# AMP-DCC Data Analysis Report

# BioMe

# Phase 2

07/10/2019 (15:45)

Prepared by Ryan Koesterer on behalf of the AMP-DCC Data Analysis Team at Broad Institute

Contact: amp-dcc-dat@broadinstitute.org

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

## Contents

# 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

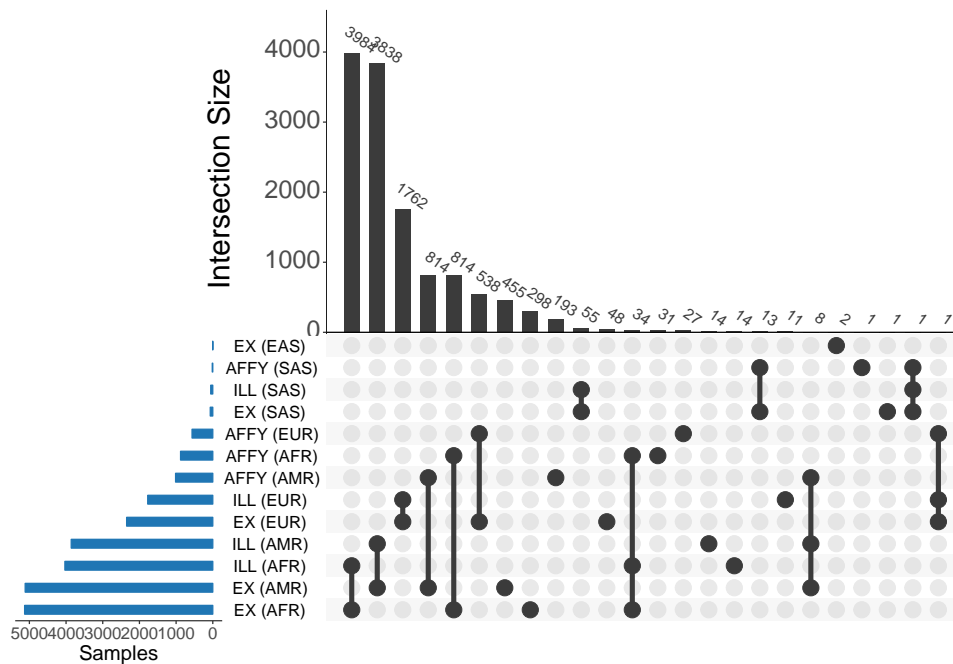| ID | Filename | Format | LiftOver |
|---|---|---|---|
| EX | BioMe_EXOMECHIP | bfile | N/A |
| ILL | BioMe_ILLUMINA | bfile | N/A |
| AFFY | BioMe_AFFY | bfile | N/A |

Figure 1: Samples remaining for analysis after quality control
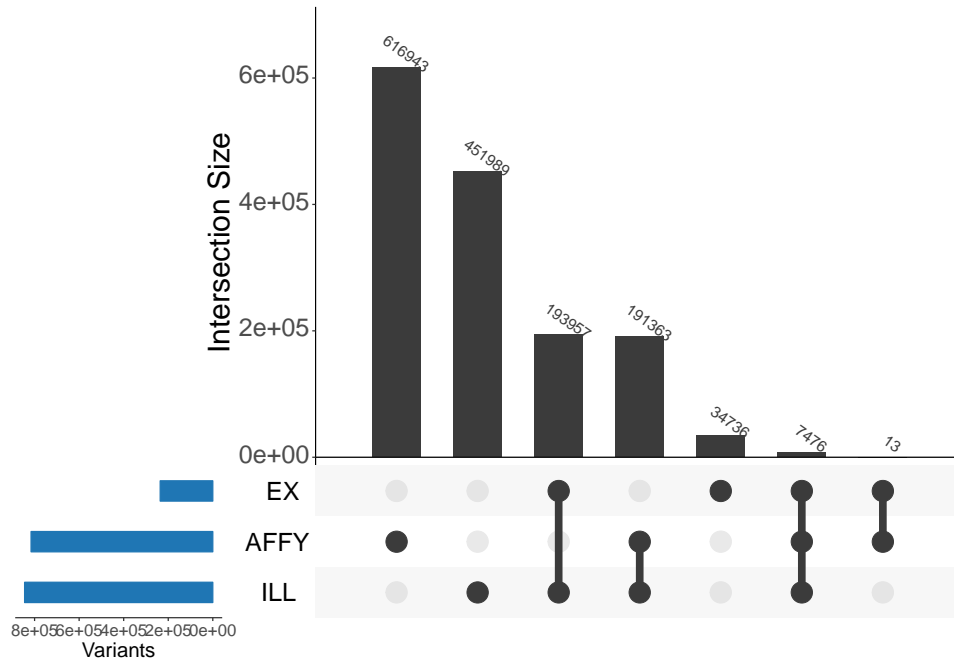
Figure 2: Variants remaining for analysis after quality control

# 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 $MAF >= 0.01$ and $callrate >= 0.98$ 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 ($kinship >= 0.0884$) to a sample from any preceeding 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 ($p <= 0.05$), 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   Serum Creatinine (SERUM_CREATININE)

## 3.1   Summary
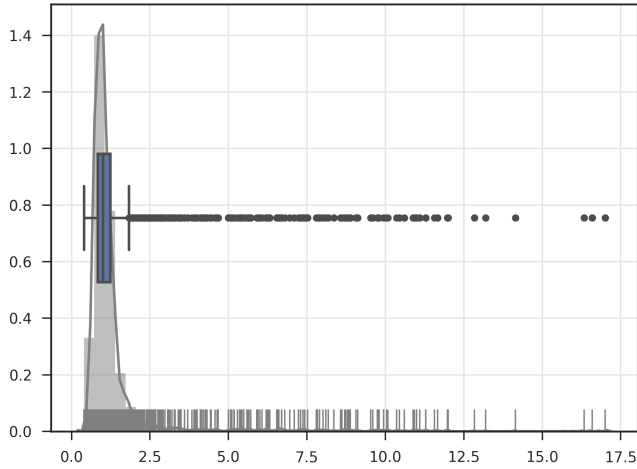


(a) EX_AFR
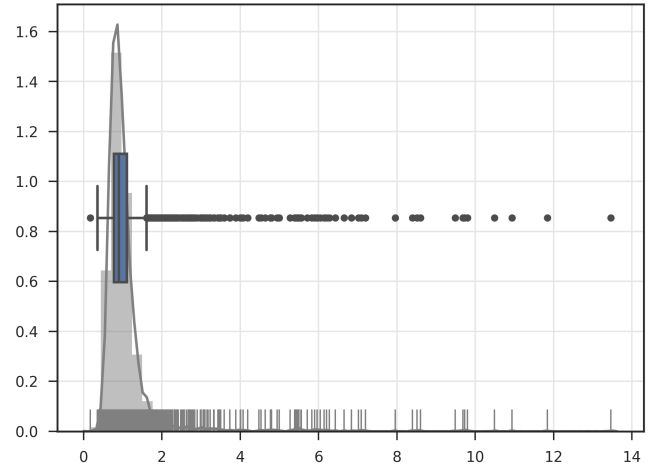
(b) EX_AMR
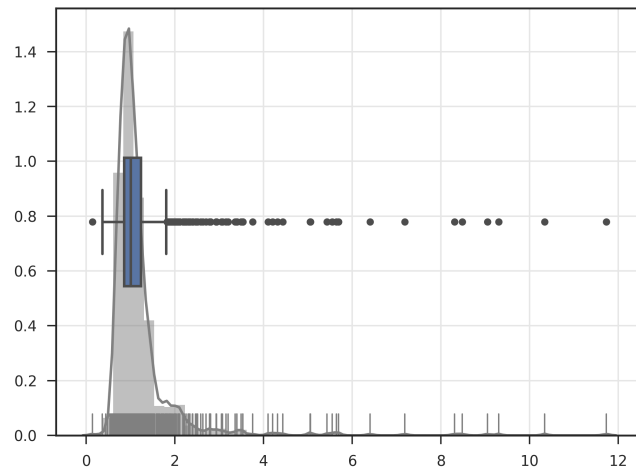
(c) EX_EUR

Figure 3: Distribution of SERUM_CREATININE in META_EX by cohort

(a) AFFY_AFR

(b) AFFY_AMR

(c) AFFY_EUR

(d) ILL_AFR

(e) ILL_AMR
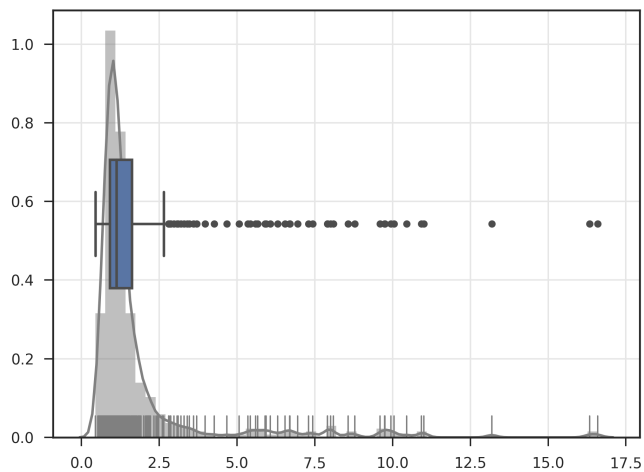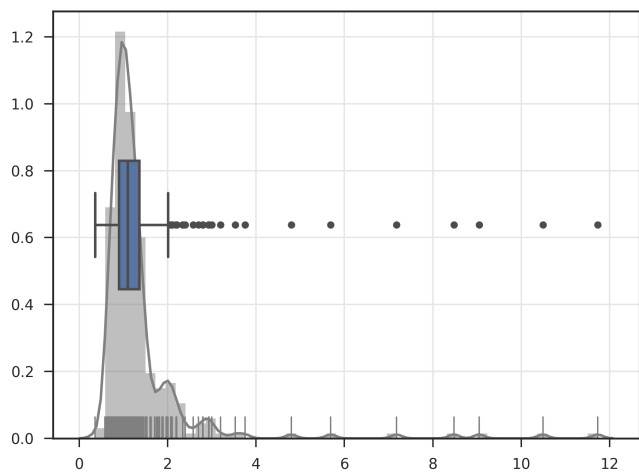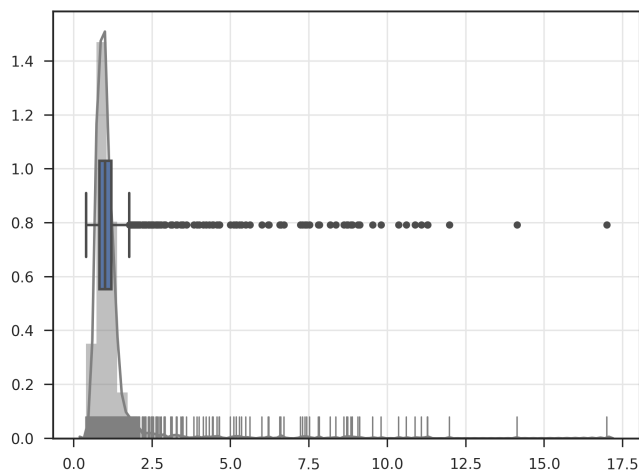


(f) ILL_EUR
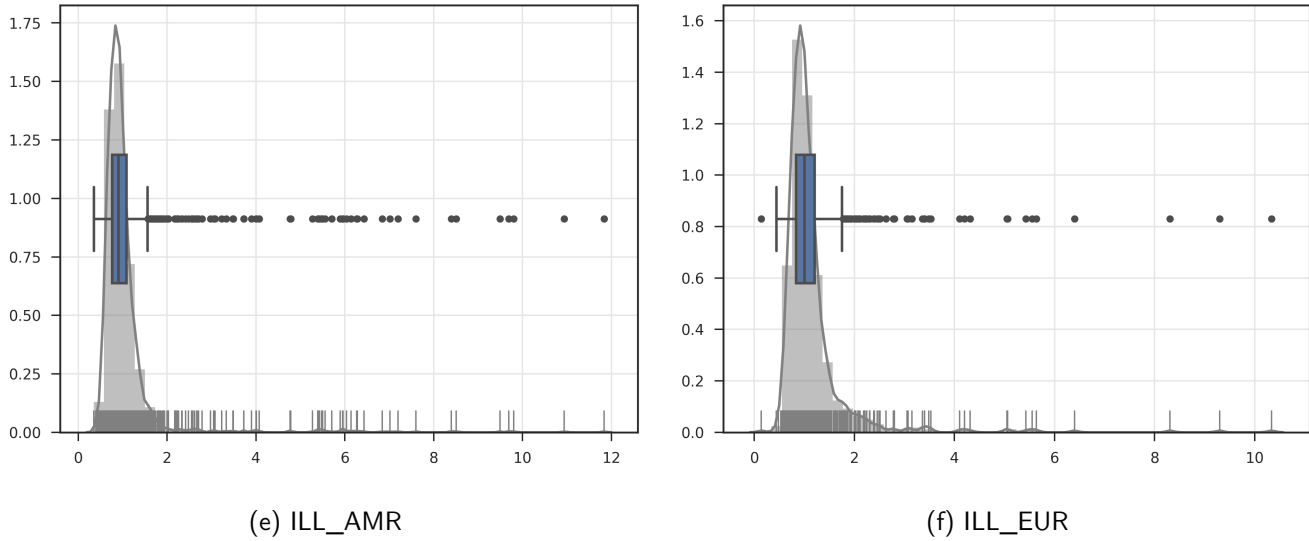
Figure 4: Distribution of SERUM_CREATININE in META_GWAS by cohort

Table 5: Summary of samples removed from Serum Creatinine analysis by cohort and model

| Cohort | Array | Ancestry | Trans | Covars | Total | -SampleQc | -missObs | -Kinship | -PcOutlier |
|---|---|---|---|---|---|---|---|---|---|
| META_EX EX_AFR | EX | AFR | invn | AGE_SERUM_CREATININE+SEX | 5172 | 44 | 2385 | 173 | 51 |
| META_EX EX_AMR | EX | AMR | invn | AGE_SERUM_CREATININE+SEX | 5144 | 32 | 2545 | 260 | 0 |
| META_EX EX_EUR | EX | EUR | invn | AGE_SERUM_CREATININE+SEX | 2379 | 30 | 1273 | 3 | 0 |
| META_GWAS AFFY_AFR | AFFY | AFR | invn | AGE_SERUM_CREATININE+SEX | 897 | 18 | 353 | 97 | 0 |
| META_GWAS AFFY_AMR | AFFY | AMR | invn | AGE_SERUM_CREATININE+SEX | 1035 | 20 | 439 | 122 | 0 |
| META_GWAS AFFY_EUR | AFFY | EUR | invn | AGE_SERUM_CREATININE+SEX | 578 | 12 | 288 | 5 | 0 |
| META_GWAS ILL_AFR | ILL | AFR | invn | AGE_SERUM_CREATININE+SEX | 4077 | 46 | 1921 | 0 | 37 |
| META_GWAS ILL_AMR | ILL | AMR | invn | AGE_SERUM_CREATININE+SEX | 3884 | 26 | 1956 | 0 | 0 |
| META_GWAS ILL_EUR | ILL | EUR | invn | AGE_SERUM_CREATININE+SEX | 1797 | 23 | 983 | 0 | 0 |

Table 6: Summary of samples remaining for Serum Creatinine analysis by cohort and model

| Cohort | Array | Ancestry | Trans | Covars | PCs | N | Male | Female | Max | Min | $\mu$ | $\tilde{x}$ | $\sigma$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| META_EX EX_AFR | EX | AFR | invn | AGE_SERUM_CREATININE+SEX | 8 | 2545 | 972 | 1573 | 17.0 | 0.39 | 1.331 | 1.0 | 1.447 |
| META_EX EX_AMR | EX | AMR | invn | AGE_SERUM_CREATININE+SEX | 1 | 2322 | 940 | 1382 | 13.46 | 0.35 | 1.103 | 0.91 | 0.925 |
| META_EX EX_EUR | EX | EUR | invn | AGE_SERUM_CREATININE+SEX | 1 | 1086 | 747 | 339 | 11.73 | 0.14 | 1.205 | 1.0 | 0.887 |
| META_GWAS AFFY_AFR | AFFY | AFR | invn | AGE_SERUM_CREATININE+SEX | 0 | 434 | 197 | 237 | 16.59 | 0.44 | 1.82 | 1.125 | 2.137 |
| META_GWAS AFFY_AMR | AFFY | AMR | invn | AGE_SERUM_CREATININE+SEX | 0 | 460 | 205 | 255 | 13.46 | 0.38 | 1.463 | 1.09 | 1.368 |
| META_GWAS AFFY_EUR | AFFY | EUR | invn | AGE_SERUM_CREATININE+SEX | 0 | 280 | 238 | 42 | 11.73 | 0.36 | 1.36 | 1.1 | 1.131 |
| META_GWAS ILL_AFR | ILL | AFR | invn | AGE_SERUM_CREATININE+SEX | 9 | 2091 | 777 | 1314 | 17.0 | 0.39 | 1.209 | 0.98 | 1.169 |
| META_GWAS ILL_AMR | ILL | AMR | invn | AGE_SERUM_CREATININE+SEX | 1 | 1914 | 757 | 1157 | 11.84 | 0.35 | 1.035 | 0.9 | 0.812 |
| META_GWAS ILL_EUR | ILL | EUR | invn | AGE_SERUM_CREATININE+SEX | 1 | 801 | 507 | 294 | 10.34 | 0.14 | 1.151 | 0.99 | 0.779 |

## 3.2 Calibration



$\lambda \approx 1.011$
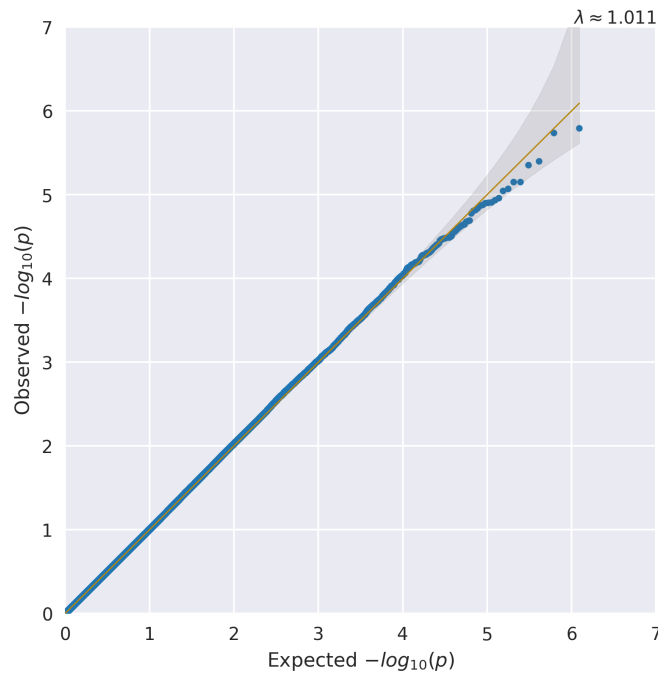
(a) invn Adjusted AGE_SERUM_CREATININE+SEX

Figure 5: QQ plots for SERUM_CREATININE in the MERGE analysis



$gws \approx 5.4e - 08$
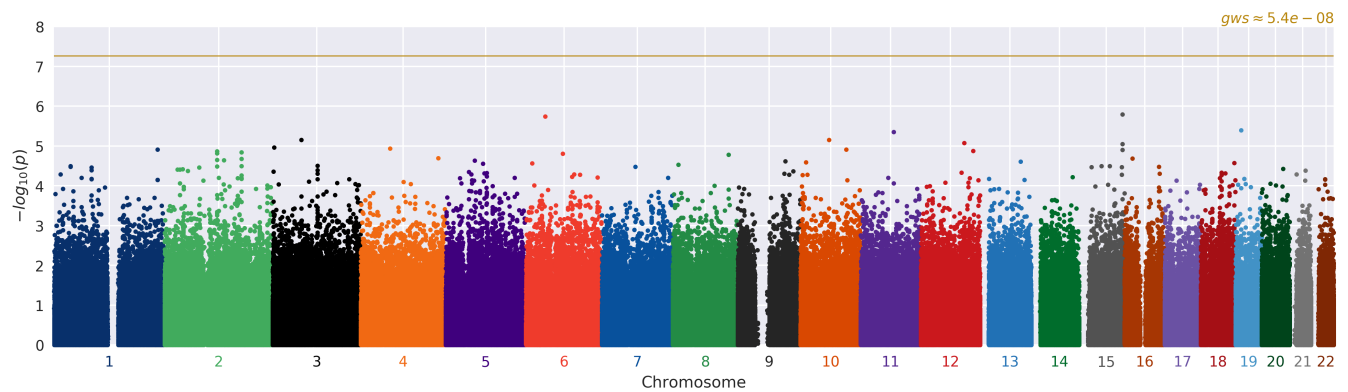
(a) invn Adjusted AGE_SERUM_CREATININE+SEX

Figure 6: Manhattan plots for SERUM_CREATININE in the MERGE analysis

## 3.3 Top associations

Table 7: Top variants in the MERGE invn Adjusted AGE_SERUM_CREATININE+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 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 15 | 97587651 | rs234538 | T | G | SPATA8 | META_GWAS | +++xxx | 4,804 | 2,041 | 2,763 | 0.427 | 0.341 | 0.512 | $9.89 \cdot 10^{-2}$ | $2.06 \cdot 10^{-2}$ | 1.104 | 4.798 | $1.61 \cdot 10^{-6}$ |
| 6 | 43303503 | rs2651202 | A | G | ZNF318 | META_GWAS | +++xxx | 4,806 | 2,041 | 2,765 | $1.53 \cdot 10^{-2}$ | $4.3 \cdot 10^{-3}$ | $3.93 \cdot 10^{-2}$ | 0.398 | $8.34 \cdot 10^{-2}$ | 1.489 | 4.772 | $1.82 \cdot 10^{-6}$ |
| 19 | 13035722 | rs35087277 | T | C | FARSA | META_EX | +++ | 5,953 | 2,659 | 3,294 | $8.32 \cdot 10^{-3}$ | $5.7 \cdot 10^{-3}$ | $1.75 \cdot 10^{-2}$ | 0.456 | $9.89 \cdot 10^{-2}$ | 1.578 | $-4.612$ | $3.99 \cdot 10^{-6}$ |
| 11 | 74170978 | rs3867279 | C | A | KCNE3 | META_GWAS | +++xxx | 4,806 | 2,041 | 2,765 | 0.169 | 0.128 | 0.202 | 0.126 | $2.74 \cdot 10^{-2}$ | 1.134 | $-4.591$ | $4.42 \cdot 10^{-6}$ |
| 3 | 64206296 | rs696231 | A | G | PRICKLE2 | META_GWAS | +++xxx | 4,806 | 2,041 | 2,765 | $9.95 \cdot 10^{-2}$ | $7.68 \cdot 10^{-2}$ | 0.123 | 0.152 | $3.39 \cdot 10^{-2}$ | 1.164 | 4.493 | $7.03 \cdot 10^{-6}$ |
| 10 | 64128954 | rs7096931 | C | A | ZNF365 | META_GWAS | +++xxx | 4,805 | 2,041 | 2,764 | 0.218 | 0.205 | 0.235 | 0.111 | $2.47 \cdot 10^{-2}$ | 1.117 | $-4.492$ | $7.06 \cdot 10^{-6}$ |
| 12 | 97606943 | rs12322545 | A | G | NEDD1 | META_GWAS | +++xxx | 4,805 | 2,041 | 2,764 | 0.273 | 0.166 | 0.394 | 0.104 | $2.34 \cdot 10^{-2}$ | 1.11 | 4.454 | $8.45 \cdot 10^{-6}$ |
| 3 | 3079127 | rs3749363 | T | G | CNTN4 | META_GWAS | +++xxx | 4,805 | 2,040 | 2,765 | $9 \cdot 10^{-2}$ | $6.6 \cdot 10^{-2}$ | 0.12 | 0.158 | $3.6 \cdot 10^{-2}$ | 1.171 | $-4.399$ | $1.09 \cdot 10^{-5}$ |
| 4 | 66294649 | rs7672488 | G | A | EPHA5 | META_GWAS | +++xxx | 4,801 | 2,037 | 2,764 | 0.718 | 0.645 | 0.8 | $1 \cdot 10^{-1}$ | $2.28 \cdot 10^{-2}$ | 1.105 | $-4.384$ | $1.16 \cdot 10^{-5}$ |
| 1 | 233256280 | rs717588 | G | A | PCNX2 | META_GWAS | +++xxx | 4,806 | 2,041 | 2,765 | 0.784 | 0.617 | 0.876 | 0.111 | $2.53 \cdot 10^{-2}$ | 1.117 | 4.372 | $1.23 \cdot 10^{-5}$ |
| 10 | 103067687 | rs590945 | T | C | BTRC | META_GWAS | ++++++ | 5,980 | 2,681 | 3,299 | 0.658 | 0.522 | 0.809 | $8.73 \cdot 10^{-2}$ | $2 \cdot 10^{-2}$ | 1.091 | $-4.37$ | $1.24 \cdot 10^{-5}$ |
| 12 | 118135896 | rs605265 | A | G | KSR2 | META_GWAS | ++++++ | 5,978 | 2,680 | 3,298 | 0.507 | 0.374 | 0.698 | $8.23 \cdot 10^{-2}$ | $1.89 \cdot 10^{-2}$ | 1.086 | $-4.356$ | $1.33 \cdot 10^{-5}$ |
| 2 | 117724192 | rs7608004 | G | A | DDX18 | META_GWAS | +++xxx | 4,804 | 2,040 | 2,764 | 0.495 | 0.387 | 0.565 | $8.82 \cdot 10^{-2}$ | $2.03 \cdot 10^{-2}$ | 1.092 | $-4.352$ | $1.35 \cdot 10^{-5}$ |
| 2 | 172663394 | rs6754817 | T | C | SLC25A12 | META_GWAS | xxx+++ | 1,174 | 640 | 534 | 0.293 | 0.26 | 0.327 | 0.196 | $4.51 \cdot 10^{-2}$ | 1.216 | 4.337 | $1.44 \cdot 10^{-5}$ |
| 6 | 82783397 | rs16893850 | T | C | IBTK | META_GWAS | xxx+++ | 1,169 | 639 | 530 | $4.32 \cdot 10^{-2}$ | $1.27 \cdot 10^{-2}$ | $7.99 \cdot 10^{-2}$ | 0.434 | 0.1 | 1.543 | 4.32 | $1.56 \cdot 10^{-5}$ |
| 8 | 125640964 | rs4870915 | G | A | MTSS1 | META_GWAS | xxx+++ | 1,169 | 639 | 530 | 0.235 | 0.141 | 0.356 | 0.212 | $4.93 \cdot 10^{-2}$ | 1.236 | 4.305 | $1.67 \cdot 10^{-5}$ |
| 4 | 174046753 | rs10022850 | C | A | GALNT7 | META_GWAS | xxx+++ | 1,174 | 640 | 534 | $2.73 \cdot 10^{-2}$ | $1.79 \cdot 10^{-3}$ | $5.65 \cdot 10^{-2}$ | 0.533 | 0.125 | 1.704 | 4.263 | $2.02 \cdot 10^{-5}$ |
| 16 | 17530588 | rs1559448 | C | G | XYLT1 | META_GWAS | xxx+++ | 1,173 | 639 | 534 | $2.56 \cdot 10^{-3}$ | $1.15 \cdot 10^{-3}$ | $4.35 \cdot 10^{-3}$ | 1.734 | 0.407 | 5.663 | 4.259 | $2.06 \cdot 10^{-5}$ |
| 2 | 172558172 | rs2138348 | T | G | DYNC1I2 | META_GWAS | xxx+++ | 1,174 | 640 | 534 | 0.292 | 0.258 | 0.325 | 0.193 | $4.53 \cdot 10^{-2}$ | 1.213 | 4.254 | $2.1 \cdot 10^{-5}$ |
| 2 | 132917161 | rs6707621 | G | A | ANKRD30BL | META_GWAS | xxx+++ | 1,173 | 640 | 533 | 0.13 | $1.61 \cdot 10^{-2}$ | 0.258 | 0.273 | $6.45 \cdot 10^{-2}$ | 1.314 | 4.235 | $2.28 \cdot 10^{-5}$ |

## 3.4 Previously identified risk loci

Table 8 shows statistics from the MERGE cohort for 10 loci that were shown to be significantly associated with Serum Creatinine in the 2016 Nature Communications paper by Kettunen et al [8]. 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 1 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 10 variants in both studies, 9 exhibit the same direction of effect with the known result (binomial test $p = 0.0107$).

