WFS1	1	rs4458523	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.098	2.02 · 10 ⁻¹⁵
2	227093585	rs2943640	C	A	1,581	761	820	0.787	0.658	0.91	1.084	0.418	xxxx++	META_GWAS	IRS1	1	rs2943640	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.096	2.69 · 10 ⁻¹⁴
10	94209939	rs6583813	C	T	7,760	1,891	5,869	0.202	8.55 · 10 ⁻²	0.352	1.05	0.357	+++xxx	META_GWAS	IDE	1	rs6583813	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.098	6.45 · 10 ⁻¹⁴
3	123082398	rs11717195	T	C	1,580	760	820	0.159	0.11	0.188	1.043	0.697	xxxx++	META_GWAS	ADCY5	1	rs11717195	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.112	6.47 · 10 ⁻¹⁴
10	94354204	rs3824735	T	G	7,753	1,890	5,863	0.227	0.133	0.354	1.043	0.403	+++xxx	META_GWAS	KIF11	1	rs3824735	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.097	7.43 · 10 ⁻¹³
3	12393125	rs1801282	C	G	9,350	2,650	6,700	5.27 · 10 ⁻²	1.81 · 10 ⁻²	8.79 · 10 ⁻²	1.131	0.133	+++	META_EX	PPAP2	1	rs1801282	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.113	1.05 · 10 ⁻¹²
2	227047771	rs2943653	C	T	1,581	761	820	0.612	0.516	0.661	1.029	0.72	xxxx++	META_GWAS	NYAP2	1	rs2943653	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.087	8.64 · 10 ⁻¹²
2	43690030	rs10203174	C	T	1,581	761	820	0.207	0.115	0.347	1.005	0.964	xxxx+	META_GWAS	THADA	1	rs10203174	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.144	9.5 · 10 ⁻¹²
11	2847069	rs163184	G	T	7,761	1,891	5,870	0.322	0.173	0.481	1.056	0.229	+++xxx	META_GWAS	KCNQ1	1	rs163184	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.086	1.18 · 10 ⁻¹¹
11	92673828	rs1387153	T	C	9,359	2,653	6,706	0.308	0.269	0.353	1.069	7.45 · 10 ⁻²	+++	META_EX	MTNR1B	1	rs1387153	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.093	1.59 · 10 ⁻¹¹
4	6315954	rs10804976	T	G	7,762	1,892	5,870	0.547	0.515	0.57	1.08	5.61 · 10 ⁻²	+++xxx	META_GWAS	PPP2R2C	1	rs10804976	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.085	3.77 · 10 ⁻¹¹
3	64705365	rs6795735	T	C	9,358	2,653	6,705	0.707	0.533	0.832	1.022	0.587	---	META_EX	ADAMT59	1	rs6795735	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	0.926	7.39 · 10 ⁻¹¹
10	80942631	rs12571751	A	G	9,359	2,653	6,706	0.463	0.442	0.476	1.04	0.250	+++	META_EX	ZMIZ1	1	rs12571751	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.078	1.02 · 10 ⁻¹⁰
5	76425867	rs7708285	G	A	7,755	1,891	5,864	0.764	0.667	0.854	1.005	0.913	+++xxx	META_GWAS	ZBED3	1	rs7708285	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.095	1.45 · 10 ⁻¹⁰
7	36103565	rs11263763	G	A	1,576	757	819	0.555	0.48	0.627	1.009	0.907	xxxx++	META_GWAS	HNF1B	1	rs11263763	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.099	1.57 · 10 ⁻¹⁰
11	72433098	rs1552224	C	G	9,358	2,653	6,705	6.25 · 10 ⁻²	2.73 · 10 ⁻²	0.114	1.082	0.291	+++	META_EX	ARAP1	1	rs1552224	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.107	1.79 · 10 ⁻¹⁰
7	14922007	rs10276674	T	C	7,757	1,890	5,867	0.236	0.164	0.275	1.044	0.364	+++xxx	META_GWAS	DGKB	1	rs10276674	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	0.908	2.07 · 10 ⁻¹⁰
8	41519248	rs156946	C	T	9,359	2,653	6,706	0.749	0.724	0.774	1.015	0.717	---	META_EX	ANK1	1	rs156946	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.091	2.49 · 10 ⁻¹⁰
12	27965150	rs10842994	C	T	9,358	2,653	6,705	0.109	4.37 · 10 ⁻²	0.181	1.153	1.49 · 10 ⁻²	+++	META_EX	KLHL42	1	rs10842994	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.096	6.08 · 10 ⁻¹⁰
11	17408630	rs5215	C	T	9,357	2,651	6,706	0.784	0.645	0.912	1.019	0.685	+-	META_EX	KCNJ11	1	rs5215	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.075	8.5 · 10 ⁻¹⁰
12	66212318	rs2261181	C	T	9,341	2,651	6,690	0.164	0.119	0.22	1.003	0.959	+++++	META_GWAS	HMGAA2	1	rs2261181	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	0.888	1.16 · 10 ⁻⁹
3	23454790	rs1496653	A	G	9,345	2,648	6,687	0.272	0.171	0.384	1.062	0.138	+++++	META_GWAS	UBE2E2	1	rs1496653	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.085	3.56 · 10 ⁻⁹
15	77832762	rs7177055	A	G	9,359	2,653	6,706	0.508	0.352	0.675	1.015	0.675	++	META_EX	HMC20A	1	rs7177055	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.077	4.6 · 10 ⁻⁹
11	17418477	rs757110	C	A	9,357	2,652	6,705	0.79	0.635	0.933	1.026	0.573	++	META_EX	ABCC8	1	rs757110	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.074	5 · 10 ⁻⁹
9	84308948	rs2796441	G	A	9,359	2,653	6,706	0.288	0.166	0.375	1.04	0.324	---	META_EX	TLE1	1	rs2796441	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.074	5.39 · 10 ⁻⁹
5	55806751	rs459193	G	A	9,358	2,653	6,705	0.674	0.585	0.768	1.142	4.11 · 10 ⁻⁴	+++	META_EX	AC022431.2	1	rs459193	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.081	5.99 · 10 ⁻⁹
15	91544076	rs12899811	A	G	7,759	1,891	5,868	0.534	0.322	0.638	1.017	0.68	+++xxx	META_GWAS	VPS33B	1	rs12899811	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.076	6.34 · 10 ⁻⁹
12	71439589	rs7138300	C	T	1,581	761	820	0.594	0.482	0.746	1.018	0.825	xxxx--	META_GWAS	CTD-2021H9.3	1	rs7138300	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.069	6.47 · 10 ⁻⁹
19	19407718	rs10401969	C	T	9,357	2,652	6,705	0.122	6.63 · 10 ⁻²	0.171	1.104	6.07 · 10 ⁻²	+++	META_EX	SUGP1	1	rs10401969	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.135	7.04 · 10 ⁻⁹
11	72629946	rs17244499	A	G	1,581	761	820	9.93 · 10 ⁻³	5.4 · 10 ⁻²	0.139	1.107	0.437	xxxx++	META_GWAS	FCHSD2	1	rs17244499	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.086	1.07 · 10 ⁻⁸
19	19658472	rs16996148	T	G	9,359	2,653	6,706	0.114	7.26 · 10 ⁻²	0.154	1.112	4.98 · 10 ⁻²	---	META_EX	CILP2	1	rs16996148	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.124	1.12 · 10 ⁻⁸
18	57884750	rs12970134	A	G	9,359	2,653	6,706	0.183	0.143	0.242	1.028	0.542	--	META_EX	MC4R	1	rs12970134	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.078	1.19 · 10 ⁻⁸
13	8071156	rs1359790	G	A	9,355	2,652	6,703	0.202	0.11	0.271	1.06	0.192	+++	META_EX	SPRY2	1	rs1359790	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.077	1.39 · 10 ⁻⁸
2	60585806	rs243019	T	C	1,578	758	820	0.487	0.417	0.534	1.081	0.325	xxxx++	META_GWAS	BCL11A	1	rs243019	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	0.937	2.15 · 10 ⁻⁸
2	43844833	rs17031133	G	A	1,580	760	820	0.161	0.12	0.237	1.192	0.103	xxxx++	META_GWAS	PLEKH2	1	rs17031133	1.5 · 10 ⁵	34,840	1.15 · 10 ^{5</}		

Table 10: Top known loci in MERGE model Adjusted AGE_T2D_OTHER+SEX+BMI (**bold** variants indicate matching direction of effect)

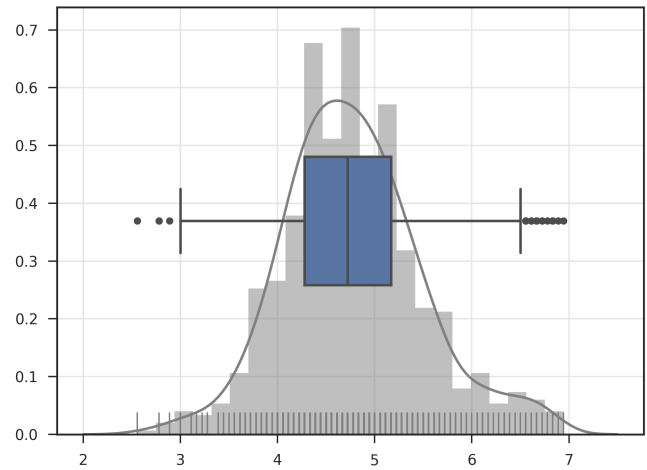
CHR	POS	ID	EA	OA	N	CASE	CTRL	FREQ _{AVG}	FREQ _{MIN}	FREQ _{MAX}	OR	P	DIR	COHORT	GENE _{CLOSEST}	R ²	ID _{KNOWN}	N _{KNOWN}	CASE _{KNOWN}	CTRL _{KNOWN}	OR _{KNOWN}	P _{KNOWN}
10	114758349	rs7903146	T	C	7,224	1,896	5,328	0.289	0.282	0.296	1.325	3.67 · 10 ⁻¹⁰	+++	META_EX	TCF7L2	1	rs7903146	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.389	1.2 · 10 ⁻¹³⁹
6	20679709	rs7756992	G	A	7,226	1,897	5,329	0.43	0.306	0.565	1.077	8.35 · 10 ⁻²	+++	META_EX	CDKAL1	1	rs7756992	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.167	6.95 · 10 ⁻³⁵
9	22134094	rs10811661	T	C	1,129	514	615	0.137	7.18 · 10 ⁻²	0.192	1.092	0.535	xxxx++	META_GWAS	CDKN2B	1	rs10811661	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.185	3.72 · 10 ⁻²⁷
3	185511687	rs4402960	T	G	7,226	1,897	5,329	0.404	0.31	0.518	1.084	5.91 · 10 ⁻²	+++	META_EX	IGF2BP2	1	rs4402960	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.131	2.39 · 10 ⁻²³
16	53819169	rs9936385	T	C	6,100	1,386	4,714	0.424	0.359	0.47	1.002	0.964	+++xxx	META_GWAS	FTO	1	rs9936385	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	0.886	2.61 · 10 ⁻²³
8	118185025	rs3802177	G	A	7,226	1,897	5,329	0.194	9.3 · 10 ⁻²	0.287	1.092	0.106	+++	META_EX	SLC30A8	1	rs3802177	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.136	1.26 · 10 ⁻²¹
10	94462882	rs1111875	C	T	1,128	513	615	0.313	0.241	0.392	1.043	0.688	xxxx++	META_GWAS	HHEX	1	rs1111875	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.111	1.98 · 10 ⁻¹⁹
7	28180556	rs864745	T	C	7,215	1,894	5,321	0.364	0.252	0.508	1.045	0.313	+++	META_EX	JAZF1	1	rs864745	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.099	2.28 · 10 ⁻¹⁶
4	6289986	rs4458523	G	T	7,229	1,900	5,329	0.613	0.573	0.645	1.064	0.145	+++++	META_GWAS	WFS1	1	rs4458523	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.098	2.02 · 10 ⁻¹⁵
2	227093585	rs2943640	C	A	1,129	514	615	0.787	0.656	0.911	1.134	0.309	xxxx++	META_GWAS	IRS1	1	rs2943640	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.096	2.69 · 10 ⁻¹⁴
10	94209939	rs6583813	T	C	6,098	1,385	4,713	0.204	8.89 · 10 ⁻²	0.356	1.06	0.346	+++xxx	META_GWAS	IDE	1	rs6583813	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.098	6.45 · 10 ⁻¹⁴
3	123082398	rs11717195	C	T	1,129	514	615	0.156	0.107	0.187	1.098	0.472	xxxx++	META_GWAS	ADCY5	1	rs11717195	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.112	6.47 · 10 ⁻¹⁴
10	94354204	rs3824735	C	G	6,095	1,385	4,710	0.228	0.132	0.359	1.041	0.495	+++xxx	META_GWAS	KIF11	1	rs3824735	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.097	7.43 · 10 ⁻¹³
3	12393125	rs1801282	C	G	7,218	1,895	5,323	5.17 · 10 ⁻²	1.84 · 10 ⁻²	8.52 · 10 ⁻²	1.217	4.84 · 10 ⁻²	+++	META_EX	PPARG	1	rs1801282	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.13	1.05 · 10 ⁻¹²
2	227047771	rs2943653	C	T	1,129	514	615	0.605	0.522	0.654	1.008	0.93	xxxx++	META_GWAS	NYAP2	1	rs2943653	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.087	8.64 · 10 ⁻¹²
2	43690030	rs10203174	C	T	1,129	514	615	0.209	0.111	0.347	1.057	0.645	xxxx++	META_GWAS	THADA	1	rs10203174	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.144	9.5 · 10 ⁻¹²
11	2847069	rs163184	G	T	6,099	1,385	4,714	0.321	0.171	0.485	1.075	0.168	+++xxx	META_GWAS	KCNQ1	1	rs163184	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.086	1.18 · 10 ⁻¹¹
11	92673828	rs1387153	T	C	7,226	1,897	5,329	0.308	0.27	0.351	1.137	3.77 · 10 ⁻³	+++	META_EX	MTRNR1B	1	rs1387153	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.093	1.59 · 10 ⁻¹¹
4	6315954	rs10804976	G	T	6,100	1,386	4,714	0.545	0.511	0.571	1.051	0.284	---xxx	META_GWAS	PPP2R2C	1	rs10804976	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.085	3.77 · 10 ⁻¹¹
3	64705365	rs6795735	T	C	7,225	1,897	5,328	0.709	0.534	0.832	1.015	0.751	+++	META_EX	ADAMTS9	1	rs6795735	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	0.926	7.39 · 10 ⁻¹¹
10	80942631	rs12571751	A	G	7,226	1,897	5,329	0.462	0.447	0.476	1.081	6.01 · 10 ⁻²	+++	META_EX	ZMIZ1	1	rs12571751	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.078	1.02 · 10 ⁻¹⁰
5	76425867	rs7708285	A	G	6,095	1,385	4,710	0.763	0.665	0.853	1.045	0.431	+++xxx	META_GWAS	ZBED3	1	rs7708285	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	0.913	1.45 · 10 ⁻¹⁰
17	36103565	rs11263763	A	G	1,126	511	615	0.562	0.487	0.617	1.04	0.671	xxxx++	META_GWAS	HNF1B	1	rs11263763	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	0.91	1.57 · 10 ⁻¹⁰
11	72433098	rs1552224	A	G	7,225	1,897	5,328	6.21 · 10 ⁻²	2.71 · 10 ⁻²	0.118	1.101	0.282	+++	META_EX	ARAP1	1	rs1552224	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.107	1.79 · 10 ⁻¹⁰
7	14922007	rs10276674	C	T	6,095	1,384	4,711	0.236	0.167	0.275	1.008	0.883	+++xxx	META_GWAS	DGKB	1	rs10276674	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.102	2.07 · 10 ⁻¹⁰
8	41519248	rs516946	C	T	7,226	1,897	5,329	0.75	0.721	0.773	1.021	0.666	++	META_EX	ANK1	1	rs516946	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	0.916	2.49 · 10 ⁻¹⁰
12	27965150	rs10842994	C	T	7,225	1,897	5,328	0.108	4.5 · 10 ⁻²	0.177	1.201	8.66 · 10 ⁻³	+++	META_EX	KLHL42	1	rs10842994	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.096	6.08 · 10 ⁻¹⁰
11	17408630	rs5215	C	T	7,225	1,896	5,329	0.79	0.653	0.915	1.021	0.7	+++	META_EX	KCNJ11	1	rs5215	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.075	8.5 · 10 ⁻¹⁰
12	66212318	rs2261181	T	C	7,228	1,899	5,329	0.163	0.119	0.21	1.014	0.808	++++	META_GWAS	HMG2	1	rs2261181	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.126	1.16 · 10 ⁻⁹
3	23454790	rs1496653	A	G	7,223	1,897	5,326	0.272	0.17	0.381	1.086	8.4 · 10 ⁻²	++++	META_GWAS	UBE2E2	1	rs1496653	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.085	3.56 · 10 ⁻⁹
15	77832762	rs7177055	A	G	7,226	1,897	5,329	0.507	0.355	0.672	1.025	0.563	++	META_EX	HMG20A	1	rs7177055	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.077	4.6 · 10 ⁻⁹
11	17418477	rs757110	A	G	7,225	1,896	5,329	0.796	0.642	0.934	1.039	0.494	++	META_EX	ABCC8	1	rs757110	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.074	5 · 10 ⁻⁹
9	84308948	rs2796441	G	A	7,226	1,897	5,329	0.285	0.162	0.376	1.036	0.454	+++	META_EX	TLE1	1	rs2796441	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.074	5.39 · 10 ⁻⁹
5	55806751	rs459193	G	A	7,225	1,897	5,328	0.672	0.582	0.769	1.119	1.09 · 10 ⁻²	+++	META_EX	AC022431.2	1	rs459193	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.081	5.99 · 10 ⁻⁹
15	91544076	rs12899811	G	A	6,097	1,385	4,712	0.535	0.326	0.637	1.033	0.489	+++xxx	META_GWAS	VPS33B	1	rs12899811	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.076	6.34 · 10 ⁻⁹
12	71439589	rs7138300	T	C	1,129	514	615	0.596	0.5	0.744	1.048	0.633	xxxx++	META_GWAS	CTD-2021H9.3	1	rs7138300	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	0.935	6.47 · 10 ⁻⁹
19	19407718	rs10401969	C	T	7,224	1,896	5,328	0.123	6.3 · 10 ⁻²	0.174	1.13	4.83 · 10 ⁻²	+++	META_EX	SUGP1	1	rs10401969	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.135	7.04 · 10 ⁻⁹
11	72629946	rs17244499	A	G	1,129	514	615	9.74 · 10 ⁻²	5.74 · 10 ⁻²	0.132	1.196	0.272	xxxxxxx	META_GWAS	FCHSD2	1	rs17244499	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.086	1.07 · 10 ⁻⁸
19	19658472	rs16996148	A	G	7,226	1,897	5,329	0.114	7.11 · 10 ⁻²	0.155	1.15	2.72 · 10 ⁻²	+++	META_EX	CILP2	1	rs16996148	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.124	1.12 · 10 ⁻⁸
18	57884750	rs12970134	A	G	7,226	1,897	5,329	0.182	0.144	0.244	1.057	0.3	++	META_EX	MC4R	1	rs12970134	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.078	1.19 · 10 ⁻⁸
13	80717156	rs1359790	A	G	7,223	1,896	5,327	0.203	0.109	0.278	1.049	0.368	++	META_EX	SPRY2	1	rs1359790	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	1.077	1.39 · 10 ⁻⁸
2	60585806	rs243019	T	C	1,129	514	615	0.486	0.424	0.526	1.008	0.936	xxxx++	META_GWAS	BCL11A	1	rs243019	1.5 · 10 ⁵	34,840	1.15 · 10 ⁵	0.937	2.15 · 10 ⁻⁸
2	4384833	rs17031133	A	G	1,128	513	615	0.164	0.123	0.239	1.108	0.233	xxxx++	META_GWAS	PLEKH2	1	rs17031133	1.5 · 10 ⁵	34,840			