Table 8: Top known loci in MERGE model invn Adjusted AGE_SERUM_CREATININE+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$_{KNOWN}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 15 | 45636584 | **rs1153860** | T | C | 1,174 | 0.661 | 0.4 | 0.876 | $1.42 \cdot 10^{-2}$ | $4.66 \cdot 10^{-2}$ | 0.76 | xxx+-+ | META_GWAS | GATM | 1 | rs1153860 | 24,925 | $7.34 \cdot 10^{-2}$ | $9.4 \cdot 10^{-3}$ | $6.99 \cdot 10^{-15}$ |
| 15 | 45683795 | **rs1145077** | T | G | 1,172 | 0.662 | 0.394 | 0.88 | $8.56 \cdot 10^{-3}$ | $4.69 \cdot 10^{-2}$ | 0.855 | xxx+-+ | META_GWAS | SPATA5L1 | 1 | rs1145077 | 24,925 | $7.35 \cdot 10^{-2}$ | $9.44 \cdot 10^{-3}$ | $8.05 \cdot 10^{-15}$ |
| 17 | 59465697 | **rs2079742** | C | T | 1,174 | 0.202 | 0.151 | 0.266 | $3.07 \cdot 10^{-2}$ | $5.1 \cdot 10^{-2}$ | 0.547 | xxx+-+ | META_GWAS | BCAS3 | 1 | rs2079742 | 24,925 | $9.59 \cdot 10^{-2}$ | $1.28 \cdot 10^{-2}$ | $8.61 \cdot 10^{-14}$ |
| 15 | 45609773 | rs1719250 | A | G | 1,174 | 0.611 | 0.541 | 0.667 | $3.06 \cdot 10^{-2}$ | $4.08 \cdot 10^{-2}$ | 0.453 | xxx-++ | META_GWAS | SLC28A2 | 1 | rs1719250 | 24,925 | $-6.51 \cdot 10^{-2}$ | $9.52 \cdot 10^{-3}$ | $8.52 \cdot 10^{-12}$ |
| 15 | 45729123 | **rs1974981** | G | A | 5,977 | 0.31 | 0.264 | 0.385 | $2.69 \cdot 10^{-2}$ | $1.98 \cdot 10^{-2}$ | 0.174 | +-+++ | META_GWAS | C15orf48 | 1 | rs1974981 | 24,925 | $7.03 \cdot 10^{-2}$ | $1.03 \cdot 10^{-2}$ | $9.04 \cdot 10^{-12}$ |
| 7 | 151415041 | **rs10224002** | G | A | 5,955 | 0.35 | 0.285 | 0.407 | $2.18 \cdot 10^{-2}$ | $1.94 \cdot 10^{-2}$ | 0.263 | +++ | META_EX | PRKAG2 | 1 | rs10224002 | 24,925 | $7.07 \cdot 10^{-2}$ | $1.11 \cdot 10^{-2}$ | $1.89 \cdot 10^{-10}$ |
| 4 | 77420784 | **rs1986734** | T | C | 4,806 | 0.343 | 0.237 | 0.483 | $2.32 \cdot 10^{-2}$ | $2.2 \cdot 10^{-2}$ | 0.291 | -++xxx | META_GWAS | SHROOM3 | 1 | rs1986734 | 24,925 | $6.19 \cdot 10^{-2}$ | $9.8 \cdot 10^{-3}$ | $3.04 \cdot 10^{-10}$ |
| 6 | 160693107 | **rs3119311** | C | T | 4,806 | 0.145 | 0.101 | 0.196 | $4.8 \cdot 10^{-2}$ | $2.89 \cdot 10^{-2}$ | $9.73 \cdot 10^{-2}$ | +++xxx | META_GWAS | SLC22A2 | 1 | rs3119311 | 24,925 | $9.08 \cdot 10^{-2}$ | $1.55 \cdot 10^{-2}$ | $5.29 \cdot 10^{-9}$ |
| 17 | 59483766 | **rs8068318** | C | T | 5,954 | 0.434 | 0.271 | 0.699 | $3.79 \cdot 10^{-2}$ | $1.97 \cdot 10^{-2}$ | $5.42 \cdot 10^{-2}$ | +++ | META_EX | TBX2 | 1 | rs8068318 | 24,925 | $6.21 \cdot 10^{-2}$ | $1.08 \cdot 10^{-2}$ | $8.69 \cdot 10^{-9}$ |
| 15 | 45801035 | **rs950027** | C | T | 5,979 | 0.745 | 0.48 | 0.916 | $5.81 \cdot 10^{-2}$ | $2.23 \cdot 10^{-2}$ | $9.26 \cdot 10^{-3}$ | +++++ | META_GWAS | SLC30A4 | 1 | rs950027 | 24,925 | $5.28 \cdot 10^{-2}$ | $9.32 \cdot 10^{-3}$ | $1.59 \cdot 10^{-8}$ |

# 4 Systolic Blood Pressure (SBP15)
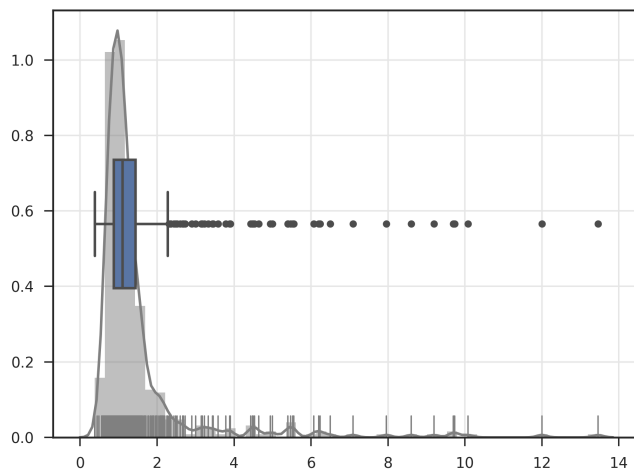
## 4.1 Summary
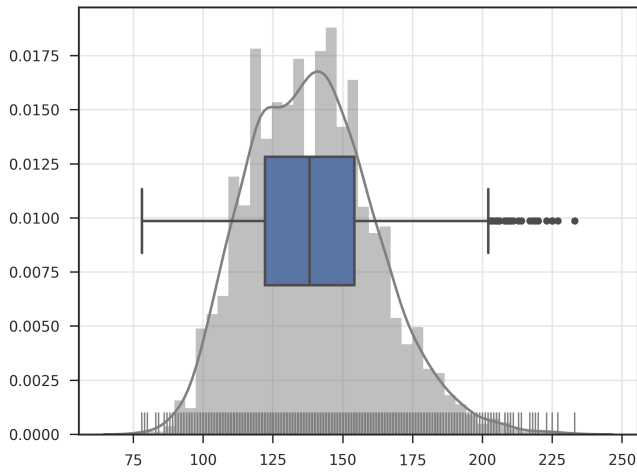


(a) EX_AFR
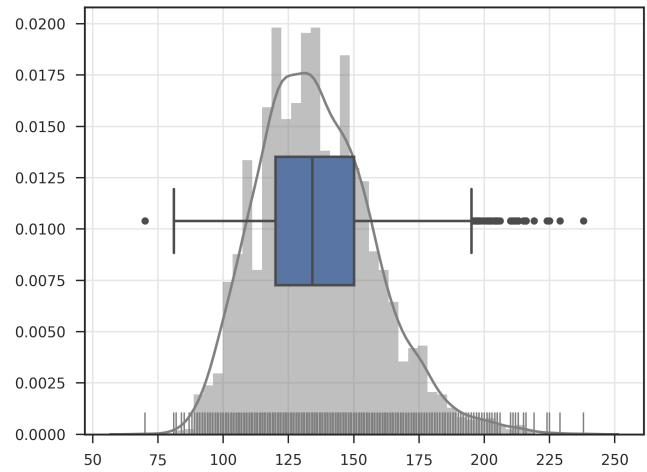


(b) EX_AMR
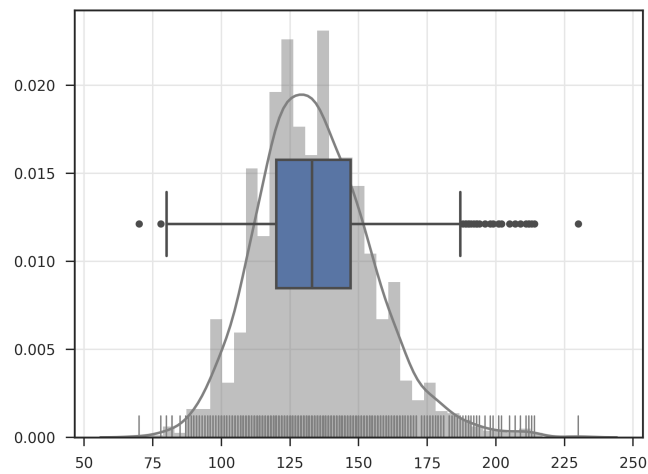


(c) EX_EUR

Figure 7: Distribution of SBP15 in META_EX by cohort

(a) AFFY_AFR



(b) AFFY_AMR



(c) AFFY_EUR



(d) ILL_AFR

(e) ILL_AMR
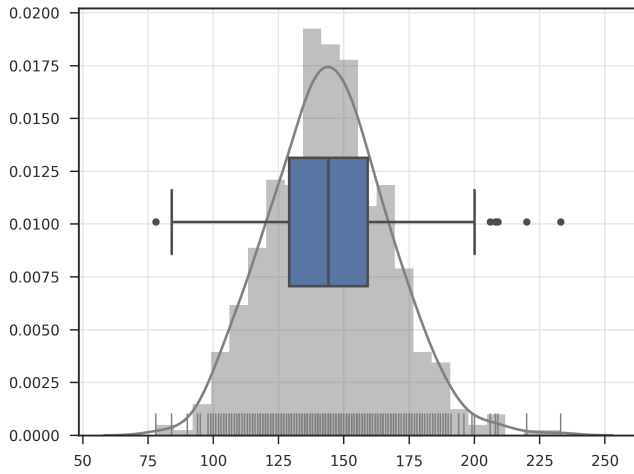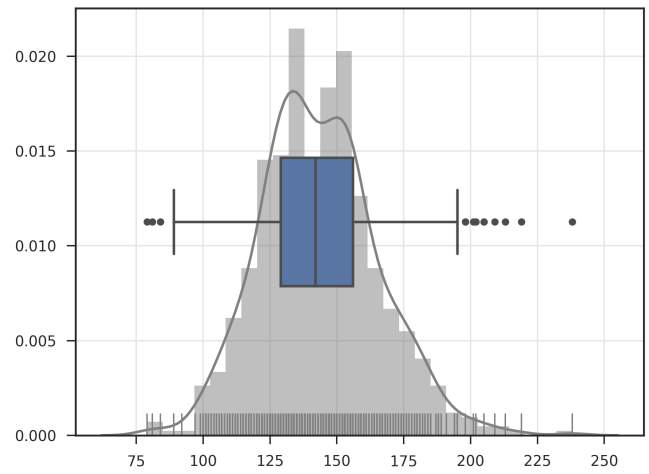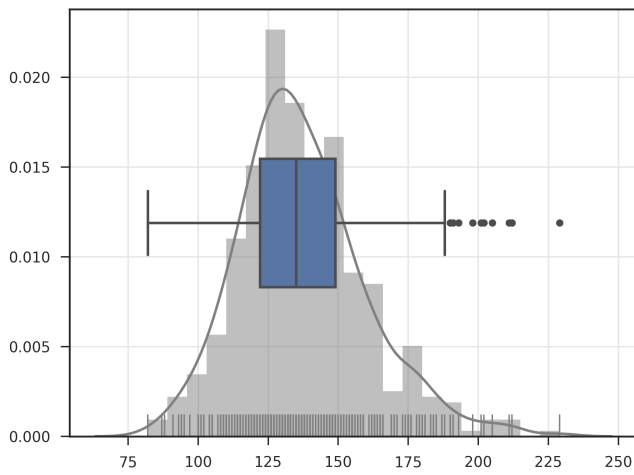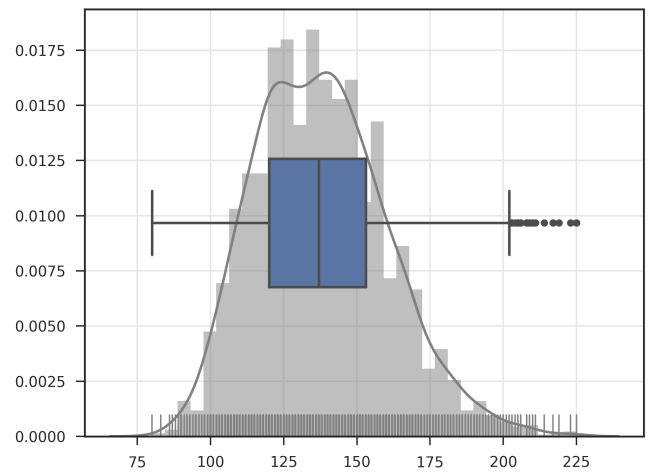


(f) ILL_EUR
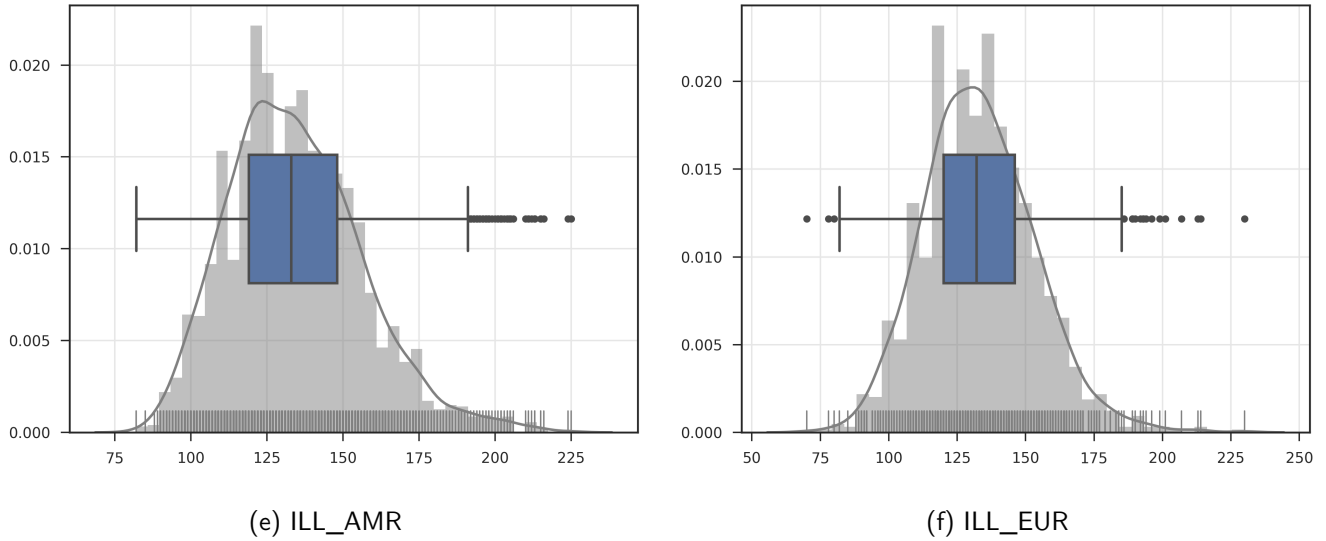
Figure 8: Distribution of SBP15 in META_GWAS by cohort

Table 9: Summary of samples removed from Systolic Blood Pressure analysis by cohort and model

| Cohort | Array | Ancestry | Trans | Covars | Total | -SampleQc | -missObs | -Kinship | -PcOutlier |
|---|---|---|---|---|---|---|---|---|---|
| META_EX EX_AFR | EX | AFR | invn | AGE_BP+AGE_BP2+SEX+BMI | 5172 | 44 | 1132 | 285 | 5 |
| META_EX EX_AMR | EX | AMR | invn | AGE_BP+AGE_BP2+SEX+BMI | 5144 | 32 | 1144 | 424 | 0 |
| META_EX EX_EUR | EX | EUR | invn | AGE_BP+AGE_BP2+SEX+BMI | 2379 | 30 | 626 | 6 | 1 |
| META_GWAS AFFY_AFR | AFFY | AFR | invn | AGE_BP+AGE_BP2+SEX+BMI | 897 | 18 | 208 | 127 | 0 |
| META_GWAS AFFY_AMR | AFFY | AMR | invn | AGE_BP+AGE_BP2+SEX+BMI | 1035 | 20 | 227 | 164 | 0 |
| META_GWAS AFFY_EUR | AFFY | EUR | invn | AGE_BP+AGE_BP2+SEX+BMI | 578 | 12 | 173 | 8 | 0 |
| META_GWAS ILL_AFR | ILL | AFR | invn | AGE_BP+AGE_BP2+SEX+BMI | 4077 | 46 | 893 | 4 | 0 |
| META_GWAS ILL_AMR | ILL | AMR | invn | AGE_BP+AGE_BP2+SEX+BMI | 3884 | 26 | 870 | 2 | 0 |
| META_GWAS ILL_EUR | ILL | EUR | invn | AGE_BP+AGE_BP2+SEX+BMI | 1797 | 23 | 456 | 1 | 0 |

Table 10: Summary of samples remaining for Systolic Blood Pressure analysis by cohort and model

| Cohort | Array | Ancestry | Trans | Covars | PCs | N | Male | Female | Max | Min | $\mu$ | $\tilde{x}$ | $\sigma$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| META_EX EX_AFR | EX | AFR | invn | AGE_BP+AGE_BP2+SEX+BMI | 0 | 3719 | 1311 | 2408 | 233.0 | 79.0 | 139.229 | 139.0 | 22.635 |
| META_EX EX_AMR | EX | AMR | invn | AGE_BP+AGE_BP2+SEX+BMI | 1 | 3553 | 1392 | 2161 | 238.0 | 81.0 | 135.615 | 134.0 | 22.326 |
| META_EX EX_EUR | EX | EUR | invn | AGE_BP+AGE_BP2+SEX+BMI | 8 | 1723 | 1150 | 573 | 230.0 | 70.0 | 134.22 | 133.0 | 20.786 |
| META_GWAS AFFY_AFR | AFFY | AFR | invn | AGE_BP+AGE_BP2+SEX+BMI | 0 | 550 | 240 | 310 | 233.0 | 79.0 | 144.856 | 145.0 | 22.874 |
| META_GWAS AFFY_AMR | AFFY | AMR | invn | AGE_BP+AGE_BP2+SEX+BMI | 0 | 627 | 273 | 354 | 238.0 | 81.0 | 143.046 | 141.0 | 21.842 |
| META_GWAS AFFY_EUR | AFFY | EUR | invn | AGE_BP+AGE_BP2+SEX+BMI | 0 | 391 | 319 | 72 | 212.0 | 82.0 | 137.235 | 135.0 | 22.431 |
| META_GWAS ILL_AFR | ILL | AFR | invn | AGE_BP+AGE_BP2+SEX+BMI | 0 | 3146 | 1080 | 2066 | 225.0 | 80.0 | 138.076 | 137.0 | 22.313 |
| META_GWAS ILL_AMR | ILL | AMR | invn | AGE_BP+AGE_BP2+SEX+BMI | 3 | 2994 | 1143 | 1851 | 225.0 | 82.0 | 134.365 | 133.0 | 22.02 |
| META_GWAS ILL_EUR | ILL | EUR | invn | AGE_BP+AGE_BP2+SEX+BMI | 0 | 1324 | 828 | 496 | 230.0 | 70.0 | 133.292 | 132.0 | 20.038 |

## 4.2   Calibration
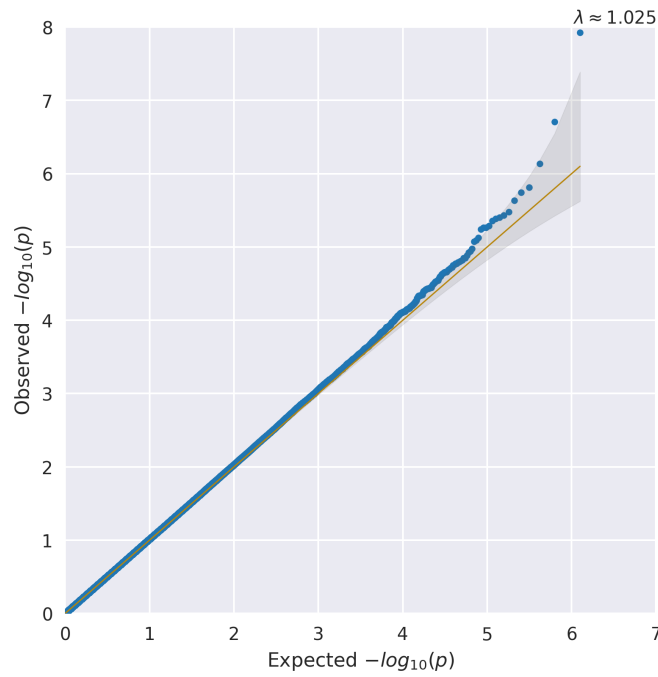


(a) invn Adjusted AGE_BP+AGE_BP2+SEX+BMI

Figure 9: QQ plots for SBP15 in the MERGE analysis
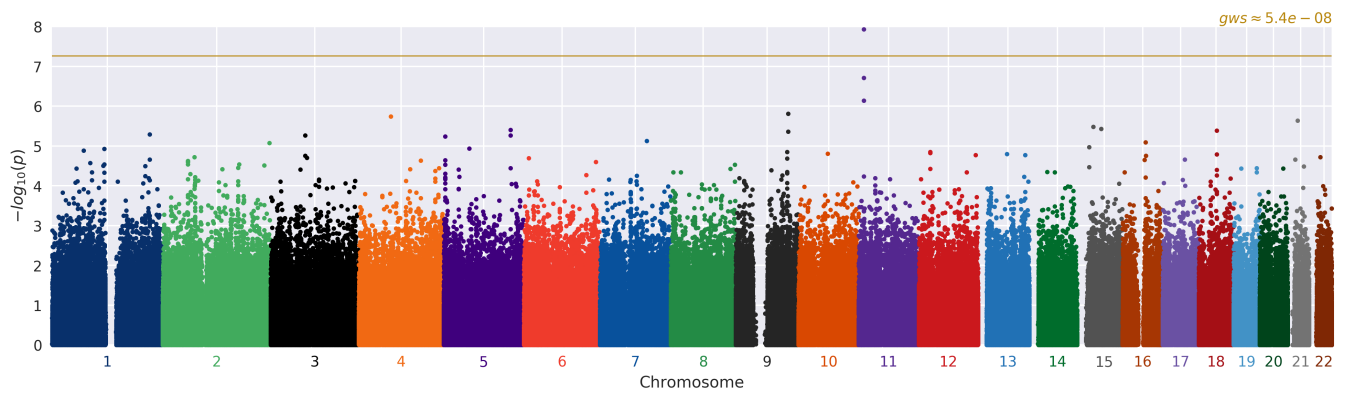


(a) invn Adjusted AGE_BP+AGE_BP2+SEX+BMI

Figure 10: Manhattan plots for SBP15 in the MERGE analysis

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## 4.3 Top associations

Table 11: Top variants in the MERGE invn Adjusted AGE_BP+AGE_BP2+SEX+BMI model (**bold** variants indicate previously identified associations)

| CHR | POS | ID | EA | OA | GENE$_{\text{CLOSEST}}$ | COHORT | DIR | N | MALE | FEMALE | FREQ$_{\text{AVG}}$ | FREQ$_{\text{MIN}}$ | FREQ$_{\text{MAX}}$ | EFFECT | STDERR | OR | ZSCORE | P |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 11 | 11386594 | rs1843784 | T | A | GALNT18 | META_GWAS | xxx+++ | 1,568 | 832 | 736 | 0.217 | 0.131 | 0.289 | 0.251 | $4.41 \cdot 10^{-2}$ | 1.286 | $-5.703$ | $1.18 \cdot 10^{-8}$ |
| 9 | 117502242 | rs2185935 | C | T | TNFSF15 | META_GWAS | +++++- | 9,032 | 3,883 | 5,149 | 0.183 | $8.74 \cdot 10^{-2}$ | 0.353 | $9.43 \cdot 10^{-2}$ | $1.96 \cdot 10^{-2}$ | 1.099 | $-4.805$ | $1.54 \cdot 10^{-6}$ |
| 4 | 71984094 | rs1985134 | G | A | SLC4A4 | META_GWAS | xxx+++ | 1,567 | 832 | 735 | 0.18 | 0.123 | 0.248 | 0.221 | $4.63 \cdot 10^{-2}$ | 1.247 | 4.774 | $1.81 \cdot 10^{-6}$ |
| 21 | 22624941 | rs2826754 | A | G | NCAM2 | META_GWAS | +++xxx | 7,460 | 3,050 | 4,410 | 0.311 | 0.25 | 0.378 | $8.34 \cdot 10^{-2}$ | $1.77 \cdot 10^{-2}$ | 1.087 | $-4.724$ | $2.32 \cdot 10^{-6}$ |
| 15 | 36780723 | rs7168196 | C | T | C15orf41 | META_GWAS | ++++-+ | 9,030 | 3,881 | 5,149 | 0.335 | 0.281 | 0.416 | $7.38 \cdot 10^{-2}$ | $1.59 \cdot 10^{-2}$ | 1.077 | 4.65 | $3.32 \cdot 10^{-6}$ |
| 15 | 54201160 | rs2255116 | G | T | UNC13C | META_GWAS | xxx+++ | 1,562 | 831 | 731 | $8.26 \cdot 10^{-2}$ | $1.28 \cdot 10^{-3}$ | 0.182 | 0.307 | $6.64 \cdot 10^{-2}$ | 1.36 | 4.628 | $3.69 \cdot 10^{-6}$ |
| 5 | 150282784 | rs2290989 | T | C | ZNF300 | META_GWAS | xxx+++ | 1,568 | 832 | 736 | $3.44 \cdot 10^{-2}$ | $2.09 \cdot 10^{-2}$ | $4.99 \cdot 10^{-2}$ | 0.447 | $9.7 \cdot 10^{-2}$ | 1.564 | $-4.613$ | $3.96 \cdot 10^{-6}$ |
| 18 | 40453910 | rs41444547 | C | A | RIT2 | META_GWAS | xxx+++ | 1,562 | 829 | 733 | $8.99 \cdot 10^{-2}$ | $3.19 \cdot 10^{-2}$ | 0.146 | 0.297 | $6.45 \cdot 10^{-2}$ | 1.346 | $-4.607$ | $4.08 \cdot 10^{-6}$ |
| 9 | 117483943 | rs7026324 | G | A | RP11-402G3 | META_GWAS | +++xxx | 7,464 | 3,051 | 4,413 | 0.219 | 0.1 | 0.42 | $9.39 \cdot 10^{-2}$ | $2.04 \cdot 10^{-2}$ | 1.098 | $-4.592$ | $4.39 \cdot 10^{-6}$ |
| 1 | 220228658 | rs10863529 | A | G | BPNT1 | META_GWAS | +++xxx | 7,459 | 3,050 | 4,409 | 0.503 | 0.365 | 0.69 | $7.59 \cdot 10^{-2}$ | $1.67 \cdot 10^{-2}$ | 1.079 | 4.56 | $5.12 \cdot 10^{-6}$ |
| 3 | 77419441 | rs4234495 | T | C | ROBO2 | META_GWAS | xxx+++ | 1,568 | 832 | 736 | 0.805 | 0.767 | 0.827 | 0.204 | $4.48 \cdot 10^{-2}$ | 1.226 | $-4.548$ | $5.42 \cdot 10^{-6}$ |
| 5 | 150199238 | rs12659091 | T | C | AC010441 | META_GWAS | xxx+++ | 1,568 | 832 | 736 | $3.41 \cdot 10^{-2}$ | $1.91 \cdot 10^{-2}$ | $4.99 \cdot 10^{-2}$ | 0.443 | $9.74 \cdot 10^{-2}$ | 1.557 | $-4.547$ | $5.44 \cdot 10^{-6}$ |
| 5 | 3470914 | rs2914204 | T | C | IRX1 | META_GWAS | xxx+++ | 1,564 | 829 | 735 | 0.765 | 0.56 | 0.926 | 0.204 | $4.5 \cdot 10^{-2}$ | 1.226 | $-4.535$ | $5.75 \cdot 10^{-6}$ |
| 7 | 105554522 | rs17152281 | C | A | ATXN7L1 | META_GWAS | xxx+++ | 1,556 | 826 | 730 | 0.141 | 0.129 | 0.161 | 0.234 | $5.22 \cdot 10^{-2}$ | 1.263 | $-4.481$ | $7.43 \cdot 10^{-6}$ |
| 16 | 51656556 | rs9674344 | T | A | SALL1 | META_GWAS | xxx+++ | 1,568 | 832 | 736 | $6.7 \cdot 10^{-2}$ | $1.28 \cdot 10^{-3}$ | 0.122 | 0.317 | $7.1 \cdot 10^{-2}$ | 1.373 | 4.463 | $8.07 \cdot 10^{-6}$ |
| 2 | 239600686 | rs7594129 | A | C | TWIST2 | META_GWAS | +++-++ | 9,032 | 3,883 | 5,149 | 0.588 | 0.459 | 0.727 | $6.87 \cdot 10^{-2}$ | $1.54 \cdot 10^{-2}$ | 1.071 | 4.453 | $8.46 \cdot 10^{-6}$ |
| 15 | 27183589 | rs1864793 | T | C | GABRB3 | META_GWAS | xxx+++ | 1,567 | 832 | 735 | 0.445 | 0.384 | 0.488 | 0.158 | $3.6 \cdot 10^{-2}$ | 1.172 | 4.405 | $1.06 \cdot 10^{-5}$ |
| 5 | 57939227 | rs4997647 | T | G | RAB3C | META_GWAS | +++xxx | 7,462 | 3,049 | 4,413 | $9.29 \cdot 10^{-2}$ | $7.02 \cdot 10^{-2}$ | 0.103 | 0.124 | $2.84 \cdot 10^{-2}$ | 1.132 | 4.387 | $1.15 \cdot 10^{-5}$ |
| 1 | 118017634 | rs10923312 | A | T | MAN1A2 | META_GWAS | xxx+++ | 1,568 | 832 | 736 | 0.125 | 0.112 | 0.141 | 0.235 | $5.37 \cdot 10^{-2}$ | 1.265 | $-4.38$ | $1.19 \cdot 10^{-5}$ |
| 1 | 71024268 | rs4612577 | G | T | CTH | META_GWAS | xxx+++ | 1,568 | 832 | 736 | 0.471 | 0.403 | 0.5 | 0.157 | $3.61 \cdot 10^{-2}$ | 1.17 | 4.36 | $1.3 \cdot 10^{-5}$ |
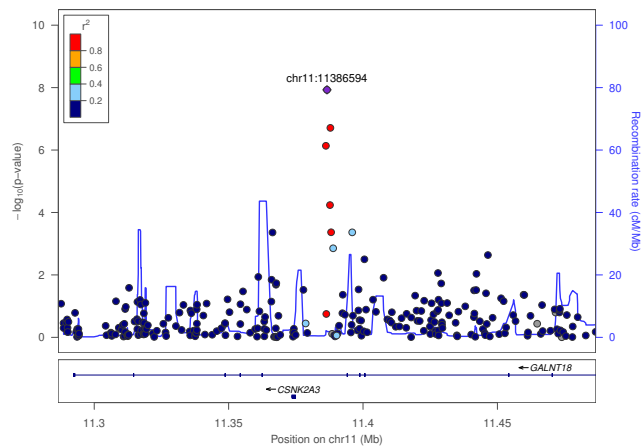


Figure 11: Regional plot for cohort MERGE model invn Adjusted AGE_BP+AGE_BP2+SEX+BMI: rs1843784 $\pm 100 kb$

## 4.4 Previously identified risk loci

Table 12 shows statistics from the MERGE cohort for 22 loci that were shown to be significantly associated with Systolic Blood Pressure in the 2011 Nature paper by Ehret et al [17]. 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 2 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 20 variants in both studies, 8 exhibit the same direction of effect with the known result (binomial test $p = 0.868$).

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Table 12: Top known loci in MERGE model invn Adjusted AGE_BP+AGE_BP2+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$_{CLOSEST}$ | R² | ID$_{KNOWN}$ | N$_{KNOWN}$ | EFFECT$_{KNOWN}$ | STDERR$_{KNOWN}$ | P$_{KNOWN}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 12 | 90060586 | **rs17249754** | G | A | 8,994 | 0.136 | 0.12 | 0.194 | $7.26 \cdot 10^{-2}$ | $2.16 \cdot 10^{-2}$ | $7.98 \cdot 10^{-4}$ | +++ | META_EX | ATP2B1 | 1 | rs17249754 | $2 \cdot 10^5$ | 0.955 | 0.134 | $9.73 \cdot 10^{-13}$ |
| 1 | 11862778 | rs17367504 | A | G | 8,997 | 0.109 | 0.105 | 0.122 | $1.91 \cdot 10^{-2}$ | $2.38 \cdot 10^{-2}$ | 0.423 | ++- | META_EX | MTHFR | 1 | rs17367504 | $2 \cdot 10^5$ | −0.861 | 0.136 | $2.11 \cdot 10^{-10}$ |
| 1 | 11883731 | rs12567136 | C | T | 9,032 | 0.112 | 0.107 | 0.137 | $5.29 \cdot 10^{-3}$ | $2.32 \cdot 10^{-2}$ | 0.82 | ++++- | META_GWAS | CLCN6 | 1 | rs12567136 | $2 \cdot 10^5$ | −0.847 | 0.135 | $3.41 \cdot 10^{-10}$ |
| 15 | 75077367 | **rs1378942** | C | A | 1,568 | 0.356 | 0.106 | 0.619 | $6.17 \cdot 10^{-2}$ | $4.19 \cdot 10^{-2}$ | 0.141 | xxx+++ | META_GWAS | CSK | 1 | rs1378942 | $2 \cdot 10^5$ | 0.632 | 0.101 | $3.43 \cdot 10^{-10}$ |
| 10 | 104846178 | **rs11191548** | T | C | 8,997 | $7.62 \cdot 10^{-2}$ | $4.55 \cdot 10^{-2}$ | 0.103 | $3.49 \cdot 10^{-2}$ | $2.81 \cdot 10^{-2}$ | 0.215 | +++ | META_EX | CNNM2 | 1 | rs11191548 | $2 \cdot 10^5$ | 1.083 | 0.174 | $5.03 \cdot 10^{-10}$ |
| 10 | 104594507 | **rs1004467** | G | A | 8,995 | 0.162 | 0.102 | 0.199 | $3.04 \cdot 10^{-4}$ | $2.04 \cdot 10^{-2}$ | 0.988 | -+- | META_EX | CYP17A1 | 1 | rs1004467 | $2 \cdot 10^5$ | 1.01 | 0.164 | $6.61 \cdot 10^{-10}$ |
| 10 | 104906211 | **rs11191580** | T | C | 8,994 | $6.39 \cdot 10^{-2}$ | $2.11 \cdot 10^{-2}$ | $9.67 \cdot 10^{-2}$ | $2.62 \cdot 10^{-2}$ | $3.07 \cdot 10^{-2}$ | 0.394 | +++ | META_EX | NT5C2 | 1 | rs11191580 | $2 \cdot 10^5$ | 1.058 | 0.173 | $9.16 \cdot 10^{-10}$ |
| 12 | 112007756 | rs653178 | C | T | 8,997 | 0.744 | 0.439 | 0.926 | $7.24 \cdot 10^{-3}$ | $1.86 \cdot 10^{-2}$ | 0.697 | --+ | META_EX | ATXN2 | 1 | rs653178 | $2 \cdot 10^5$ | −0.605 | $9.88 \cdot 10^{-2}$ | $9.3 \cdot 10^{-10}$ |
| 12 | 89942390 | rs11105328 | A | G | 9,030 | 0.135 | 0.108 | 0.194 | $7.53 \cdot 10^{-2}$ | $2.18 \cdot 10^{-2}$ | $5.4 \cdot 10^{-4}$ | +++++ | META_GWAS | POC1B-GALNT4 | 1 | rs11105328 | $2 \cdot 10^5$ | −0.838 | 0.137 | $1.08 \cdot 10^{-9}$ |
| 10 | 104660004 | rs11191454 | A | G | 8,997 | $6.27 \cdot 10^{-2}$ | $2.08 \cdot 10^{-2}$ | $9.47 \cdot 10^{-2}$ | $3.89 \cdot 10^{-2}$ | $3.1 \cdot 10^{-2}$ | 0.209 | +++ | META_EX | BORCS7-ASMT | 1 | rs11191454 | $2 \cdot 10^5$ | −1.043 | 0.171 | $1.12 \cdot 10^{-9}$ |
| 12 | 111884608 | **rs3184504** | T | C | 8,997 | 0.744 | 0.44 | 0.926 | $8.1 \cdot 10^{-3}$ | $1.86 \cdot 10^{-2}$ | 0.664 | --+ | META_EX | SH2B3 | 1 | rs3184504 | $2 \cdot 10^5$ | 0.598 | $9.93 \cdot 10^{-2}$ | $1.69 \cdot 10^{-9}$ |
| 4 | 81164723 | **rs1458038** | T | C | 7,463 | 0.173 | $8.3 \cdot 10^{-2}$ | 0.26 | $3.53 \cdot 10^{-2}$ | $2.21 \cdot 10^{-2}$ | 0.11 | +++xxx | META_GWAS | FGF5 | 1 | rs1458038 | $2 \cdot 10^5$ | 0.662 | 0.111 | $2.12 \cdot 10^{-9}$ |
| 11 | 16902268 | rs381815 | C | T | 7,463 | 0.229 | 0.191 | 0.279 | $3.65 \cdot 10^{-2}$ | $1.95 \cdot 10^{-2}$ | $6.08 \cdot 10^{-2}$ | +++xxx | META_GWAS | PLEKHA7 | 1 | rs381815 | $2 \cdot 10^5$ | −0.655 | 0.11 | $2.45 \cdot 10^{-9}$ |
| 10 | 104638480 | rs3740390 | C | T | 1,566 | $8.3 \cdot 10^{-2}$ | $5.74 \cdot 10^{-2}$ | 0.104 | $2.92 \cdot 10^{-2}$ | $6.53 \cdot 10^{-2}$ | 0.655 | xxx++- | META_GWAS | AS3MT | 1 | rs3740390 | $2 \cdot 10^5$ | −1.005 | 0.172 | $4.61 \cdot 10^{-9}$ |
| 10 | 104546284 | rs486955 | C | T | 7,464 | 0.792 | 0.726 | 0.9 | $1.98 \cdot 10^{-2}$ | $2.05 \cdot 10^{-2}$ | 0.335 | -++xxx | META_EX | WBP1L | 1 | rs486955 | $2 \cdot 10^5$ | −0.895 | 0.156 | $9.47 \cdot 10^{-9}$ |
| 15 | 75107880 | rs7176022 | A | C | 1,568 | 0.614 | 0.585 | 0.701 | $5.92 \cdot 10^{-2}$ | $3.76 \cdot 10^{-2}$ | 0.116 | xxx+++ | META_GWAS | LMAN1L | 1 | rs7176022 | $2 \cdot 10^5$ | −0.602 | 0.107 | $2.11 \cdot 10^{-8}$ |
| 12 | 112072424 | **rs11065987** | G | A | 8,996 | 0.237 | $6.57 \cdot 10^{-2}$ | 0.526 | $6.86 \cdot 10^{-3}$ | $1.91 \cdot 10^{-2}$ | 0.719 | -++ | META_EX | BRAP | 1 | rs11065987 | $2 \cdot 10^5$ | 0.57 | 0.102 | $2.12 \cdot 10^{-8}$ |
| 15 | 75057203 | rs4886406 | G | T | 7,464 | 0.677 | 0.617 | 0.721 | $3.84 \cdot 10^{-4}$ | $1.77 \cdot 10^{-2}$ | 0.983 | ++xxx | META_GWAS | CYP1A2 | 1 | rs4886406 | $2 \cdot 10^5$ | −0.599 | 0.108 | $3.06 \cdot 10^{-8}$ |
| 12 | 112486818 | rs17696736 | A | G | 8,996 | 0.24 | $6.65 \cdot 10^{-2}$ | 0.54 | $1.23 \cdot 10^{-3}$ | $1.9 \cdot 10^{-2}$ | 0.949 | ++- | META_EX | NAA25 | 1 | rs17696736 | $2 \cdot 10^5$ | −0.549 | $9.96 \cdot 10^{-2}$ | $3.43 \cdot 10^{-8}$ |
| 12 | 112906415 | rs11066320 | A | G | 7,464 | 0.767 | 0.46 | 0.933 | $4.89 \cdot 10^{-3}$ | $2.1 \cdot 10^{-2}$ | 0.816 | -++xxx | META_GWAS | PTPN11 | 1 | rs11066320 | $2 \cdot 10^5$ | −0.544 | $9.96 \cdot 10^{-2}$ | $4.56 \cdot 10^{-8}$ |
| 12 | 112486818 | rs17696736 | A | G | 8,996 | 0.24 | $6.65 \cdot 10^{-2}$ | 0.54 | $1.23 \cdot 10^{-3}$ | $1.9 \cdot 10^{-2}$ | 0.949 | ++- | META_EX | TRAFD1 | 0.922 | rs17630235 | $2 \cdot 10^5$ | −0.569 | 0.1 | $1.45 \cdot 10^{-8}$ |
| 12 | 112486818 | rs17696736 | A | G | 8,996 | 0.24 | $6.65 \cdot 10^{-2}$ | 0.54 | $1.23 \cdot 10^{-3}$ | $1.9 \cdot 10^{-2}$ | 0.949 | ++- | META_EX | HECTD4 | 0.913 | rs11066188 | $2 \cdot 10^5$ | −0.567 | 0.101 | $1.72 \cdot 10^{-8}$ |