4 Fasting Glucose (GLU_FAST)

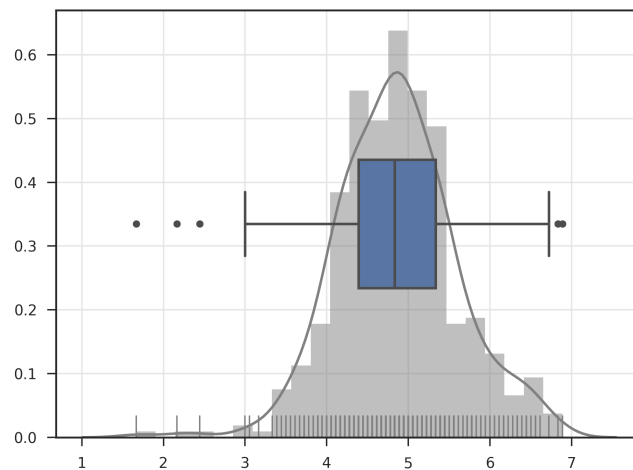
4.1 Summary



(a) EX_AFR

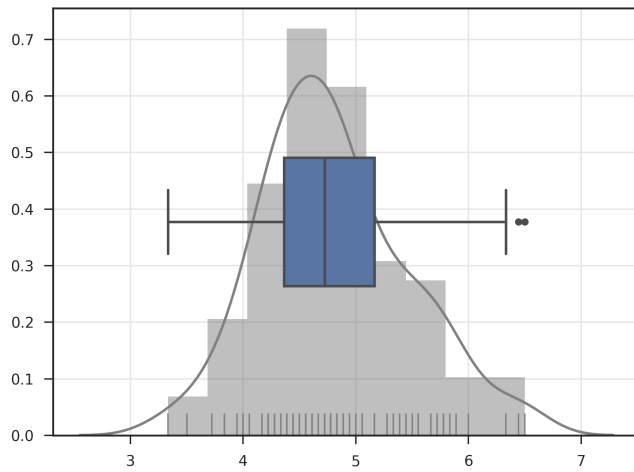


(b) EX_AMR

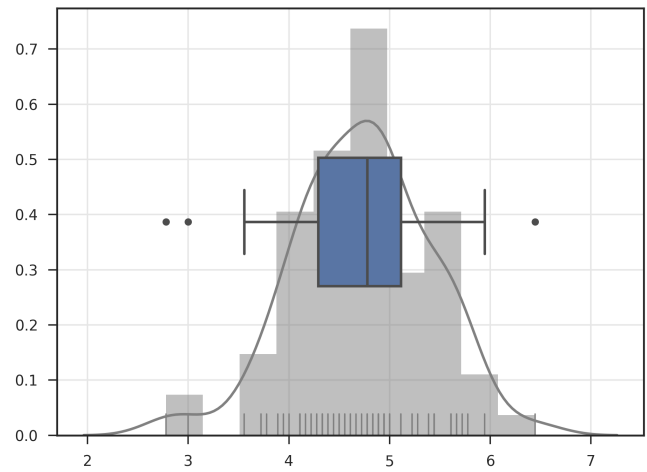


(c) EX_EUR

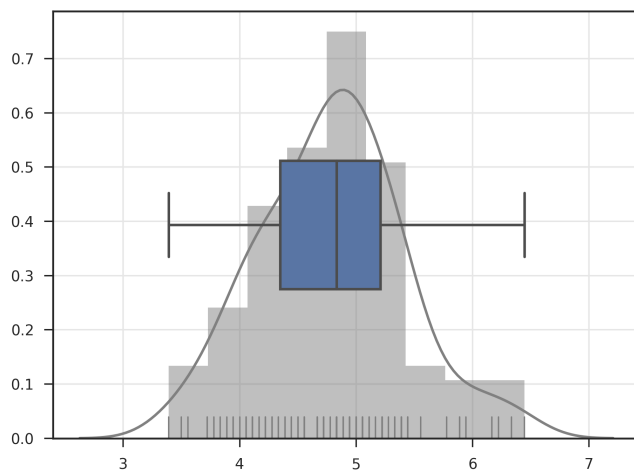
Figure 9: Distribution of GLU_FAST in META_EX by cohort



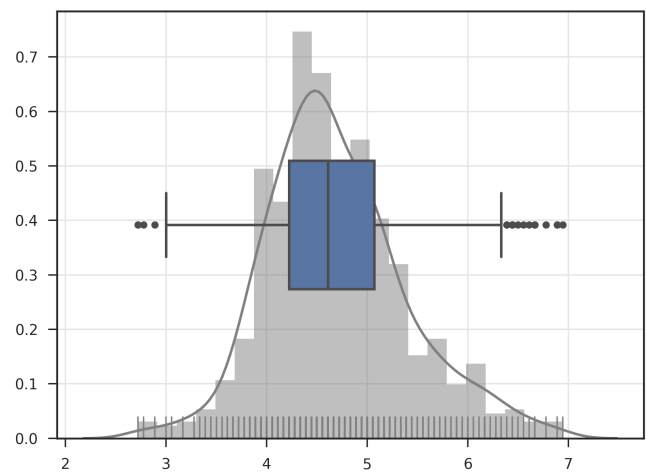
(a) AFFY_AFR



(b) AFFY_AMR



(c) AFFY_EUR



(d) ILL_AFR

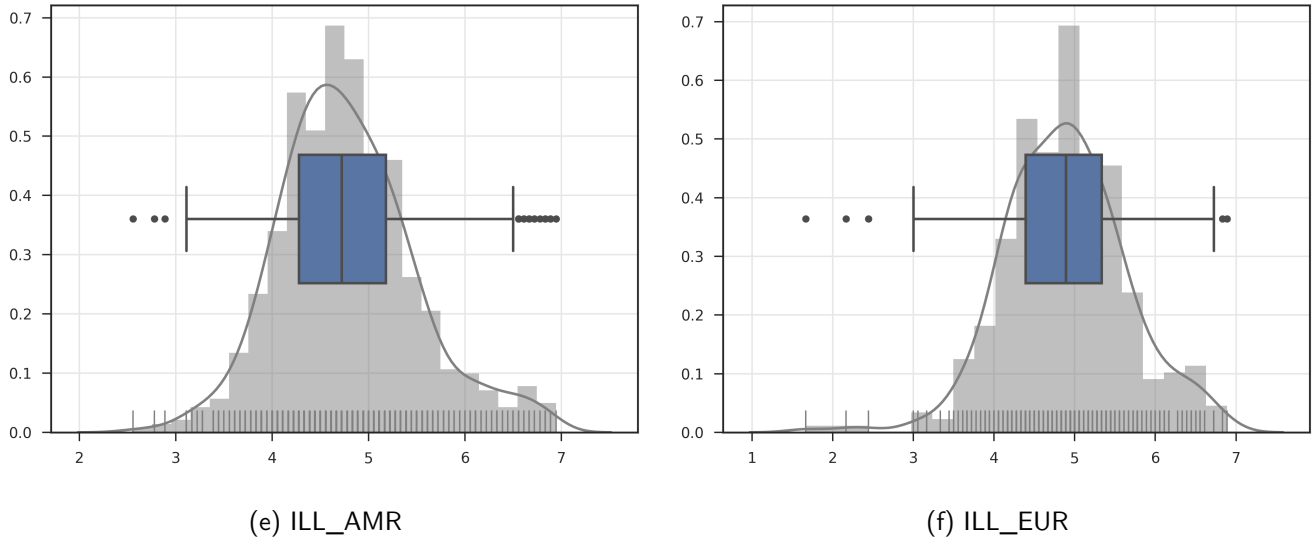


Figure 10: Distribution of GLU_FAST in META_GWAS by cohort

Table 11: Summary of samples removed from Fasting Glucose analysis by cohort and model

Cohort	Array	Ancestry	Trans	Covars	Total	-SampleQc	-missObs	-Kinship	-PcOutlier
META_EX EX_AFR	EX	AFR	invn	AGE_GLU_INS_FAST+SEX+BMI	5172	44	4354	53	0
			invn	AGE_GLU_INS_FAST+SEX	5172	44	4301	53	0
META_EX EX_AMR	EX	AMR	invn	AGE_GLU_INS_FAST+SEX	5144	32	4338	70	1
			invn	AGE_GLU_INS_FAST+SEX+BMI	5144	32	4380	66	0
META_EX EX_EUR	EX	EUR	invn	AGE_GLU_INS_FAST+SEX+BMI	2379	30	1949	0	0
			invn	AGE_GLU_INS_FAST+SEX	2379	30	1922	0	0
META_GWAS AFFY_AFR	AFFY	AFR	invn	AGE_GLU_INS_FAST+SEX+BMI	897	18	800	14	0
			invn	AGE_GLU_INS_FAST+SEX	897	18	793	16	2
META_GWAS AFFY_AMR	AFFY	AMR	invn	AGE_GLU_INS_FAST+SEX	1035	20	956	8	0
			invn	AGE_GLU_INS_FAST+SEX+BMI	1035	20	961	9	0
META_GWAS AFFY_EUR	AFFY	EUR	invn	AGE_GLU_INS_FAST+SEX+BMI	578	12	478	1	0
			invn	AGE_GLU_INS_FAST+SEX	578	12	467	0	0
META_GWAS ILL_AFR	ILL	AFR	invn	AGE_GLU_INS_FAST+SEX	4077	46	3341	0	0
			invn	AGE_GLU_INS_FAST+SEX+BMI	4077	46	3388	1	0
META_GWAS ILL_AMR	ILL	AMR	invn	AGE_GLU_INS_FAST+SEX	3884	26	3212	0	0
			invn	AGE_GLU_INS_FAST+SEX+BMI	3884	26	3248	0	0
META_GWAS ILL_EUR	ILL	EUR	invn	AGE_GLU_INS_FAST+SEX	1797	23	1452	0	1
			invn	AGE_GLU_INS_FAST+SEX+BMI	1797	23	1469	0	0

Table 12: Summary of samples remaining for Fasting Glucose analysis by cohort and model

Cohort	Array	Ancestry	Trans	Covars	PCs	N	Male	Female	Max	Min	μ	\bar{x}	σ
META_EX EX_AFR	EX	AFR	invn	AGE_GLU_INS_FAST+SEX+BMI	0	760	292	468	6.944	2.722	4.716	4.611	0.69
				AGE_GLU_INS_FAST+SEX	0	813	315	498	6.944	2.722	4.713	4.611	0.69
META_EX EX_AMR	EX	AMR	invn	AGE_GLU_INS_FAST+SEX	0	728	319	409	6.944	2.556	4.767	4.722	0.716
				AGE_GLU_INS_FAST+SEX+BMI	0	690	296	394	6.944	2.556	4.757	4.722	0.713
META_EX EX_EUR	EX	EUR	invn	AGE_GLU_INS_FAST+SEX+BMI	0	422	287	135	6.889	1.667	4.863	4.833	0.713
				AGE_GLU_INS_FAST+SEX	0	449	307	142	6.889	1.667	4.859	4.833	0.733
META_GWAS AFFY_AFR	AFFY	AFR	invn	AGE_GLU_INS_FAST+SEX+BMI	0	82	38	44	6.444	3.333	4.768	4.722	0.624
				AGE_GLU_INS_FAST+SEX	0	86	41	45	6.5	3.333	4.807	4.722	0.653
META_GWAS AFFY_AMR	AFFY	AMR	invn	AGE_GLU_INS_FAST+SEX	2	69	28	41	6.444	2.778	4.713	4.778	0.681
				AGE_GLU_INS_FAST+SEX+BMI	2	63	26	37	6.444	2.778	4.691	4.722	0.694
META_GWAS AFFY_EUR	AFFY	EUR	invn	AGE_GLU_INS_FAST+SEX+BMI	0	97	80	17	6.444	3.5	4.802	4.833	0.563
				AGE_GLU_INS_FAST+SEX	0	109	90	19	6.444	3.389	4.794	4.833	0.605
META_GWAS ILL_AFR	ILL	AFR	invn	AGE_GLU_INS_FAST+SEX	0	727	276	451	6.944	2.722	4.695	4.611	0.701
				AGE_GLU_INS_FAST+SEX+BMI	0	680	257	423	6.944	2.722	4.706	4.611	0.704
META_GWAS ILL_AMR	ILL	AMR	invn	AGE_GLU_INS_FAST+SEX	0	664	293	371	6.944	2.556	4.78	4.722	0.717
				AGE_GLU_INS_FAST+SEX+BMI	0	629	273	356	6.944	2.556	4.77	4.722	0.713
META_GWAS ILL_EUR	ILL	EUR	invn	AGE_GLU_INS_FAST+SEX	2	338	213	125	6.889	1.667	4.876	4.889	0.765
				AGE_GLU_INS_FAST+SEX+BMI	2	322	204	118	6.889	1.667	4.876	4.889	0.75