# 5 HDL Cholesterol (HDL)

## 5.1 Summary
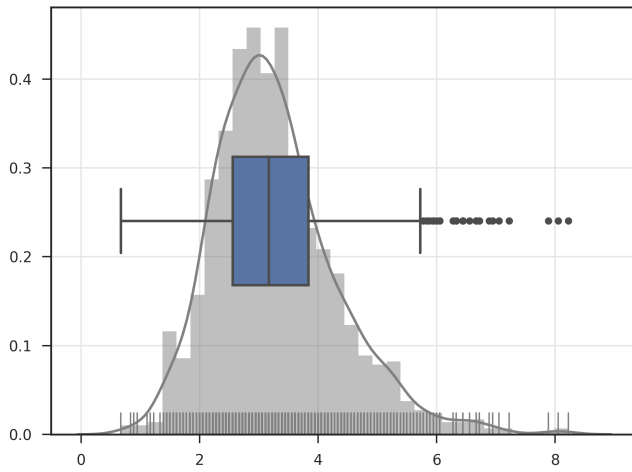


(a) EX_AFR
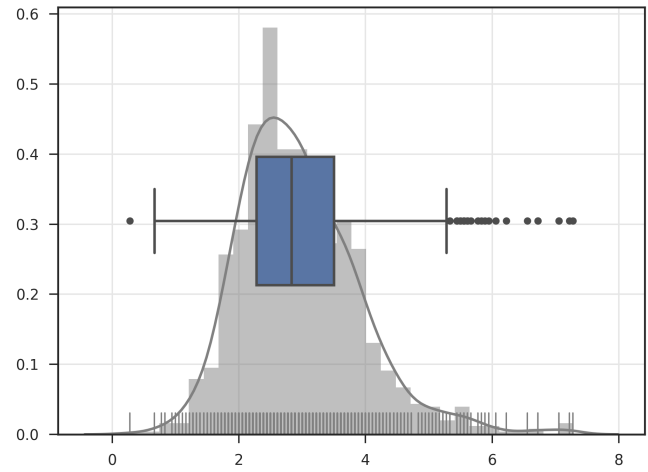
(b) EX_AMR
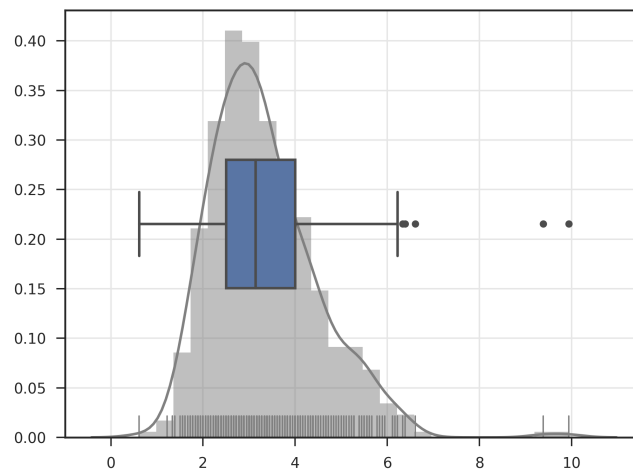
(c) EX_EUR

Figure 12: Distribution of HDL in META_EX by cohort
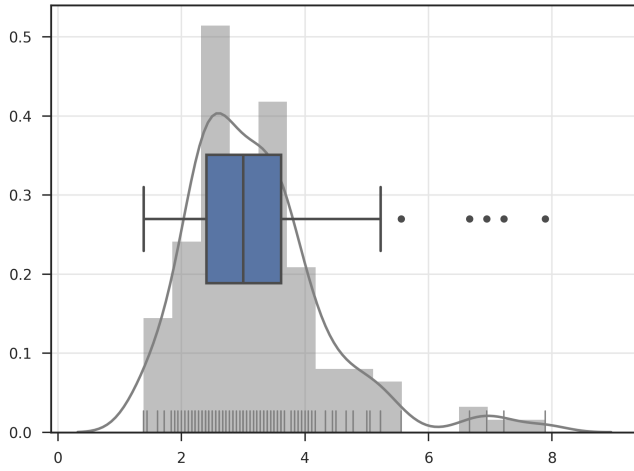
(a) AFFY_AFR
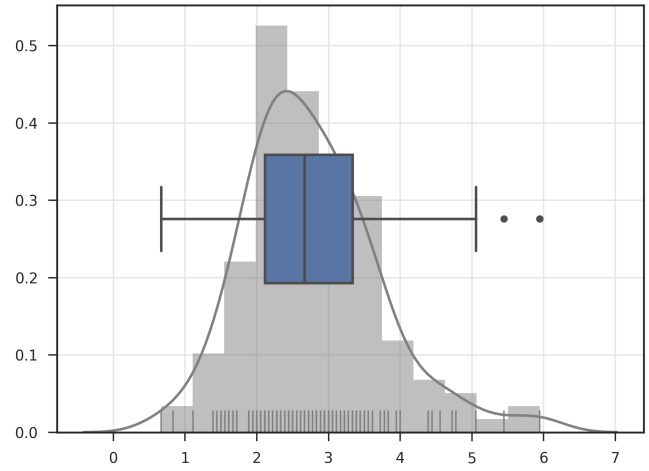
(b) AFFY_AMR
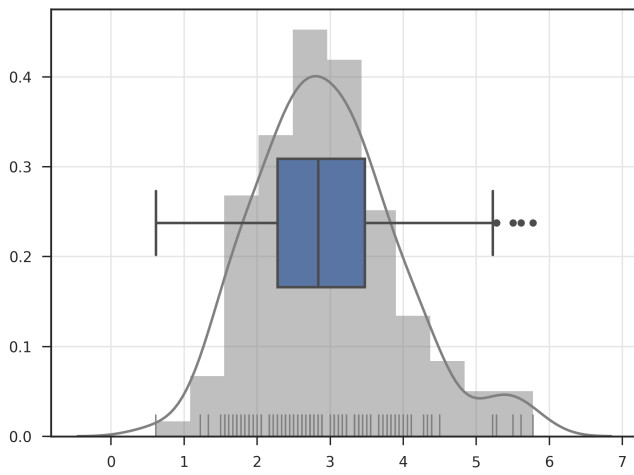
(c) AFFY_EUR
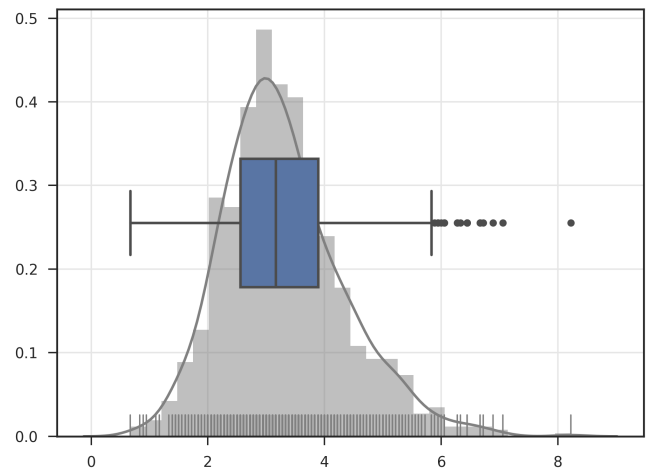
(d) ILL_AFR

(e) ILL_AMR                                      (f) ILL_EUR
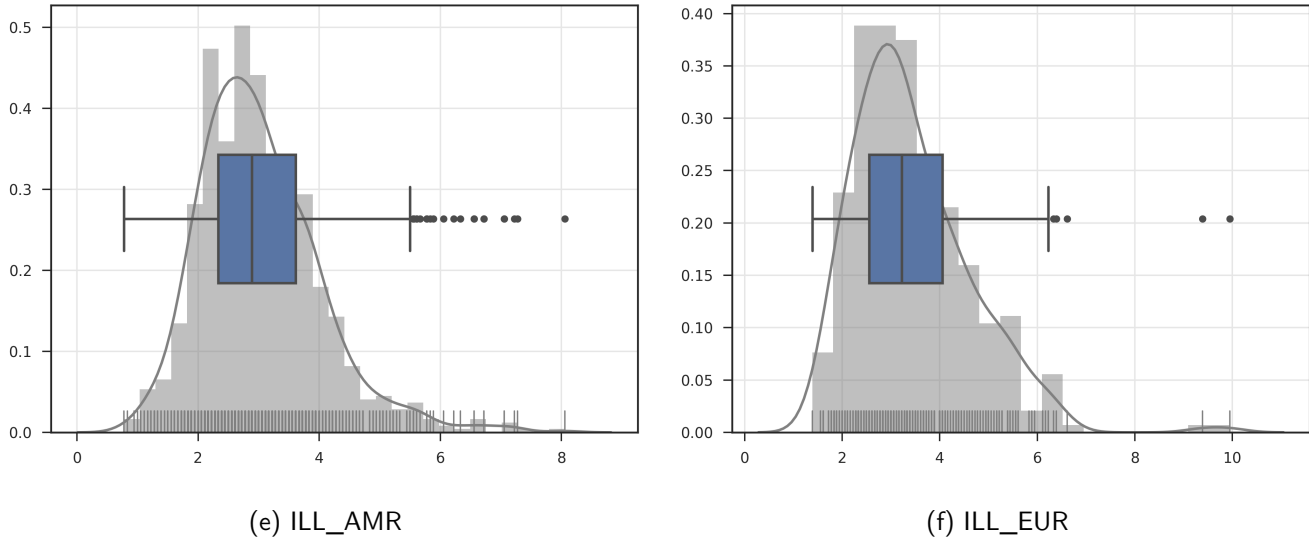
Figure 13: Distribution of HDL in META_GWAS by cohort

Table 13: Summary of samples removed from HDL Cholesterol analysis by cohort and model

| Cohort | Array | Ancestry | Trans | Covars | Total | -SampleQc | -missObs | -Kinship | -PcOutlier |
|---|---|---|---|---|---|---|---|---|---|
| META_EX EX_AFR | EX | AFR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 5172 | 44 | 4004 | 82 | 0 |
| META_EX EX_AMR | EX | AMR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 5144 | 32 | 4095 | 111 | 0 |
| META_EX EX_EUR | EX | EUR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 2379 | 30 | 1945 | 1 | 0 |
| META_GWAS AFFY_AFR | AFFY | AFR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 897 | 18 | 734 | 27 | 0 |
| META_GWAS AFFY_AMR | AFFY | AMR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 1035 | 20 | 897 | 27 | 6 |
| META_GWAS AFFY_EUR | AFFY | EUR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 578 | 12 | 467 | 1 | 0 |
| META_GWAS ILL_AFR | ILL | AFR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 4077 | 46 | 3121 | 1 | 14 |
| META_GWAS ILL_AMR | ILL | AMR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 3884 | 26 | 3039 | 0 | 1 |
| META_GWAS ILL_EUR | ILL | EUR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 1797 | 23 | 1475 | 0 | 4 |

Table 14: Summary of samples remaining for HDL Cholesterol analysis by cohort and model

| Cohort | Array | Ancestry | Trans | Covars | PCs | N | Male | Female | Max | Min | $\mu$ | $\tilde{x}$ | $\sigma$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| META_EX EX_AFR | EX | AFR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 0 | 1078 | 387 | 691 | 8.222 | 0.667 | 3.281 | 3.111 | 1.049 |
| META_EX EX_AMR | EX | AMR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 2 | 931 | 383 | 548 | 7.222 | 0.667 | 2.963 | 2.833 | 0.943 |
| META_EX EX_EUR | EX | EUR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 0 | 425 | 273 | 152 | 9.944 | 0.611 | 3.349 | 3.167 | 1.179 |
| META_GWAS AFFY_AFR | AFFY | AFR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 0 | 134 | 64 | 70 | 7.889 | 1.389 | 3.147 | 3.0 | 1.124 |
| META_GWAS AFFY_AMR | AFFY | AMR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 0 | 104 | 46 | 58 | 5.944 | 0.667 | 2.658 | 2.583 | 0.851 |
| META_GWAS AFFY_EUR | AFFY | EUR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 0 | 107 | 85 | 22 | 5.778 | 0.611 | 3.002 | 2.889 | 0.983 |
| META_GWAS ILL_AFR | ILL | AFR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 3 | 929 | 318 | 611 | 8.222 | 0.667 | 3.307 | 3.167 | 1.037 |
| META_GWAS ILL_AMR | ILL | AMR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 0 | 839 | 341 | 498 | 7.278 | 0.833 | 2.999 | 2.833 | 0.977 |
| META_GWAS ILL_EUR | ILL | EUR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 10 | 314 | 186 | 128 | 9.944 | 1.389 | 3.46 | 3.222 | 1.22 |

## 5.2   Calibration
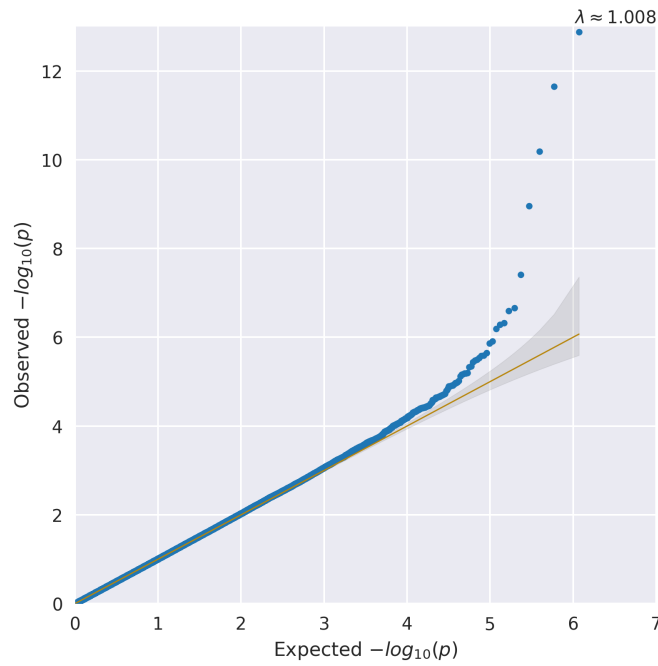


(a) invn Adjusted AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI

Figure 14: QQ plots for HDL in the MERGE analysis
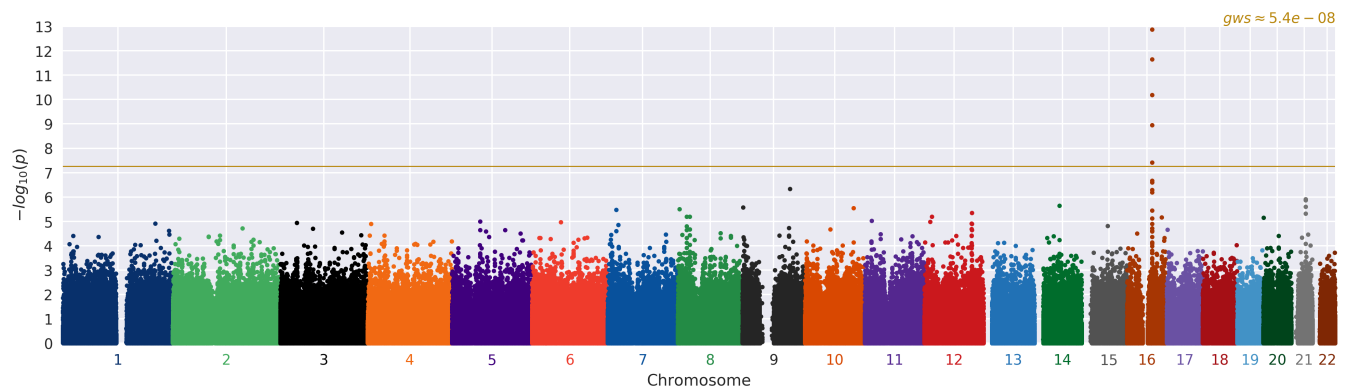


(a) invn Adjusted AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI

Figure 15: Manhattan plots for HDL in the MERGE analysis

## 5.3 Top associations

Table 15: Top variants in the MERGE invn Adjusted AGE_LIPIDS+AGE_LIPIDS2+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 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 16 | 56989590 | **rs247616** | T | C | **CETP** | META_EX | +++ | 2,433 | 1,042 | 1,391 | 0.272 | 0.258 | 0.294 | 0.235 | $3.18 \cdot 10^{-2}$ | 1.265 | 7.403 | $1.33 \cdot 10^{-13}$ |
| 9 | 107180109 | rs10991262 | A | G | OR13F1 | META_GWAS | +++xxx | 2,082 | 845 | 1,237 | 0.336 | 0.313 | 0.428 | 0.166 | $3.29 \cdot 10^{-2}$ | 1.18 | 5.038 | $4.7 \cdot 10^{-7}$ |
| 21 | 32659136 | rs2251255 | G | A | TIAM1 | META_GWAS | xxx+++ | 345 | 195 | 150 | 0.106 | $3.36 \cdot 10^{-2}$ | 0.192 | 0.64 | 0.132 | 1.897 | −4.852 | $1.22 \cdot 10^{-6}$ |
| 14 | 56960032 | rs1189273 | T | C | TMEM260 | META_GWAS | +++xxx | 2,080 | 845 | 1,235 | 0.628 | 0.57 | 0.713 | 0.151 | $3.19 \cdot 10^{-2}$ | 1.163 | 4.73 | $2.25 \cdot 10^{-6}$ |
| 9 | 1472056 | rs7853203 | C | A | DMRT2 | META_GWAS | xxx+++ | 345 | 195 | 150 | $4.78 \cdot 10^{-2}$ | $1.87 \cdot 10^{-2}$ | $7.48 \cdot 10^{-2}$ | 0.813 | 0.173 | 2.256 | −4.698 | $2.63 \cdot 10^{-6}$ |
| 10 | 109888333 | rs2151875 | C | T | SORCS1 | META_GWAS | +++xxx | 2,081 | 845 | 1,236 | 0.129 | $9.55 \cdot 10^{-2}$ | 0.169 | 0.216 | $4.61 \cdot 10^{-2}$ | 1.241 | −4.679 | $2.88 \cdot 10^{-6}$ |
| 8 | 3720473 | rs2975366 | A | G | CSMD1 | META_GWAS | xxx+++ | 345 | 195 | 150 | 0.332 | 0.266 | 0.403 | 0.359 | $7.7 \cdot 10^{-2}$ | 1.432 | −4.661 | $3.14 \cdot 10^{-6}$ |
| 7 | 19461203 | rs10486347 | C | A | TWISTNB | META_GWAS | xxx+++ | 343 | 194 | 149 | 0.35 | 0.235 | 0.43 | 0.38 | $8.18 \cdot 10^{-2}$ | 1.463 | −4.651 | $3.3 \cdot 10^{-6}$ |
| 12 | 107159405 | rs10778508 | T | C | RFX4 | META_GWAS | xxx+++ | 345 | 195 | 150 | 0.441 | 0.409 | 0.489 | 0.329 | $7.17 \cdot 10^{-2}$ | 1.39 | 4.589 | $4.46 \cdot 10^{-6}$ |
| 8 | 19824492 | **rs13702** | C | T | **LPL** | META_EX | -++ | 2,434 | 1,043 | 1,391 | 0.429 | 0.335 | 0.532 | 0.131 | $2.91 \cdot 10^{-2}$ | 1.14 | 4.513 | $6.38 \cdot 10^{-6}$ |
| 8 | 26848328 | rs17056484 | A | G | ADRA1A | META_GWAS | xxx+++ | 344 | 195 | 149 | 0.112 | $6.54 \cdot 10^{-2}$ | 0.175 | 0.546 | 0.121 | 1.726 | 4.51 | $6.47 \cdot 10^{-6}$ |
| 12 | 16747034 | rs10846380 | T | C | LMO3 | META_GWAS | ++++-+ | 2,424 | 1,038 | 1,386 | 0.285 | 0.222 | 0.392 | 0.142 | $3.16 \cdot 10^{-2}$ | 1.153 | 4.51 | $6.49 \cdot 10^{-6}$ |
| 16 | 78209069 | rs11643308 | T | G | WWOX | META_GWAS | ++++++ | 2,427 | 1,040 | 1,387 | 0.365 | 0.295 | 0.411 | 0.132 | $2.94 \cdot 10^{-2}$ | 1.142 | −4.5 | $6.8 \cdot 10^{-6}$ |
| 20 | 283877 | rs4815112 | T | C | ZCCHC3 | META_GWAS | ++++++ | 2,426 | 1,040 | 1,386 | 0.533 | 0.365 | 0.725 | 0.135 | $3.01 \cdot 10^{-2}$ | 1.145 | −4.495 | $6.95 \cdot 10^{-6}$ |
| 11 | 15443681 | rs10766251 | G | A | INSC | META_GWAS | xxx+++ | 345 | 195 | 150 | 0.629 | 0.467 | 0.728 | 0.353 | $7.98 \cdot 10^{-2}$ | 1.424 | −4.428 | $9.53 \cdot 10^{-6}$ |
| 5 | 63098636 | rs10075397 | C | T | HTR1A | META_GWAS | xxx+++ | 345 | 195 | 150 | 0.635 | 0.5 | 0.769 | 0.335 | $7.58 \cdot 10^{-2}$ | 1.397 | −4.413 | $1.02 \cdot 10^{-5}$ |
| 12 | 12812881 | rs759747 | A | G | GPR19 | META_GWAS | xxx+++ | 344 | 194 | 150 | 0.967 | 0.952 | 0.981 | 0.89 | 0.202 | 2.436 | −4.406 | $1.05 \cdot 10^{-5}$ |
| 6 | 65657069 | rs12200181 | A | G | EYS | META_GWAS | xxx+++ | 345 | 195 | 150 | 0.175 | $9.33 \cdot 10^{-2}$ | 0.266 | 0.437 | $9.93 \cdot 10^{-2}$ | 1.548 | −4.402 | $1.07 \cdot 10^{-5}$ |
| 3 | 37487580 | rs9844749 | T | G | ITGA9 | META_GWAS | +++-+- | 2,426 | 1,040 | 1,386 | 0.144 | $2.34 \cdot 10^{-2}$ | 0.242 | 0.186 | $4.23 \cdot 10^{-2}$ | 1.204 | −4.39 | $1.13 \cdot 10^{-5}$ |
| 1 | 209800230 | rs2076349 | C | T | LAMB3 | META_EX | +++ | 2,432 | 1,042 | 1,390 | 0.199 | $2.47 \cdot 10^{-2}$ | 0.269 | 0.162 | $3.71 \cdot 10^{-2}$ | 1.176 | −4.375 | $1.21 \cdot 10^{-5}$ |
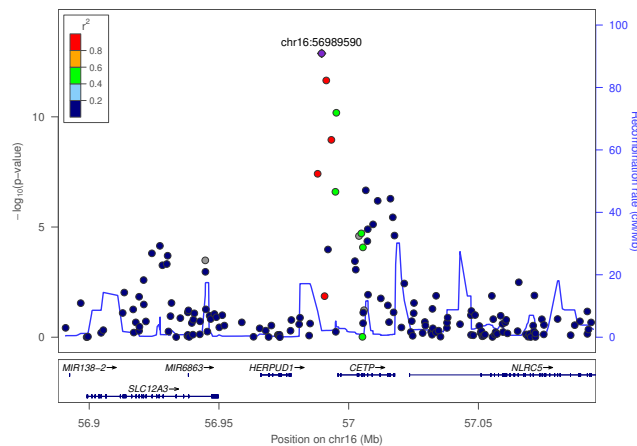


Figure 16: Regional plot for cohort MERGE model invn Adjusted AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI: rs247616 $\pm 100 kb$

## 5.4 Previously identified risk loci

Table 16 shows statistics from the MERGE cohort for 50 loci that were shown to be significantly associated with HDL Cholesterol in the 2013 Nature Genetics paper by Willer et al [12]. Where a previously reported variant was not genotyped in the study (indicated by $\bar{R}^2 < 1$), if available, a tagging variant in LD with the reported variant ($\bar{R}^2 >= 0.7$ 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 50 variants in both studies, 38 exhibit the same direction of effect with the known result (binomial test $p = 0.000153$).

Table 16: Top known loci in MERGE model invn Adjusted AGE_LIPIDS+AGE_LIPIDS2+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$_{CLOSEST}$ | R² | ID$_{KNOWN}$ | N$_{KNOWN}$ | EFFECT$_{KNOWN}$ | STDERR$_{KNOWN}$ | P$_{KNOWN}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 16 | 57005479 | **rs1532624** | A | C | 2,433 | 0.26 | 0.151 | 0.399 | 0.133 | $3.37 \cdot 10^{-2}$ | $8.22 \cdot 10^{-5}$ | +++ | META_EX | CETP | 1 | rs1532624 | 94,595 | 0.204 | $3.5 \cdot 10^{-3}$ | 0 |
| 16 | 56985139 | **rs9989419** | G | A | 2,433 | 0.511 | 0.4 | 0.619 | $3.32 \cdot 10^{-2}$ | $2.89 \cdot 10^{-2}$ | 0.25 | ++- | META_EX | HERPUD1 | 1 | rs9989419 | 94,595 | 0.147 | $3.6 \cdot 10^{-3}$ | 0 |
| 15 | 58678512 | **rs10468017** | T | C | 2,433 | 0.212 | 0.157 | 0.294 | $4.22 \cdot 10^{-2}$ | $3.57 \cdot 10^{-2}$ | 0.238 | +++ | META_EX | LIPC | 1 | rs10468017 | 94,595 | 0.118 | $3.8 \cdot 10^{-3}$ | $1.21 \cdot 10^{-188}$ |
| 8 | 19824492 | **rs13702** | C | T | 2,433 | 0.429 | 0.334 | 0.532 | 0.129 | $2.91 \cdot 10^{-2}$ | $8.76 \cdot 10^{-6}$ | -++ | META_EX | LPL | 1 | rs13702 | 94,595 | 0.106 | $3.8 \cdot 10^{-3}$ | $1.28 \cdot 10^{-160}$ |
| 8 | 19928582 | **rs9644568** | A | G | 345 | $9.13 \cdot 10^{-2}$ | $5.6 \cdot 10^{-2}$ | 0.136 | 0.176 | 0.133 | 0.186 | xxx++ | META_GWAS | SLC18A1 | 1 | rs9644568 | 94,595 | 0.127 | $5.4 \cdot 10^{-3}$ | $4.07 \cdot 10^{-110}$ |
| 18 | 47167214 | **rs4939883** | C | T | 2,432 | 0.689 | 0.537 | 0.866 | $4.67 \cdot 10^{-2}$ | $3.24 \cdot 10^{-2}$ | 0.15 | -++ | META_EX | LIPG | 1 | rs4939883 | 94,595 | $7.99 \cdot 10^{-2}$ | $4.5 \cdot 10^{-3}$ | $1.8 \cdot 10^{-66}$ |
| 9 | 107664301 | **rs1883025** | C | T | 2,433 | 0.298 | 0.253 | 0.319 | $8.51 \cdot 10^{-2}$ | $3.11 \cdot 10^{-2}$ | $6.15 \cdot 10^{-3}$ | +++ | META_EX | ABCA1 | 1 | rs1883025 | 94,595 | $6.98 \cdot 10^{-2}$ | $4.1 \cdot 10^{-3}$ | $1.5 \cdot 10^{-65}$ |
| 16 | 56866196 | rs2241770 | C | T | 2,082 | $8.72 \cdot 10^{-2}$ | $6.21 \cdot 10^{-2}$ | $9.63 \cdot 10^{-2}$ | $5.16 \cdot 10^{-2}$ | $5.45 \cdot 10^{-2}$ | 0.345 | +++xxx | META_GWAS | NUP93 | 1 | rs2241770 | 94,595 | $-9.89 \cdot 10^{-2}$ | $5.7 \cdot 10^{-3}$ | $6.78 \cdot 10^{-60}$ |
| 2 | 21231524 | rs676210 | G | A | 2,433 | 0.183 | 0.15 | 0.233 | $2.05 \cdot 10^{-2}$ | $3.69 \cdot 10^{-2}$ | 0.578 | -++ | META_EX | APOB | 1 | rs676210 | 94,595 | $-6.6 \cdot 10^{-2}$ | $4 \cdot 10^{-3}$ | $2.35 \cdot 10^{-54}$ |
| 16 | 67928042 | **rs16942887** | A | G | 2,433 | 0.176 | 0.111 | 0.211 | $2.77 \cdot 10^{-2}$ | $3.7 \cdot 10^{-2}$ | 0.454 | ++- | META_EX | PSKH1 | 1 | rs16942887 | 94,595 | $8.31 \cdot 10^{-2}$ | $5.1 \cdot 10^{-3}$ | $8.28 \cdot 10^{-54}$ |
| 16 | 67897487 | **rs1124324** | T | C | 2,427 | 0.177 | $9.35 \cdot 10^{-2}$ | 0.228 | $5.14 \cdot 10^{-2}$ | $3.7 \cdot 10^{-2}$ | 0.165 | ++-++ | META_GWAS | NUTF2 | 1 | rs1124324 | 94,595 | $8.28 \cdot 10^{-2}$ | $5.1 \cdot 10^{-3}$ | $1.82 \cdot 10^{-53}$ |
| 16 | 67879400 | **rs3809630** | A | G | 2,082 | 0.177 | 0.118 | 0.207 | $4.98 \cdot 10^{-2}$ | $3.97 \cdot 10^{-2}$ | 0.21 | ++-xxx | META_GWAS | CENPT | 1 | rs3809630 | 94,595 | $8.28 \cdot 10^{-2}$ | $5.1 \cdot 10^{-3}$ | $2.05 \cdot 10^{-53}$ |
| 16 | 67758778 | **rs4474673** | T | C | 2,082 | 0.174 | $9.39 \cdot 10^{-2}$ | 0.212 | $7.08 \cdot 10^{-2}$ | $4.01 \cdot 10^{-2}$ | $7.76 \cdot 10^{-2}$ | ++-xxx | META_GWAS | RANBP10 | 1 | rs4474673 | 94,595 | $8.46 \cdot 10^{-2}$ | $5.3 \cdot 10^{-3}$ | $9.34 \cdot 10^{-52}$ |
| 16 | 67997920 | **rs3785100** | C | T | 2,433 | 0.185 | 0.138 | 0.212 | $2.99 \cdot 10^{-2}$ | $3.61 \cdot 10^{-2}$ | 0.408 | ++- | META_EX | SLC12A4 | 1 | rs3785100 | 94,595 | $7.97 \cdot 10^{-2}$ | $5 \cdot 10^{-3}$ | $2.22 \cdot 10^{-51}$ |
| 16 | 67861134 | rs2292316 | G | C | 345 | 0.18 | $9.81 \cdot 10^{-2}$ | 0.235 | 0.101 | 0.101 | 0.591 | xxx-++ | META_GWAS | TSNAXIP1 | 1 | rs2292316 | 94,595 | $-7.88 \cdot 10^{-2}$ | $5.1 \cdot 10^{-3}$ | $3.2 \cdot 10^{-48}$ |
| 11 | 116648917 | rs964184 | C | G | 2,430 | 0.8 | 0.788 | 0.854 | $6.2 \cdot 10^{-2}$ | $3.65 \cdot 10^{-2}$ | $8.9 \cdot 10^{-2}$ | +++ | META_EX | ZPR1 | 1 | rs964184 | 94,595 | $-0.107$ | $7.1 \cdot 10^{-3}$ | $6.09 \cdot 10^{-48}$ |
| 16 | 68039850 | **rs16957696** | T | C | 2,082 | 0.116 | $7.75 \cdot 10^{-2}$ | 0.154 | $3.11 \cdot 10^{-4}$ | $4.87 \cdot 10^{-2}$ | 0.995 | +-xxx | META_GWAS | DPEP2 | 1 | rs16957696 | 94,595 | $7.45 \cdot 10^{-2}$ | $4.9 \cdot 10^{-3}$ | $1.31 \cdot 10^{-46}$ |
| 16 | 56933519 | **rs11643718** | A | G | 2,432 | $6.95 \cdot 10^{-2}$ | $2.55 \cdot 10^{-2}$ | 0.105 | $3.28 \cdot 10^{-4}$ | $5.85 \cdot 10^{-2}$ | 0.996 | -+ | META_EX | SLC12A3 | 1 | rs11643718 | 94,595 | $8.22 \cdot 10^{-2}$ | $5.4 \cdot 10^{-3}$ | $2.98 \cdot 10^{-46}$ |
| 16 | 68099821 | **rs7201742** | G | T | 2,082 | 0.228 | 0.162 | 0.277 | $2.34 \cdot 10^{-2}$ | $3.7 \cdot 10^{-2}$ | 0.526 | ++-xxx | META_GWAS | DUS2 | 1 | rs7201742 | 94,595 | $7.36 \cdot 10^{-2}$ | $4.8 \cdot 10^{-3}$ | $5.13 \cdot 10^{-46}$ |
| 11 | 116603724 | **rs12272004** | C | A | 2,433 | 0.125 | $6.94 \cdot 10^{-2}$ | 0.147 | $6.24 \cdot 10^{-2}$ | $4.31 \cdot 10^{-2}$ | 0.148 | +++ | META_EX | BUD13 | 1 | rs12272004 | 94,595 | 0.102 | $7 \cdot 10^{-3}$ | $1.16 \cdot 10^{-45}$ |
| 8 | 9183596 | **rs4841132** | G | A | 2,433 | 0.874 | 0.856 | 0.934 | 0.143 | $4.33 \cdot 10^{-2}$ | $9.9 \cdot 10^{-4}$ | +++ | META_EX | PPP1R3B | 1 | rs4841132 | 94,595 | $8.16 \cdot 10^{-2}$ | $5.8 \cdot 10^{-3}$ | $4.83 \cdot 10^{-45}$ |
| 16 | 68150527 | rs12447640 | A | G | 2,079 | 0.101 | $5.02 \cdot 10^{-2}$ | 0.158 | $3.41 \cdot 10^{-2}$ | $5.2 \cdot 10^{-2}$ | 0.948 | -+xxx | META_GWAS | NFATC3 | 1 | rs12447640 | 94,595 | $-7.3 \cdot 10^{-2}$ | $4.9 \cdot 10^{-3}$ | $5.07 \cdot 10^{-45}$ |
| 2 | 21123352 | rs6711016 | C | A | 345 | 0.148 | $4.85 \cdot 10^{-2}$ | 0.229 | 0.148 | 0.117 | 0.205 | xxx+++ | META_GWAS | LDAH | 1 | rs6711016 | 94,595 | $-5.69 \cdot 10^{-2}$ | $4 \cdot 10^{-3}$ | $9.32 \cdot 10^{-43}$ |
| 1 | 230295691 | **rs4846914** | A | G | 2,433 | 0.341 | 0.128 | 0.587 | $6.12 \cdot 10^{-2}$ | $3.35 \cdot 10^{-2}$ | $6.74 \cdot 10^{-2}$ | +++ | META_EX | GALNT2 | 1 | rs4846914 | 94,595 | $4.79 \cdot 10^{-2}$ | $3.4 \cdot 10^{-3}$ | $3.51 \cdot 10^{-41}$ |
| 8 | 19746876 | **rs17482310** | T | G | 2,427 | $8.59 \cdot 10^{-2}$ | $4.52 \cdot 10^{-2}$ | 0.196 | $9.43 \cdot 10^{-2}$ | $5.13 \cdot 10^{-2}$ | $6.63 \cdot 10^{-2}$ | -+++-+ | META_GWAS | INTS10 | 1 | rs17482310 | 94,595 | $6.36 \cdot 10^{-2}$ | $4.6 \cdot 10^{-3}$ | $1.01 \cdot 10^{-40}$ |
| 15 | 58579956 | rs2899624 | G | A | 2,082 | 0.134 | 0.133 | 0.134 | $9.49 \cdot 10^{-3}$ | $4.5 \cdot 10^{-2}$ | 0.833 | ++xxx | META_GWAS | ALDH1A2 | 1 | rs2899624 | 94,595 | $-7.14 \cdot 10^{-2}$ | $4.9 \cdot 10^{-3}$ | $1.39 \cdot 10^{-40}$ |
| 16 | 68280317 | rs3826164 | G | A | 345 | 0.104 | $5.97 \cdot 10^{-2}$ | 0.144 | $6.93 \cdot 10^{-2}$ | 0.122 | 0.571 | xxx++- | META_GWAS | PLA2G15 | 1 | rs3826164 | 94,595 | $-7.34 \cdot 10^{-2}$ | $5.2 \cdot 10^{-3}$ | $2.56 \cdot 10^{-40}$ |
| 16 | 67922342 | rs10468274 | A | G | 345 | 0.399 | 0.154 | 0.631 | $1.75 \cdot 10^{-2}$ | $8.01 \cdot 10^{-2}$ | 0.827 | xxx+-- | META_GWAS | NRN1L | 1 | rs10468274 | 94,595 | $6.39 \cdot 10^{-2}$ | $4.6 \cdot 10^{-3}$ | $2.39 \cdot 10^{-39}$ |
| 11 | 47294626 | **rs10501321** | A | G | 345 | 0.468 | 0.29 | 0.634 | 0.161 | $7.59 \cdot 10^{-2}$ | $3.38 \cdot 10^{-2}$ | xxx++++ | META_GWAS | MADD | 1 | rs10501321 | 94,595 | $4.83 \cdot 10^{-2}$ | $3.6 \cdot 10^{-3}$ | $3.54 \cdot 10^{-38}$ |
| 20 | 44576502 | rs7679 | C | T | 2,427 | $9.37 \cdot 10^{-2}$ | $3.96 \cdot 10^{-2}$ | 0.161 | $1.36 \cdot 10^{-2}$ | $4.96 \cdot 10^{-2}$ | 0.784 | -+ | META_EX | PCIF1 | 1 | rs7679 | 94,595 | $-5.87 \cdot 10^{-2}$ | $4.4 \cdot 10^{-3}$ | $6.73 \cdot 10^{-38}$ |
| 11 | 47354787 | **rs1052373** | T | C | 2,432 | 0.41 | 0.282 | 0.506 | $2.11 \cdot 10^{-2}$ | $2.96 \cdot 10^{-2}$ | 0.476 | +++ | META_EX | MYBPC3 | 1 | rs1052373 | 94,595 | $4.78 \cdot 10^{-2}$ | $3.7 \cdot 10^{-3}$ | $1.55 \cdot 10^{-36}$ |
| 20 | 44547068 | **rs17447545** | A | G | 2,081 | 0.184 | 0.175 | 0.195 | $3.31 \cdot 10^{-2}$ | $4.03 \cdot 10^{-2}$ | 0.412 | ++-xxx | META_GWAS | PLTP | 1 | rs17447545 | 94,595 | $5.62 \cdot 10^{-2}$ | $4.4 \cdot 10^{-3}$ | $3.98 \cdot 10^{-36}$ |
| 11 | 47260272 | **rs2013867** | C | T | 345 | 0.433 | 0.271 | 0.567 | 0.108 | $7.51 \cdot 10^{-2}$ | 0.149 | xxx+++ | META_GWAS | DDB2 | 1 | rs2013867 | 94,595 | $4.8 \cdot 10^{-2}$ | $3.7 \cdot 10^{-3}$ | $4.88 \cdot 10^{-36}$ |
| 11 | 116660686 | **rs2266788** | A | G | 2,433 | 0.948 | 0.917 | 0.983 | $6.69 \cdot 10^{-2}$ | | 0.82 | -++ | META_EX | APOA5 | 1 | rs2266788 | 94,595 | $9.22 \cdot 10^{-2}$ | $6.8 \cdot 10^{-3}$ | $1.19 \cdot 10^{-35}$ |
| 18 | 47243912 | **rs6507945** | C | A | 2,427 | 0.665 | 0.556 | 0.773 | $2.81 \cdot 10^{-2}$ | $3.13 \cdot 10^{-2}$ | 0.369 | -+++ | META_GWAS | ACAA2 | 1 | rs6507945 | 94,595 | $4.41 \cdot 10^{-2}$ | $3.4 \cdot 10^{-3}$ | $1.33 \cdot 10^{-34}$ |
| 20 | 43042364 | **rs1800961** | C | T | 2,433 | $2.4 \cdot 10^{-2}$ | $6.49 \cdot 10^{-3}$ | $4.09 \cdot 10^{-2}$ | 0.178 | $9.56 \cdot 10^{-2}$ | $6.31 \cdot 10^{-2}$ | -++ | META_EX | HNF4A | 1 | rs1800961 | 94,595 | 0.127 | $9.9 \cdot 10^{-3}$ | $1.64 \cdot 10^{-34}$ |
| 11 | 47275064 | **rs10838681** | A | G | 2,427 | 0.369 | 0.225 | 0.493 | $1.98 \cdot 10^{-2}$ | $2.96 \cdot 10^{-2}$ | 0.504 | -++++ | META_GWAS | NR1H3 | 1 | rs10838681 | 94,595 | $4.8 \cdot 10^{-2}$ | $3.8 \cdot 10^{-3}$ | $1.72 \cdot 10^{-33}$ |
| 12 | 125261441 | rs838879 | A | G | 345 | 0.549 | 0.369 | 0.673 | $1.01 \cdot 10^{-2}$ | $7.96 \cdot 10^{-2}$ | 0.899 | xxx++- | META_GWAS | SCARB1 | 1 | rs838879 | 94,595 | $-4.93 \cdot 10^{-2}$ | $4 \cdot 10^{-3}$ | $9.37 \cdot 10^{-33}$ |
| 19 | 54797848 | rs103294 | T | C | 2,081 | 0.124 | $8.89 \cdot 10^{-2}$ | 0.157 | $3.65 \cdot 10^{-2}$ | $4.64 \cdot 10^{-2}$ | 0.432 | +++xxx | META_GWAS | LILRB2 | 1 | rs103294 | 94,595 | $5.23 \cdot 10^{-2}$ | $4.4 \cdot 10^{-3}$ | $4 \cdot 10^{-30}$ |
| 8 | 126495818 | rs10808546 | C | T | 2,082 | 0.344 | 0.331 | 0.382 | $2.95 \cdot 10^{-2}$ | $3.33 \cdot 10^{-2}$ | 0.374 | ++xxx | META_GWAS | TRIB1 | 1 | rs10808546 | 94,595 | $-4.09 \cdot 10^{-2}$ | $3.4 \cdot 10^{-3}$ | $4.11 \cdot 10^{-30}$ |
| 16 | 68335392 | **rs11350** | C | T | 2,426 | 0.148 | 0.116 | 0.194 | $4.83 \cdot 10^{-2}$ | $4.01 \cdot 10^{-2}$ | 0.229 | ++-++ | META_GWAS | SLC7A6 | 1 | rs11350 | 94,595 | $6.19 \cdot 10^{-2}$ | $5.1 \cdot 10^{-3}$ | $1.05 \cdot 10^{-29}$ |
| 11 | 47270255 | **rs2167079** | T | C | 2,433 | 0.441 | 0.265 | 0.564 | $1.81 \cdot 10^{-2}$ | $2.93 \cdot 10^{-2}$ | 0.538 | +++ | META_EX | ACP2 | 1 | rs2167079 | 94,595 | $5.77 \cdot 10^{-2}$ | $4.8 \cdot 10^{-3}$ | $1.19 \cdot 10^{-28}$ |
| 16 | 67671804 | rs6499137 | T | G | 2,082 | 0.214 | $7.17 \cdot 10^{-2}$ | 0.326 | $3.61 \cdot 10^{-2}$ | $3.92 \cdot 10^{-2}$ | 0.357 | -+xxx | META_GWAS | CTCF | 1 | rs6499137 | 94,595 | $-7.22 \cdot 10^{-2}$ | $6.2 \cdot 10^{-3}$ | $5.9 \cdot 10^{-28}$ |
| 11 | 61557803 | **rs102275** | T | C | 2,433 | 0.567 | 0.344 | 0.667 | $4.25 \cdot 10^{-2}$ | $3.02 \cdot 10^{-2}$ | 0.159 | ++ | META_EX | TMEM258 | 1 | rs102275 | 94,595 | $3.91 \cdot 10^{-2}$ | $3.5 \cdot 10^{-3}$ | $6.4 \cdot 10^{-28}$ |
| 11 | 61569830 | **rs174546** | C | T | 2,433 | 0.231 | $7.28 \cdot 10^{-2}$ | 0.375 | $3.88 \cdot 10^{-2}$ | $3.73 \cdot 10^{-2}$ | 0.299 | ++ | META_EX | FADS1 | 1 | rs174546 | 94,595 | $3.91 \cdot 10^{-2}$ | $3.5 \cdot 10^{-3}$ | $8.3 \cdot 10^{-28}$ |
| 11 | 61551356 | **rs174535** | T | C | 2,082 | 0.296 | 0.187 | 0.407 | $1.32 \cdot 10^{-3}$ | $3.5 \cdot 10^{-2}$ | 0.97 | +-xxx | META_GWAS | MYRF | 1 | rs174535 | 94,595 | $3.92 \cdot 10^{-2}$ | $3.5 \cdot 10^{-3}$ | $9.04 \cdot 10^{-28}$ |
| 11 | 47901269 | **rs1872167** | T | C | 345 | 0.238 | 0.164 | 0.332 | 0.177 | $8.6 \cdot 10^{-2}$ | $3.9 \cdot 10^{-2}$ | xxx+++ | META_GWAS | NUP160 | 1 | rs1872167 | 94,595 | $5.48 \cdot 10^{-2}$ | $4.8 \cdot 10^{-3}$ | $2.71 \cdot 10^{-27}$ |
| 9 | 15304782 | **rs686030** | A | C | 2,082 | 0.897 | 0.842 | 0.914 | $9.63 \cdot 10^{-2}$ | $4.99 \cdot 10^{-2}$ | $5.35 \cdot 10^{-2}$ | +++xxx | META_GWAS | TTC39B | 1 | rs686030 | 94,595 | $5.5 \cdot 10^{-2}$ | $4.9 \cdot 10^{-3}$ | $4.29 \cdot 10^{-27}$ |
| 11 | 61597972 | **rs1535** | A | G | 2,433 | 0.277 | 0.156 | 0.397 | $1.54 \cdot 10^{-2}$ | $3.39 \cdot 10^{-2}$ | 0.649 | ++ | META_EX | FADS2 | 1 | rs1535 | 94,595 | $3.91 \cdot 10^{-2}$ | $3.6 \cdot 10^{-3}$ | $5.74 \cdot 10^{-27}$ |
| 18 | 47457559 | **rs1787328** | C | T | 2,082 | 0.574 | 0.518 | 0.593 | $3.35 \cdot 10^{-2}$ | $3.07 \cdot 10^{-2}$ | 0.275 | +++xxx | META_GWAS | MYO5B | 1 | rs1787328 | 94,595 | $4.11 \cdot 10^{-2}$ | $3.7 \cdot 10^{-3}$ | $2.3 \cdot 10^{-26}$ |

# 6 Estimated Glomerular Filtration Rate (eGFR)

## 6.1 Summary



(a) EX_AFR

(b) EX_AMR

(c) EX_EUR
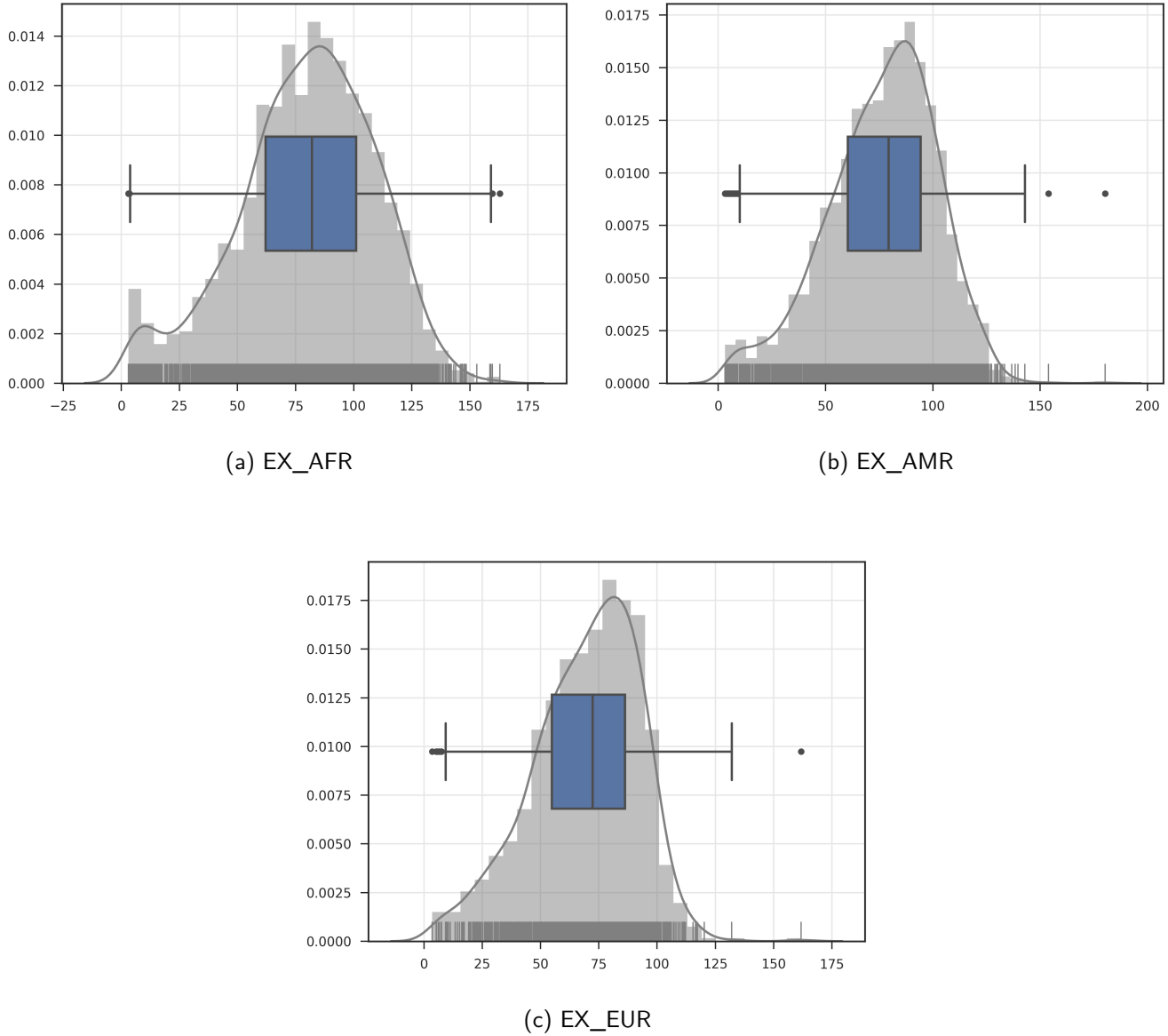
Figure 17: Distribution of eGFR in META_EX by cohort
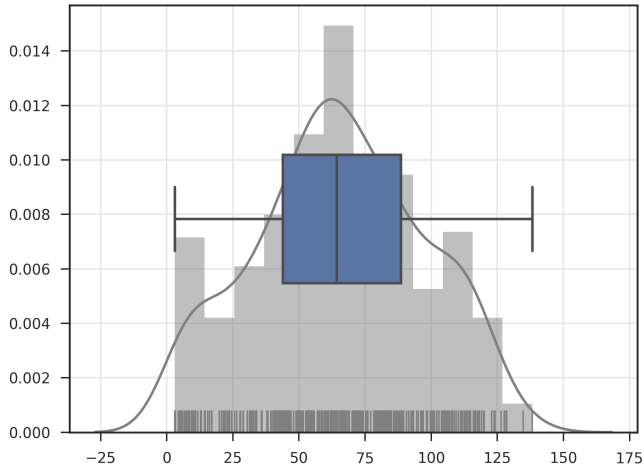
(a) AFFY_AFR
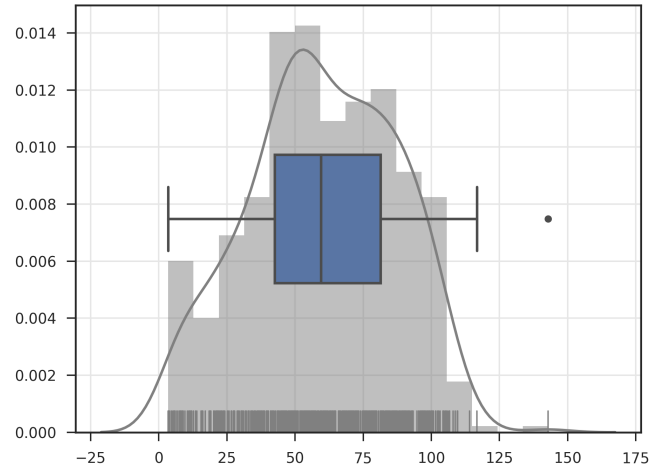


(b) AFFY_AMR
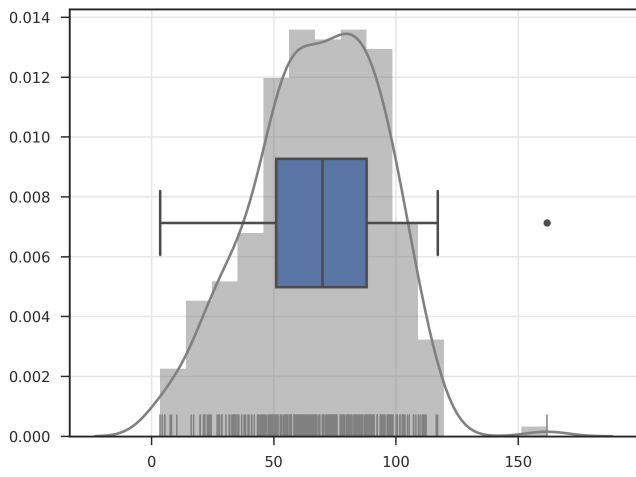


(c) AFFY_EUR
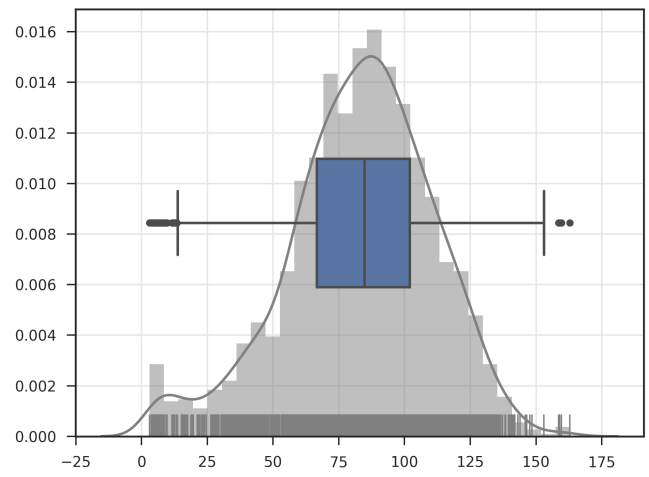


(d) ILL_AFR

(e) ILL_AMR                                    (f) ILL_EUR
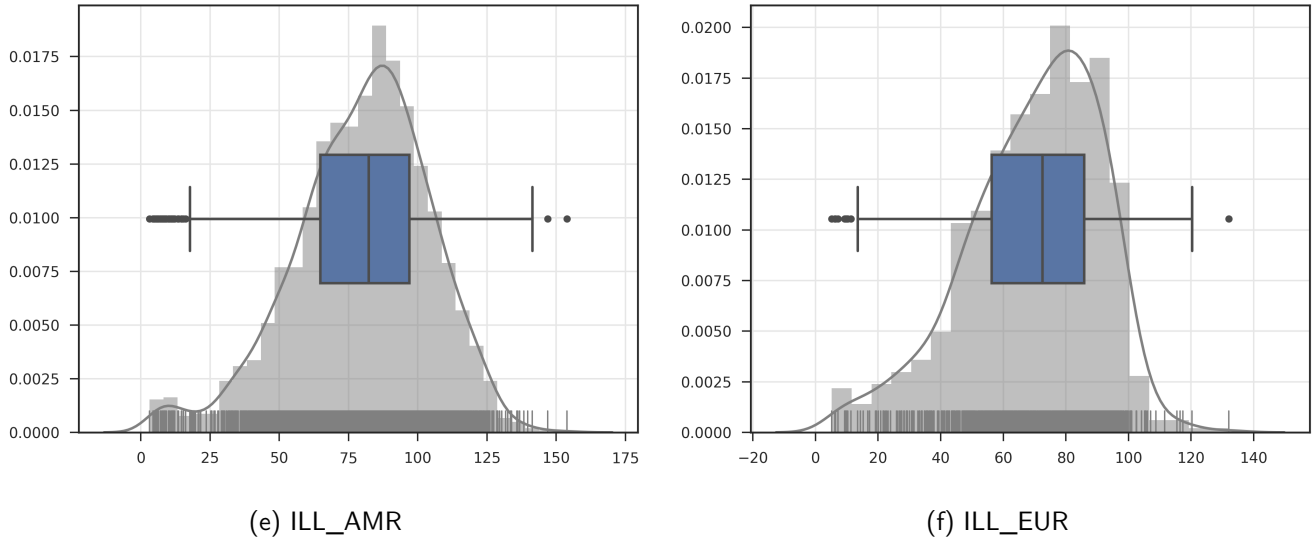
Figure 18: Distribution of eGFR in META_GWAS by cohort

Table 17: Summary of samples removed from Estimated Glomerular Filtration Rate analysis by cohort and model

| Cohort | Array | Ancestry | Trans | Covars | Total | –SampleQc | –missObs | –Kinship | –PcOutlier |
|---|---|---|---|---|---|---|---|---|---|
| META_EX EX_AFR | EX | AFR | invn | | 5172 | 44 | 2385 | 172 | 51 |
| META_EX EX_AMR | EX | AMR | invn | | 5144 | 32 | 2545 | 259 | 0 |
| META_EX EX_EUR | EX | EUR | invn | | 2379 | 30 | 1273 | 3 | 0 |
| META_GWAS AFFY_AFR | AFFY | AFR | invn | | 897 | 18 | 353 | 97 | 0 |
| META_GWAS AFFY_AMR | AFFY | AMR | invn | | 1035 | 20 | 439 | 122 | 0 |
| META_GWAS AFFY_EUR | AFFY | EUR | invn | | 578 | 12 | 288 | 5 | 13 |
| META_GWAS ILL_AFR | ILL | AFR | invn | | 4077 | 46 | 1921 | 0 | 4 |
| META_GWAS ILL_AMR | ILL | AMR | invn | | 3884 | 26 | 1956 | 0 | 0 |
| META_GWAS ILL_EUR | ILL | EUR | invn | | 1797 | 23 | 983 | 0 | 5 |

Table 18: Summary of samples remaining for Estimated Glomerular Filtration Rate analysis by cohort and model

| Cohort | Array | Ancestry | Trans | Covars | PCs | N | Male | Female | Max | Min | $\mu$ | $\tilde{x}$ | $\sigma$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| META_EX EX_AFR | EX | AFR | invn | | 8 | 2546 | 974 | 1572 | 162.894 | 3.003 | 79.565 | 81.835 | 29.591 |
| META_EX EX_AMR | EX | AMR | invn | | 3 | 2323 | 941 | 1382 | 153.861 | 3.157 | 76.127 | 79.22 | 25.365 |
| META_EX EX_EUR | EX | EUR | invn | | 1 | 1086 | 747 | 339 | 161.756 | 3.514 | 69.307 | 72.276 | 22.572 |
| META_GWAS AFFY_AFR | AFFY | AFR | invn | | 0 | 434 | 197 | 237 | 138.222 | 3.003 | 65.339 | 64.228 | 31.573 |
| META_GWAS AFFY_AMR | AFFY | AMR | invn | | 0 | 460 | 205 | 255 | 142.856 | 3.692 | 60.091 | 59.134 | 26.455 |
| META_GWAS AFFY_EUR | AFFY | EUR | invn | | 3 | 270 | 233 | 37 | 161.756 | 3.514 | 67.786 | 70.28 | 25.585 |
| META_GWAS ILL_AFR | ILL | AFR | invn | | 1 | 2122 | 788 | 1334 | 162.894 | 3.003 | 83.187 | 84.708 | 27.861 |
| META_GWAS ILL_AMR | ILL | AMR | invn | | 3 | 1914 | 757 | 1157 | 153.861 | 3.157 | 79.623 | 82.018 | 23.949 |
| META_GWAS ILL_EUR | ILL | EUR | invn | | 4 | 796 | 505 | 291 | 131.997 | 5.202 | 69.718 | 72.562 | 21.273 |