4.2 Calibration

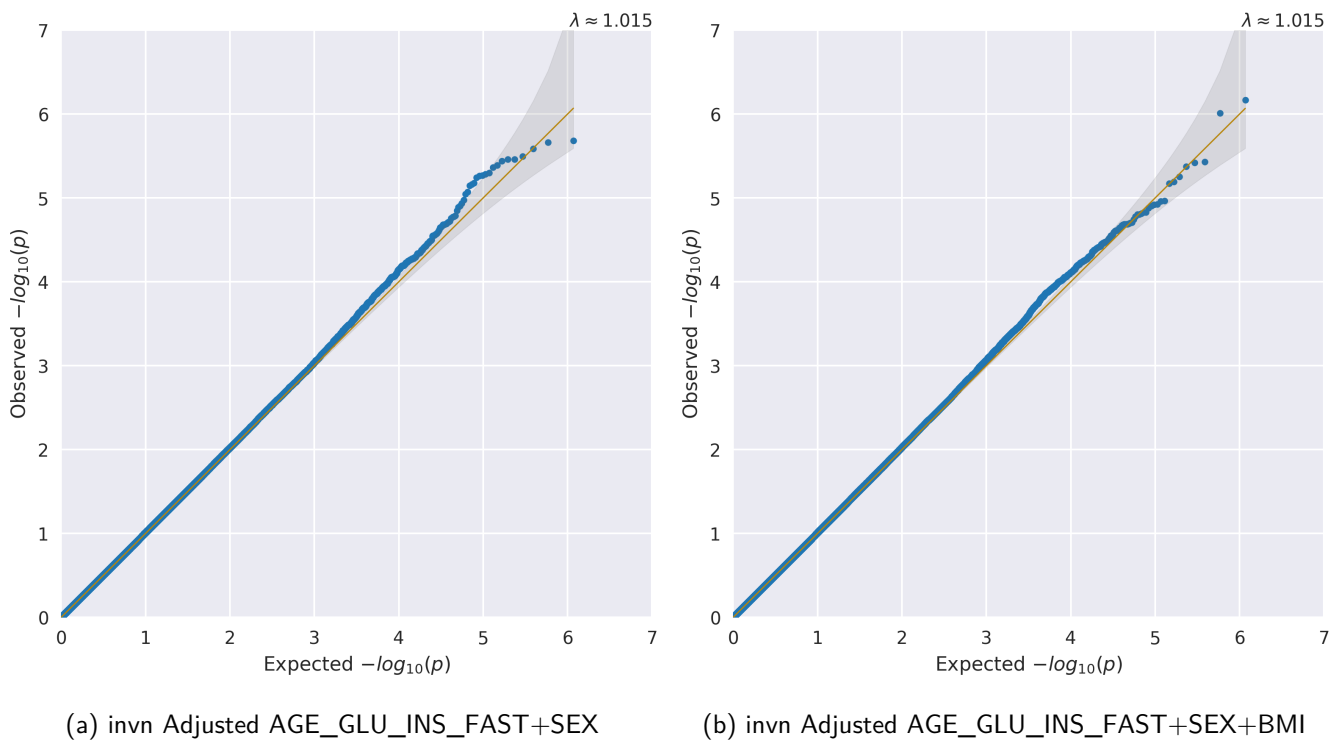
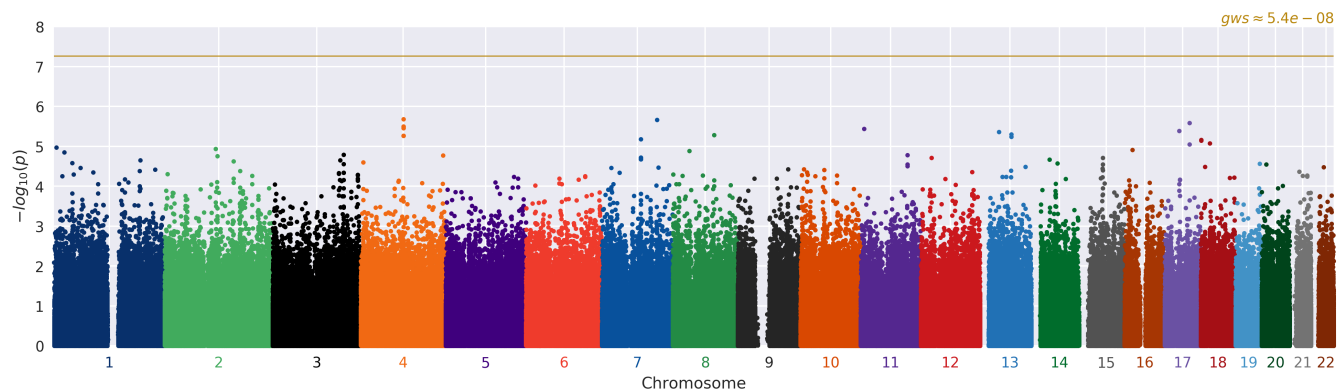
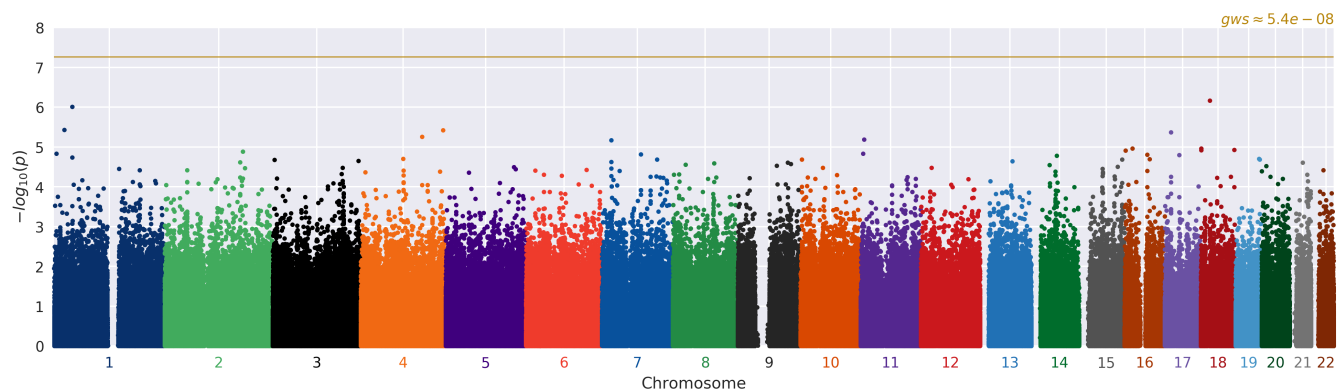


Figure 11: QQ plots for GLU_FAST in the MERGE analysis



(a) invn Adjusted AGE_GLU_INS_FAST+SEX



(b) invn Adjusted AGE_GLU_INS_FAST+SEX+BMI

Figure 12: Manhattan plots for GLU_FAST in the MERGE analysis

4.3 Top associations

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

CHR	POS	ID	EA	OA	GENE _{CLOSEST}	COHORT	DIR	N	MALE	FEMALE	FREQ _{AVG}	FREQ _{MIN}	FREQ _{MAX}	EFFECT	STDERR	OR	ZSCORE	P
4	96259018	rs4699424	G	A	UNC5C	META_GWAS	xxx+++	264	159	105	0.328	0.203	0.431	0.433	9.12 · 10 ⁻²	1.541	-4.746	2.07 · 10 ⁻⁶
7	123801762	rs1860484	T	C	TMEM229A	META_GWAS	xxx+++	264	159	105	0.383	0.291	0.431	0.439	9.28 · 10 ⁻²	1.552	-4.736	2.18 · 10 ⁻⁶
17	55880068	rs2586098	C	A	MRPS23	META_GWAS	xxx+++	264	159	105	0.663	0.535	0.725	0.438	9.32 · 10 ⁻²	1.55	-4.702	2.58 · 10 ⁻⁶
11	7892797	rs16933247	G	C	OR5P3	META_GWAS	xxx+++	264	159	105	8.9 · 10 ⁻²	3.67 · 10 ⁻²	0.163	0.674	0.146	1.963	-4.63	3.65 · 10 ⁻⁶
17	32883256	rs988199	A	G	TMEM132E	META_GWAS	+++++	1,993	941	1,052	0.166	9.77 · 10 ⁻²	0.28	0.198	4.29 · 10 ⁻²	1.219	4.608	4.07 · 10 ⁻⁶
13	42102635	rs9532874	A	C	VWA8	META_GWAS	xxx+++	264	159	105	0.718	0.669	0.78	0.402	8.74 · 10 ⁻²	1.494	-4.596	4.32 · 10 ⁻⁶
13	69713670	rs9599417	C	T	KLHL1	META_GWAS	xxx+++	263	159	104	0.103	4.07 · 10 ⁻²	0.161	0.613	0.134	1.847	-4.565	5 · 10 ⁻⁶
8	92976563	rs2976501	T	G	RUNX1T1	META_GWAS	+++xxx	1,725	780	945	0.657	0.518	0.797	0.165	3.62 · 10 ⁻²	1.179	-4.556	5.2 · 10 ⁻⁶
7	87323145	rs17328880	T	C	ABC1	META_GWAS	+++xxx	1,729	782	947	2.37 · 10 ⁻²	1.86 · 10 ⁻²	4.29 · 10 ⁻²	0.509	0.113	1.663	4.505	6.65 · 10 ⁻⁶
18	722644	rs17516202	A	G	YES1	META_GWAS	+++xxx	1,719	780	939	0.111	0.104	0.12	0.245	5.46 · 10 ⁻²	1.278	-4.498	6.85 · 10 ⁻⁶
18	20832557	rs6507568	G	A	CABLES1	META_GWAS	xxx+++	264	159	105	0.816	0.732	0.89	0.469	0.105	1.599	-4.453	8.46 · 10 ⁻⁶
1	5471517	rs7418357	A	G	NPHP4	META_GWAS	+++++	1,993	941	1,052	0.377	0.226	0.485	0.145	3.29 · 10 ⁻²	1.156	4.404	1.06 · 10 ⁻⁵
2	114979501	rs3105493	G	A	DPP10	META_GWAS	+++xxx	1,729	782	947	0.149	8.43 · 10 ⁻²	0.229	0.208	4.74 · 10 ⁻²	1.231	-4.384	1.16 · 10 ⁻⁵
16	17270508	rs7206082	G	A	XYLT1	META_GWAS	xxx+++	264	159	105	9.28 · 10 ⁻²	6.4 · 10 ⁻²	0.123	0.618	0.141	1.855	-4.37	1.24 · 10 ⁻⁵
8	37046050	rs6981452	A	C	KCNU1	META_GWAS	xxx+++	263	159	104	0.251	0.142	0.448	0.446	0.102	1.562	4.361	1.29 · 10 ⁻⁵
1	23098982	rs12410046	A	G	EPHB2	META_GWAS	+++xxx	1,729	782	947	7.17 · 10 ⁻²	2.13 · 10 ⁻²	0.119	0.285	6.57 · 10 ⁻²	1.33	4.343	1.41 · 10 ⁻⁵
3	159302274	rs9829229	C	T	SCHIP1	META_GWAS	xxx+++	264	159	105	0.244	2.29 · 10 ⁻²	0.599	0.504	0.117	1.655	4.31	1.63 · 10 ⁻⁵
11	104912012	rs17103597	G	T	CARD16	META_GWAS	xxx+++	264	159	105	0.206	0.198	0.217	0.446	0.103	1.561	-4.306	1.66 · 10 ⁻⁵
4	185365540	rs890195	A	C	IRF2	META_GWAS	xxx+++	264	159	105	6.25 · 10 ⁻²	4.59 · 10 ⁻³	0.157	0.8	0.186	2.225	4.304	1.68 · 10 ⁻⁵
2	118280869	rs17047049	T	C	DDX18	META_GWAS	xxx+++	264	159	105	5.11 · 10 ⁻²	7.25 · 10 ⁻³	0.14	0.845	0.197	2.329	-4.295	1.75 · 10 ⁻⁵

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

CHR	POS	ID	EA	OA	GENE _{CLOSEST}	COHORT	DIR	N	MALE	FEMALE	FREQ _{AVG}	FREQ _{MIN}	FREQ _{MAX}	EFFECT	STDERR	OR	ZSCORE	P
18	20832557	rs6507568	G	A	CABLES1	META_GWAS	xxx+++	242	144	98	0.822	0.73	0.902	0.542	0.109	1.72	-4.966	6.83 · 10 ⁻⁷
1	41010454	rs11208363	A	G	ZNF684	META_GWAS	+++++	1,871	878	993	0.307	0.125	0.395	0.179	3.65 · 10 ⁻²	1.195	-4.897	9.75 · 10 ⁻⁷
1	23098982	rs12410046	A	G	EPHB2	META_GWAS	+++xxx	1,631	734	897	7.3 · 10 ⁻²	2.21 · 10 ⁻²	0.121	0.309	6.68 · 10 ⁻²	1.362	4.627	3.71 · 10 ⁻⁶
4	185365540	rs890195	A	C	IRF2	META_GWAS	xxx+++	242	144	98	6.2 · 10 ⁻²	5.15 · 10 ⁻³	0.146	0.867	0.188	2.379	4.621	3.82 · 10 ⁻⁶
17	14156055	rs9903896	G	T	CDRT15	META_GWAS	xxx+++	242	144	98	0.419	0.384	0.444	0.396	8.62 · 10 ⁻²	1.487	4.599	4.24 · 10 ⁻⁶
4	137669438	rs1903270	G	A	PCDH18	META_GWAS	xxx+++	241	144	97	0.396	0.311	0.46	0.403	8.87 · 10 ⁻²	1.496	-4.541	5.59 · 10 ⁻⁶
11	7892797	rs16933247	G	C	OR5P3	META_GWAS	xxx+++	242	144	98	9.09 · 10 ⁻²	3.61 · 10 ⁻²	0.165	0.674	0.149	1.962	-4.512	6.43 · 10 ⁻⁶
7	20784134	rs6947306	C	G	ABC5	META_GWAS	xxx+++	241	143	98	0.803	0.753	0.865	0.463	0.103	1.589	-4.502	6.72 · 10 ⁻⁶
18	722644	rs17516202	A	G	YES1	META_GWAS	+++xxx	1,623	732	891	0.111	0.103	0.117	0.248	5.64 · 10 ⁻²	1.282	-4.399	1.09 · 10 ⁻⁵
16	17270508	rs7206082	G	A	XYLT1	META_GWAS	xxx+++	242	144	98	8.88 · 10 ⁻²	6.1 · 10 ⁻²	0.127	0.652	0.148	1.919	-4.398	1.1 · 10 ⁻⁵
18	75143743	rs6565969	G	A	GALR1	META_GWAS	xxx+++	242	144	98	0.519	0.428	0.595	0.378	8.63 · 10 ⁻²	1.459	-4.38	1.19 · 10 ⁻⁵
16	1988617	rs4987018	C	A	MSRB1	META_GWAS	+++xxx	1,629	734	895	1.75 · 10 ⁻²	8.11 · 10 ⁻³	4.35 · 10 ⁻²	0.591	0.135	1.805	-4.371	1.24 · 10 ⁻⁵
2	175594914	rs2600698	A	C	CHRNA1	META_GWAS	+++xxx	1,631	734	897	0.33	0.205	0.466	0.167	3.83 · 10 ⁻²	1.182	4.357	1.32 · 10 ⁻⁵
11	5484514	rs1039216	C	T	HBE1	META_GWAS	xxx+++	242	144	98	0.585	0.378	0.746	0.393	9.08 · 10 ⁻²	1.482	4.331	1.48 · 10 ⁻⁵
1	5471517	rs7418357	A	G	NPHP4	META_GWAS	+++++	1,873	878	995	0.373	0.225	0.476	0.147	3.4 · 10 ⁻²	1.159	4.331	1.48 · 10 ⁻⁵
7	87323145	rs17328880	T	C	ABC1	META_GWAS	+++xxx	1,631	734	897	2.45 · 10 ⁻²	1.91 · 10 ⁻²	4.5 · 10 ⁻²	0.496	0.115	1.642	4.324	1.53 · 10 ⁻⁵
16	50787483	rs7342715	A	G	CYLD	META_GWAS	xxx+++	242	144	98	0.618	0.51	0.744	0.383	8.87 · 10 ⁻²	1.467	-4.318	1.58 · 10 ⁻⁵
17	32883256	rs988199	A	G	TMEM132E	META_GWAS	+++++	1,873	878	995	0.167	9.71 · 10 ⁻²	0.278	0.19	4.4 · 10 ⁻²	1.209	4.318	1.58 · 10 ⁻⁵
14	56807717	rs17691681	A	G	PELI2	META_GWAS	xxx+++	242	144	98	8.68 · 10 ⁻²	4.27 · 10 ⁻²	0.159	0.631	0.146	1.879	-4.305	1.67 · 10 ⁻⁵
4	95298214	rs11935851	T	A	HPGDS	META_GWAS	xxx++	242	144	98	3.51 · 10 ⁻²	5.15 · 10 ⁻³	6.71 · 10 ⁻²	1.006	0.236	2.735	4.268	1.97 · 10 ⁻⁵

4.4 Previously identified risk loci

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 ($\bar{R}^2 \geq 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. There are 7 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 50 variants in both

studies, 33 exhibit the same direction of effect with the known result (binomial test $p = 0.0164$).