## 6.2   Calibration
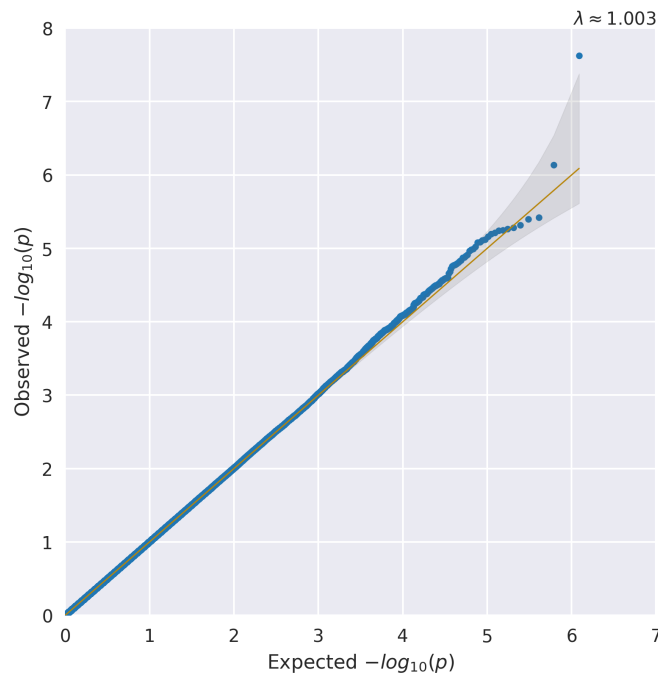


(a) invn Unadjusted

Figure 19: QQ plots for eGFR in the MERGE analysis
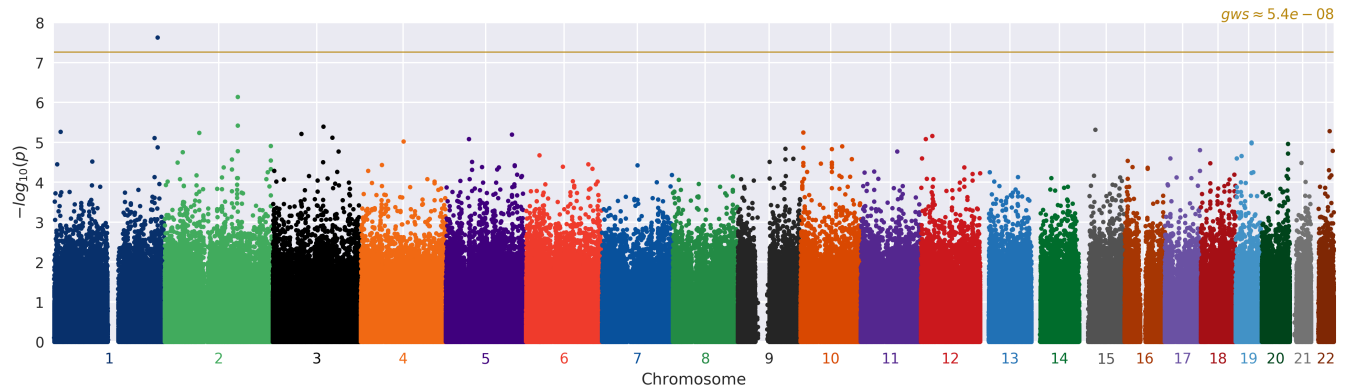
(a) invn Unadjusted

Figure 20: Manhattan plots for eGFR in the MERGE analysis

## 6.3　Top associations

Table 19: Top variants in the MERGE invn Unadjusted 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 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 233256280 | rs717588 | A | G | PCNX2 | META_GWAS | +++xxx | 4,832 | 2,050 | 2,782 | 0.785 | 0.618 | 0.876 | 0.141 | $2.52 \cdot 10^{-2}$ | 1.151 | $-5.584$ | $2.36 \cdot 10^{-8}$ |
| 2 | 164332357 | rs2704367 | C | T | FIGN | META_GWAS | xxx+++ | 1,159 | 633 | 526 | 0.444 | 0.411 | 0.48 | 0.209 | $4.22 \cdot 10^{-2}$ | 1.233 | $-4.954$ | $7.28 \cdot 10^{-7}$ |
| 3 | 113815580 | rs12494543 | C | A | QTRT2 | META_GWAS | xxx+++ | 1,164 | 635 | 529 | 0.216 | 0.181 | 0.227 | 0.227 | $4.93 \cdot 10^{-2}$ | 1.255 | $-4.61$ | $4.02 \cdot 10^{-6}$ |
| 15 | 36116795 | rs11073126 | A | G | DPH6 | META_GWAS | +++xxx | 4,831 | 2,050 | 2,781 | 0.108 | $4.69 \cdot 10^{-2}$ | 0.185 | 0.151 | $3.3 \cdot 10^{-2}$ | 1.163 | 4.574 | $4.79 \cdot 10^{-6}$ |
| 22 | 41661154 | rs2235852 | T | G | RANGAP1 | META_GWAS | +++-++ | 5,993 | 2,683 | 3,310 | 0.317 | 0.214 | 0.404 | $9.09 \cdot 10^{-2}$ | $1.99 \cdot 10^{-2}$ | 1.095 | 4.556 | $5.22 \cdot 10^{-6}$ |
| 1 | 14831919 | rs10754859 | T | C | KAZN | META_GWAS | xxx+++ | 1,164 | 635 | 529 | 0.791 | 0.772 | 0.809 | 0.23 | $5.05 \cdot 10^{-2}$ | 1.258 | $-4.547$ | $5.44 \cdot 10^{-6}$ |
| 10 | 6210312 | rs642104 | T | C | PFKFB3 | META_GWAS | xxx+++ | 1,162 | 633 | 529 | 0.172 | $9.7 \cdot 10^{-2}$ | 0.269 | 0.242 | $5.34 \cdot 10^{-2}$ | 1.274 | 4.54 | $5.64 \cdot 10^{-6}$ |
| 2 | 77225981 | rs17013535 | C | T | LRRTM4 | META_GWAS | xxx+++ | 1,164 | 635 | 529 | $7.95 \cdot 10^{-2}$ | $1.3 \cdot 10^{-2}$ | 0.128 | 0.345 | $7.6 \cdot 10^{-2}$ | 1.412 | $-4.536$ | $5.74 \cdot 10^{-6}$ |
| 3 | 64527128 | rs17070965 | A | C | ADAMTS9 | META_GWAS | -++xxx | 4,832 | 2,050 | 2,782 | $1.27 \cdot 10^{-2}$ | $2.12 \cdot 10^{-3}$ | $2.87 \cdot 10^{-2}$ | 0.419 | $9.27 \cdot 10^{-2}$ | 1.521 | $-4.523$ | $6.09 \cdot 10^{-6}$ |
| 5 | 148659664 | rs1438692 | A | G | AFAP1L1 | META_GWAS | +++xxx | 4,828 | 2,049 | 2,779 | 0.33 | 0.269 | 0.394 | $9.78 \cdot 10^{-2}$ | $2.17 \cdot 10^{-2}$ | 1.103 | 4.515 | $6.33 \cdot 10^{-6}$ |
| 12 | 25993356 | rs41518252 | G | A | RASSF8 | META_GWAS | xxx+++ | 1,163 | 634 | 529 | $6.88 \cdot 10^{-2}$ | $5.54 \cdot 10^{-2}$ | $7.72 \cdot 10^{-2}$ | 0.378 | $8.41 \cdot 10^{-2}$ | 1.459 | 4.496 | $6.91 \cdot 10^{-6}$ |
| 3 | 134079064 | rs2241558 | T | C | AMOTL2 | META_GWAS | xxx+++ | 1,159 | 631 | 528 | $4.31 \cdot 10^{-3}$ | $3.75 \cdot 10^{-3}$ | $4.62 \cdot 10^{-3}$ | 1.405 | 0.314 | 4.074 | 4.478 | $7.54 \cdot 10^{-6}$ |
| 1 | 226055595 | rs2292564 | G | A | TMEM63A | META_GWAS | +++xxx | 4,831 | 2,050 | 2,781 | 0.361 | 0.262 | 0.456 | $9.59 \cdot 10^{-2}$ | $2.15 \cdot 10^{-2}$ | 1.101 | $-4.47$ | $7.81 \cdot 10^{-6}$ |
| 12 | 11586582 | rs2416674 | C | A | PRB1 | META_GWAS | xxx+++ | 1,164 | 635 | 529 | 0.626 | 0.465 | 0.773 | 0.19 | $4.27 \cdot 10^{-2}$ | 1.21 | $-4.459$ | $8.23 \cdot 10^{-6}$ |
| 5 | 51912216 | rs830890 | T | G | ITGA1 | META_GWAS | +++xxx | 4,831 | 2,050 | 2,781 | 0.141 | 0.104 | 0.161 | 0.128 | $2.88 \cdot 10^{-2}$ | 1.137 | $-4.457$ | $8.33 \cdot 10^{-6}$ |
| 4 | 96025302 | rs7665167 | T | G | BMPR1B | META_GWAS | xxx+++ | 1,161 | 634 | 527 | 0.827 | 0.806 | 0.856 | 0.24 | $5.42 \cdot 10^{-2}$ | 1.272 | $-4.429$ | $9.47 \cdot 10^{-6}$ |
| 19 | 36392355 | rs7254113 | G | A | NFKBID | META_GWAS | -++xxx | 4,830 | 2,049 | 2,781 | 0.13 | $2.7 \cdot 10^{-2}$ | 0.218 | 0.137 | $3.11 \cdot 10^{-2}$ | 1.147 | $-4.415$ | $1.01 \cdot 10^{-5}$ |
| 20 | 58698287 | rs2145554 | C | G | CDH26 | META_GWAS | xxx+++ | 1,164 | 635 | 529 | $7.13 \cdot 10^{-2}$ | $5.11 \cdot 10^{-2}$ | $8.76 \cdot 10^{-2}$ | 0.356 | $8.1 \cdot 10^{-2}$ | 1.428 | 4.399 | $1.09 \cdot 10^{-5}$ |
| 2 | 238143803 | rs4490127 | T | G | COL6A3 | META_GWAS | +++xxx | 4,832 | 2,050 | 2,782 | 0.728 | 0.541 | 0.883 | 0.105 | $2.41 \cdot 10^{-2}$ | 1.111 | 4.373 | $1.22 \cdot 10^{-5}$ |
| 10 | 93810872 | rs1776209 | G | A | CPEB3 | META_GWAS | ++++-+ | 5,994 | 2,685 | 3,309 | 0.176 | $6.55 \cdot 10^{-2}$ | 0.307 | 0.108 | $2.48 \cdot 10^{-2}$ | 1.114 | 4.366 | $1.26 \cdot 10^{-5}$ |
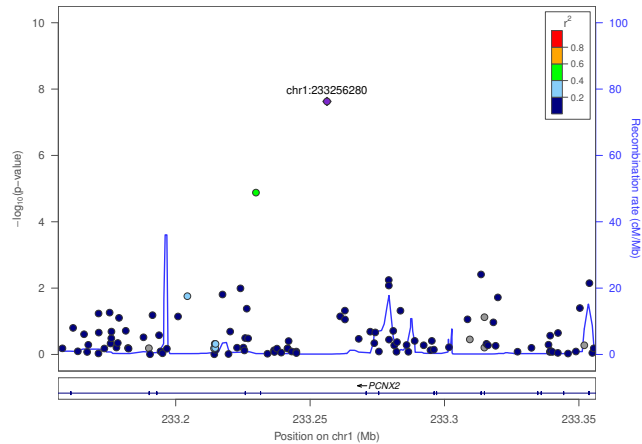
Figure 21: Regional plot for cohort MERGE model invn Unadjusted: rs717588 $\pm 100kb$

## 6.4    Previously identified risk loci

Table 20 shows statistics from the MERGE cohort for 50 loci that were shown to be significantly associated with Estimated Glomerular Filtration Rate in the 2016 Nature Communications paper by Pattaro et al [13]. 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 7 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 50 variants in both studies, 36 exhibit the same direction of effect with the known result (binomial test $p = 0.0013$).

Table 20: Top known loci in MERGE model invn Unadjusted (**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$_{KNOWN}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 15 | 45683795 | **rs1145077** | G | T | 1,162 | 0.664 | 0.392 | 0.88 | $8.32 \cdot 10^{-3}$ | $4.72 \cdot 10^{-2}$ | 0.86 | xxx+-+ | META_GWAS | SPATA5L1 | 1 | rs1145077 | $1.33 \cdot 10^5$ | $1.2 \cdot 10^{-2}$ | $9.2 \cdot 10^{-4}$ | $3.5 \cdot 10^{-42}$ |
| 16 | 20367690 | **rs12917707** | T | G | 5,954 | 0.111 | $4.78 \cdot 10^{-2}$ | 0.164 | $7.3 \cdot 10^{-2}$ | $2.96 \cdot 10^{-2}$ | $1.37 \cdot 10^{-2}$ | +++ | META_EX | UMOD | 1 | rs12917707 | $1.33 \cdot 10^5$ | $1.6 \cdot 10^{-2}$ | $1.2 \cdot 10^{-3}$ | $1.2 \cdot 10^{-41}$ |
| 15 | 45636584 | **rs1153860** | C | T | 1,164 | 0.663 | 0.398 | 0.876 | $1.12 \cdot 10^{-2}$ | $4.69 \cdot 10^{-2}$ | 0.812 | xxx+-+ | META_GWAS | GATM | 1 | rs1153860 | $1.33 \cdot 10^5$ | $1.2 \cdot 10^{-2}$ | $9.2 \cdot 10^{-4}$ | $4.5 \cdot 10^{-41}$ |
| 4 | 77368847 | **rs17319721** | G | A | 5,954 | 0.293 | 0.211 | 0.403 | $8.26 \cdot 10^{-3}$ | $2.05 \cdot 10^{-2}$ | 0.687 | --+ | META_EX | SHROOM3 | 1 | rs17319721 | $1.33 \cdot 10^5$ | $1.1 \cdot 10^{-2}$ | $9.2 \cdot 10^{-4}$ | $1.3 \cdot 10^{-37}$ |
| 15 | 45723983 | **rs1547487** | A | G | 4,832 | 0.695 | 0.443 | 0.865 | $6.9 \cdot 10^{-2}$ | $2.37 \cdot 10^{-2}$ | $3.56 \cdot 10^{-3}$ | +++xx | META_GWAS | C15orf48 | 1 | rs1547487 | $1.33 \cdot 10^5$ | $1.1 \cdot 10^{-2}$ | $9.2 \cdot 10^{-4}$ | $2 \cdot 10^{-32}$ |
| 16 | 20400839 | **rs11864909** | T | C | 4,831 | 0.189 | $9.97 \cdot 10^{-2}$ | 0.263 | $3.49 \cdot 10^{-2}$ | $2.65 \cdot 10^{-2}$ | 0.187 | +++xxx | META_GWAS | PDILT | 1 | rs11864909 | $1.33 \cdot 10^5$ | $1.2 \cdot 10^{-2}$ | $1 \cdot 10^{-3}$ | $1 \cdot 10^{-30}$ |
| 7 | 151407801 | **rs7805747** | G | A | 5,953 | 0.295 | 0.251 | 0.342 | $3.11 \cdot 10^{-2}$ | $2.01 \cdot 10^{-2}$ | 0.122 | +++ | META_EX | PRKAG2 | 1 | rs7805747 | $1.33 \cdot 10^5$ | $1.3 \cdot 10^{-2}$ | $1.1 \cdot 10^{-3}$ | $8 \cdot 10^{-29}$ |
| 15 | 45609773 | rs1719250 | G | A | 1,164 | 0.612 | 0.541 | 0.667 | $3.72 \cdot 10^{-2}$ | $4.09 \cdot 10^{-2}$ | 0.363 | xxx-++ | META_GWAS | SLC28A2 | 1 | rs1719250 | $1.33 \cdot 10^5$ | $-1 \cdot 10^{-2}$ | $9.2 \cdot 10^{-4}$ | $4.5 \cdot 10^{-27}$ |
| 15 | 45801035 | **rs950027** | T | C | 5,995 | 0.746 | 0.48 | 0.916 | $5.52 \cdot 10^{-2}$ | $2.25 \cdot 10^{-2}$ | $1.4 \cdot 10^{-2}$ | +-++- | META_GWAS | SLC30A4 | 1 | rs950027 | $1.33 \cdot 10^5$ | $8.8 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $8.1 \cdot 10^{-23}$ |
| 5 | 176817636 | **rs6420094** | A | G | 5,954 | 0.269 | 0.21 | 0.36 | $6.36 \cdot 10^{-3}$ | $2.08 \cdot 10^{-2}$ | 0.759 | ++ | META_EX | SLC34A1 | 1 | rs6420094 | $1.33 \cdot 10^5$ | $9.6 \cdot 10^{-3}$ | $1 \cdot 10^{-3}$ | $4.9 \cdot 10^{-22}$ |
| 5 | 176801131 | rs10866705 | C | A | 5,985 | 0.773 | 0.728 | 0.811 | $5.6 \cdot 10^{-3}$ | $2.16 \cdot 10^{-2}$ | 0.795 | +--+++ | META_GWAS | RGS14 | 1 | rs10866705 | $1.33 \cdot 10^5$ | $-9.9 \cdot 10^{-3}$ | $1 \cdot 10^{-3}$ | $1.2 \cdot 10^{-21}$ |
| 17 | 59456589 | **rs9895661** | T | C | 5,954 | 0.61 | 0.537 | 0.776 | $9.8 \cdot 10^{-3}$ | $1.92 \cdot 10^{-2}$ | 0.609 | ++ | META_EX | BCAS3 | 1 | rs9895661 | $1.33 \cdot 10^5$ | $1.1 \cdot 10^{-2}$ | $1.2 \cdot 10^{-3}$ | $2.8 \cdot 10^{-21}$ |
| 5 | 39397132 | **rs11959928** | A | T | 4,829 | 0.375 | 0.311 | 0.446 | $2.03 \cdot 10^{-2}$ | $2.13 \cdot 10^{-2}$ | 0.342 | -++xx | META_GWAS | DAB2 | 1 | rs11959928 | $1.33 \cdot 10^5$ | $8.3 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $1.7 \cdot 10^{-20}$ |
| 2 | 73679280 | rs6546838 | A | G | 5,952 | 0.534 | 0.224 | 0.761 | $4.35 \cdot 10^{-3}$ | $2.07 \cdot 10^{-2}$ | 0.834 | ++ | META_EX | ALMS1 | 1 | rs6546838 | $1.33 \cdot 10^5$ | $-9.3 \cdot 10^{-3}$ | $1 \cdot 10^{-3}$ | $7.7 \cdot 10^{-20}$ |
| 5 | 39362039 | **rs700229** | C | T | 1,164 | 0.352 | 0.267 | 0.42 | $1.42 \cdot 10^{-2}$ | $4.38 \cdot 10^{-2}$ | 0.745 | xxx+-- | META_GWAS | C9 | 1 | rs700229 | $1.33 \cdot 10^5$ | $8.1 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $9.8 \cdot 10^{-20}$ |
| 4 | 77254804 | rs907446 | T | C | 1,164 | 0.239 | $7.83 \cdot 10^{-2}$ | 0.415 | $5.27 \cdot 10^{-2}$ | $5.11 \cdot 10^{-2}$ | 0.302 | xxx+++ | META_GWAS | CCDC158 | 1 | rs907446 | $1.33 \cdot 10^5$ | $-8 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $1 \cdot 10^{-19}$ |
| 4 | 77220837 | **rs12506745** | T | G | 5,993 | 0.246 | 0.107 | 0.426 | $2.1 \cdot 10^{-3}$ | $2.21 \cdot 10^{-2}$ | 0.924 | -+--- | META_GWAS | FAM47E-STBD1 | 1 | rs12506745 | $1.33 \cdot 10^5$ | $8 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $3.7 \cdot 10^{-19}$ |
| 6 | 160575764 | **rs316009** | T | C | 4,832 | 0.908 | 0.888 | 0.92 | $6.14 \cdot 10^{-2}$ | $3.53 \cdot 10^{-2}$ | $8.16 \cdot 10^{-2}$ | +++xx | META_GWAS | SLC22A2 | 1 | rs316009 | $1.33 \cdot 10^5$ | $1.3 \cdot 10^{-2}$ | $1.4 \cdot 10^{-3}$ | $4.4 \cdot 10^{-19}$ |
| 11 | 30760335 | **rs3925584** | C | T | 5,954 | 0.278 | 0.117 | 0.479 | $4.85 \cdot 10^{-3}$ | $2.18 \cdot 10^{-2}$ | 0.824 | ++- | META_EX | DCDC1 | 1 | rs3925584 | $1.33 \cdot 10^5$ | $7.6 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $7.6 \cdot 10^{-18}$ |
| 8 | 23728271 | **rs6999484** | G | A | 4,826 | 0.335 | 0.325 | 0.38 | $7.3 \cdot 10^{-3}$ | $2.15 \cdot 10^{-2}$ | 0.735 | -++xxx | META_GWAS | STC1 | 1 | rs6999484 | $1.33 \cdot 10^5$ | $7.1 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $1.9 \cdot 10^{-15}$ |
| 15 | 53946593 | **rs491567** | C | A | 5,952 | 0.415 | 0.18 | 0.567 | $1 \cdot 10^{-2}$ | $1.96 \cdot 10^{-2}$ | 0.611 | ++ | META_EX | WDR72 | 1 | rs491567 | $1.33 \cdot 10^5$ | $8.4 \cdot 10^{-3}$ | $1 \cdot 10^{-3}$ | $2.9 \cdot 10^{-15}$ |
| 6 | 43806609 | rs881858 | A | G | 5,954 | 0.527 | 0.371 | 0.693 | $2.25 \cdot 10^{-3}$ | $1.92 \cdot 10^{-2}$ | 0.907 | -++ | META_EX | VEGFA | 1 | rs881858 | $1.33 \cdot 10^5$ | $-8.1 \cdot 10^{-3}$ | $1 \cdot 10^{-3}$ | $7.5 \cdot 10^{-15}$ |
| 9 | 71433212 | **rs1556751** | T | C | 4,832 | 0.636 | 0.574 | 0.705 | $4.39 \cdot 10^{-2}$ | $2.15 \cdot 10^{-2}$ | $4.1 \cdot 10^{-2}$ | +++xxx | META_GWAS | PIP5K1B | 1 | rs1556751 | $1.33 \cdot 10^5$ | $7 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $9.9 \cdot 10^{-15}$ |
| 17 | 37516722 | rs8076494 | T | C | 1,164 | 0.365 | 0.23 | 0.469 | $7.94 \cdot 10^{-2}$ | $4.32 \cdot 10^{-2}$ | $6.58 \cdot 10^{-2}$ | xxx++- | META_GWAS | FBXL20 | 1 | rs8076494 | $1.33 \cdot 10^5$ | $-7.6 \cdot 10^{-3}$ | $1 \cdot 10^{-3}$ | $2.3 \cdot 10^{-14}$ |
| 17 | 37665554 | rs12936996 | A | G | 1,164 | 0.543 | 0.341 | 0.769 | $3.59 \cdot 10^{-2}$ | $4.34 \cdot 10^{-2}$ | 0.408 | xxx++- | META_GWAS | CDK12 | 1 | rs12936996 | $1.33 \cdot 10^5$ | $-7.6 \cdot 10^{-3}$ | $1 \cdot 10^{-3}$ | $2.4 \cdot 10^{-14}$ |
| 2 | 27730940 | rs1260326 | C | T | 5,953 | 0.735 | 0.524 | 0.864 | $2.22 \cdot 10^{-2}$ | $2.16 \cdot 10^{-2}$ | 0.304 | --+ | META_EX | GCKR | 1 | rs1260326 | $1.33 \cdot 10^5$ | $-6.8 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $3.4 \cdot 10^{-14}$ |
| 17 | 37591422 | **rs10445306** | A | G | 4,830 | 0.507 | 0.343 | 0.72 | $1.29 \cdot 10^{-2}$ | $2.13 \cdot 10^{-2}$ | 0.544 | -++xxx | META_GWAS | MED1 | 1 | rs10445306 | $1.33 \cdot 10^5$ | $7.5 \cdot 10^{-3}$ | $1 \cdot 10^{-3}$ | $4.1 \cdot 10^{-14}$ |
| 9 | 71397747 | **rs2017** | C | T | 4,830 | 0.602 | 0.527 | 0.678 | $1.65 \cdot 10^{-2}$ | $2.11 \cdot 10^{-2}$ | 0.435 | ++-xxx | META_GWAS | FAM122A | 1 | rs2017 | $1.33 \cdot 10^5$ | $6.8 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $4.7 \cdot 10^{-14}$ |
| 2 | 73878352 | **rs6759452** | T | C | 5,990 | 0.116 | $5.2 \cdot 10^{-2}$ | 0.16 | $5.91 \cdot 10^{-2}$ | $2.83 \cdot 10^{-2}$ | $3.67 \cdot 10^{-2}$ | ++++++ | META_GWAS | NAT8 | 1 | rs6759452 | $1.33 \cdot 10^5$ | $9 \cdot 10^{-3}$ | $1.2 \cdot 10^{-3}$ | $4.7 \cdot 10^{-14}$ |
| 15 | 76158983 | **rs1394125** | G | A | 5,952 | 0.342 | 0.308 | 0.404 | $1.46 \cdot 10^{-2}$ | $1.93 \cdot 10^{-2}$ | 0.45 | ++ | META_EX | UBE2Q2 | 1 | rs1394125 | $1.33 \cdot 10^5$ | $7.3 \cdot 10^{-3}$ | $1 \cdot 10^{-3}$ | $5.5 \cdot 10^{-14}$ |
| 3 | 141724644 | rs2861422 | C | T | 1,162 | 0.308 | 0.25 | 0.372 | $3.05 \cdot 10^{-2}$ | $4.46 \cdot 10^{-2}$ | 0.494 | xxx-++ | META_GWAS | TFDP2 | 1 | rs2861422 | $1.33 \cdot 10^5$ | $-7.4 \cdot 10^{-3}$ | $1 \cdot 10^{-3}$ | $9.1 \cdot 10^{-14}$ |
| 19 | 33356891 | **rs12460876** | C | T | 5,954 | 0.351 | 0.269 | 0.47 | $2.34 \cdot 10^{-3}$ | $1.94 \cdot 10^{-2}$ | 0.904 | --+ | META_EX | SLC7A9 | 1 | rs12460876 | $1.33 \cdot 10^5$ | $6.6 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $1.9 \cdot 10^{-13}$ |
| 15 | 76304503 | **rs10851885** | A | G | 5,985 | 0.158 | 0.102 | 0.238 | $1.31 \cdot 10^{-2}$ | $2.52 \cdot 10^{-2}$ | 0.602 | -++++ | META_GWAS | NRG4 | 1 | rs10851885 | $1.33 \cdot 10^5$ | $7.5 \cdot 10^{-3}$ | $1 \cdot 10^{-3}$ | $2.5 \cdot 10^{-13}$ |
| 17 | 59483766 | **rs8068318** | T | C | 5,953 | 0.434 | 0.271 | 0.699 | $6.16 \cdot 10^{-3}$ | $1.98 \cdot 10^{-2}$ | $1.86 \cdot 10^{-1}$ | +++ | META_EX | TBX2 | 1 | rs8068318 | $1.33 \cdot 10^5$ | $7.6 \cdot 10^{-3}$ | $1 \cdot 10^{-3}$ | $3 \cdot 10^{-13}$ |
| 1 | 150951477 | **rs267734** | C | T | 5,954 | $9.29 \cdot 10^{-2}$ | $3.05 \cdot 10^{-2}$ | 0.186 | $3.82 \cdot 10^{-2}$ | $3.23 \cdot 10^{-2}$ | 0.238 | ++ | META_EX | ANXA9 | 1 | rs267734 | $1.33 \cdot 10^5$ | $7.9 \cdot 10^{-3}$ | $1.1 \cdot 10^{-3}$ | $4 \cdot 10^{-13}$ |
| 4 | 77198986 | **rs6812193** | T | C | 5,952 | 0.383 | 0.34 | 0.436 | $6.54 \cdot 10^{-3}$ | $1.9 \cdot 10^{-2}$ | 0.731 | -+- | META_EX | FAM47E | 1 | rs6812193 | $1.33 \cdot 10^5$ | $6.6 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $4.1 \cdot 10^{-13}$ |
| 20 | 52732362 | rs17216707 | T | C | 1,164 | 0.167 | $6.34 \cdot 10^{-2}$ | 0.235 | $2.75 \cdot 10^{-3}$ | $5.66 \cdot 10^{-2}$ | 0.961 | xxx-+ | META_GWAS | CYP24A1 | 1 | rs17216707 | $1.33 \cdot 10^5$ | $-8.4 \cdot 10^{-3}$ | $1.1 \cdot 10^{-3}$ | $6 \cdot 10^{-13}$ |
| 19 | 33364628 | **rs8101881** | C | T | 5,953 | 0.469 | 0.406 | 0.515 | $1.25 \cdot 10^{-2}$ | $1.87 \cdot 10^{-2}$ | 0.504 | --+ | META_EX | CEP89 | 1 | rs8101881 | $1.33 \cdot 10^5$ | $6.4 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $8.1 \cdot 10^{-13}$ |
| 5 | 176755841 | **rs6860069** | C | T | 4,831 | 0.38 | 0.343 | 0.426 | $1.35 \cdot 10^{-2}$ | $2.1 \cdot 10^{-2}$ | 0.519 | +-xxx | META_GWAS | LMAN2 | 1 | rs6860069 | $1.33 \cdot 10^5$ | $6.8 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $8.2 \cdot 10^{-13}$ |
| 7 | 77467459 | **rs17807736** | A | C | 5,996 | 0.185 | 0.15 | 0.246 | $8.61 \cdot 10^{-3}$ | $2.37 \cdot 10^{-2}$ | 0.717 | ++++- | META_GWAS | PHTF2 | 1 | rs17807736 | $1.33 \cdot 10^5$ | $7 \cdot 10^{-3}$ | $1 \cdot 10^{-3}$ | $9.5 \cdot 10^{-13}$ |
| 7 | 77423152 | **rs1045463** | C | T | 4,830 | 0.162 | 0.11 | 0.238 | $2.79 \cdot 10^{-3}$ | $2.81 \cdot 10^{-2}$ | 0.921 | +-xxx | META_GWAS | TMEM60 | 1 | rs1045463 | $1.33 \cdot 10^5$ | $7 \cdot 10^{-3}$ | $1 \cdot 10^{-3}$ | $1.1 \cdot 10^{-12}$ |
| 1 | 150940625 | **rs267738** | C | T | 5,953 | $9.43 \cdot 10^{-2}$ | $3.07 \cdot 10^{-2}$ | 0.188 | $4.37 \cdot 10^{-2}$ | $3.22 \cdot 10^{-2}$ | 0.174 | ++-xxx | META_GWAS | CERS2 | 1 | rs267738 | $1.33 \cdot 10^5$ | $7.7 \cdot 10^{-3}$ | $1.1 \cdot 10^{-3}$ | $1.3 \cdot 10^{-12}$ |
| 17 | 37726423 | rs903507 | C | T | 1,164 | 0.252 | 0.165 | 0.313 | $1.61 \cdot 10^{-2}$ | $4.87 \cdot 10^{-2}$ | 0.74 | xxx++- | META_GWAS | NEUROD2 | 1 | rs903507 | $1.33 \cdot 10^5$ | $-8.5 \cdot 10^{-3}$ | $1.2 \cdot 10^{-3}$ | $1.7 \cdot 10^{-12}$ |
| 12 | 349298 | rs10774021 | T | C | 5,948 | 0.509 | 0.484 | 0.601 | $1.43 \cdot 10^{-2}$ | $1.82 \cdot 10^{-2}$ | 0.431 | ++ | META_EX | SLC6A13 | 1 | rs10774021 | $1.33 \cdot 10^5$ | $-6.3 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $4.8 \cdot 10^{-12}$ |
| 7 | 77416439 | rs6465825 | C | T | 5,951 | 0.426 | 0.355 | 0.492 | $2.56 \cdot 10^{-3}$ | $1.88 \cdot 10^{-2}$ | 0.891 | -++ | META_EX | RSBN1L | 1 | rs6465825 | $1.33 \cdot 10^5$ | $-6.2 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $4.9 \cdot 10^{-12}$ |
| 2 | 15793014 | **rs807601** | T | G | 1,164 | 0.555 | 0.319 | 0.766 | $1.81 \cdot 10^{-2}$ | $4.41 \cdot 10^{-2}$ | 0.681 | xxx+-+ | META_GWAS | DDX1 | 1 | rs807601 | $1.33 \cdot 10^5$ | $6.4 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $6.6 \cdot 10^{-12}$ |
| 2 | 211547400 | rs13386028 | C | A | 4,826 | 0.399 | 0.376 | 0.425 | $2.85 \cdot 10^{-2}$ | $2.08 \cdot 10^{-2}$ | 0.172 | xxx-++ | META_GWAS | CPS1 | 1 | rs13386028 | $1.33 \cdot 10^5$ | $-6.3 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $6.8 \cdot 10^{-12}$ |
| 2 | 73942233 | **rs6755500** | G | A | 1,164 | 0.509 | 0.355 | 0.683 | $5.9 \cdot 10^{-3}$ | $4.25 \cdot 10^{-2}$ | 0.89 | xxx-+ | META_GWAS | TPRKB | 1 | rs6755500 | $1.33 \cdot 10^5$ | $6.4 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $6.9 \cdot 10^{-12}$ |
| 15 | 45902779 | **rs12909221** | C | T | 4,826 | 0.706 | 0.594 | 0.78 | $5.7 \cdot 10^{-2}$ | $2.23 \cdot 10^{-2}$ | $1.04 \cdot 10^{-2}$ | +-+xx | META_GWAS | BLOC1S6 | 1 | rs12909221 | $1.33 \cdot 10^5$ | $6.4 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $1 \cdot 10^{-11}$ |
| 17 | 19440538 | **rs894680** | G | A | 4,832 | 0.242 | 0.14 | 0.405 | $3.23 \cdot 10^{-2}$ | $2.44 \cdot 10^{-2}$ | 0.186 | ++-xxx | META_GWAS | SLC47A1 | 1 | rs894680 | $1.33 \cdot 10^5$ | $6.5 \cdot 10^{-3}$ | $9.2 \cdot 10^{-4}$ | $1 \cdot 10^{-11}$ |

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# 7 Diastolic Blood Pressure (DBP10)

## 7.1 Summary



(a) EX_AFR

(b) EX_AMR

(c) EX_EUR

Figure 22: Distribution of DBP10 in META_EX by cohort

(a) AFFY_AFR



(b) AFFY_AMR



(c) AFFY_EUR



(d) ILL_AFR

(e) ILL_AMR
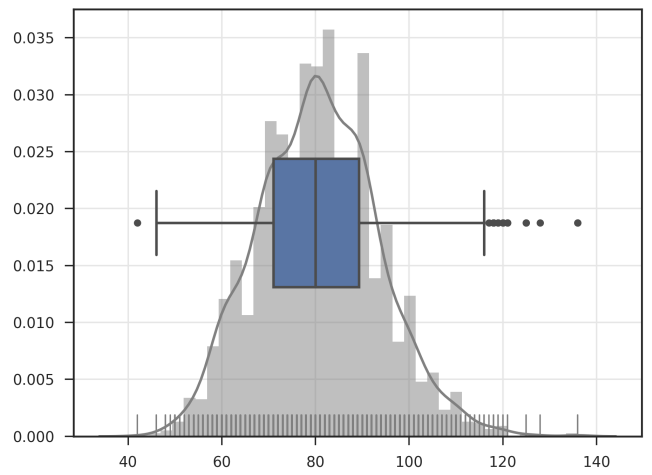
(f) ILL_EUR
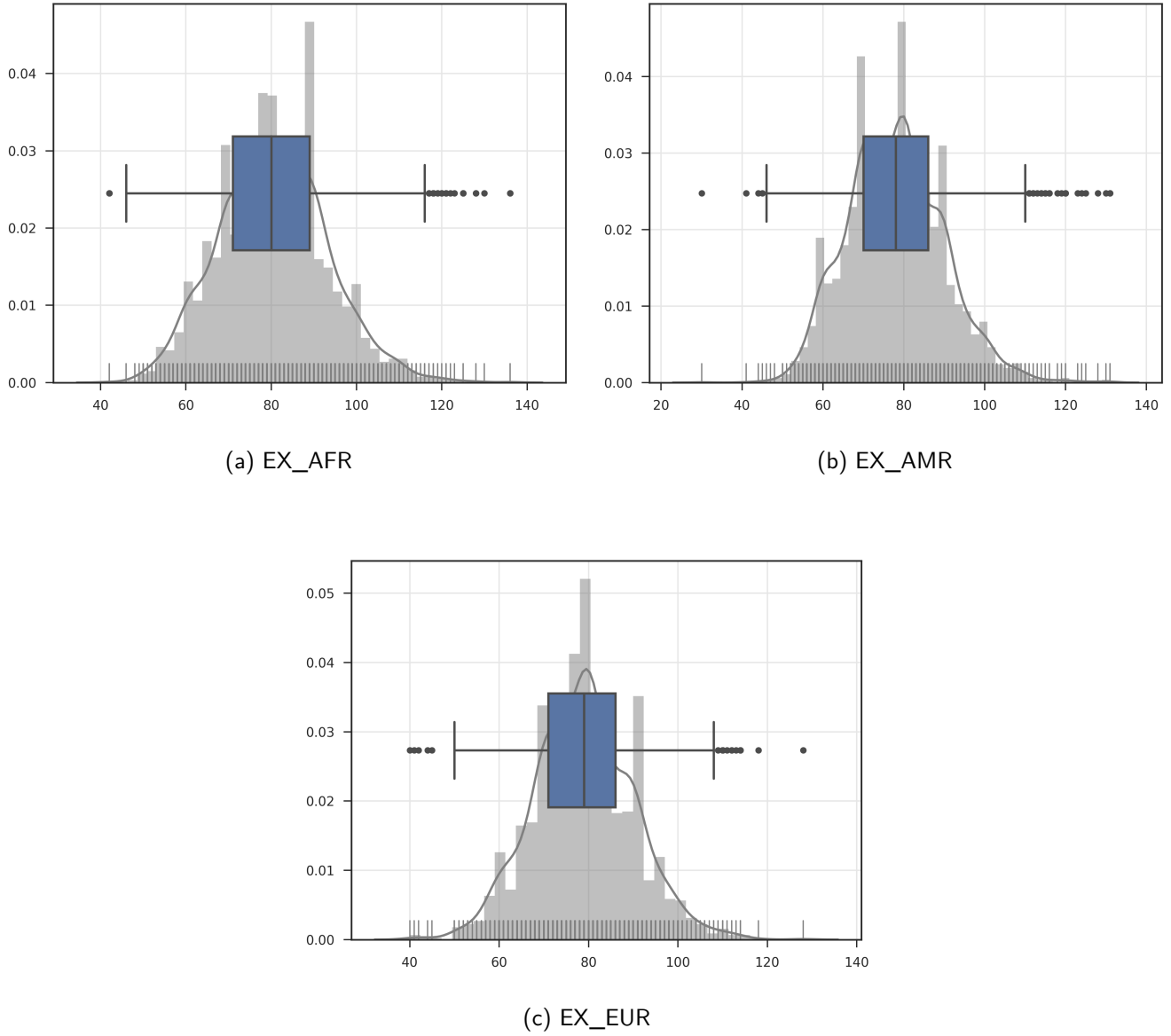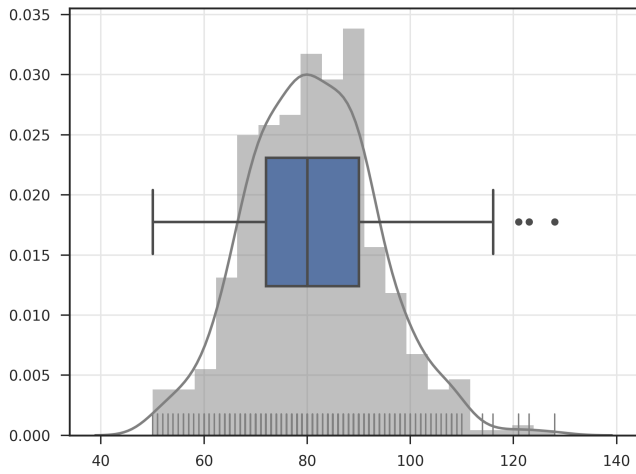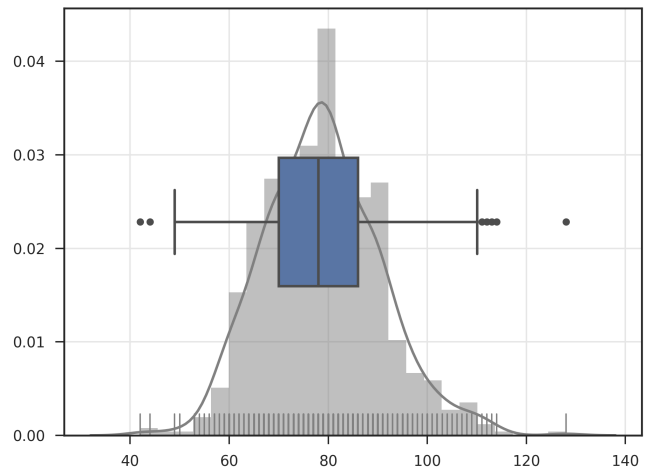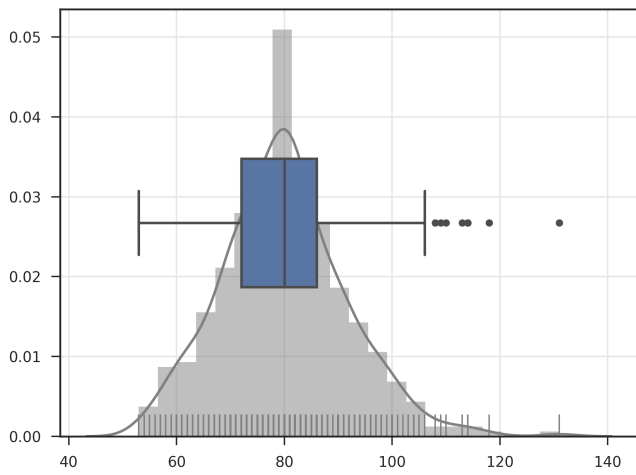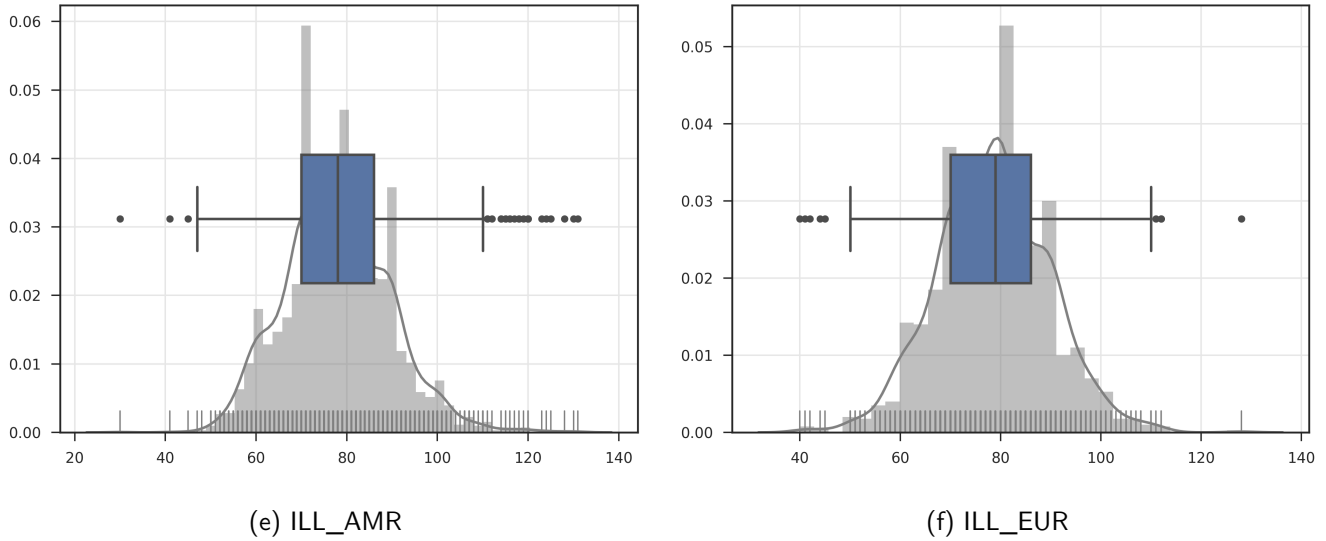
Figure 23: Distribution of DBP10 in META_GWAS by cohort

Table 21: Summary of samples removed from Diastolic Blood Pressure analysis by cohort and model

| Cohort | Array | Ancestry | Trans | Covars | Total | –SampleQc | –missObs | –Kinship | –PcOutlier |
|---|---|---|---|---|---|---|---|---|---|
| META_EX EX_AFR | EX | AFR | invn | AGE_BP+AGE_BP2+SEX+BMI | 5172 | 44 | 1132 | 285 | 5 |
| META_EX EX_AMR | EX | AMR | invn | AGE_BP+AGE_BP2+SEX+BMI | 5144 | 32 | 1144 | 424 | 0 |
| META_EX EX_EUR | EX | EUR | invn | AGE_BP+AGE_BP2+SEX+BMI | 2379 | 30 | 626 | 6 | 1 |
| META_GWAS AFFY_AFR | AFFY | AFR | invn | AGE_BP+AGE_BP2+SEX+BMI | 897 | 18 | 208 | 127 | 14 |
| META_GWAS AFFY_AMR | AFFY | AMR | invn | AGE_BP+AGE_BP2+SEX+BMI | 1035 | 20 | 227 | 166 | 0 |
| META_GWAS AFFY_EUR | AFFY | EUR | invn | AGE_BP+AGE_BP2+SEX+BMI | 578 | 12 | 173 | 8 | 0 |
| META_GWAS ILL_AFR | ILL | AFR | invn | AGE_BP+AGE_BP2+SEX+BMI | 4077 | 46 | 893 | 4 | 6 |
| META_GWAS ILL_AMR | ILL | AMR | invn | AGE_BP+AGE_BP2+SEX+BMI | 3884 | 26 | 870 | 2 | 0 |
| META_GWAS ILL_EUR | ILL | EUR | invn | AGE_BP+AGE_BP2+SEX+BMI | 1797 | 23 | 456 | 1 | 0 |

Table 22: Summary of samples remaining for Diastolic Blood Pressure analysis by cohort and model

| Cohort | Array | Ancestry | Trans | Covars | PCs | N | Male | Female | Max | Min | $\mu$ | $\tilde{x}$ | $\sigma$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| META_EX EX_AFR | EX | AFR | invn | AGE_BP+AGE_BP2+SEX+BMI | 0 | 3719 | 1311 | 2408 | 136.0 | 42.0 | 80.732 | 80.0 | 12.782 |
| META_EX EX_AMR | EX | AMR | invn | AGE_BP+AGE_BP2+SEX+BMI | 3 | 3553 | 1392 | 2161 | 131.0 | 41.0 | 78.019 | 78.0 | 11.712 |
| META_EX EX_EUR | EX | EUR | invn | AGE_BP+AGE_BP2+SEX+BMI | 8 | 1723 | 1150 | 573 | 128.0 | 40.0 | 78.906 | 79.0 | 11.186 |
| META_GWAS AFFY_AFR | AFFY | AFR | invn | AGE_BP+AGE_BP2+SEX+BMI | 0 | 539 | 234 | 305 | 128.0 | 42.0 | 81.557 | 81.0 | 12.502 |
| META_GWAS AFFY_AMR | AFFY | AMR | invn | AGE_BP+AGE_BP2+SEX+BMI | 3 | 625 | 273 | 352 | 113.0 | 44.0 | 78.541 | 78.0 | 11.406 |
| META_GWAS AFFY_EUR | AFFY | EUR | invn | AGE_BP+AGE_BP2+SEX+BMI | 0 | 391 | 319 | 72 | 118.0 | 53.0 | 80.003 | 80.0 | 11.466 |
| META_GWAS ILL_AFR | ILL | AFR | invn | AGE_BP+AGE_BP2+SEX+BMI | 0 | 3140 | 1076 | 2064 | 136.0 | 42.0 | 80.619 | 80.0 | 12.756 |
| META_GWAS ILL_AMR | ILL | AMR | invn | AGE_BP+AGE_BP2+SEX+BMI | 1 | 2994 | 1143 | 1851 | 131.0 | 41.0 | 77.822 | 78.0 | 11.713 |
| META_GWAS ILL_EUR | ILL | EUR | invn | AGE_BP+AGE_BP2+SEX+BMI | 0 | 1324 | 828 | 496 | 128.0 | 40.0 | 78.491 | 79.0 | 11.057 |

## 7.2  Calibration



$\lambda \approx 1.005$
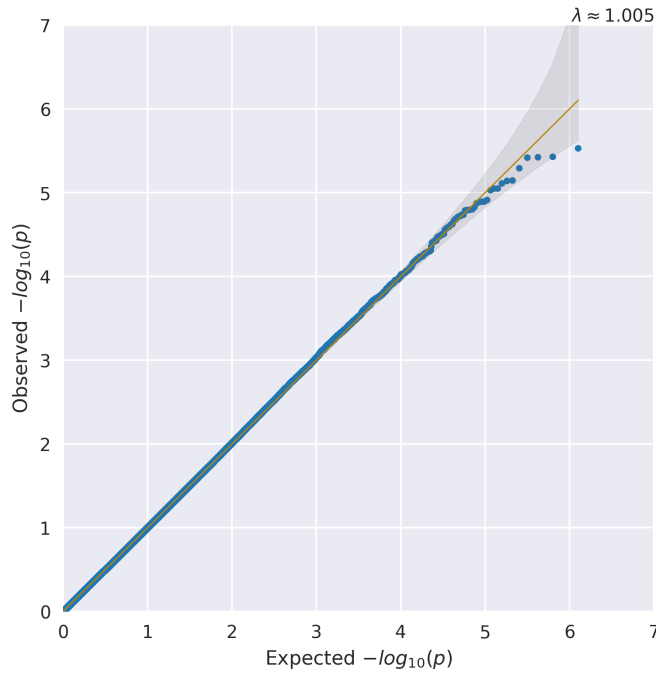
(a) invn Adjusted AGE_BP+AGE_BP2+SEX+BMI

Figure 24: QQ plots for DBP10 in the MERGE analysis
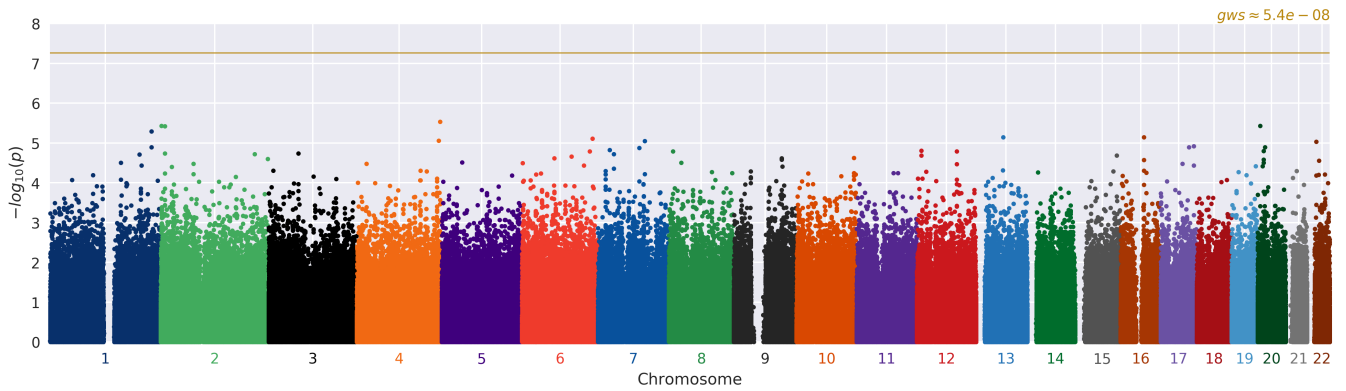


(a) invn Adjusted AGE_BP+AGE_BP2+SEX+BMI

Figure 25: Manhattan plots for DBP10 in the MERGE analysis

## 7.3  Top associations

Table 23: Top variants in the MERGE invn Adjusted AGE_BP+AGE_BP2+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 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 4 | 187813575 | rs736880 | A | C | FAT1 | META_GWAS | +++-++ | 9,013 | 3,873 | 5,140 | 0.804 | 0.722 | 0.92 | $8.88 \cdot 10^{-2}$ | $1.9 \cdot 10^{-2}$ | 1.093 | $-4.675$ | $2.94 \cdot 10^{-6}$ |
| 2 | 1981503 | rs6721182 | C | A | MYT1L | META_GWAS | +++xxx | 7,456 | 3,045 | 4,411 | 0.227 | 0.166 | 0.287 | $9.18 \cdot 10^{-2}$ | $1.98 \cdot 10^{-2}$ | 1.096 | 4.627 | $3.72 \cdot 10^{-6}$ |
| 20 | 5644184 | rs8119133 | A | C | GPCPD1 | META_GWAS | +++-++ | 9,012 | 3,872 | 5,140 | 0.309 | 0.261 | 0.446 | $7.5 \cdot 10^{-2}$ | $1.62 \cdot 10^{-2}$ | 1.078 | 4.625 | $3.75 \cdot 10^{-6}$ |
| 2 | 9389812 | rs2666214 | G | T | ASAP2 | META_GWAS | xxx+++ | 1,553 | 826 | 727 | 0.533 | 0.438 | 0.676 | 0.168 | $3.63 \cdot 10^{-2}$ | 1.183 | $-4.623$ | $3.79 \cdot 10^{-6}$ |
| 1 | 228633197 | rs16848614 | T | C | HIST3H2A | META_GWAS | +++xxx | 7,449 | 3,042 | 4,407 | $7.16 \cdot 10^{-2}$ | $4.07 \cdot 10^{-2}$ | $9.4 \cdot 10^{-2}$ | 0.146 | $3.19 \cdot 10^{-2}$ | 1.157 | $-4.56$ | $5.1 \cdot 10^{-6}$ |
| 16 | 52172190 | rs11645663 | G | A | TOX3 | META_GWAS | xxx+++ | 1,555 | 826 | 729 | 0.159 | $8.53 \cdot 10^{-2}$ | 0.233 | 0.224 | $4.99 \cdot 10^{-2}$ | 1.251 | $-4.489$ | $7.16 \cdot 10^{-6}$ |
| 13 | 60616431 | rs9646034 | T | C | DIAPH3 | META_GWAS | ++++++ | 9,009 | 3,873 | 5,136 | $1.41 \cdot 10^{-2}$ | $6.05 \cdot 10^{-3}$ | $4.6 \cdot 10^{-2}$ | 0.283 | $6.31 \cdot 10^{-2}$ | 1.328 | 4.487 | $7.22 \cdot 10^{-6}$ |
| 6 | 158502528 | exm590335 | G | A | SYNJ2 | META_EX | +++ | 8,995 | 3,853 | 5,142 | $2.78 \cdot 10^{-4}$ | $1.34 \cdot 10^{-4}$ | $5.8 \cdot 10^{-4}$ | 1.994 | 0.446 | 7.347 | $-4.472$ | $7.74 \cdot 10^{-6}$ |
| 4 | 184572036 | rs4547833 | T | C | RWDD4 | META_GWAS | +++xxx | 7,456 | 3,047 | 4,409 | 0.226 | 0.214 | 0.237 | $8.65 \cdot 10^{-2}$ | $1.95 \cdot 10^{-2}$ | 1.09 | 4.444 | $8.83 \cdot 10^{-6}$ |
| 7 | 105554522 | rs17152281 | C | A | ATXN7L1 | META_GWAS | xxx+++ | 1,544 | 821 | 723 | 0.142 | 0.13 | 0.161 | 0.232 | $5.21 \cdot 10^{-2}$ | 1.26 | $-4.442$ | $8.93 \cdot 10^{-6}$ |
| 22 | 21003610 | rs4822389 | T | C | PI4KA | META_GWAS | +++xxx | 7,444 | 3,041 | 4,403 | 0.164 | $7.43 \cdot 10^{-2}$ | 0.24 | $9.93 \cdot 10^{-2}$ | $2.24 \cdot 10^{-2}$ | 1.104 | $-4.434$ | $9.27 \cdot 10^{-6}$ |
| 17 | 74546939 | rs752049 | T | C | CYGB | META_GWAS | ++++++ | 9,012 | 3,872 | 5,140 | 0.233 | 0.2 | 0.253 | $7.72 \cdot 10^{-2}$ | $1.76 \cdot 10^{-2}$ | 1.08 | 4.376 | $1.21 \cdot 10^{-5}$ |
| 1 | 228579788 | rs4653951 | C | T | TRIM11 | META_GWAS | ++++++ | 9,005 | 3,870 | 5,135 | $6.65 \cdot 10^{-2}$ | $3.34 \cdot 10^{-2}$ | $8.99 \cdot 10^{-2}$ | 0.129 | $2.96 \cdot 10^{-2}$ | 1.138 | $-4.365$ | $1.27 \cdot 10^{-5}$ |
| 20 | 16783688 | rs7267583 | T | C | OTOR | META_GWAS | +++-++ | 9,010 | 3,872 | 5,138 | $9.02 \cdot 10^{-2}$ | $1.89 \cdot 10^{-3}$ | 0.163 | 0.116 | $2.65 \cdot 10^{-2}$ | 1.123 | 4.365 | $1.27 \cdot 10^{-5}$ |
| 17 | 63371880 | rs4790945 | G | A | RGS9 | META_GWAS | +++xxx | 7,458 | 3,047 | 4,411 | 0.15 | $9.82 \cdot 10^{-2}$ | 0.208 | 0.101 | $2.32 \cdot 10^{-2}$ | 1.107 | $-4.362$ | $1.29 \cdot 10^{-5}$ |
| 7 | 93083708 | rs17165475 | T | C | CALCR | -++-+- | 9,005 | 3,872 | 5,133 | 0.116 | $1.89 \cdot 10^{-3}$ | 0.223 | 0.106 | $2.44 \cdot 10^{-2}$ | 1.112 | 4.355 | $1.33 \cdot 10^{-5}$ |
| 7 | 25968712 | rs7810017 | A | G | NFE2L3 | META_GWAS | xxx+++ | 1,555 | 826 | 729 | 0.397 | 0.356 | 0.415 | 0.157 | $3.61 \cdot 10^{-2}$ | 1.169 | $-4.331$ | $1.49 \cdot 10^{-5}$ |
| 12 | 10437066 | rs7297855 | A | G | KLRD1 | META_GWAS | -++xxx | 7,457 | 3,046 | 4,411 | $7.46 \cdot 10^{-2}$ | $7.55 \cdot 10^{-4}$ | 0.135 | 0.138 | $3.19 \cdot 10^{-2}$ | 1.148 | 4.319 | $1.57 \cdot 10^{-5}$ |
| 20 | 13035593 | rs1431431 | C | T | SPTLC3 | META_GWAS | +++-++ | 9,011 | 3,872 | 5,139 | 0.297 | 0.237 | 0.352 | $7.02 \cdot 10^{-2}$ | $1.63 \cdot 10^{-2}$ | 1.073 | $-4.317$ | $1.58 \cdot 10^{-5}$ |
| 8 | 9877986 | rs9329211 | G | A | MSRA | META_GWAS | ++++++ | 9,013 | 3,873 | 5,140 | 0.172 | $7.67 \cdot 10^{-3}$ | 0.317 | $8.99 \cdot 10^{-2}$ | $2.09 \cdot 10^{-2}$ | 1.094 | $-4.313$ | $1.61 \cdot 10^{-5}$ |

## 7.4  Previously identified risk loci

Table 24 shows statistics from the MERGE cohort for 26 loci that were shown to be significantly associated with Diastolic Blood Pressure in the 2011 Nature paper by Ehret et al [10]. Where a previously reported variant was not genotyped in the study (indicated by $\bar{R}^2 < 1$), if available, a tagging variant in LD with the reported variant ($\bar{R}^2 >= 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. There are 2 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 24 variants in both studies, 8 exhibit the same direction of effect with the known result (binomial test $p = 0.968$).

Table 24: Top known loci in MERGE model invn Adjusted AGE_BP+AGE_BP2+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$_{KNOWN}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 12 | 112007756 | rs653178 | C | T | 8,998 | 0.744 | 0.439 | 0.927 | $2.54 \cdot 10^{-2}$ | $1.9 \cdot 10^{-2}$ | 0.181 | +++ | META_EX | ATXN2 | 1 | rs653178 | $2 \cdot 10^5$ | $-0.48$ | $6.26 \cdot 10^{-2}$ | $1.64 \cdot 10^{-14}$ |
| 12 | 111884608 | **rs3184504** | T | C | 8,998 | 0.744 | 0.44 | 0.926 | $2.46 \cdot 10^{-2}$ | $1.9 \cdot 10^{-2}$ | 0.195 | ++ | META_EX | SH2B3 | 1 | rs3184504 | $2 \cdot 10^5$ | 0.48 | $6.29 \cdot 10^{-2}$ | $2.33 \cdot 10^{-14}$ |
| 4 | 81164723 | **rs1458038** | T | C | 7,457 | 0.173 | $8.3 \cdot 10^{-2}$ | 0.26 | $3.69 \cdot 10^{-2}$ | $2.21 \cdot 10^{-2}$ | $9.47 \cdot 10^{-2}$ | +++xxx | META_GWAS | FGF5 | 1 | rs1458038 | $2 \cdot 10^5$ | 0.503 | $7.02 \cdot 10^{-2}$ | $7.91 \cdot 10^{-13}$ |
| 12 | 112072424 | **rs11065987** | G | A | 8,997 | 0.237 | $6.56 \cdot 10^{-2}$ | 0.526 | $2.67 \cdot 10^{-2}$ | $1.94 \cdot 10^{-2}$ | 0.168 | +++ | META_EX | BRAP | 1 | rs11065987 | $2 \cdot 10^5$ | 0.449 | $6.46 \cdot 10^{-2}$ | $3.43 \cdot 10^{-12}$ |
| 15 | 75077367 | **rs1378942** | C | A | 1,556 | 0.357 | 0.106 | 0.619 | $6.47 \cdot 10^{-3}$ | $4.29 \cdot 10^{-2}$ | 0.88 | xxx+-+ | META_GWAS | CSK | 1 | rs1378942 | $2 \cdot 10^5$ | 0.445 | $6.4 \cdot 10^{-2}$ | $3.47 \cdot 10^{-12}$ |
| 12 | 112486818 | **rs17696736** | G | A | 8,997 | 0.24 | $6.64 \cdot 10^{-2}$ | 0.54 | $2.33 \cdot 10^{-2}$ | $1.93 \cdot 10^{-2}$ | 0.229 | +++ | META_EX | NAA25 | 1 | rs17696736 | $2 \cdot 10^5$ | 0.422 | $6.34 \cdot 10^{-2}$ | $2.8 \cdot 10^{-11}$ |
| 12 | 112906415 | rs11066320 | A | G | 7,458 | 0.767 | 0.46 | 0.933 | $8.6 \cdot 10^{-3}$ | $2.08 \cdot 10^{-2}$ | 0.68 | +-+xxx | META_GWAS | PTPN11 | 1 | rs11066320 | $2 \cdot 10^5$ | $-0.413$ | $6.32 \cdot 10^{-2}$ | $6.32 \cdot 10^{-11}$ |
| 15 | 75057203 | **rs4886406** | T | G | 7,458 | 0.677 | 0.617 | 0.721 | $9.87 \cdot 10^{-3}$ | $1.77 \cdot 10^{-2}$ | 0.577 | ++-xxx | META_GWAS | CYP1A2 | 1 | rs4886406 | $2 \cdot 10^5$ | 0.426 | $6.85 \cdot 10^{-2}$ | $4.83 \cdot 10^{-10}$ |
| 15 | 75125645 | **rs6495122** | C | A | 8,997 | 0.395 | 0.272 | 0.504 | $3.19 \cdot 10^{-3}$ | $1.57 \cdot 10^{-2}$ | 0.839 | $-$+ | META_EX | CPLX3 | 1 | rs6495122 | $2 \cdot 10^5$ | 0.383 | $6.23 \cdot 10^{-2}$ | $8.41 \cdot 10^{-10}$ |
| 15 | 75115895 | rs7162232 | A | G | 7,458 | 0.619 | 0.586 | 0.705 | $1.42 \cdot 10^{-3}$ | $1.7 \cdot 10^{-2}$ | 0.402 | ++-xxx | META_GWAS | LMAN1L | 1 | rs7162232 | $2 \cdot 10^5$ | $-0.416$ | $6.89 \cdot 10^{-2}$ | $1.58 \cdot 10^{-9}$ |
| 7 | 2512545 | rs2969070 | A | G | 1,555 | 0.759 | 0.584 | 0.917 | $7.83 \cdot 10^{-2}$ | $4.37 \cdot 10^{-2}$ | $7.3 \cdot 10^{-2}$ | xxx+++ | META_GWAS | GRIFIN | 1 | rs2969070 | $2 \cdot 10^5$ | $-0.386$ | $6.47 \cdot 10^{-2}$ | $2.57 \cdot 10^{-9}$ |
| 12 | 90008959 | rs2681472 | A | G | 8,993 | 0.125 | $9.68 \cdot 10^{-2}$ | 0.195 | $1.76 \cdot 10^{-2}$ | $2.25 \cdot 10^{-2}$ | 0.435 | ++- | META_EX | ATP2B1 | 1 | rs2681472 | $2 \cdot 10^5$ | $-0.492$ | $8.36 \cdot 10^{-2}$ | $3.9 \cdot 10^{-9}$ |
| 15 | 75140854 | **rs3765066** | G | A | 7,457 | 0.385 | 0.164 | 0.62 | $2.34 \cdot 10^{-2}$ | $1.83 \cdot 10^{-2}$ | 0.199 | +++xxx | META_GWAS | SCAMP2 | 1 | rs3765066 | $2 \cdot 10^5$ | 0.382 | $6.51 \cdot 10^{-2}$ | $4.17 \cdot 10^{-9}$ |
| 10 | 63524591 | rs1530440 | C | T | 8,998 | 0.125 | $6.13 \cdot 10^{-2}$ | 0.201 | $4.51 \cdot 10^{-2}$ | $2.29 \cdot 10^{-2}$ | $4.84 \cdot 10^{-2}$ | +++ | META_EX | C10orf107 | 1 | rs1530440 | $2 \cdot 10^5$ | $-0.459$ | $7.92 \cdot 10^{-2}$ | $6.71 \cdot 10^{-9}$ |
| 1 | 11883731 | rs12567136 | C | T | 9,014 | 0.112 | 0.107 | 0.137 | $4.08 \cdot 10^{-2}$ | $2.32 \cdot 10^{-2}$ | $7.94 \cdot 10^{-2}$ | ++++-- | META_GWAS | CLCN6 | 1 | rs12567136 | $2 \cdot 10^5$ | $-0.488$ | $8.56 \cdot 10^{-2}$ | $1.15 \cdot 10^{-8}$ |
| 1 | 11862778 | rs17367504 | A | G | 8,998 | 0.109 | 0.105 | 0.122 | $3.48 \cdot 10^{-2}$ | $2.38 \cdot 10^{-2}$ | 0.144 | ++ | META_EX | MTHFR | 1 | rs17367504 | $2 \cdot 10^5$ | $-0.49$ | $8.61 \cdot 10^{-2}$ | $1.29 \cdot 10^{-8}$ |
| 12 | 89942390 | rs11105328 | A | G | 9,013 | 0.135 | 0.107 | 0.194 | $3.28 \cdot 10^{-2}$ | $2.18 \cdot 10^{-2}$ | 0.132 | ++-++ | META_GWAS | POC1B-GALNT4 | 1 | rs11105328 | $2 \cdot 10^5$ | $-0.487$ | $8.66 \cdot 10^{-2}$ | $1.83 \cdot 10^{-8}$ |
| 12 | 111818701 | rs11065884 | A | G | 7,457 | 0.508 | 0.197 | 0.734 | $1.49 \cdot 10^{-2}$ | $1.79 \cdot 10^{-2}$ | 0.405 | --+xxx | META_GWAS | FAM109A | 1 | rs11065884 | $2 \cdot 10^5$ | $-0.409$ | $7.42 \cdot 10^{-2}$ | $3.57 \cdot 10^{-8}$ |
| 15 | 75234610 | rs11072518 | C | T | 7,456 | 0.578 | 0.54 | 0.606 | $1.47 \cdot 10^{-2}$ | $1.67 \cdot 10^{-2}$ | 0.379 | +++xxx | META_GWAS | COX5A | 1 | rs11072518 | $2 \cdot 10^5$ | $-0.355$ | $6.45 \cdot 10^{-2}$ | $3.78 \cdot 10^{-8}$ |
| 6 | 26107463 | rs198846 | A | G | 8,996 | 0.87 | 0.846 | 0.882 | $2.82 \cdot 10^{-2}$ | $2.22 \cdot 10^{-2}$ | 0.202 | +++ | META_EX | HIST1H1T | 1 | rs198846 | $2 \cdot 10^5$ | $-0.487$ | $8.85 \cdot 10^{-2}$ | $3.8 \cdot 10^{-8}$ |
| 6 | 26091179 | rs1799945 | G | C | 8,996 | $7.89 \cdot 10^{-2}$ | $2.63 \cdot 10^{-2}$ | 0.144 | $5.84 \cdot 10^{-2}$ | $2.81 \cdot 10^{-2}$ | $3.74 \cdot 10^{-2}$ | +++ | META_EX | HFE | 1 | rs1799945 | $2 \cdot 10^5$ | $-0.482$ | $8.82 \cdot 10^{-2}$ | $4.78 \cdot 10^{-8}$ |
| 12 | 111780644 | rs7306529 | C | T | 1,549 | 0.328 | 0.159 | 0.429 | $1.53 \cdot 10^{-2}$ | $3.91 \cdot 10^{-2}$ | 0.695 | xxx-++ | META_GWAS | CUX2 | 1 | rs7306529 | $2 \cdot 10^5$ | $-0.413$ | $7.56 \cdot 10^{-2}$ | $4.87 \cdot 10^{-8}$ |
| 15 | 75185670 | rs7495739 | A | G | 1,555 | 0.455 | 0.348 | 0.514 | $1.93 \cdot 10^{-2}$ | $3.61 \cdot 10^{-2}$ | 0.594 | xxx++ | META_GWAS | MPI | 1 | rs7495739 | $2 \cdot 10^5$ | $-0.335$ | $6.15 \cdot 10^{-2}$ | $5.02 \cdot 10^{-8}$ |
| 6 | 26107463 | rs198846 | A | G | 8,996 | 0.87 | 0.846 | 0.882 | $2.82 \cdot 10^{-2}$ | $2.22 \cdot 10^{-2}$ | 0.202 | +++ | META_EX | HIST1H2BC | 1 | rs198833 | $2 \cdot 10^5$ | $-0.485$ | $8.88 \cdot 10^{-2}$ | $4.58 \cdot 10^{-8}$ |
| 12 | 112486818 | **rs17696736** | G | A | 8,997 | 0.24 | $6.64 \cdot 10^{-2}$ | 0.54 | $2.33 \cdot 10^{-2}$ | $1.93 \cdot 10^{-2}$ | 0.229 | +++ | META_EX | TRAFD1 | 0.922 | rs17630235 | $2 \cdot 10^5$ | 0.447 | $6.4 \cdot 10^{-2}$ | $2.92 \cdot 10^{-12}$ |
| 12 | 112486818 | **rs17696736** | G | A | 8,997 | 0.24 | $6.64 \cdot 10^{-2}$ | 0.54 | $2.33 \cdot 10^{-2}$ | $1.93 \cdot 10^{-2}$ | 0.229 | +++ | META_EX | HECTD4 | 0.913 | rs11066188 | $2 \cdot 10^5$ | 0.447 | $6.41 \cdot 10^{-2}$ | $3.06 \cdot 10^{-12}$ |