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

CHR	POS	ID	EA	OA	N	FREQ _{AVG}	FREQ _{MIN}	FREQ _{MAX}	EFFECT	STDERR	P	DIR	COHORT	GENE _{CLOSEST}	R ²	ID _{KNOWN}	N _{KNOWN}	EFFECT _{KNOWN}	STDERR _{KNOWN}	P _{KNOWN}
2	169763148	rs560887	C	T	1,986	0.859	0.716	0.958	0.178	4.67 · 10 ⁻²	1.44 · 10 ⁻⁴	+++	META_EX	G6PC2	1	rs560887	1.33 · 10 ⁵	7.1 · 10 ⁻²	2.5 · 10 ⁻³	1.4 · 10 ⁻¹⁷⁸
2	169802252	rs853787	T	G	1,729	0.78	0.666	0.838	0.132	4.15 · 10 ⁻²	1.51 · 10 ⁻³	++++xxx	META_GWAS	ABCB11	1	rs853787	1.33 · 10 ⁵	6.1 · 10 ⁻²	2.2 · 10 ⁻³	5.51 · 10 ⁻¹⁶⁶
11	92673828	rs1387153	C	T	1,992	0.314	0.273	0.351	2.71 · 10 ⁻²	3.43 · 10 ⁻²	0.43	+++	META_EX	MTNR1B	1	rs1387153	1.33 · 10 ⁵	-6.1 · 10 ⁻²	2.4 · 10 ⁻³	3.91 · 10 ⁻¹⁴³
7	44231886	rs6975024	C	T	1,992	0.133	7.81 · 10 ⁻²	0.175	8.58 · 10 ⁻²	4.69 · 10 ⁻²	6.7 · 10 ⁻²	+++	META_EX	GCK	1	rs6975024	1.33 · 10 ⁵	6.1 · 10 ⁻²	2.9 · 10 ⁻³	2.88 · 10 ⁻⁹⁹
7	44248828	rs2908282	A	G	264	0.188	0.142	0.227	7.19 · 10 ⁻²	0.109	0.511	xxx++	META_GWAS	YKT6	1	rs2908282	1.33 · 10 ⁵	5.7 · 10 ⁻²	2.9 · 10 ⁻³	1.04 · 10 ⁻⁸⁸
2	169750483	rs477224	C	T	1,727	0.559	0.497	0.655	6.36 · 10 ⁻²	3.41 · 10 ⁻²	6.6 · 10 ⁻²	++++xxx	META_GWAS	SPC25	1	rs477224	1.33 · 10 ⁵	3.6 · 10 ⁻²	2.3 · 10 ⁻³	6.02 · 10 ⁻⁵⁷
7	15064309	rs2191349	T	G	1,992	0.541	0.49	0.581	2.1 · 10 ⁻²	3.18 · 10 ⁻²	0.508	++	META_EX	DGKB	1	rs2191349	1.33 · 10 ⁵	2.9 · 10 ⁻²	2.1 · 10 ⁻³	1.28 · 10 ⁻⁴²
2	27730940	rs1260326	C	T	1,991	0.713	0.498	0.859	3.4 · 10 ⁻³	3.69 · 10 ⁻²	0.927	++	META_EX	GCKR	1	rs1260326	1.33 · 10 ⁵	2.9 · 10 ⁻²	2.1 · 10 ⁻³	2.17 · 10 ⁻⁴¹
8	118185733	rs11558471	G	A	1,992	0.204	9.78 · 10 ⁻²	0.302	2.53 · 10 ⁻³	4.07 · 10 ⁻²	0.95	++	META_EX	SLC30A8	1	rs11558471	1.33 · 10 ⁵	-2.9 · 10 ⁻²	2.3 · 10 ⁻³	7.8 · 10 ⁻³⁷
2	169703974	rs11676084	G	A	264	0.178	6.98 · 10 ⁻²	0.257	2.67 · 10 ⁻²	0.11	0.808	xxx++	META_GWAS	NOSTRIN	1	rs11676084	1.33 · 10 ⁵	2.8 · 10 ⁻²	2.4 · 10 ⁻³	3.65 · 10 ⁻³²
15	62383155	rs4502156	C	T	1,992	0.594	0.382	0.727	3.33 · 10 ⁻³	3.39 · 10 ⁻²	0.922	++	META_EX	C2CD4A	1	rs4502156	1.33 · 10 ⁵	-2.2 · 10 ⁻²	2.1 · 10 ⁻³	1.38 · 10 ⁻²⁵
10	114758349	rs7903146	C	T	1,991	0.285	0.274	0.303	2.05 · 10 ⁻³	3.48 · 10 ⁻²	0.953	++	META_EX	TCF7L2	1	rs7903146	1.33 · 10 ⁵	-2.2 · 10 ⁻²	2.4 · 10 ⁻³	2.71 · 10 ⁻²⁰
2	27839539	rs2068834	T	C	264	0.309	0.198	0.362	0.117	8.95 · 10 ⁻²	0.19	xxx++	META_GWAS	ZNF512	1	rs2068834	1.33 · 10 ⁵	2.1 · 10 ⁻²	2.3 · 10 ⁻³	9.68 · 10 ⁻²⁰
10	61603510	rs174576	C	A	1,729	0.354	0.28	0.437	3.97 · 10 ⁻²	3.56 · 10 ⁻²	0.264	++++xxx	META_GWAS	FADS2	1	rs174576	1.33 · 10 ⁵	2 · 10 ⁻²	2.2 · 10 ⁻³	1.18 · 10 ⁻¹⁸
3	123065778	rs11708067	A	G	1,992	0.176	0.152	0.203	2.25 · 10 ⁻²	4.17 · 10 ⁻²	0.589	+++	META_EX	ADCY5	1	rs11708067	1.33 · 10 ⁵	2.3 · 10 ⁻²	2.6 · 10 ⁻³	1.3 · 10 ⁻¹⁸
2	22134094	rs10811661	T	C	264	0.165	8.14 · 10 ⁻²	0.22	0.174	0.112	0.12	xxx++	META_GWAS	CDKN2B	1	rs10811661	1.33 · 10 ⁵	2.4 · 10 ⁻²	2.8 · 10 ⁻³	5.65 · 10 ⁻¹⁸
3	170717096	rs11924648	A	G	1,991	0.273	0.129	0.406	3.88 · 10 ⁻²	3.66 · 10 ⁻²	0.289	+++	META_GWAS	SLC2A2	1	rs11924648	1.33 · 10 ⁵	2.6 · 10 ⁻²	3.1 · 10 ⁻³	1.02 · 10 ⁻¹⁷
11	61571348	rs174548	G	C	264	0.282	0.243	0.355	0.205	9.8 · 10 ⁻²	3.66 · 10 ⁻²	xxx++	META_GWAS	FADS1	1	rs174548	1.33 · 10 ⁵	-1.9 · 10 ⁻²	2.3 · 10 ⁻³	1.02 · 10 ⁻¹⁷
11	61551356	rs174535	T	C	1,729	0.307	0.188	0.418	3.49 · 10 ⁻²	3.76 · 10 ⁻²	0.353	++++xxx	META_GWAS	MYRF	1	rs174535	1.33 · 10 ⁵	1.9 · 10 ⁻²	2.2 · 10 ⁻³	2.38 · 10 ⁻¹⁷
11	61557803	rs102275	C	T	1,992	0.554	0.342	0.67	1.31 · 10 ⁻²	3.29 · 10 ⁻²	0.691	+++	META_EX	TMEM258	1	rs102275	1.33 · 10 ⁵	-1.9 · 10 ⁻²	2.2 · 10 ⁻³	4.97 · 10 ⁻¹⁷
5	95539448	rs4869272	T	C	1,992	0.75	0.679	0.809	4.88 · 10 ⁻²	3.6 · 10 ⁻²	0.175	++	META_EX	PCSK1	1	rs4869272	1.33 · 10 ⁵	1.8 · 10 ⁻²	2.2 · 10 ⁻³	1.02 · 10 ⁻¹⁵
13	28847599	rs11619319	G	A	1,991	0.24	0.164	0.297	8.79 · 10 ⁻²	3.8 · 10 ⁻²	2.09 · 10 ⁻²	+++	META_EX	PDX1	1	rs11619319	1.33 · 10 ⁵	2 · 10 ⁻²	2.4 · 10 ⁻³	1.33 · 10 ⁻¹⁵
11	47318157	rs749067	C	T	1,728	0.192	6.53 · 10 ⁻²	0.386	3.61 · 10 ⁻²	4.61 · 10 ⁻²	0.434	++++xxx	META_GWAS	MADD	1	rs749067	1.33 · 10 ⁵	-1.7 · 10 ⁻²	2.2 · 10 ⁻³	6.12 · 10 ⁻¹⁵
8	9177732	rs983309	G	T	1,729	0.784	0.709	0.917	1.01 · 10 ⁻²	4.12 · 10 ⁻²	0.806	+++	META_GWAS	RP11-10A14.4	1	rs983309	1.33 · 10 ⁵	-2.6 · 10 ⁻²	3.3 · 10 ⁻³	6.29 · 10 ⁻¹⁵
2	28003174	rs13030345	G	T	264	0.163	5.23 · 10 ⁻²	0.271	0.168	0.109	0.124	xxx++	META_GWAS	MRPL33	1	rs13030345	1.33 · 10 ⁵	2.1 · 10 ⁻²	2.8 · 10 ⁻³	3.84 · 10 ⁻¹⁴
11	47659135	rs7118178	A	G	1,729	0.157	4.81 · 10 ⁻²	0.315	1.11 · 10 ⁻⁵	4.87 · 10 ⁻²	1	++xxx	META_GWAS	MTCH2	1	rs7118178	1.33 · 10 ⁵	-1.8 · 10 ⁻²	2.4 · 10 ⁻³	3.84 · 10 ⁻¹⁴
11	47600438	rs2280231	T	C	1,729	0.157	4.81 · 10 ⁻²	0.315	1.11 · 10 ⁻⁵	4.87 · 10 ⁻²	1	--xxx	META_GWAS	KBTBD4	1	rs2280231	1.33 · 10 ⁵	-1.8 · 10 ⁻²	2.4 · 10 ⁻³	1.67 · 10 ⁻¹³
2	169605967	rs2390732	G	A	1,729	0.705	0.556	0.796	5.62 · 10 ⁻³	3.79 · 10 ⁻²	0.882	++++xxx	META_GWAS	CERS6	1	rs2390732	1.33 · 10 ⁵	-1.5 · 10 ⁻²	2.1 · 10 ⁻³	7.1 · 10 ⁻¹³
9	4292083	rs10758593	A	G	1,992	0.465	0.403	0.495	9.09 · 10 ⁻³	3.15 · 10 ⁻²	0.773	++	META_EX	GLIS3	1	rs10758593	1.33 · 10 ⁵	1.6 · 10 ⁻²	2.2 · 10 ⁻³	1.17 · 10 ⁻¹²
7	50791579	rs6943153	T	C	1,992	0.487	0.283	0.736	6.23 · 10 ⁻²	3.35 · 10 ⁻²	6.32 · 10 ⁻²	++	META_EX	GRB10	1	rs6943153	1.33 · 10 ⁵	1.5 · 10 ⁻²	2.2 · 10 ⁻³	1.63 · 10 ⁻¹²
7	44178743	rs82020	T	C	263	0.183	0.174	0.192	6.91 · 10 ⁻²	0.107	0.52	xxx+++	META_GWAS	MYL7	1	rs82020	1.33 · 10 ⁵	2.1 · 10 ⁻²	3 · 10 ⁻³	3.04 · 10 ⁻¹²
1	214150445	rs1712208	A	T	264	2.65 · 10 ⁻²	7.25 · 10 ⁻³	4.13 · 10 ⁻²	0.169	0.278	0.542	xxx+++	META_GWAS	PROX1	1	rs1712208	1.33 · 10 ⁵	5.1 · 10 ⁻²	7.4 · 10 ⁻³	3.22 · 10 ⁻¹²
2	27860258	rs2141371	G	A	1,993	0.539	0.453	0.716	2.61 · 10 ⁻⁵	3.21 · 10 ⁻²	0.999	+++++	META_GWAS	GNP1	1	rs2141371	1.33 · 10 ⁵	1.7 · 10 ⁻²	2.5 · 10 ⁻³	6.59 · 10 ⁻¹²
11	72432985	rs11603334	A	G	1,992	7.4 · 10 ⁻²	5.17 · 10 ⁻²	0.125	2.05 · 10 ⁻²	6.03 · 10 ⁻²	0.734	++	META_EX	ARAP1	1	rs11603334	1.33 · 10 ⁵	-1.9 · 10 ⁻²	2.8 · 10 ⁻³	1.12 · 10 ⁻¹¹
2	27951658	rs867282	T	C	1,992	0.591	0.488	0.769	1.28 · 10 ⁻²	3.22 · 10 ⁻²	0.691	+++++	META_GWAS	AC074091.13	1	rs867282	1.33 · 10 ⁵	1.7 · 10 ⁻²	2.5 · 10 ⁻³	1.76 · 10 ⁻¹¹
7	44162355	rs2979422	C	T	1,993	0.245	0.165	0.366	4.34 · 10 ⁻²	3.66 · 10 ⁻²	0.235	+++++	META_GWAS	POLD2	1	rs2979422	1.33 · 10 ⁵	2 · 10 ⁻²	3 · 10 ⁻³	1.78 · 10 ⁻¹¹
20	22557099	rs6113722	G	A	1,992	0.113	6.57 · 10 ⁻²	0.175	0.1	5.02 · 10 ⁻²	4.58 · 10 ⁻²	+++	META_EX	FOXA2	1	rs6113722	1.33 · 10 ⁵	3.5 · 10 ⁻²	5.3 · 10 ⁻³	2.49 · 10 ⁻¹¹
11	11680359	rs16913693	G	T	1,992	0.113	1.89 · 10 ⁻²	0.218	1.91 · 10 ⁻²	5.24 · 10 ⁻²	0.715	++	META_EX	IKBKAP	1	rs16913693	1.33 · 10 ⁵	-4.3 · 10 ⁻²	6.6 · 10 ⁻³	3.51 · 10 ⁻¹¹
2	27152874	rs1371614	C	T	1,728	0.335	0.253	0.369	3.76 · 10 ⁻³	3.62 · 10 ⁻²	0.917	++xxx	META_GWAS	DPYSL5	1	rs1371614	1.33 · 10 ⁵	-1.6 · 10 ⁻²	2.4 · 10 ⁻³	7.09 · 10 ⁻¹¹
11	47275064	rs10838681	A	G	1,993	0.359	0.219	0.453	1.59 · 10 ⁻²	3.35 · 10 ⁻²	0.635	+++++	META_GWAS	NR1H3	1	rs10838681	1.33 · 10 ⁵	1.5 · 10 ⁻²	2.4 · 10 ⁻³	8.84 · 10 ⁻¹¹
11	48009074	rs11039482	C	T	1,992	7.08 · 10 ⁻²	2.28 · 10 ⁻²	0.129	0.156	6.22 · 10 ⁻²	1.25 · 10 ⁻²	+++	META_EX	PTRJ	1	rs11039482	1.33 · 10 ⁵	2 · 10 ⁻²	3 · 10 ⁻³	9.36 · 10 ⁻¹¹
15	62424649	rs4775471	C	T	1,728	0.146	8.82 · 10 ⁻²	0.207	0.103	4.74 · 10 ⁻²	3.03 · 10 ⁻²	++xxx	META_GWAS	C2CD4B	1	rs4775471	1.33 · 10 ⁵	1.6 · 10 ⁻²	2.5 · 10 ⁻³	9.73 · 10 ⁻¹¹
9	139256766	rs3829109	A	G	1,992	0.227	0.171	0.274	4.61 · 10 ⁻²	3.81 · 10 ⁻²	0.226	++	META_EX							

Table 16: Top known loci in MERGE model invn Adjusted AGE_GLU_INS_FAST+SEX+BMI (**bold** variants indicate matching direction of effect)

CHR	POS	ID	EA	OA	N	FREQ _{AVG}	FREQ _{MIN}	FREQ _{MAX}	EFFECT	STDERR	P	DIR	COHORT	GENE _{CLOSEST}	R ²	ID _{KNOWN}	N _{KNOWN}	EFFECT _{KNOWN}	STDERR _{KNOWN}	P _{KNOWN}
2	169763148	rs560887	C	T	1,866	0.859	0.718	0.958	0.179	4.8 · 10 ⁻²	1.87 · 10 ⁻⁴	+++	META_EX	G6PC2	1	rs560887	1,33 · 10 ⁵	7.1 · 10 ⁻²	2.5 · 10 ⁻³	1.4 · 10 ⁻¹⁷⁸
2	169802252	rs853787	T	G	1,631	0.781	0.668	0.84	0.129	4.27 · 10 ⁻²	2.42 · 10 ⁻³	+++xxx	META_GWAS	ABC11	1	rs853787	1,33 · 10 ⁵	6.1 · 10 ⁻²	2.2 · 10 ⁻³	5.51 · 10 ⁻¹⁶⁶
11	92673828	rs1387153	C	T	1,872	0.313	0.275	0.349	3.26 · 10 ⁻²	3.53 · 10 ⁻²	0.356	++	META_EX	MTNR1B	1	rs1387153	1,33 · 10 ⁵	-6.1 · 10 ⁻²	2.4 · 10 ⁻³	3.91 · 10 ⁻¹⁴³
7	44231886	rs6975024	C	T	1,872	0.134	7.89 · 10 ⁻²	0.174	0.105	4.82 · 10 ⁻²	2.96 · 10 ⁻²	+++	META_EX	GCK	1	rs6975024	1,33 · 10 ⁵	6.1 · 10 ⁻²	2.9 · 10 ⁻³	2.88 · 10 ⁻⁹⁹
7	44248828	rs2908282	A	G	242	0.19	0.139	0.23	4.94 · 10 ⁻²	0.115	0.667	xxx++	META_GWAS	YKT6	1	rs2908282	1,33 · 10 ⁵	5.7 · 10 ⁻²	2.9 · 10 ⁻³	1.04 · 10 ⁻⁸⁸
2	169750483	rs477224	C	T	1,629	0.563	0.502	0.658	5.28 · 10 ⁻²	3.52 · 10 ⁻²	0.134	+++xxx	META_GWAS	SPC25	1	rs477224	1,33 · 10 ⁵	3.6 · 10 ⁻²	2.3 · 10 ⁻³	6.02 · 10 ⁻⁵⁷
7	15064309	rs2191349	T	G	1,872	0.539	0.49	0.578	1.7 · 10 ⁻²	3.29 · 10 ⁻²	0.605	++	META_EX	DGKB	1	rs2191349	1,33 · 10 ⁵	2.9 · 10 ⁻²	2.1 · 10 ⁻³	1.28 · 10 ⁻⁴²
2	27730940	rs1260326	C	T	1,871	0.714	0.496	0.86	5.57 · 10 ⁻³	3.81 · 10 ⁻²	0.884	++	META_EX	GCKR	1	rs1260326	1,33 · 10 ⁵	2.9 · 10 ⁻²	2.1 · 10 ⁻³	2.17 · 10 ⁻⁴¹
8	118185733	rs11558471	G	A	1,872	0.205	0.101	0.297	4.2 · 10 ⁻³	4.16 · 10 ⁻²	0.92	+-	META_EX	SLC30A8	1	rs11558471	1,33 · 10 ⁵	-2.9 · 10 ⁻²	2.3 · 10 ⁻³	7.8 · 10 ⁻³⁷
2	169703974	rs11676084	G	A	242	0.178	7.32 · 10 ⁻²	0.268	0.108	0.115	0.346	xxx++	META_GWAS	NOSTRIN	1	rs11676084	1,33 · 10 ⁵	2.8 · 10 ⁻²	2.4 · 10 ⁻³	3.65 · 10 ⁻³²
15	62383155	rs4502156	C	T	1,872	0.595	0.384	0.724	1.12 · 10 ⁻²	3.5 · 10 ⁻²	0.749	++	META_EX	C2CD4A	1	rs4502156	1,33 · 10 ⁵	-2.2 · 10 ⁻²	2.1 · 10 ⁻³	1.78 · 10 ⁻²⁵
10	114758349	rs7903146	C	T	1,871	0.285	0.273	0.307	1.23 · 10 ⁻³	3.58 · 10 ⁻²	0.973	++	META_EX	TCF7L2	1	rs7903146	1,33 · 10 ⁵	-2.2 · 10 ⁻²	2.4 · 10 ⁻³	2.31 · 10 ⁻²⁰
2	27839539	rs2068834	T	C	242	0.314	0.201	0.389	7.69 · 10 ⁻²	9.33 · 10 ⁻²	0.409	xxx++	META_GWAS	ZNF512	1	rs2068834	1,33 · 10 ⁵	2.1 · 10 ⁻²	2.3 · 10 ⁻³	9.68 · 10 ⁻²⁰
11	61603510	rs174576	C	A	1,631	0.352	0.276	0.437	4.07 · 10 ⁻²	3.66 · 10 ⁻²	0.266	+++xxx	META_GWAS	FADS2	1	rs174576	1,33 · 10 ⁵	2 · 10 ⁻²	2.2 · 10 ⁻³	1.18 · 10 ⁻¹⁸
3	123065578	rs11708067	A	G	1,872	0.177	0.155	0.202	2.31 · 10 ⁻²	4.29 · 10 ⁻²	0.591	+++	META_EX	ADCY5	1	rs11708067	1,33 · 10 ⁵	2.3 · 10 ⁻²	2.6 · 10 ⁻³	1.3 · 10 ⁻¹⁸
2	22134094	rs10811661	T	C	242	0.159	7.93 · 10 ⁻²	0.211	0.17	0.116	0.144	xxx++	META_GWAS	CDKN2B	1	rs10811661	1,33 · 10 ⁵	2.4 · 10 ⁻²	2.8 · 10 ⁻³	5.65 · 10 ⁻¹⁸
3	170717996	rs11924648	A	G	1,871	0.278	0.132	0.42	3.25 · 10 ⁻²	3.78 · 10 ⁻²	0.391	+++	META_GWAS	SLC2A2	1	rs11924648	1,33 · 10 ⁵	2.6 · 10 ⁻²	3.1 · 10 ⁻³	1.02 · 10 ⁻¹⁷
11	61571348	rs174548	G	C	242	0.279	0.253	0.325	0.194	0.104	6.21 · 10 ⁻²	xxx++	META_GWAS	FADS1	1	rs174548	1,33 · 10 ⁵	-1.9 · 10 ⁻²	2.3 · 10 ⁻³	1.02 · 10 ⁻¹⁷
11	61551356	rs174535	T	C	1,631	0.31	0.193	0.419	4.1 · 10 ⁻²	3.86 · 10 ⁻²	0.288	+++xxx	META_GWAS	MYRF	1	rs174535	1,33 · 10 ⁵	1.9 · 10 ⁻²	2.2 · 10 ⁻³	2.38 · 10 ⁻¹⁷
11	61557803	rs102275	C	T	1,872	0.553	0.341	0.671	3.09 · 10 ⁻²	3.39 · 10 ⁻²	0.362	++	META_EX	TMEM258	1	rs102275	1,33 · 10 ⁵	-1.9 · 10 ⁻²	2.2 · 10 ⁻³	4.97 · 10 ⁻¹⁷
5	95539448	rs4869272	T	C	1,872	0.749	0.679	0.808	4.21 · 10 ⁻²	3.72 · 10 ⁻²	0.258	++	META_EX	PCSK1	1	rs4869272	1,33 · 10 ⁵	1.8 · 10 ⁻²	2.2 · 10 ⁻³	1.02 · 10 ⁻¹⁵
13	28487599	rs11619319	G	A	1,871	0.241	0.166	0.3	9.03 · 10 ⁻³	3.9 · 10 ⁻²	2.06 · 10 ⁻²	+++	META_EX	PDX1	1	rs11619319	1,33 · 10 ⁵	2 · 10 ⁻²	2.4 · 10 ⁻³	1.33 · 10 ⁻¹⁵
11	47318157	rs749067	T	C	1,630	0.192	6.69 · 10 ⁻²	0.382	2.24 · 10 ⁻²	4.71 · 10 ⁻²	0.634	+++	META_GWAS	MADD	1	rs749067	1,33 · 10 ⁵	-1.7 · 10 ⁻²	2.2 · 10 ⁻³	6.12 · 10 ⁻¹⁵
8	9177732	rs983309	G	T	1,631	0.784	0.707	0.919	1.56 · 10 ⁻²	4.26 · 10 ⁻²	0.714	+++xxx	META_GWAS	RP11-10A14.4	1	rs983309	1,33 · 10 ⁵	-2.6 · 10 ⁻²	3.3 · 10 ⁻³	6.29 · 10 ⁻¹⁵
2	28003174	rs13030345	G	T	242	0.161	5.49 · 10 ⁻²	0.263	0.165	0.113	0.145	xxx++	META_GWAS	MRPL33	1	rs13030345	1,33 · 10 ⁵	2.1 · 10 ⁻²	2.8 · 10 ⁻³	3.84 · 10 ⁻¹⁴
11	47659135	rs7118178	A	G	1,631	0.156	4.93 · 10 ⁻²	0.309	3.2 · 10 ⁻³	5 · 10 ⁻²	0.949	++xxx	META_GWAS	MTCH2	1	rs7118178	1,33 · 10 ⁵	-1.8 · 10 ⁻²	2.4 · 10 ⁻³	3.84 · 10 ⁻¹⁴
11	47600438	rs2280231	T	C	1,631	0.156	4.93 · 10 ⁻²	0.309	3.2 · 10 ⁻³	5 · 10 ⁻²	0.949	++xxx	META_GWAS	KBTBD4	1	rs2280231	1,33 · 10 ⁵	-1.8 · 10 ⁻²	2.4 · 10 ⁻³	1.67 · 10 ⁻¹³
2	169605967	rs2390732	G	A	1,631	0.704	0.554	0.799	1.29 · 10 ⁻³	3.91 · 10 ⁻²	0.974	+++xxx	META_GWAS	CERS6	1	rs2390732	1,33 · 10 ⁵	-1.5 · 10 ⁻²	2.1 · 10 ⁻³	7.1 · 10 ⁻¹³
4	4292083	rs10758593	A	G	1,872	0.466	0.405	0.491	1.88 · 10 ⁻²	3.24 · 10 ⁻²	0.562	+++	META_EX	GLIS3	1	rs10758593	1,33 · 10 ⁵	1.6 · 10 ⁻²	2.2 · 10 ⁻³	1.17 · 10 ⁻¹²
7	50791579	rs6943153	T	C	1,872	0.487	0.277	0.736	6.9 · 10 ⁻²	3.46 · 10 ⁻²	4.62 · 10 ⁻²	+++	META_EX	GRB10	1	rs6943153	1,33 · 10 ⁵	1.5 · 10 ⁻²	2.2 · 10 ⁻³	1.63 · 10 ⁻¹²
7	44178743	rs882020	T	C	241	0.181	0.177	0.185	1.7 · 10 ⁻²	0.112	0.879	xxx++	META_GWAS	MYL7	1	rs882020	1,33 · 10 ⁵	2.1 · 10 ⁻²	3 · 10 ⁻³	3.04 · 10 ⁻¹²
1	214150445	rs17712208	A	T	242	2.89 · 10 ⁻²	7.94 · 10 ⁻³	4.64 · 10 ⁻²	0.206	0.278	0.46	xxx+++	META_GWAS	PROX1	1	rs17712208	1,33 · 10 ⁵	5.1 · 10 ⁻²	7.4 · 10 ⁻³	3.22 · 10 ⁻¹²
2	27860258	rs2141371	G	A	1,873	0.539	0.433	0.722	5.29 · 10 ⁻³	3.33 · 10 ⁻²	0.874	+++	META_GWAS	GNP1	1	rs2141371	1,33 · 10 ⁵	1.7 · 10 ⁻²	2.5 · 10 ⁻³	6.59 · 10 ⁻¹²
11	72432985	rs11603334	A	G	1,872	7.56 · 10 ⁻²	5.33 · 10 ⁻²	0.129	7.49 · 10 ⁻³	6.16 · 10 ⁻²	0.903	+-	META_EX	ARAP1	1	rs11603334	1,33 · 10 ⁵	-1.9 · 10 ⁻²	2.8 · 10 ⁻³	1.12 · 10 ⁻¹¹
2	27951658	rs867282	T	C	1,872	0.591	0.463	0.773	2.43 · 10 ⁻²	3.32 · 10 ⁻²	0.465	++++	META_GWAS	AC074091.13	1	rs867282	1,33 · 10 ⁵	1.7 · 10 ⁻²	2.5 · 10 ⁻³	1.76 · 10 ⁻¹¹
7	44162355	rs2979422	C	T	1,873	0.247	0.17	0.354	4.82 · 10 ⁻²	3.77 · 10 ⁻²	0.201	+++++	META_GWAS	POLD2	1	rs2979422	1,33 · 10 ⁵	2 · 10 ⁻²	3 · 10 ⁻³	1.78 · 10 ⁻¹¹
20	22557099	rs6113722	G	A	1,872	0.114	6.52 · 10 ⁻²	0.175	0.119	5.17 · 10 ⁻²	2.17 · 10 ⁻²	+++	META_EX	FOXA2	1	rs6113722	1,33 · 10 ⁵	3.5 · 10 ⁻²	5.3 · 10 ⁻³	2.49 · 10 ⁻¹¹
9	111680359	rs16913693	G	T	1,872	0.111	1.78 · 10 ⁻²	0.212	1.39 · 10 ⁻²	5.47 · 10 ⁻²	0.799	+-	META_EX	IKBKAP	1	rs16913693	1,33 · 10 ⁵	-4.3 · 10 ⁻²	6.6 · 10 ⁻³	3.51 · 10 ⁻¹¹
2	27152874	rs1371614	C	T	1,631	0.338	0.256	0.373	7.85 · 10 ⁻³	3.72 · 10 ⁻²	0.833	++xxx	META_GWAS	DPYSL5	1	rs1371614	1,33 · 10 ⁵	-1.6 · 10 ⁻²	2.4 · 10 ⁻³	7.09 · 10 ⁻¹¹
11	47275064	rs10838681	A	G	1,873	0.358	0.225	0.451	8.1 · 10 ⁻³	3.45 · 10 ⁻²	0.815	+++	META_GWAS	NR1H3	1	rs10838681	1,33 · 10 ⁵	1.5 · 10 ⁻²	2.4 · 10 ⁻³	8.84 · 10 ⁻¹¹
11	48090074	rs11039482	C	T	1,872	7.08 · 10 ⁻²	2.3 · 10 ⁻²	0.128	0.141	6.41 · 10 ⁻²	2.81 · 10 ⁻²	+++	META_EX	PTPRJ	1	rs11039482	1,33 · 10 ⁵	2 · 10 ⁻²	3 · 10 ⁻³	9.36 · 10 ⁻¹¹
15	62426469	rs4775471	T	C	1,630	0.144	8.62 · 10 ⁻²	0.205	0.102	4.89 · 10 ⁻²	3.67 · 10 ⁻²	++xxx	META_GWAS	C2CD4B	1	rs4775471	1,33 · 10 ⁵	1.6 · 10 ⁻²	2.5 · 10 ⁻³	9.73 · 10 ⁻¹¹
9	139256766	rs3829109	A	G	1,872	0.228	0.174	0.275	5.42 · 10 ⁻²	3.91 · 10 ⁻²	0.166	++	META_EX	DNLZ	1	rs3829109	1,33 · 10 ⁵	-1.7 · 10 ⁻²	2.7 · 10 ⁻³	1.13 · 1