# 8 LDL Cholesterol (LDL_DIRECT)

## 8.1 Summary
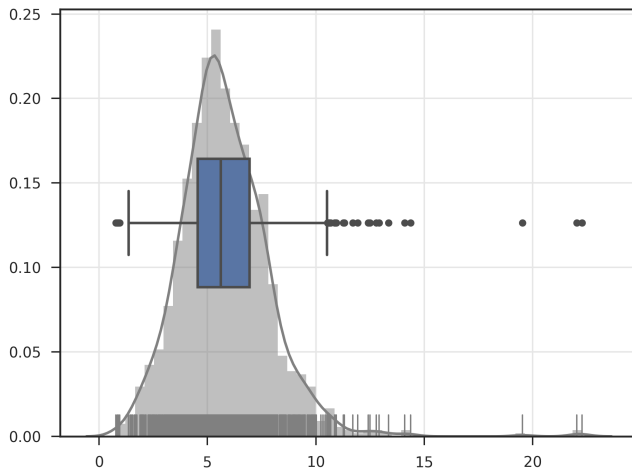


(a) EX_AFR
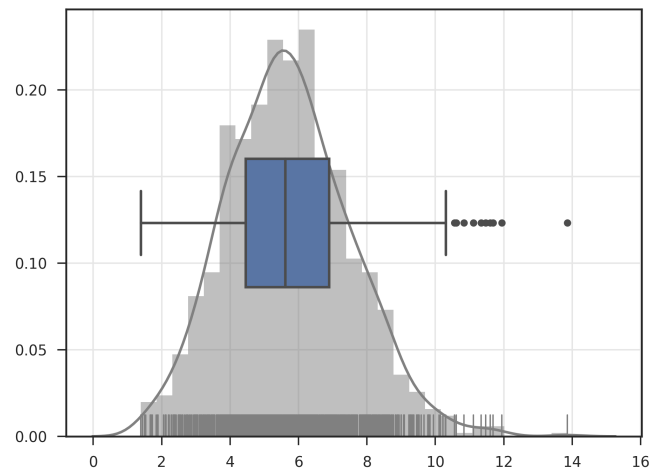
(b) EX_AMR
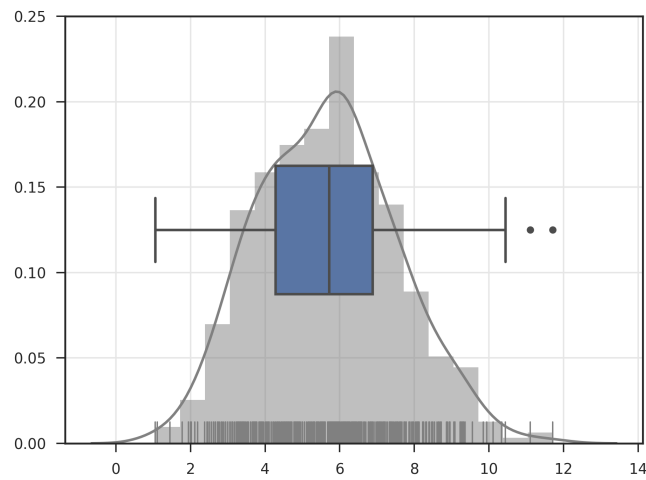
(c) EX_EUR

Figure 26: Distribution of LDL_DIRECT in META_EX by cohort

(a) AFFY_AFR

(b) AFFY_AMR

(c) AFFY_EUR

(d) ILL_AFR

(e) ILL_AMR
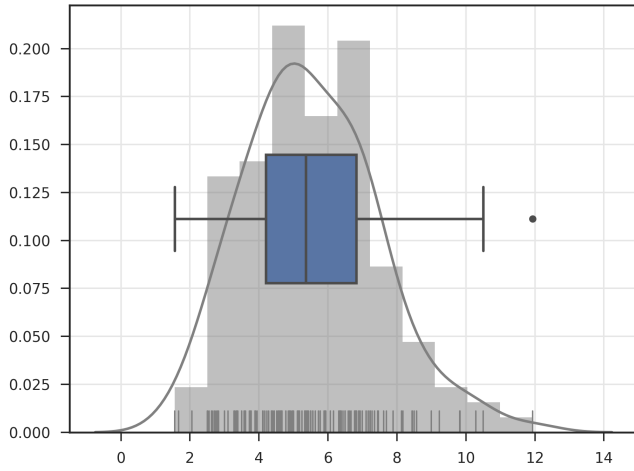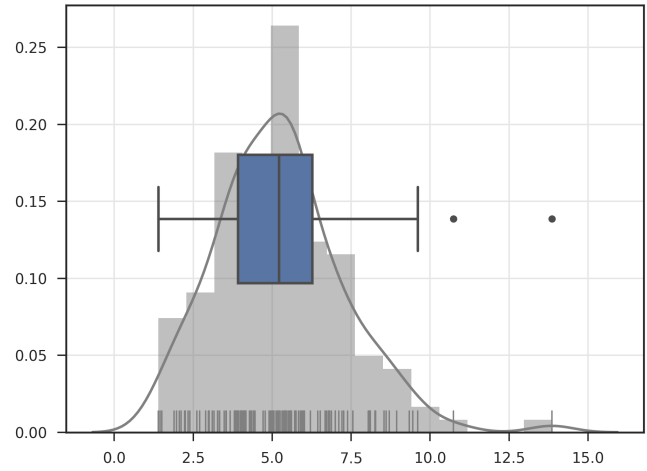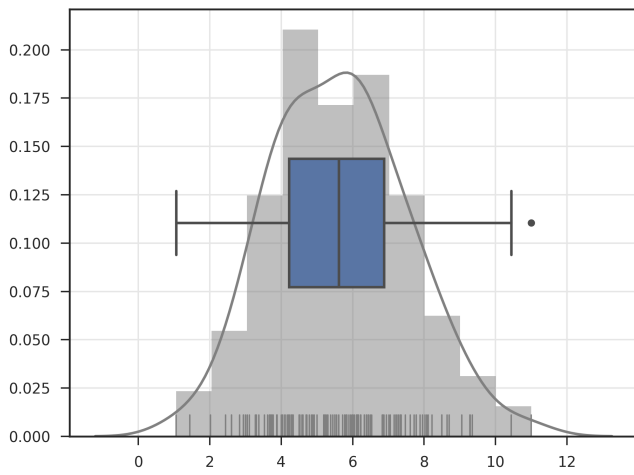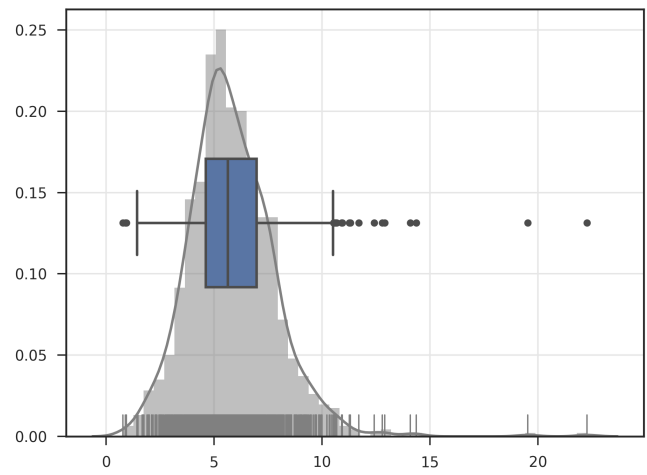
(f) ILL_EUR
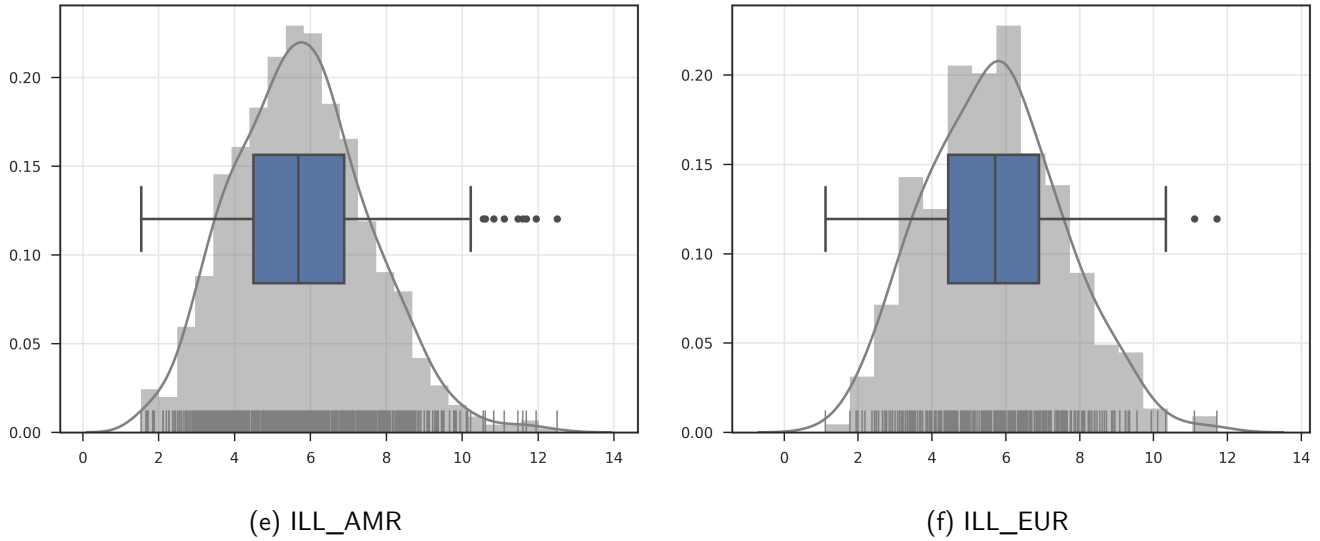
Figure 27: Distribution of LDL_DIRECT in META_GWAS by cohort

Table 25: Summary of samples removed from LDL Cholesterol analysis by cohort and model

| Cohort | Array | Ancestry | Trans | Covars | Total | -SampleQc | -missObs | -Kinship | -PcOutlier |
|---|---|---|---|---|---|---|---|---|---|
| META_EX EX_AFR | EX | AFR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 5172 | 44 | 4000 | 81 | 21 |
| META_EX EX_AMR | EX | AMR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 5144 | 32 | 4084 | 111 | 0 |
| META_EX EX_EUR | EX | EUR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 2379 | 30 | 1942 | 1 | 0 |
| META_GWAS AFFY_AFR | AFFY | AFR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 897 | 18 | 734 | 27 | 0 |
| META_GWAS AFFY_AMR | AFFY | AMR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 1035 | 20 | 895 | 27 | 11 |
| META_GWAS AFFY_EUR | AFFY | EUR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 578 | 12 | 465 | 1 | 0 |
| META_GWAS ILL_AFR | ILL | AFR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 4077 | 46 | 3117 | 1 | 0 |
| META_GWAS ILL_AMR | ILL | AMR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 3884 | 26 | 3031 | 0 | 0 |
| META_GWAS ILL_EUR | ILL | EUR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 1797 | 23 | 1474 | 0 | 1 |

Table 26: Summary of samples remaining for LDL Cholesterol analysis by cohort and model

| Cohort | Array | Ancestry | Trans | Covars | PCs | N | Male | Female | Max | Min | $\mu$ | $\tilde{x}$ | $\sigma$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| META_EX EX_AFR | EX | AFR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 7 | 1062 | 382 | 680 | 22.278 | 0.778 | 5.794 | 5.583 | 2.086 |
| META_EX EX_AMR | EX | AMR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 6 | 942 | 389 | 553 | 11.944 | 1.389 | 5.697 | 5.611 | 1.779 |
| META_EX EX_EUR | EX | EUR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 0 | 428 | 276 | 152 | 11.711 | 1.056 | 5.706 | 5.728 | 1.855 |
| META_GWAS AFFY_AFR | AFFY | AFR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 0 | 134 | 64 | 70 | 11.933 | 1.667 | 5.459 | 5.344 | 1.845 |
| META_GWAS AFFY_AMR | AFFY | AMR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 0 | 101 | 46 | 55 | 10.744 | 1.389 | 5.124 | 5.167 | 1.851 |
| META_GWAS AFFY_EUR | AFFY | EUR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 0 | 109 | 87 | 22 | 11.0 | 1.056 | 5.599 | 5.5 | 1.866 |
| META_GWAS ILL_AFR | ILL | AFR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 0 | 946 | 326 | 620 | 22.278 | 0.778 | 5.823 | 5.65 | 2.027 |
| META_GWAS ILL_AMR | ILL | AMR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 0 | 847 | 345 | 502 | 11.944 | 1.533 | 5.756 | 5.667 | 1.778 |
| META_GWAS ILL_EUR | ILL | EUR | invn | AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI | 0 | 318 | 188 | 130 | 11.711 | 1.111 | 5.739 | 5.739 | 1.849 |

## 8.2  Calibration
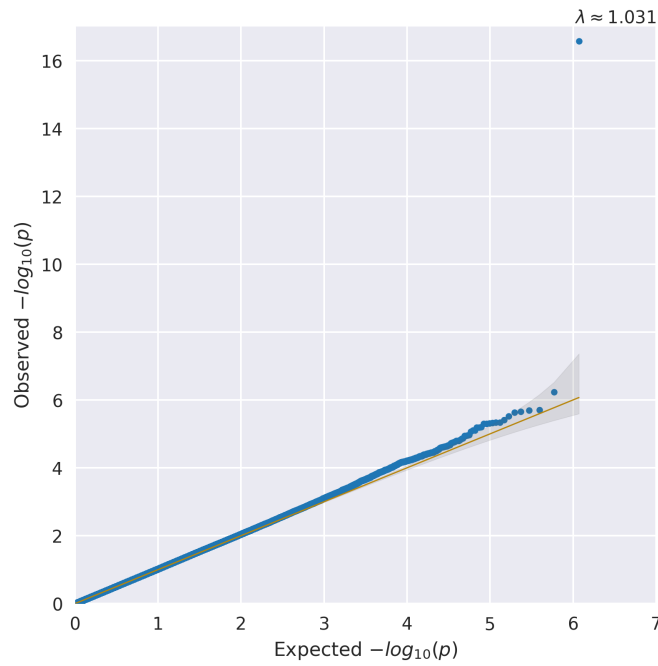


(a) invn Adjusted AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI

Figure 28: QQ plots for LDL_DIRECT in the MERGE analysis
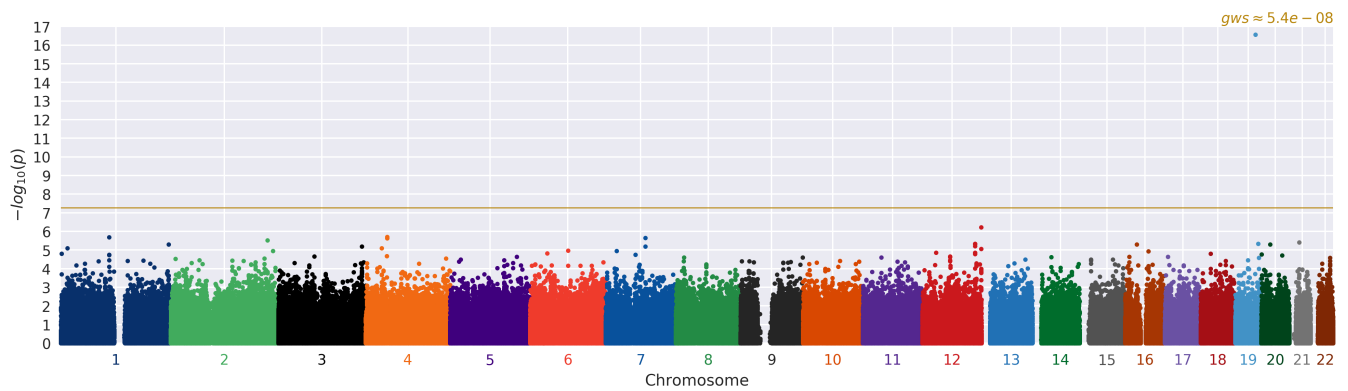


(a) invn Adjusted AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI

Figure 29: Manhattan plots for LDL_DIRECT in the MERGE analysis

## 8.3 Top associations

Table 27: Top variants in the MERGE invn Adjusted AGE_LIPIDS+AGE_LIPIDS2+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 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 19 | 45412079 | **rs7412** | C | T | **APOE** | META_EX | +++ | 2,432 | 1,047 | 1,385 | $8.26 \cdot 10^{-2}$ | $5.1 \cdot 10^{-2}$ | 0.116 | 0.439 | $5.19 \cdot 10^{-2}$ | 1.551 | $-8.459$ | $2.7 \cdot 10^{-17}$ |
| 12 | 133021330 | rs4883531 | G | A | MUC8 | META_GWAS | +++xxx | 2,111 | 859 | 1,252 | 0.635 | 0.61 | 0.66 | 0.157 | $3.14 \cdot 10^{-2}$ | 1.17 | 4.994 | $5.92 \cdot 10^{-7}$ |
| 4 | 48222160 | rs16851721 | C | T | TEC | META_GWAS | xxx+++ | 344 | 197 | 147 | 0.657 | 0.596 | 0.703 | 0.381 | $8.01 \cdot 10^{-2}$ | 1.464 | 4.755 | $1.98 \cdot 10^{-6}$ |
| 1 | 109817192 | **rs7528419** | A | G | **CELSR2** | META_GWAS | -++xxx | 2,110 | 859 | 1,251 | 0.252 | 0.195 | 0.279 | 0.163 | $3.44 \cdot 10^{-2}$ | 1.177 | $-4.749$ | $2.05 \cdot 10^{-6}$ |
| 7 | 90135511 | rs10487118 | C | A | CLDN12 | META_GWAS | xxx+++ | 344 | 197 | 147 | 0.11 | $4.1 \cdot 10^{-2}$ | 0.161 | 0.559 | 0.118 | 1.749 | 4.734 | $2.2 \cdot 10^{-6}$ |
| 2 | 218680591 | rs41383244 | A | G | TNS1 | META_GWAS | xxx+++ | 344 | 197 | 147 | 0.211 | $7.09 \cdot 10^{-2}$ | 0.372 | 0.445 | $9.52 \cdot 10^{-2}$ | 1.56 | $-4.671$ | $2.99 \cdot 10^{-6}$ |
| 21 | 22926491 | rs7281895 | A | G | NCAM2 | META_GWAS | +++xxx | 2,111 | 859 | 1,252 | 0.694 | 0.525 | 0.769 | 0.156 | $3.39 \cdot 10^{-2}$ | 1.169 | $-4.618$ | $3.87 \cdot 10^{-6}$ |
| 12 | 119482036 | rs11064646 | G | A | SRRM4 | META_GWAS | xxx+++ | 344 | 197 | 147 | 0.61 | 0.522 | 0.702 | 0.365 | $7.96 \cdot 10^{-2}$ | 1.44 | 4.585 | $4.54 \cdot 10^{-6}$ |
| 19 | 51572155 | rs1001538 | C | T | KLK13 | META_GWAS | +++xxx | 2,111 | 859 | 1,252 | 0.46 | 0.324 | 0.575 | 0.145 | $3.16 \cdot 10^{-2}$ | 1.156 | 4.581 | $4.62 \cdot 10^{-6}$ |
| 20 | 19806241 | rs17371935 | G | A | RIN2 | META_GWAS | xxx+++ | 343 | 196 | 147 | $2.92 \cdot 10^{-2}$ | $1.12 \cdot 10^{-2}$ | $5.05 \cdot 10^{-2}$ | 0.982 | 0.215 | 2.669 | 4.569 | $4.91 \cdot 10^{-6}$ |
| 16 | 26328263 | rs1424211 | T | C | HS3ST4 | META_GWAS | +++xxx | 2,111 | 859 | 1,252 | 0.939 | 0.899 | 0.964 | 0.293 | $6.41 \cdot 10^{-2}$ | 1.34 | $-4.566$ | $4.97 \cdot 10^{-6}$ |
| 1 | 244155946 | rs7511723 | T | C | ZBTB18 | META_GWAS | +++xxx | 2,106 | 857 | 1,249 | 0.236 | 0.12 | 0.301 | 0.168 | $3.68 \cdot 10^{-2}$ | 1.183 | $-4.562$ | $5.06 \cdot 10^{-6}$ |
| 7 | 90140673 | rs17867686 | A | C | CDK14 | META_GWAS | xxx+++ | 344 | 197 | 147 | 0.105 | $3.73 \cdot 10^{-2}$ | 0.161 | 0.544 | 0.121 | 1.723 | 4.513 | $6.4 \cdot 10^{-6}$ |
| 3 | 189017265 | rs7647662 | C | T | TPRG1 | META_GWAS | xxx+++ | 344 | 197 | 147 | 0.499 | 0.33 | 0.694 | 0.336 | $7.45 \cdot 10^{-2}$ | 1.399 | $-4.509$ | $6.5 \cdot 10^{-6}$ |
| 1 | 15589886 | rs10927751 | G | A | FHAD1 | META_GWAS | xxx+++ | 344 | 197 | 147 | 0.128 | $8.72 \cdot 10^{-2}$ | 0.179 | 0.535 | 0.12 | 1.707 | $-4.467$ | $7.94 \cdot 10^{-6}$ |
| 4 | 35807973 | rs4832782 | A | G | ARAP2 | META_GWAS | xxx+++ | 344 | 197 | 147 | 0.14 | 0.124 | 0.158 | 0.462 | 0.104 | 1.588 | $-4.467$ | $7.94 \cdot 10^{-6}$ |
| 6 | 86059902 | rs9450247 | A | G | NT5E | META_GWAS | ++++++ | 2,445 | 1,052 | 1,393 | 0.174 | $8.91 \cdot 10^{-2}$ | 0.25 | 0.17 | $3.87 \cdot 10^{-2}$ | 1.186 | $-4.403$ | $1.07 \cdot 10^{-5}$ |
| 2 | 231326201 | rs11681514 | G | C | SP100 | META_GWAS | xxx+++ | 344 | 197 | 147 | 0.219 | 0.174 | 0.248 | 0.388 | $8.83 \cdot 10^{-2}$ | 1.474 | 4.395 | $1.11 \cdot 10^{-5}$ |
| 7 | 25276424 | rs757202 | C | T | NPVF | META_GWAS | ++++++ | 2,455 | 1,056 | 1,399 | 0.665 | 0.541 | 0.757 | 0.135 | $3.08 \cdot 10^{-2}$ | 1.145 | 4.391 | $1.13 \cdot 10^{-5}$ |
| 16 | 52575907 | rs4784223 | A | G | TOX3 | META_GWAS | xxx+++ | 342 | 197 | 145 | 0.332 | 0.22 | 0.399 | 0.354 | $8.07 \cdot 10^{-2}$ | 1.425 | $-4.388$ | $1.15 \cdot 10^{-5}$ |
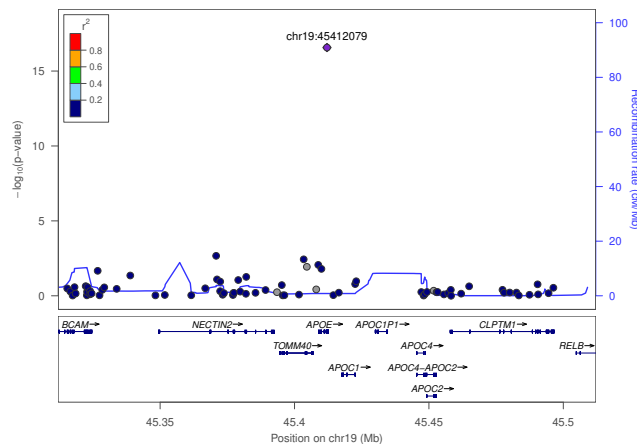


Figure 30: Regional plot for cohort MERGE model invn Adjusted AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI: rs7412 $\pm 100kb$

## 8.4 Previously identified risk loci

Table 28 shows statistics from the MERGE cohort for 50 loci that were shown to be significantly associated with LDL Cholesterol in the 2013 Nature Genetics paper by Willer 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 7 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 50 variants in both studies, 35 exhibit the same direction of effect with the known result (binomial test $p = 0.0033$).