5 Hemoglobin A1c (HBA1C)

5.1 Summary

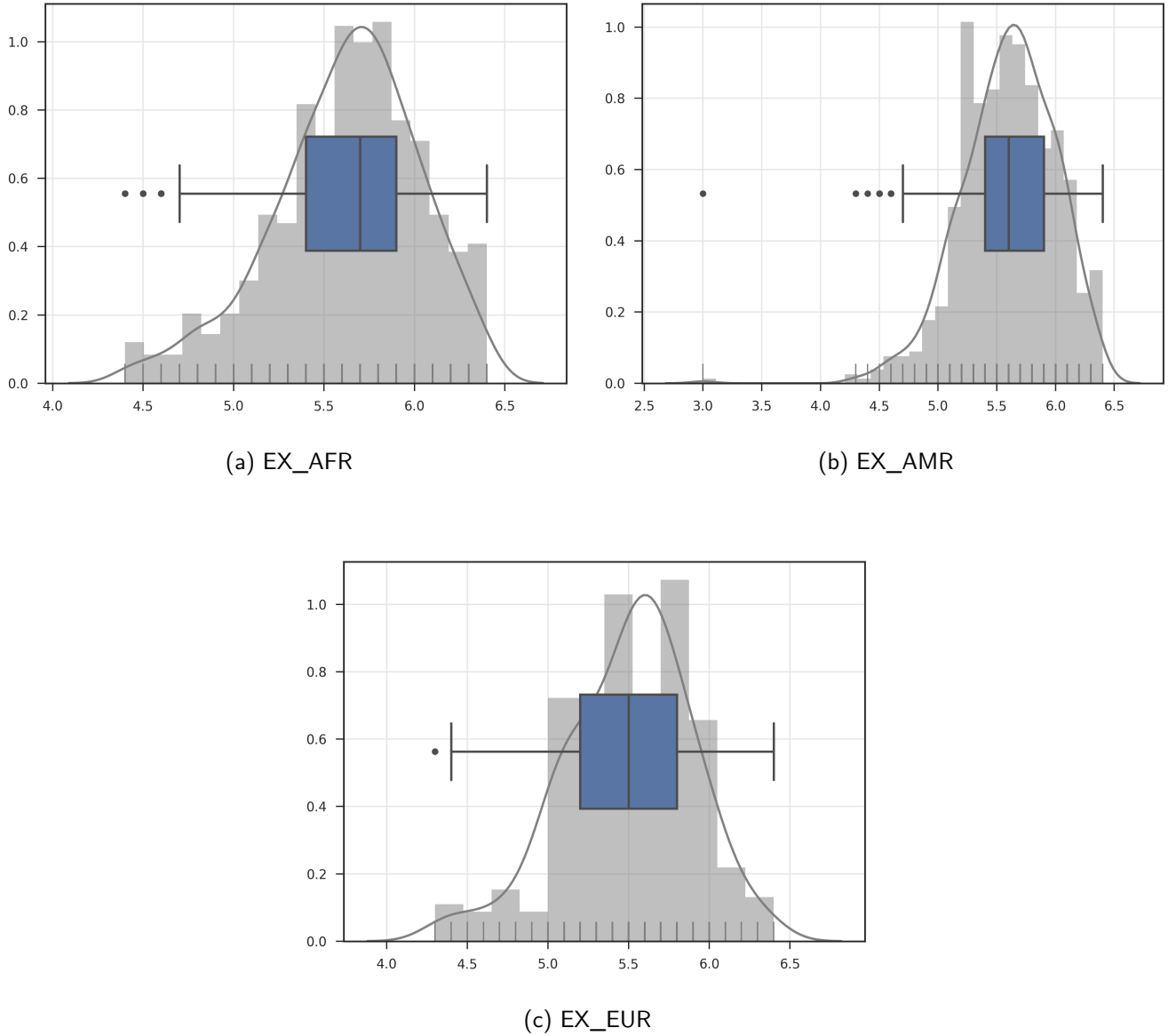
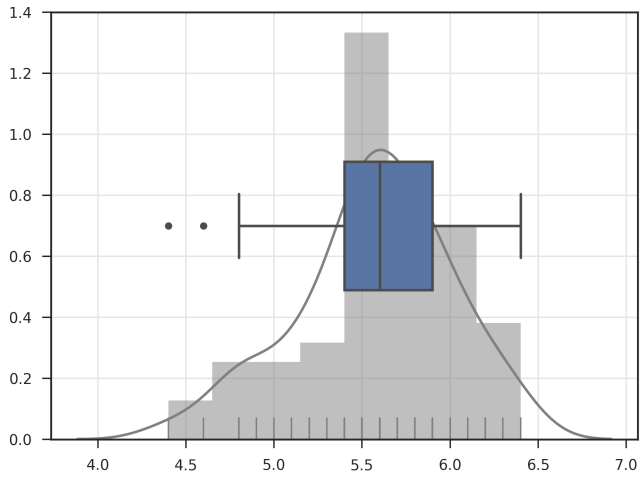
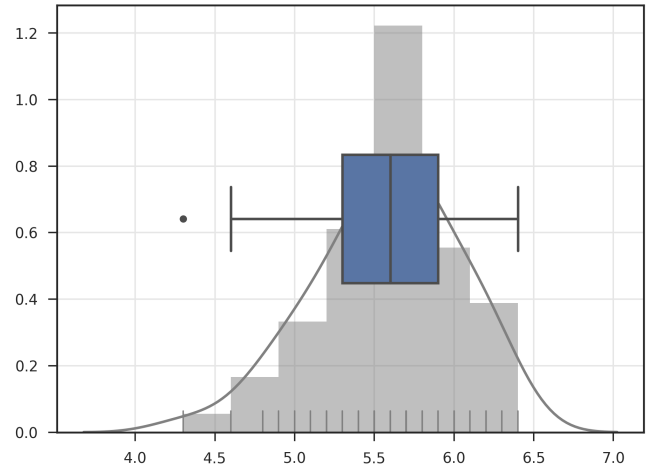


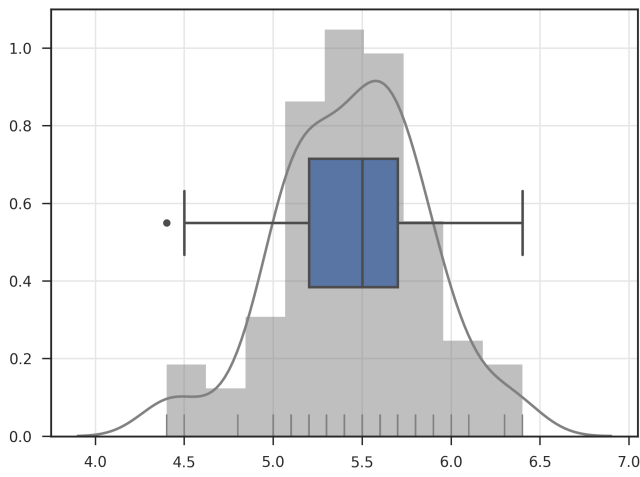
Figure 13: Distribution of HBA1C in META_EX by cohort



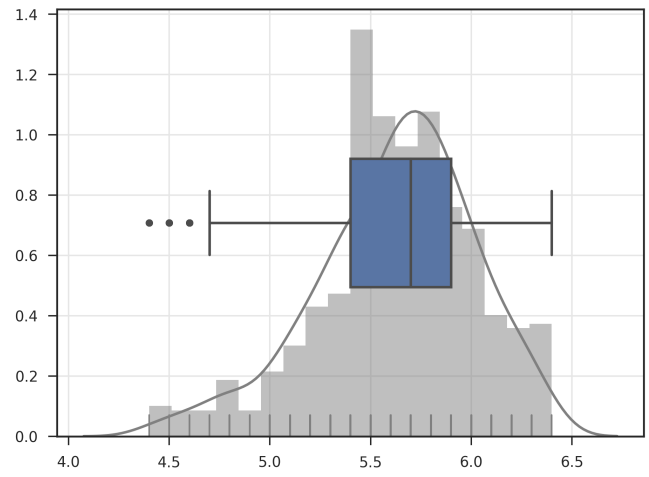
(a) AFFY_AFR



(b) AFFY_AMR



(c) AFFY_EUR



(d) ILL_AFR

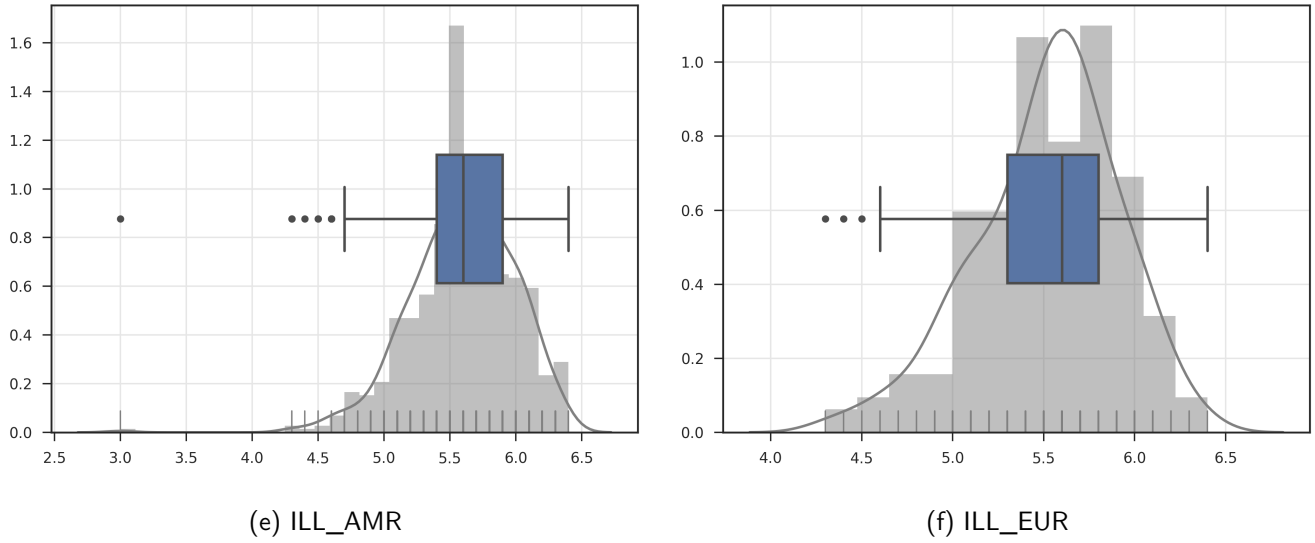


Figure 14: Distribution of HBA1C in META_GWAS by cohort

Table 17: Summary of samples removed from Hemoglobin A1c analysis by cohort and model

Cohort	Array	Ancestry	Trans	Covars	Total	-SampleQc	-missObs	-Kinship	-PcOutlier
META_EX EX_AFR	EX	AFR	invn	AGE_HBA1C+SEX	5172	44	4381	57	0
			invn	AGE_HBA1C+SEX+BMI	5172	44	4404	56	0
META_EX EX_AMR	EX	AMR	invn	AGE_HBA1C+SEX+BMI	5144	32	4427	82	0
			invn	AGE_HBA1C+SEX	5144	32	4412	82	0
META_EX EX_EUR	EX	EUR	invn	AGE_HBA1C+SEX	2379	30	2114	1	0
			invn	AGE_HBA1C+SEX+BMI	2379	30	2123	1	0
META_GWAS AFFY_AFR	AFFY	AFR	invn	AGE_HBA1C+SEX	897	18	815	17	2
			invn	AGE_HBA1C+SEX+BMI	897	18	819	16	2
META_GWAS AFFY_AMR	AFFY	AMR	invn	AGE_HBA1C+SEX+BMI	1035	20	966	13	0
			invn	AGE_HBA1C+SEX	1035	20	964	12	0
META_GWAS AFFY_EUR	AFFY	EUR	invn	AGE_HBA1C+SEX+BMI	578	12	512	0	0
			invn	AGE_HBA1C+SEX	578	12	505	0	0
META_GWAS ILL_AFR	ILL	AFR	invn	AGE_HBA1C+SEX	4077	46	3401	0	13
			invn	AGE_HBA1C+SEX+BMI	4077	46	3421	0	14
META_GWAS ILL_AMR	ILL	AMR	invn	AGE_HBA1C+SEX+BMI	3884	26	3298	0	0
			invn	AGE_HBA1C+SEX	3884	26	3285	0	0
META_GWAS ILL_EUR	ILL	EUR	invn	AGE_HBA1C+SEX	1797	23	1610	0	3
			invn	AGE_HBA1C+SEX+BMI	1797	23	1612	0	4

Table 18: Summary of samples remaining for Hemoglobin A1c analysis by cohort and model

Cohort	Array	Ancestry	Trans	Covars	PCs	N	Male	Female	Max	Min	μ	\bar{x}	σ
META_EX EX_AFR	EX	AFR	invn	AGE_HBA1C+SEX	0	733	247	486	6.4	4.4	5.614	5.6	0.407
			invn	AGE_HBA1C+SEX+BMI	0	711	240	471	6.4	4.4	5.616	5.7	0.408
META_EX EX_AMR	EX	AMR	invn	AGE_HBA1C+SEX+BMI	2	630	240	390	6.4	4.3	5.598	5.6	0.39
			invn	AGE_HBA1C+SEX	2	645	245	400	6.4	4.3	5.596	5.6	0.39
META_EX EX_EUR	EX	EUR	invn	AGE_HBA1C+SEX	2	260	178	82	6.4	4.3	5.491	5.5	0.4
			invn	AGE_HBA1C+SEX+BMI	2	251	172	79	6.4	4.3	5.498	5.5	0.394
META_GWAS AFFY_AFR	AFFY	AFR	invn	AGE_HBA1C+SEX	8	61	29	32	6.4	4.4	5.584	5.6	0.455
			invn	AGE_HBA1C+SEX+BMI	7	58	28	30	6.4	4.4	5.61	5.6	0.447
META_GWAS AFFY_AMR	AFFY	AMR	invn	AGE_HBA1C+SEX+BMI	0	55	18	37	6.3	4.3	5.582	5.6	0.437
			invn	AGE_HBA1C+SEX	0	58	19	39	6.3	4.3	5.56	5.6	0.439
META_GWAS AFFY_EUR	AFFY	EUR	invn	AGE_HBA1C+SEX+BMI	0	64	53	11	6.4	4.4	5.453	5.45	0.398
			invn	AGE_HBA1C+SEX	0	71	59	12	6.4	4.4	5.448	5.5	0.408
META_GWAS ILL_AFR	ILL	AFR	invn	AGE_HBA1C+SEX	2	659	213	446	6.4	4.4	5.627	5.7	0.394
			invn	AGE_HBA1C+SEX+BMI	2	638	207	431	6.4	4.4	5.628	5.7	0.394
META_GWAS ILL_AMR	ILL	AMR	invn	AGE_HBA1C+SEX+BMI	0	583	223	360	6.4	3.0	5.59	5.6	0.399
			invn	AGE_HBA1C+SEX	0	596	227	369	6.4	3.0	5.59	5.6	0.397
META_GWAS ILL_EUR	ILL	EUR	invn	AGE_HBA1C+SEX	0	181	115	66	6.4	4.3	5.52	5.6	0.391
			invn	AGE_HBA1C+SEX+BMI	6	178	114	64	6.4	4.3	5.524	5.6	0.388

5.2 Calibration

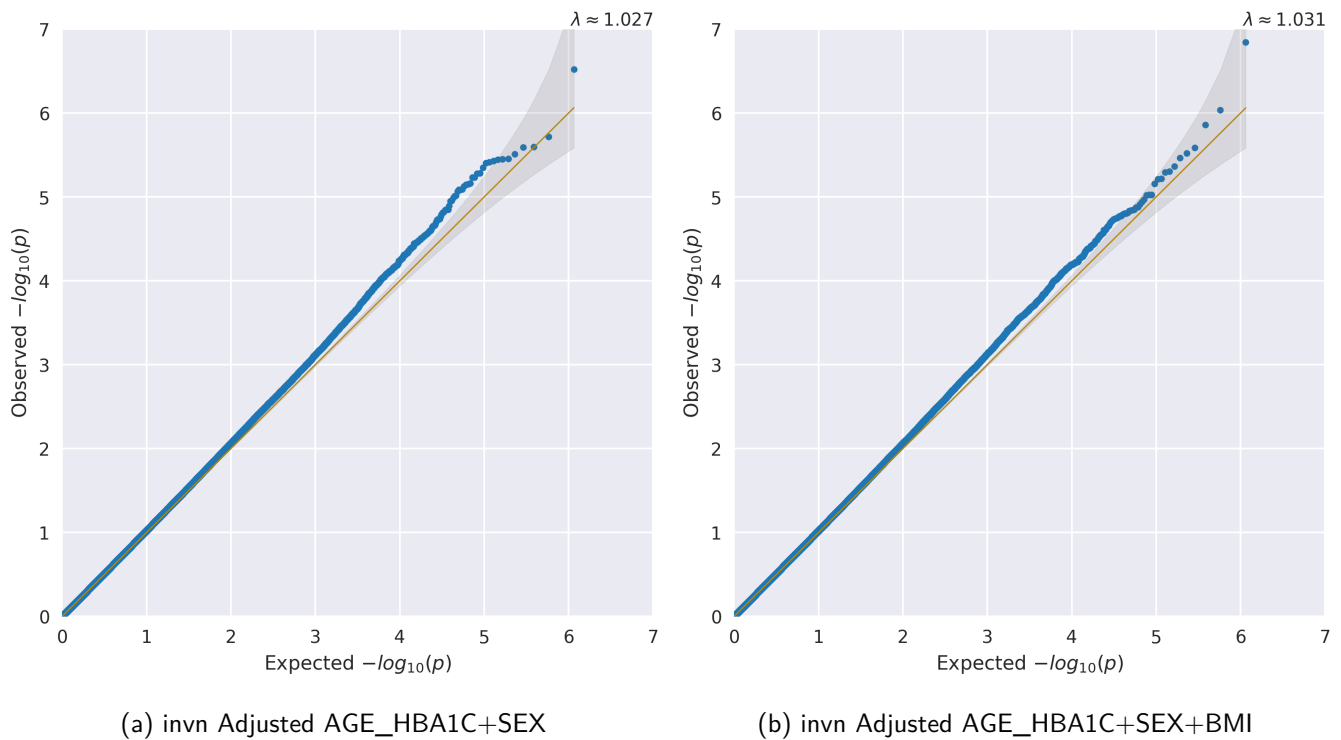
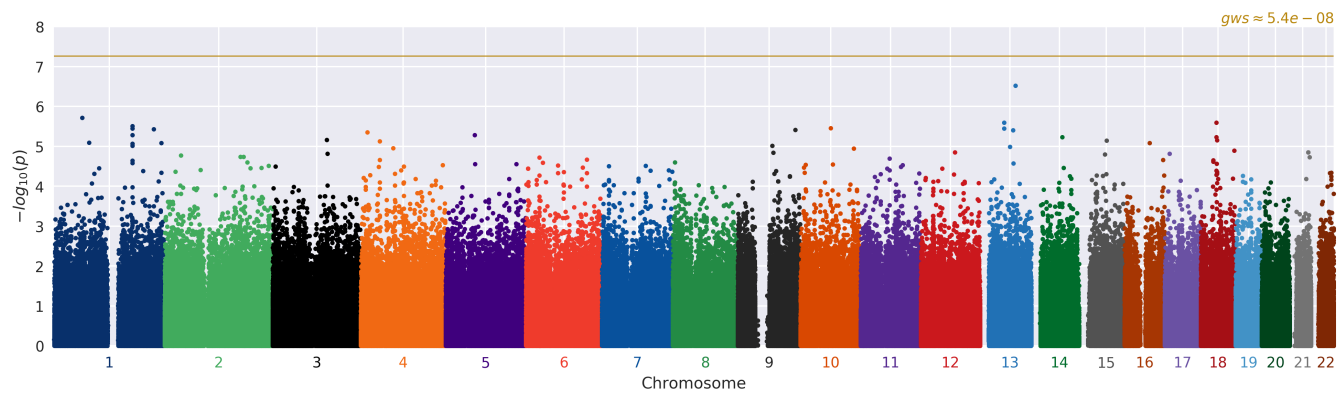
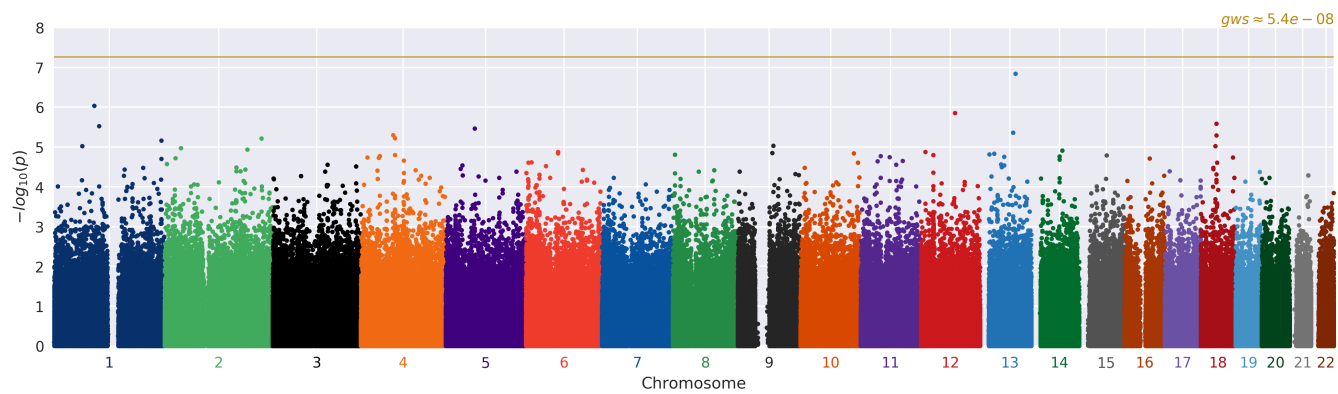


Figure 15: QQ plots for HBA1C in the MERGE analysis



(a) invn Adjusted AGE_HBA1C+SEX



(b) invn Adjusted AGE_HBA1C+SEX+BMI

Figure 16: Manhattan plots for HBA1C in the MERGE analysis

5.3 Top associations

Table 19: Top variants in the MERGE invn Adjusted AGE_HBA1C+SEX model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	GENE _{CLOSEST}	COHORT	DIR	N	MALE	FEMALE	FREQ _{AVG}	FREQ _{MIN}	FREQ _{MAX}	EFFECT	STDERR	OR	ZSCORE	P
13	79168311	rs9530803	A	G	POU4F1	META_GWAS	+++xxx	1,436	555	881	$5.47 \cdot 10^{-2}$	$1.9 \cdot 10^{-2}$	$8.56 \cdot 10^{-2}$	0.416	$8.12 \cdot 10^{-2}$	1.516	5.122	$3.03 \cdot 10^{-7}$
1	63805122	rs932748	T	G	FOXD3	META_GWAS	+++xxx	1,433	554	879	0.9	0.893	0.917	0.297	$6.24 \cdot 10^{-2}$	1.346	4.763	$1.91 \cdot 10^{-6}$
18	35295330	rs1187256	C	T	CELF4	META_GWAS	+++++	1,626	662	964	$6.27 \cdot 10^{-2}$	$8.2 \cdot 10^{-3}$	0.146	0.335	$7.11 \cdot 10^{-2}$	1.397	-4.705	$2.54 \cdot 10^{-6}$
13	53646075	rs2806948	A	G	OLFM4	META_GWAS	xxx+++	189	106	83	0.429	0.369	0.479	0.474	0.101	1.607	4.703	$2.57 \cdot 10^{-6}$
1	176385265	rs2938154	T	G	PAPPA2	META_GWAS	xxx+++	190	107	83	0.439	0.369	0.486	0.486	0.104	1.625	-4.666	$3.08 \cdot 10^{-6}$
10	67759125	rs10822690	A	C	CTNNA3	META_GWAS	xxx+++	190	107	83	0.279	0.267	0.289	0.508	0.11	1.662	4.638	$3.52 \cdot 10^{-6}$
1	224707101	rs7541917	A	G	WDR26	META_GWAS	xxx+++	190	107	83	0.289	0.148	0.459	0.469	0.101	1.598	4.627	$3.72 \cdot 10^{-6}$
9	129446591	rs3861877	A	G	LMX1B	META_GWAS	xxx+++	190	107	83	0.239	$8.2 \cdot 10^{-2}$	0.373	0.568	0.123	1.764	-4.62	$3.83 \cdot 10^{-6}$
13	73903556	rs7984199	A	G	KLF5	META_GWAS	xxx+++	190	107	83	0.858	0.73	0.937	0.631	0.137	1.879	4.615	$3.93 \cdot 10^{-6}$
4	14674246	rs7679323	T	C	CPEB2	META_GWAS	+++xxx	1,436	555	881	0.279	0.247	0.305	0.19	$4.15 \cdot 10^{-2}$	1.21	-4.589	$4.45 \cdot 10^{-6}$
5	65669141	rs979031	A	C	SREK1	META_GWAS	+++++	1,436	555	881	0.159	0.159	0.307	0.207	$4.54 \cdot 10^{-2}$	1.23	4.558	$5.18 \cdot 10^{-6}$
14	69074016	rs10143573	T	C	RAD51B	META_GWAS	+++++	1,624	662	962	0.545	0.521	0.606	0.157	$3.46 \cdot 10^{-2}$	1.17	-4.532	$5.85 \cdot 10^{-6}$
3	121728846	rs2001212	A	G	ILDR1	META_GWAS	+++xxx	1,436	555	881	0.648	0.591	0.699	0.177	$3.94 \cdot 10^{-2}$	1.194	4.499	$6.84 \cdot 10^{-6}$
15	62102570	rs12901220	G	A	VPS13C	META_GWAS	+++++	1,623	661	962	0.585	0.421	0.79	0.168	$3.75 \cdot 10^{-2}$	1.183	-4.49	$7.11 \cdot 10^{-6}$
4	42924962	rs1450918	A	G	GRXCR1	META_GWAS	xxx+++	190	107	83	0.711	0.697	0.724	0.465	0.104	1.592	-4.481	$7.44 \cdot 10^{-6}$
1	79002304	exm70307	A	G	PTGFR	META_EX	+++	1,638	670	968	$2.14 \cdot 10^{-3}$	$6.82 \cdot 10^{-4}$	$9.62 \cdot 10^{-3}$	1.649	0.369	5.202	-4.463	$8.09 \cdot 10^{-6}$
16	56583516	rs1012075	G	T	MT4	META_GWAS	xxx+++	190	107	83	0.268	0.246	0.293	0.471	0.106	1.602	4.46	$8.18 \cdot 10^{-6}$
1	241740770	rs1582096	G	C	KMO	META_GWAS	xxx+++	189	106	83	0.259	0.189	0.357	0.493	0.111	1.637	4.459	$8.24 \cdot 10^{-6}$
1	176263240	rs352306	G	A	RFWD2	META_GWAS	xxx+++	188	105	83	0.457	0.383	0.507	0.437	$9.82 \cdot 10^{-2}$	1.548	-4.451	$8.55 \cdot 10^{-6}$
9	77669665	rs773146	C	T	NMRK1	META_GWAS	xxx+++	190	107	83	0.832	0.796	0.861	0.599	0.135	1.82	4.422	$9.77 \cdot 10^{-6}$

Table 20: Top variants in the MERGE invn Adjusted AGE_HBA1C+SEX+BMI model (**bold** variants indicate previously identified associations)

CHR	POS	ID	EA	OA	GENE _{CLOSEST}	COHORT	DIR	N	MALE	FEMALE	FREQ _{AVG}	FREQ _{MIN}	FREQ _{MAX}	EFFECT	STDERR	OR	ZSCORE	P
13	79168311	rs9530803	A	G	POU4F1	META_GWAS	+++xxx	1,399	544	855	$5.43 \cdot 10^{-2}$	$1.96 \cdot 10^{-2}$	$8.4 \cdot 10^{-2}$	0.435	$8.27 \cdot 10^{-2}$	1.545	5.261	$1.43 \cdot 10^{-7}$
1	90780392	rs4475731	G	A	ZNF326	META_GWAS	xxx+++	177	99	78	0.192	0.109	0.302	0.634	0.129	1.886	-4.908	$9.19 \cdot 10^{-7}$
12	77107258	rs7975942	C	T	ZDHHC17	META_GWAS	+++++	1,576	643	933	0.214	0.128	0.351	0.209	$4.32 \cdot 10^{-2}$	1.232	-4.827	$1.39 \cdot 10^{-6}$
18	35295330	rs1187256	C	T	CELF4	META_GWAS	+++++	1,576	643	933	$6.35 \cdot 10^{-2}$	$8.62 \cdot 10^{-3}$	0.149	0.341	$7.26 \cdot 10^{-2}$	1.407	-4.701	$2.59 \cdot 10^{-6}$
1	101604781	rs7524946	G	A	S1PR1	META_GWAS	xxx+++	177	99	78	$6.5 \cdot 10^{-2}$	$4.31 \cdot 10^{-2}$	$9.38 \cdot 10^{-2}$	0.988	0.212	2.686	-4.671	$3 \cdot 10^{-6}$
5	65669141	rs979031	A	C	SREK1	META_GWAS	+++xxx	1,399	544	855	0.216	0.16	0.306	0.213	$4.58 \cdot 10^{-2}$	1.237	4.642	$3.44 \cdot 10^{-6}$
13	73903556	rs7984199	A	G	KLF5	META_GWAS	xxx+++	177	99	78	0.85	0.724	0.93	0.641	0.139	1.898	4.595	$4.32 \cdot 10^{-6}$
4	73124044	rs16847723	T	A	ADAMTS3	META_GWAS	xxx+++	177	99	78	$5.37 \cdot 10^{-2}$	$7.81 \cdot 10^{-3}$	0.147	0.883	0.193	2.418	4.566	$4.98 \cdot 10^{-6}$
4	76872684	rs3796483	A	G	AC110615	META_GWAS	xxx+++	177	99	78	0.212	0.164	0.258	0.57	0.126	1.769	-4.525	$6.04 \cdot 10^{-6}$
2	217903776	rs2372943	G	A	TNP1	META_GWAS	+++++	1,576	643	933	0.185	0.151	0.273	0.205	$4.53 \cdot 10^{-2}$	1.227	-4.523	$6.09 \cdot 10^{-6}$
1	241740770	rs1582096	G	C	KMO	META_GWAS	xxx+++	176	98	78	0.247	0.19	0.333	0.528	0.117	1.696	4.495	$6.95 \cdot 10^{-6}$
9	80144700	rs9650760	T	C	GNA14	META_GWAS	xxx+++	177	99	78	$3.11 \cdot 10^{-2}$	$9.09 \cdot 10^{-3}$	$5.17 \cdot 10^{-2}$	1.28	0.289	3.598	4.431	$9.39 \cdot 10^{-6}$
1	63805122	rs932748	T	G	FOXD3	META_GWAS	+++xxx	1,396	543	853	0.9	0.893	0.916	0.281	$6.34 \cdot 10^{-2}$	1.324	4.43	$9.41 \cdot 10^{-6}$
18	32778133	rs4799371	C	T	ZNF397	META_GWAS	xxx+++	177	99	78	0.774	0.69	0.891	0.51	0.115	1.666	-4.427	$9.55 \cdot 10^{-6}$
2	36399224	rs17404177	T	C	CRIM1	META_GWAS	xxx+++	176	99	77	0.162	$8.62 \cdot 10^{-2}$	0.213	0.587	0.133	1.798	4.401	$1.08 \cdot 10^{-5}$
2	186025368	rs9288109	T	C	ZNF804A	META_GWAS	xxx+++	177	99	78	0.181	$9.38 \cdot 10^{-2}$	0.276	0.559	0.127	1.748	-4.387	$1.15 \cdot 10^{-5}$
14	69074016	rs10143573	T	C	RAD51B	META_GWAS	+++++	1,574	643	931	0.546	0.516	0.605	0.153	$3.51 \cdot 10^{-2}$	1.166	-4.372	$1.23 \cdot 10^{-5}$
6	72203005	rs9351817	A	G	OGFRL1	META_GWAS	+++xxx	1,399	544	855	0.334	0.261	0.407	0.172	$3.96 \cdot 10^{-2}$	1.188	4.357	$1.32 \cdot 10^{-5}$
12	10754656	rs11053877	G	A	MAGOHB	META_GWAS	xxx+++	176	98	78	0.17	$7.02 \cdot 10^{-2}$	0.227	0.597	0.137	1.816	-4.354	$1.34 \cdot 10^{-5}$
9	77669665	rs773146	C	T	NMRK1	META_GWAS	xxx+++	177	99	78	0.839	0.797	0.871	0.618	0.142	1.856	4.342	$1.41 \cdot 10^{-5}$

5.4 Previously identified risk loci

Table 21 shows statistics from the MERGE cohort for 20 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 ($\bar{R}^2 \geq 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. There are 8 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 20 variants in both

studies, 17 exhibit the same direction of effect with the known result (binomial test $p = 0.00129$).

Table 21: Top known loci in MERGE model invn Adjusted AGE_HBA1C+SEX (**bold** variants indicate matching direction of effect)

CHR	POS	ID	EA	OA	N	FREQ _{AVG}	FREQ _{MIN}	FREQ _{MAX}	EFFECT	STDERR	P	DIR	COHORT	GENECLOSEST	R ²	ID _{KNOWN}	N _{KNOWN}	EFFECT _{KNOWN}	STDERR _{KNOWN}	P _{KNOWN}
17	80685533	rs1046896	T	C	1,637	0.311	0.241	0.381	0.134	3.68 · 10 ⁻²	2.73 · 10 ⁻⁴	+++	META_EX	FN3KRP	1	rs1046896	46,368	3.46 · 10 ⁻²	3.2 · 10 ⁻³	1.58 · 10 ⁻²⁶
10	71099888	rs10159477	A	G	1,436	0.139	0.111	0.163	3.84 · 10 ⁻²	5.39 · 10 ⁻²	0.476	+++xxx	META_GWAS	HK1	1	rs10159477	46,368	-5.86 · 10 ⁻²	5.6 · 10 ⁻³	3.19 · 10 ⁻²⁵
7	44229068	rs1799884	T	C	1,636	0.178	0.16	0.201	8.38 · 10 ⁻²	4.49 · 10 ⁻²	6.19 · 10 ⁻²	+++	META_EX	GCK	1	rs1799884	46,368	3.8 · 10 ⁻²	4.1 · 10 ⁻³	1.45 · 10 ⁻²⁰
17	80795783	rs7225515	A	G	190	0.263	0.164	0.345	0.242	0.112	3.04 · 10 ⁻²	xxx+++	META_GWAS	ZNF750	1	rs7225515	46,368	3.56 · 10 ⁻²	3.9 · 10 ⁻³	2.31 · 10 ⁻²⁰
6	26093141	rs1800562	G	A	1,637	1.8 · 10 ⁻²	1.16 · 10 ⁻²	5.19 · 10 ⁻²	0.103	0.134	0.445	++	META_EX	HFE	1	rs1800562	46,368	6.36 · 10 ⁻²	6.9 · 10 ⁻³	2.59 · 10 ⁻²⁰
17	80873067	rs9912684	T	C	1,436	0.202	0.143	0.293	0.113	4.59 · 10 ⁻²	1.36 · 10 ⁻²	+++xxx	META_GWAS	TBCD	1	rs9912684	46,368	3.48 · 10 ⁻²	3.9 · 10 ⁻³	3.07 · 10 ⁻¹⁹
7	44248828	rs2908282	A	G	190	0.187	0.141	0.221	0.123	0.131	0.347	xxx+++	META_GWAS	YKT6	1	rs2908282	46,368	4.04 · 10 ⁻²	4.5 · 10 ⁻³	3.55 · 10 ⁻¹⁹
2	169791438	rs552976	G	A	1,637	0.65	0.613	0.689	4.39 · 10 ⁻²	3.64 · 10 ⁻²	0.227	+++	META_EX	ABCB11	1	rs552976	46,368	2.9 · 10 ⁻²	3.4 · 10 ⁻³	8.16 · 10 ⁻¹⁸
2	169763148	rs560887	C	T	1,634	0.873	0.717	0.962	0.111	5.53 · 10 ⁻²	4.5 · 10 ⁻²	+++	META_EX	G6PC2	1	rs560887	46,368	3.18 · 10 ⁻²	3.7 · 10 ⁻³	1.04 · 10 ⁻¹⁷
22	37462936	rs855791	G	A	1,637	0.7	0.562	0.848	2.24 · 10 ⁻²	4.02 · 10 ⁻²	0.577	++	META_EX	TMPRSS6	1	rs855791	46,368	-2.71 · 10 ⁻²	3.6 · 10 ⁻³	2.74 · 10 ⁻¹⁴
6	25842951	rs1408272	T	G	1,637	1.95 · 10 ⁻²	1.02 · 10 ⁻²	4.62 · 10 ⁻²	0.128	0.129	0.32	+++	META_EX	SLC17A3	1	rs1408272	46,368	6.05 · 10 ⁻²	8.4 · 10 ⁻³	6.29 · 10 ⁻¹³
6	25821770	rs17342717	C	T	1,637	3.57 · 10 ⁻²	1.36 · 10 ⁻²	7.12 · 10 ⁻²	4.88 · 10 ⁻²	9.53 · 10 ⁻²	0.609	++	META_EX	SLC17A1	1	rs17342717	46,368	4.49 · 10 ⁻²	6.3 · 10 ⁻³	1.26 · 10 ⁻¹²
8	41630405	rs4737009	A	G	1,629	0.401	0.263	0.54	2 · 10 ⁻²	3.72 · 10 ⁻²	0.591	++	META_EX	ANK1	1	rs4737009	46,368	2.69 · 10 ⁻²	3.9 · 10 ⁻³	6.12 · 10 ⁻¹²
11	92673828	rs1387153	C	T	1,637	0.309	0.266	0.354	4.15 · 10 ⁻²	3.77 · 10 ⁻²	0.272	++	META_EX	MTNR1B	1	rs1387153	46,368	-2.58 · 10 ⁻²	3.9 · 10 ⁻³	3.96 · 10 ⁻¹¹
2	169750483	rs477224	C	T	1,434	0.546	0.489	0.66	9.64 · 10 ⁻²	3.72 · 10 ⁻²	9.51 · 10 ⁻³	+++xxx	META_GWAS	SPC25	1	rs477224	46,368	2.36 · 10 ⁻²	3.7 · 10 ⁻³	2.05 · 10 ⁻¹⁰
13	113331868	rs7998202	G	A	1,636	0.211	0.154	0.265	9.33 · 10 ⁻²	4.33 · 10 ⁻²	3.14 · 10 ⁻²	+++	META_EX	ATP11A	1	rs7998202	46,368	3.07 · 10 ⁻²	5.3 · 10 ⁻³	5.24 · 10 ⁻⁹
1	158607935	rs857725	G	T	1,637	0.187	0.109	0.254	0.107	4.49 · 10 ⁻²	1.68 · 10 ⁻²	++	META_EX	SPTA1	1	rs857725	46,368	2.15 · 10 ⁻²	3.8 · 10 ⁻³	1.26 · 10 ⁻⁸
6	25624395	rs7765813	G	T	1,436	3.69 · 10 ⁻²	1.59 · 10 ⁻²	7.73 · 10 ⁻²	8.92 · 10 ⁻²	0.1	0.372	+++xxx	META_GWAS	LRRC16A	1	rs7765813	46,368	3.43 · 10 ⁻²	6.1 · 10 ⁻³	1.66 · 10 ⁻⁸
17	80908501	rs12949939	C	T	1,626	0.26	0.213	0.303	7.44 · 10 ⁻²	4.05 · 10 ⁻²	6.64 · 10 ⁻²	+++++	META_GWAS	B3GNTL1	1	rs12949939	46,368	2.03 · 10 ⁻²	3.7 · 10 ⁻³	3.19 · 10 ⁻⁸
17	80703380	rs2264574	T	C	190	0.687	0.656	0.704	0.31	0.108	4.16 · 10 ⁻³	xxx+++	META_GWAS	FN3K	1	rs2264574	46,368	2.19 · 10 ⁻²	3.5 · 10 ⁻³	4.84 · 10 ⁻¹⁰

Table 22 shows statistics from the MERGE cohort for 20 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 ($\bar{R}^2 \geq 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. There are 8 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 20 variants in both studies, 17 exhibit the same direction of effect with the known result (binomial test $p = 0.00129$).

Table 22: Top known loci in MERGE model invn Adjusted AGE_HBA1C+SEX+BMI (**bold** variants indicate matching direction of effect)

CHR	POS	ID	EA	OA	N	FREQ _{AVG}	FREQ _{MIN}	FREQ _{MAX}	EFFECT	STDERR	P	DIR	COHORT	GENECLOSEST	R ²	ID _{KNOWN}	N _{KNOWN}	EFFECT _{KNOWN}	STDERR _{KNOWN}	P _{KNOWN}
17	80685533	rs1046896	T	C	1,593	0.313	0.241	0.386	0.114	3.74 · 10 ⁻²	2.28 · 10 ⁻³	+++	META_EX	FN3KRP	1	rs1046896	46,368	3.46 · 10 ⁻²	3.2 · 10 ⁻³	1.58 · 10 ⁻²⁶
10	71099888	rs10159477	A	G	1,399	0.14	0.111	0.166	6.57 · 10 ⁻²	5.44 · 10 ⁻²	0.227	+++xxx	META_GWAS	HK1	1	rs10159477	46,368	-5.86 · 10 ⁻²	5.6 · 10 ⁻³	3.19 · 10 ⁻²⁵
7	44229068	rs1799884	T	C	1,592	0.178	0.161	0.203	9.15 · 10 ⁻²	4.54 · 10 ⁻²	4.37 · 10 ⁻²	+++	META_EX	GCK	1	rs1799884	46,368	3.8 · 10 ⁻²	4.1 · 10 ⁻³	1.45 · 10 ⁻²⁰
17	80795783	rs7225515	A	G	177	0.274	0.172	0.359	0.239	0.116	3.87 · 10 ⁻²	xxx+++	META_GWAS	ZNF750	1	rs7225515	46,368	3.56 · 10 ⁻²	3.9 · 10 ⁻³	2.31 · 10 ⁻²⁰
6	26093141	rs1800562	G	A	1,593	1.79 · 10 ⁻²	1.11 · 10 ⁻²	5.18 · 10 ⁻²	9.79 · 10 ⁻²	0.137	0.474	++	META_EX	HFE	1	rs1800562	46,368	6.36 · 10 ⁻²	6.9 · 10 ⁻³	2.59 · 10 ⁻²⁰
17	80873067	rs9912684	T	C	1,399	0.203	0.143	0.298	8.99 · 10 ⁻²	4.64 · 10 ⁻²	5.28 · 10 ⁻²	+++xxx	META_GWAS	TBCD	1	rs9912684	46,368	3.48 · 10 ⁻²	3.9 · 10 ⁻³	3.07 · 10 ⁻¹⁹
7	44248828	rs2908282	A	G	177	0.192	0.148	0.218	0.126	0.135	0.352	xxx++	META_GWAS	YKT6	1	rs2908282	46,368	4.04 · 10 ⁻²	4.5 · 10 ⁻³	3.55 · 10 ⁻¹⁹
2	169791438	rs552976	G	A	1,593	0.652	0.613	0.691	4.94 · 10 ⁻²	3.69 · 10 ⁻²	0.181	+++	META_EX	ABCB11	1	rs552976	46,368	2.9 · 10 ⁻²	3.4 · 10 ⁻³	8.16 · 10 ⁻¹⁸
2	169763148	rs560887	C	T	1,590	0.874	0.721	0.962	0.12	5.59 · 10 ⁻²	3.14 · 10 ⁻²	+++	META_EX	G6PC2	1	rs560887	46,368	3.18 · 10 ⁻²	3.7 · 10 ⁻³	1.04 · 10 ⁻¹⁷
22	37462936	rs855791	G	A	1,593	0.702	0.564	0.851	1.01 · 10 ⁻²	4.08 · 10 ⁻²	0.805	++	META_EX	TMPRSS6	1	rs855791	46,368	-2.71 · 10 ⁻²	3.6 · 10 ⁻³	2.74 · 10 ⁻¹⁴
6	25842951	rs1408272	T	G	1,593	1.91 · 10 ⁻²	1.05 · 10 ⁻²	4.38 · 10 ⁻²	0.102	0.132	0.44	+++	META_EX	SLC17A3	1	rs1408272	46,368	6.05 · 10 ⁻²	8.4 · 10 ⁻³	6.29 · 10 ⁻¹³
6	25821770	rs17342717	C	T	1,593	3.45 · 10 ⁻²	1.41 · 10 ⁻²	6.57 · 10 ⁻²	2.55 · 10 ⁻²	9.78 · 10 ⁻²	0.794	++	META_EX	SLC17A1	1	rs17342717	46,368	4.49 · 10 ⁻²	6.3 · 10 ⁻³	1.26 · 10 ⁻¹²
8	41630405	rs4737009	A	G	1,585	0.403	0.266	0.542	1.59 · 10 ⁻²	3.76 · 10 ⁻²	0.672	++	META_EX	ANK1	1	rs4737009	46,368	2.69 · 10 ⁻²	3.9 · 10 ⁻³	6.12 · 10 ⁻¹²
11	92673828	rs1387153	C	T	1,593	0.31	0.269	0.355	4.88 · 10 ⁻²	3.8 · 10 ⁻²	0.2	+++	META_EX	MTNR1B	1	rs1387153	46,368	-2.58 · 10 ⁻²	3.9 · 10 ⁻³	3.96 · 10 ⁻¹¹
2	169750483	rs477224	C	T	1,397	0.547	0.491	0.66	9.08 · 10 ⁻²	3.77 · 10 ⁻²	1.6 · 10 ⁻²	+++xxx	META_GWAS	SPC25	1	rs477224	46,368	2.36 · 10 ⁻²	3.7 · 10 ⁻³	2.05 · 10 ⁻¹⁰
13	113331868	rs7998202	G	A	1,592	0.213	0.155	0.268	9.69 · 10 ⁻²	4.37 · 10 ⁻²	2.67 · 10 ⁻²	+++	META_EX	ATP11A	1	rs7998202	46,368	3.07 · 10 ⁻²	5.3 · 10 ⁻³	5.24 · 10 ⁻⁹
1	158607935	rs857725	G	T	1,593	0.187	0.111	0.251	0.115	4.55 · 10 ⁻²	1.17 · 10 ⁻²	++	META_EX	SPTA1	1	rs857725	46,368	2.15 · 10 ⁻²	3.8 · 10 ⁻³	1.26 · 10 ⁻⁸
6	25624395	rs7765813	G	T	1,399	3.72 · 10 ⁻²	1.65 · 10 ⁻²	7.87 · 10 ⁻²	3.63 · 10 ⁻²	0.102	0.721	+++xxx	META_GWAS	LRRC16A	1	rs7765813	46,368	3.43 · 10 ⁻²	6.1 · 10 ⁻³	1.66 · 10 ⁻⁸
17	80908501	rs12949939	C	T	1,576	0.261	0.224	0.305	6.75 · 10 ⁻²	4.1 · 10 ⁻²	9.96 · 10 ⁻²	+++++	META_GWAS	B3GNTL1	1	rs12949939	46,368	2.03 · 10 ⁻²	3.7 · 10 ⁻³	3.19 · 10 ⁻⁸
17	80703380	rs2264574	T	C	177	0.686	0.655	0.709	0.349	0.11	1.45 · 10 ⁻³	xxx+++	META_GWAS	FN3K	1	rs2264574	46,368	2.19 · 10 ⁻²	3.5 · 10 ⁻³	4.84 · 10 ⁻¹⁰

6 Acknowledgements

We would like to acknowledge the following people for their contributions to this work.

Ryan Koesterer

Maria Costanzo

Lizz Caulkins

Noel Burt

Jason Flannick

Miriam Udler

Alisa Manning

Jose Florez

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