Table 28: Top known loci in MERGE model invn Adjusted AGE_LIPIDS+AGE_LIPIDS2+SEX+BMI (**bold** variants indicate matching direction of effect)

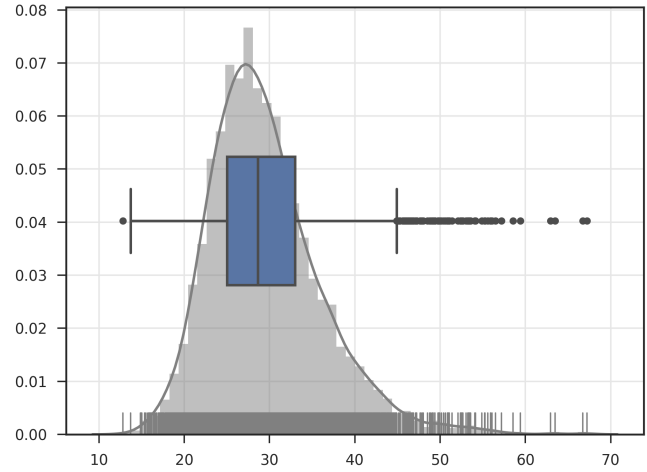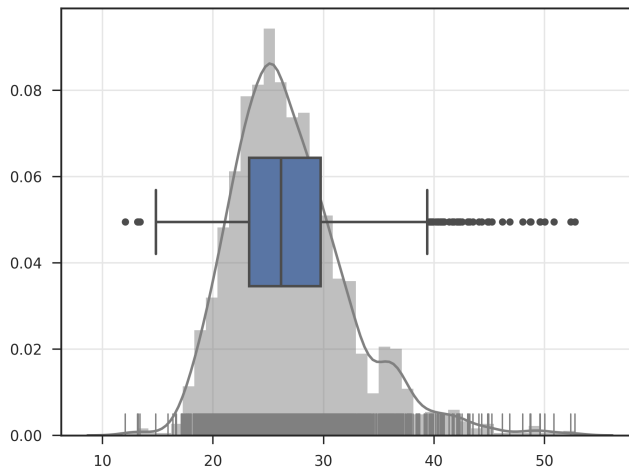| CHR | POS | ID | EA | OA | N | FREQ$_{AVG}$ | FREQ$_{MIN}$ | FREQ$_{MAX}$ | EFFECT | STDERR | P | DIR | COHORT | GENE$_{CLOSEST}$ | R$^2$ | ID$_{KNOWN}$ | N$_{KNOWN}$ | EFFECT$_{KNOWN}$ | STDERR$_{KNOWN}$ | P$_{KNOWN}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 19 | 45412079 | **rs7412** | C | T | 2,429 | $8.28 \cdot 10^{-2}$ | $5.11 \cdot 10^{-2}$ | 0.116 | 0.44 | $5.19 \cdot 10^{-2}$ | $2.2 \cdot 10^{-17}$ | +++ | META_EX | APOE | 1 | rs7412 | 94,595 | 0.59 | $1.01 \cdot 10^{-2}$ | 0 |
| 1 | 109818530 | **rs646776** | T | C | 2,111 | 0.705 | 0.651 | 0.802 | 0.137 | $3.3 \cdot 10^{-2}$ | $3.48 \cdot 10^{-5}$ | -++xxx | META_GWAS | CELSR2 | 1 | rs646776 | 94,595 | 0.16 | $4.4 \cdot 10^{-3}$ | $1.63 \cdot 10^{-272}$ |
| 1 | 109822166 | **rs599839** | A | G | 2,428 | 0.501 | 0.265 | 0.797 | $4.74 \cdot 10^{-2}$ | $3.24 \cdot 10^{-2}$ | 0.143 | -++ | META_EX | PSRC1 | 1 | rs599839 | 94,595 | 0.16 | $4.4 \cdot 10^{-3}$ | $2.75 \cdot 10^{-268}$ |
| 19 | 11202306 | **rs6511720** | G | T | 2,428 | 0.125 | 0.107 | 0.137 | 0.139 | $4.39 \cdot 10^{-2}$ | $1.55 \cdot 10^{-3}$ | +++ | META_EX | LDLR | 1 | rs6511720 | 94,595 | 0.221 | $6.1 \cdot 10^{-3}$ | $3.85 \cdot 10^{-262}$ |
| 19 | 45395619 | **rs2075650** | G | A | 2,429 | 0.115 | 0.104 | 0.123 | $5.94 \cdot 10^{-3}$ | $4.51 \cdot 10^{-2}$ | 0.895 | +-- | META_EX | TOMM40 | 1 | rs2075650 | 94,595 | 0.177 | $5.5 \cdot 10^{-3}$ | $1.72 \cdot 10^{-214}$ |
| 2 | 21263900 | **rs1367117** | A | G | 2,429 | 0.202 | 0.106 | 0.292 | $3.16 \cdot 10^{-2}$ | $3.66 \cdot 10^{-2}$ | 0.388 | +-+ | META_EX | APOB | 1 | rs1367117 | 94,595 | 0.119 | $4 \cdot 10^{-3}$ | $9.48 \cdot 10^{-183}$ |
| 19 | 45422946 | **rs4420638** | G | A | 2,429 | 0.164 | 0.111 | 0.221 | $6.32 \cdot 10^{-2}$ | $3.9 \cdot 10^{-2}$ | 0.105 | ++- | META_EX | APOC1 | 1 | rs4420638 | 94,595 | 0.225 | $7.7 \cdot 10^{-3}$ | $1.51 \cdot 10^{-178}$ |
| 19 | 45242173 | **rs1531517** | G | A | 2,111 | 0.142 | $8.38 \cdot 10^{-2}$ | 0.212 | $4.23 \cdot 10^{-2}$ | $4.42 \cdot 10^{-2}$ | 0.339 | ++xxx | META_GWAS | BCL3 | 1 | rs1531517 | 94,595 | 0.22 | $8 \cdot 10^{-3}$ | $9.51 \cdot 10^{-163}$ |
| 1 | 55505647 | **rs11591147** | G | T | 2,429 | $1.03 \cdot 10^{-2}$ | $2.83 \cdot 10^{-3}$ | $1.87 \cdot 10^{-2}$ | 0.206 | 0.145 | 0.154 | ++- | META_EX | PCSK9 | 1 | rs11591147 | 94,595 | 0.497 | $1.8 \cdot 10^{-2}$ | $8.58 \cdot 10^{-143}$ |
| 2 | 21320516 | **rs2337383** | G | A | 2,110 | 0.211 | 0.13 | 0.286 | $5.07 \cdot 10^{-2}$ | $3.77 \cdot 10^{-2}$ | 0.178 | -++xxx | META_GWAS | TDRD15 | 1 | rs2337383 | 94,595 | $9.85 \cdot 10^{-2}$ | $3.9 \cdot 10^{-3}$ | $1.08 \cdot 10^{-131}$ |
| 19 | 45333834 | **rs4803760** | C | T | 2,111 | 0.911 | 0.819 | 0.951 | $5.3 \cdot 10^{-2}$ | $5.6 \cdot 10^{-2}$ | 0.345 | +++xxx | META_GWAS | BCAM | 1 | rs4803760 | 94,595 | 0.119 | $4.9 \cdot 10^{-3}$ | $2.47 \cdot 10^{-123}$ |
| 19 | 45382034 | **rs6859** | A | G | 2,429 | 0.605 | 0.547 | 0.668 | $5.7 \cdot 10^{-2}$ | $2.93 \cdot 10^{-2}$ | $5.17 \cdot 10^{-2}$ | -++ | META_EX | NECTIN2 | 1 | rs6859 | 94,595 | $8.35 \cdot 10^{-2}$ | $3.9 \cdot 10^{-3}$ | $4.65 \cdot 10^{-88}$ |
| 2 | 44073881 | **rs6544713** | T | C | 2,429 | 0.784 | 0.703 | 0.852 | $8.34 \cdot 10^{-2}$ | $3.58 \cdot 10^{-2}$ | $1.97 \cdot 10^{-2}$ | +++ | META_EX | ABCG8 | 1 | rs6544713 | 94,595 | $8.06 \cdot 10^{-2}$ | $4.1 \cdot 10^{-3}$ | $4.84 \cdot 10^{-83}$ |
| 5 | 74656539 | **rs12916** | C | T | 2,111 | 0.296 | 0.239 | 0.396 | $5.95 \cdot 10^{-2}$ | $3.39 \cdot 10^{-2}$ | $7.94 \cdot 10^{-2}$ | ++xxx | META_GWAS | HMGCR | 1 | rs12916 | 94,595 | $7.33 \cdot 10^{-2}$ | $3.8 \cdot 10^{-3}$ | $7.79 \cdot 10^{-78}$ |
| 19 | 45176340 | rs2965157 | C | T | 344 | 0.267 | $2.75 \cdot 10^{-2}$ | 0.545 | $8.4 \cdot 10^{-2}$ | 0.103 | 0.413 | xxx+++ | META_GWAS | CEACAM19 | 1 | rs2965157 | 94,595 | $-0.189$ | $1.12 \cdot 10^{-2}$ | $7.29 \cdot 10^{-62}$ |
| 19 | 11159525 | **rs12052058** | G | T | 344 | 0.157 | $6.34 \cdot 10^{-2}$ | 0.252 | 0.115 | 0.107 | 0.284 | xxx-++ | META_GWAS | SMARCA4 | 1 | rs12052058 | 94,595 | $7.5 \cdot 10^{-2}$ | $4.3 \cdot 10^{-3}$ | $9.66 \cdot 10^{-62}$ |
| 5 | 74569856 | **rs4704200** | T | G | 2,111 | 0.59 | 0.456 | 0.707 | $6.13 \cdot 10^{-2}$ | $3.2 \cdot 10^{-2}$ | $5.59 \cdot 10^{-2}$ | +++xxx | META_GWAS | ANKRD31 | 1 | rs4704200 | 94,595 | $6.44 \cdot 10^{-2}$ | $3.7 \cdot 10^{-3}$ | $1.3 \cdot 10^{-61}$ |
| 5 | 74879890 | **rs5744680** | A | G | 344 | 0.594 | 0.395 | 0.84 | $5.75 \cdot 10^{-2}$ | $8.46 \cdot 10^{-2}$ | 0.497 | xxx+++ | META_GWAS | POLK | 1 | rs5744680 | 94,595 | $6.44 \cdot 10^{-2}$ | $3.7 \cdot 10^{-3}$ | $2.96 \cdot 10^{-61}$ |
| 19 | 45296806 | **rs3208856** | C | T | 2,429 | $3.87 \cdot 10^{-2}$ | $2.8 \cdot 10^{-2}$ | $4.85 \cdot 10^{-2}$ | $7.3 \cdot 10^{-3}$ | $7.5 \cdot 10^{-2}$ | 0.922 | ++- | META_EX | CBLC | 1 | rs3208856 | 94,595 | 0.295 | $1.91 \cdot 10^{-2}$ | $4.03 \cdot 10^{-56}$ |
| 19 | 10950125 | rs11881156 | T | C | 2,110 | 0.127 | 0.108 | 0.204 | $1.81 \cdot 10^{-2}$ | $4.67 \cdot 10^{-2}$ | 0.699 | +-+xxx | META_GWAS | C19orf38 | 1 | rs11881156 | 94,595 | $-8.11 \cdot 10^{-2}$ | $4.9 \cdot 10^{-3}$ | $1.7 \cdot 10^{-55}$ |
| 19 | 19407718 | **rs10401969** | T | C | 2,429 | 0.125 | $6.07 \cdot 10^{-2}$ | 0.166 | 0.119 | $4.42 \cdot 10^{-2}$ | $7.24 \cdot 10^{-3}$ | +++ | META_EX | SUGP1 | 1 | rs10401969 | 94,595 | 0.118 | $7.2 \cdot 10^{-3}$ | $2.65 \cdot 10^{-54}$ |
| 2 | 44065090 | rs6756629 | A | G | 2,427 | $7.79 \cdot 10^{-2}$ | $7.16 \cdot 10^{-2}$ | $8.42 \cdot 10^{-2}$ | $5.35 \cdot 10^{-2}$ | $5.37 \cdot 10^{-2}$ | 0.319 | -+- | META_EX | ABCG5 | 1 | rs6756629 | 94,595 | $-0.131$ | $8.8 \cdot 10^{-3}$ | $1.29 \cdot 10^{-49}$ |
| 8 | 126481747 | rs2980875 | G | A | 344 | 0.395 | 0.34 | 0.441 | $3.93 \cdot 10^{-2}$ | $7.67 \cdot 10^{-2}$ | 0.608 | xxx-++ | META_GWAS | TRIB1 | 1 | rs2980875 | 94,595 | $-5.47 \cdot 10^{-2}$ | $3.6 \cdot 10^{-3}$ | $2.3 \cdot 10^{-47}$ |
| 1 | 109833187 | rs17584208 | A | G | 344 | $7.99 \cdot 10^{-2}$ | $5.05 \cdot 10^{-2}$ | 0.104 | 0.151 | 0.137 | 0.271 | xxx-++ | META_GWAS | MYBPHL | 1 | rs17584208 | 94,595 | $-0.101$ | $6.7 \cdot 10^{-3}$ | $4.39 \cdot 10^{-47}$ |
| 19 | 19658472 | **rs16996148** | G | T | 2,429 | 0.114 | $6.31 \cdot 10^{-2}$ | 0.15 | $5.06 \cdot 10^{-2}$ | $4.5 \cdot 10^{-2}$ | 0.26 | -++ | META_EX | CILP2 | 1 | rs16996148 | 94,595 | $9.86 \cdot 10^{-2}$ | $6.7 \cdot 10^{-3}$ | $1.97 \cdot 10^{-45}$ |
| 19 | 45225345 | rs2965109 | T | C | 2,455 | 0.459 | 0.406 | 0.481 | $2.5 \cdot 10^{-2}$ | $2.85 \cdot 10^{-2}$ | 0.954 | +----x | META_GWAS | CEACAM16 | 1 | rs2965109 | 94,595 | $-5.46 \cdot 10^{-2}$ | $3.9 \cdot 10^{-3}$ | $6.65 \cdot 10^{-45}$ |
| 9 | 136154168 | **rs579459** | C | T | 2,429 | 0.171 | 0.137 | 0.234 | $4.84 \cdot 10^{-2}$ | $3.78 \cdot 10^{-2}$ | 0.201 | +++ | META_EX | ABO | 1 | rs579459 | 94,595 | $6.65 \cdot 10^{-2}$ | $4.5 \cdot 10^{-3}$ | $2.42 \cdot 10^{-44}$ |
| 19 | 19329924 | **rs2228603** | C | T | 2,429 | $2.68 \cdot 10^{-2}$ | $1.41 \cdot 10^{-2}$ | $5.61 \cdot 10^{-2}$ | 0.122 | $9.09 \cdot 10^{-2}$ | 0.18 | -++ | META_EX | NCAN | 1 | rs2228603 | 94,595 | 0.104 | $7.2 \cdot 10^{-3}$ | $4.43 \cdot 10^{-44}$ |
| 1 | 109782190 | rs611060 | T | C | 2,111 | 0.488 | 0.338 | 0.612 | $3.9 \cdot 10^{-4}$ | $3.06 \cdot 10^{-2}$ | 0.991 | --+xxx | META_GWAS | SARS | 1 | rs611060 | 94,595 | $-5.34 \cdot 10^{-2}$ | $3.7 \cdot 10^{-3}$ | $4.27 \cdot 10^{-42}$ |
| 16 | 72108093 | **rs2000999** | A | G | 2,426 | 0.133 | $7.68 \cdot 10^{-2}$ | 0.195 | $2.99 \cdot 10^{-2}$ | $4.25 \cdot 10^{-2}$ | 0.482 | ++- | META_EX | HPR | 1 | rs2000999 | 94,595 | $6.5 \cdot 10^{-2}$ | $4.6 \cdot 10^{-3}$ | $4.22 \cdot 10^{-41}$ |
| 11 | 61609750 | **rs174583** | C | T | 2,429 | 0.344 | 0.264 | 0.436 | $9.15 \cdot 10^{-3}$ | $3.18 \cdot 10^{-2}$ | 0.774 | ++- | META_EX | FADS2 | 1 | rs174583 | 94,595 | $5.22 \cdot 10^{-2}$ | $3.8 \cdot 10^{-3}$ | $7 \cdot 10^{-41}$ |
| 5 | 74759183 | rs4704221 | A | T | 344 | 0.599 | 0.408 | 0.84 | $3.18 \cdot 10^{-2}$ | $8.39 \cdot 10^{-2}$ | 0.705 | xxx-++ | META_GWAS | COL4A3BP | 1 | rs4704221 | 94,595 | $-6.3 \cdot 10^{-2}$ | $4.5 \cdot 10^{-3}$ | $2.03 \cdot 10^{-40}$ |
| 5 | 74924890 | rs1427924 | A | G | 344 | 0.307 | 0.252 | 0.373 | $3.23 \cdot 10^{-2}$ | $8.67 \cdot 10^{-2}$ | 0.71 | xxx+++ | META_GWAS | ANKDD1B | 1 | rs1427924 | 94,595 | $-6.28 \cdot 10^{-2}$ | $4.4 \cdot 10^{-3}$ | $2.4 \cdot 10^{-40}$ |
| 11 | 61574150 | **rs174550** | T | C | 2,429 | 0.231 | $6.79 \cdot 10^{-2}$ | 0.376 | $7.82 \cdot 10^{-2}$ | $3.79 \cdot 10^{-2}$ | $3.92 \cdot 10^{-2}$ | -++ | META_EX | FADS1 | 1 | rs174550 | 94,595 | $5.14 \cdot 10^{-2}$ | $3.8 \cdot 10^{-3}$ | $7.03 \cdot 10^{-40}$ |
| 11 | 61557803 | **rs102275** | T | C | 2,429 | 0.566 | 0.342 | 0.666 | $3.86 \cdot 10^{-2}$ | $3.05 \cdot 10^{-2}$ | 0.207 | +++ | META_EX | TMEM258 | 1 | rs102275 | 94,595 | $5.12 \cdot 10^{-2}$ | $3.8 \cdot 10^{-3}$ | $7.61 \cdot 10^{-40}$ |
| 19 | 19723215 | **rs10500212** | C | T | 2,110 | 0.116 | $6.45 \cdot 10^{-2}$ | 0.15 | $8.79 \cdot 10^{-2}$ | $4.79 \cdot 10^{-2}$ | $6.63 \cdot 10^{-2}$ | -++xxx | META_GWAS | PBX4 | 1 | rs10500212 | 94,595 | $9.15 \cdot 10^{-2}$ | $6.7 \cdot 10^{-3}$ | $8.95 \cdot 10^{-40}$ |
| 1 | 55713628 | rs4927207 | A | G | 2,111 | 0.145 | 0.128 | 0.16 | $7.34 \cdot 10^{-2}$ | $4.42 \cdot 10^{-2}$ | $9.71 \cdot 10^{-2}$ | ++xxx | META_GWAS | USP24 | 1 | rs4927207 | 94,595 | $-6.92 \cdot 10^{-2}$ | $4.9 \cdot 10^{-3}$ | $2.36 \cdot 10^{-39}$ |
| 11 | 61551356 | **rs174535** | T | C | 2,111 | 0.298 | 0.192 | 0.407 | $4.75 \cdot 10^{-2}$ | $3.45 \cdot 10^{-2}$ | 0.169 | -++xxx | META_GWAS | MYRF | 1 | rs174535 | 94,595 | $5.04 \cdot 10^{-2}$ | $3.8 \cdot 10^{-3}$ | $1.75 \cdot 10^{-38}$ |
| 19 | 19379549 | **rs58542926** | C | T | 2,429 | $4.63 \cdot 10^{-2}$ | $3.2 \cdot 10^{-2}$ | $5.84 \cdot 10^{-2}$ | 0.148 | $6.84 \cdot 10^{-2}$ | $3.03 \cdot 10^{-2}$ | +++ | META_EX | TM6SF2 | 1 | rs58542926 | 94,595 | 0.128 | $9.5 \cdot 10^{-3}$ | $1.96 \cdot 10^{-38}$ |
| 16 | 56989590 | **rs247616** | C | T | 2,428 | 0.271 | 0.258 | 0.292 | $1.56 \cdot 10^{-2}$ | $3.23 \cdot 10^{-2}$ | 0.628 | -++ | META_EX | CETP | 1 | rs247616 | 94,595 | $5.47 \cdot 10^{-2}$ | $4.1 \cdot 10^{-3}$ | $2.57 \cdot 10^{-37}$ |
| 19 | 19746151 | rs2304128 | T | G | 2,111 | 0.132 | $6.92 \cdot 10^{-2}$ | 0.169 | $2.52 \cdot 10^{-2}$ | $4.58 \cdot 10^{-2}$ | 0.582 | ++xxx | META_GWAS | GMIP | 1 | rs2304128 | 94,595 | $-9.02 \cdot 10^{-2}$ | $6.8 \cdot 10^{-3}$ | $4.23 \cdot 10^{-37}$ |
| 19 | 19505087 | **rs10415849** | C | T | 344 | 0.129 | 0.11 | 0.149 | 0.121 | 0.117 | 0.3 | xxx++- | META_GWAS | GATAD2A | 1 | rs10415849 | 94,595 | $7.28 \cdot 10^{-2}$ | $5.7 \cdot 10^{-3}$ | $4.25 \cdot 10^{-36}$ |
| 2 | 21123352 | rs6711016 | A | C | 344 | 0.148 | $4.85 \cdot 10^{-2}$ | 0.229 | $2.42 \cdot 10^{-2}$ | 0.118 | 0.838 | xxx-+- | META_GWAS | LDAH | 1 | rs6711016 | 94,595 | $-5.51 \cdot 10^{-2}$ | $4.3 \cdot 10^{-3}$ | $1.1 \cdot 10^{-35}$ |
| 11 | 61560081 | **rs174538** | G | A | 2,111 | 0.21 | $6.03 \cdot 10^{-2}$ | 0.347 | $7.34 \cdot 10^{-2}$ | $3.98 \cdot 10^{-2}$ | $6.52 \cdot 10^{-2}$ | -++xxx | META_GWAS | FEN1 | 1 | rs174538 | 94,595 | $5 \cdot 10^{-2}$ | $4 \cdot 10^{-3}$ | $1.07 \cdot 10^{-34}$ |
| 19 | 10904700 | **rs2278444** | T | C | 2,455 | 0.345 | 0.257 | 0.403 | $1.64 \cdot 10^{-2}$ | $3.03 \cdot 10^{-2}$ | 0.588 | --++xx | META_GWAS | DNM2 | 1 | rs2278444 | 94,595 | $5.12 \cdot 10^{-2}$ | $4 \cdot 10^{-3}$ | $1.76 \cdot 10^{-34}$ |
| 1 | 62996838 | rs1168013 | G | C | 344 | 0.519 | 0.332 | 0.674 | $7.98 \cdot 10^{-2}$ | $8.06 \cdot 10^{-2}$ | 0.322 | xxx++- | META_GWAS | DOCK7 | 1 | rs1168013 | 94,595 | $-4.97 \cdot 10^{-2}$ | $3.9 \cdot 10^{-3}$ | $5.71 \cdot 10^{-33}$ |
| 19 | 19789528 | rs2304130 | G | A | 2,429 | 0.149 | $5.61 \cdot 10^{-2}$ | 0.198 | $2.3 \cdot 10^{-2}$ | $4.11 \cdot 10^{-2}$ | 0.575 | ++- | META_EX | ZNF101 | 1 | rs2304130 | 94,595 | $-8.85 \cdot 10^{-2}$ | $7.2 \cdot 10^{-3}$ | $2.24 \cdot 10^{-32}$ |
| 1 | 62905893 | rs10493322 | T | C | 2,111 | 0.327 | 0.283 | 0.352 | $4.92 \cdot 10^{-4}$ | $3.25 \cdot 10^{-2}$ | 0.988 | --+xxx | META_GWAS | USP1 | 1 | rs10493322 | 94,595 | $-4.93 \cdot 10^{-2}$ | $4 \cdot 10^{-3}$ | $8.64 \cdot 10^{-32}$ |
| 5 | 156390297 | **rs6882076** | C | T | 2,428 | 0.483 | 0.341 | 0.614 | $9.19 \cdot 10^{-2}$ | $3 \cdot 10^{-2}$ | 0.759 | ++ | META_EX | TIMD4 | 1 | rs6882076 | 94,595 | $4.56 \cdot 10^{-2}$ | $3.8 \cdot 10^{-3}$ | $3.31 \cdot 10^{-31}$ |
| 1 | 109851126 | **rs413582** | T | C | 2,111 | 0.28 | $8.4 \cdot 10^{-2}$ | 0.557 | $6.55 \cdot 10^{-2}$ | $3.74 \cdot 10^{-2}$ | $7.97 \cdot 10^{-2}$ | +++xxx | META_GWAS | SORT1 | 1 | rs413582 | 94,595 | $4.38 \cdot 10^{-2}$ | $3.7 \cdot 10^{-3}$ | $4.87 \cdot 10^{-31}$ |

# 9 Body Mass Index (BMI)

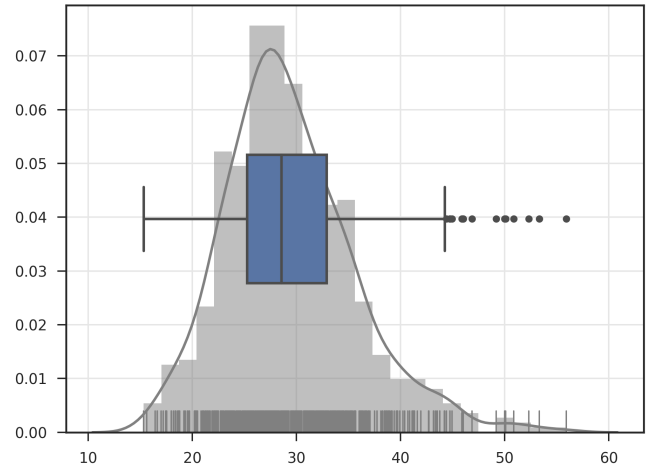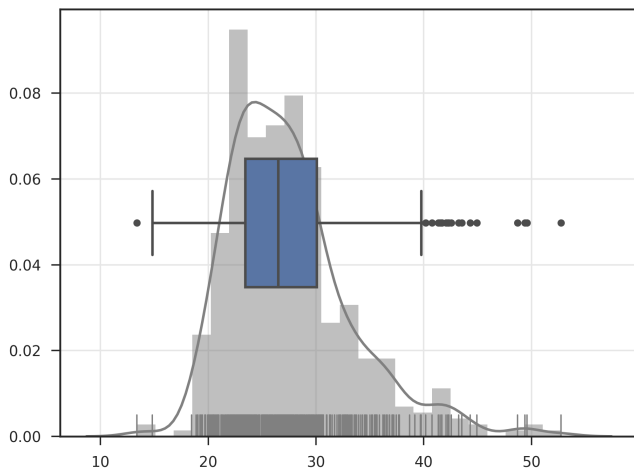## 9.1 Summary
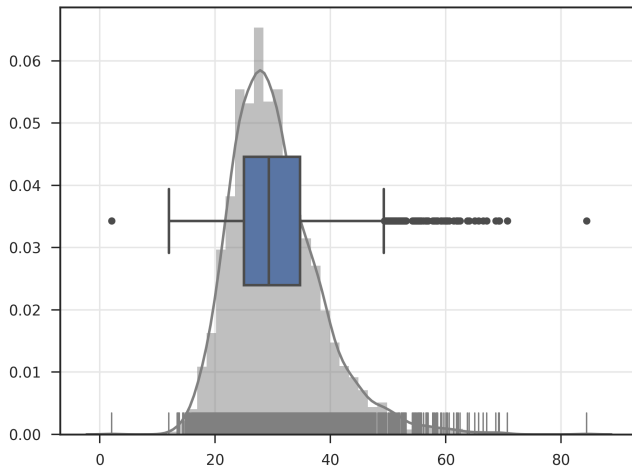


(a) EX_AFR

(b) EX_AMR

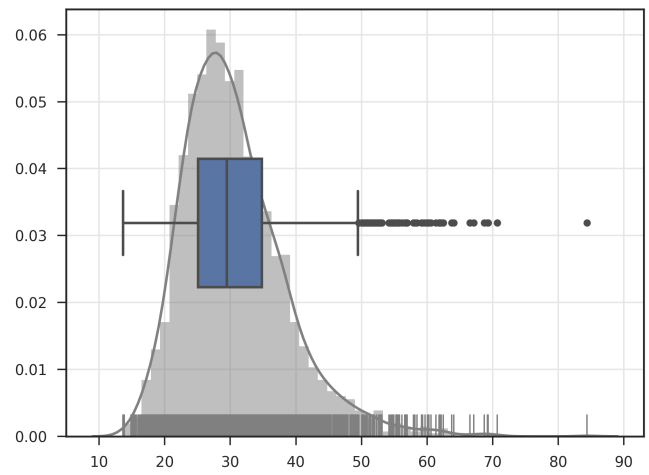(c) EX_EUR

Figure 31: Distribution of BMI in META_EX by cohort

(a) AFFY_AFR

(b) AFFY_AMR

(c) AFFY_EUR

(d) ILL_AFR

(e) ILL_AMR
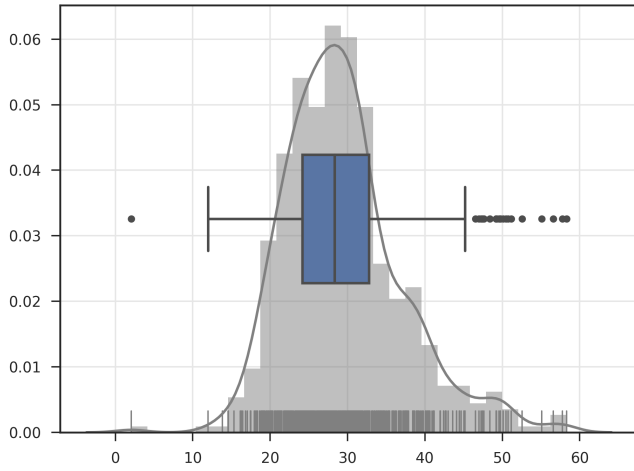
(f) ILL_EUR
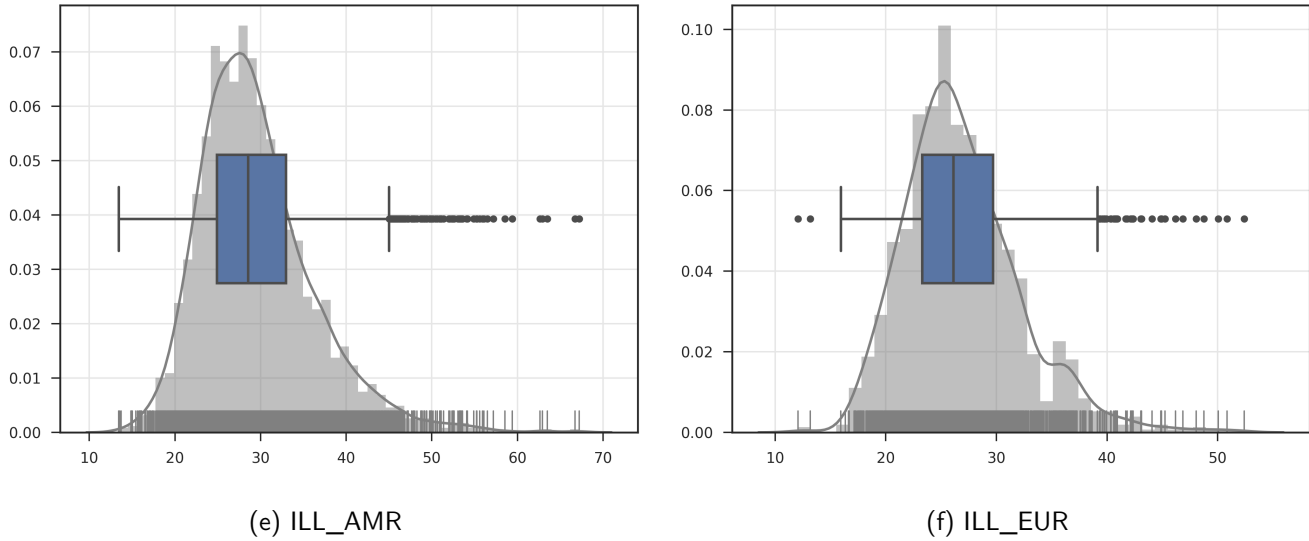
Figure 32: Distribution of BMI in META_GWAS by cohort

Table 29: Summary of samples removed from Body Mass Index analysis by cohort and model

| Cohort | Array | Ancestry | Trans | Covars | Total | -SampleQc | -missObs | -Kinship | -PcOutlier |
|---|---|---|---|---|---|---|---|---|---|
| META_EX EX_AFR | EX | AFR | invn | AGE_ANTHRO+AGE_ANTHRO2+SEX | 5172 | 44 | 1106 | 282 | 0 |
| META_EX EX_AMR | EX | AMR | invn | AGE_ANTHRO+AGE_ANTHRO2+SEX | 5144 | 32 | 1128 | 426 | 0 |
| META_EX EX_EUR | EX | EUR | invn | AGE_ANTHRO+AGE_ANTHRO2+SEX | 2379 | 30 | 586 | 6 | 0 |
| META_GWAS AFFY_AFR | AFFY | AFR | invn | AGE_ANTHRO+AGE_ANTHRO2+SEX | 897 | 18 | 200 | 129 | 15 |
| META_GWAS AFFY_AMR | AFFY | AMR | invn | AGE_ANTHRO+AGE_ANTHRO2+SEX | 1035 | 20 | 227 | 165 | 5 |
| META_GWAS AFFY_EUR | AFFY | EUR | invn | AGE_ANTHRO+AGE_ANTHRO2+SEX | 578 | 12 | 164 | 8 | 7 |
| META_GWAS ILL_AFR | ILL | AFR | invn | AGE_ANTHRO+AGE_ANTHRO2+SEX | 4077 | 46 | 872 | 4 | 0 |
| META_GWAS ILL_AMR | ILL | AMR | invn | AGE_ANTHRO+AGE_ANTHRO2+SEX | 3884 | 26 | 857 | 2 | 0 |
| META_GWAS ILL_EUR | ILL | EUR | invn | AGE_ANTHRO+AGE_ANTHRO2+SEX | 1797 | 23 | 425 | 1 | 0 |

Table 30: Summary of samples remaining for Body Mass Index analysis by cohort and model

| Cohort | Array | Ancestry | Trans | Covars | PCs | N | Male | Female | Max | Min | $\mu$ | $\tilde{x}$ | $\sigma$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| META_EX EX_AFR | EX | AFR | invn | AGE_ANTHRO+AGE_ANTHRO2+SEX | 0 | 3753 | 1323 | 2430 | 84.409 | 2.048 | 30.302 | 29.159 | 7.872 |
| META_EX EX_AMR | EX | AMR | invn | AGE_ANTHRO+AGE_ANTHRO2+SEX | 3 | 3567 | 1401 | 2166 | 67.228 | 13.714 | 29.438 | 28.498 | 6.568 |
| META_EX EX_EUR | EX | EUR | invn | AGE_ANTHRO+AGE_ANTHRO2+SEX | 0 | 1764 | 1177 | 587 | 52.743 | 12.053 | 26.953 | 26.128 | 5.398 |
| META_GWAS AFFY_AFR | AFFY | AFR | invn | AGE_ANTHRO+AGE_ANTHRO2+SEX | 0 | 544 | 237 | 307 | 58.331 | 2.048 | 29.425 | 28.342 | 7.714 |
| META_GWAS AFFY_AMR | AFFY | AMR | invn | AGE_ANTHRO+AGE_ANTHRO2+SEX | 6 | 622 | 273 | 349 | 55.913 | 15.333 | 29.358 | 28.529 | 6.212 |
| META_GWAS AFFY_EUR | AFFY | EUR | invn | AGE_ANTHRO+AGE_ANTHRO2+SEX | 0 | 395 | 324 | 71 | 52.743 | 13.383 | 27.308 | 26.306 | 5.716 |
| META_GWAS ILL_AFR | ILL | AFR | invn | AGE_ANTHRO+AGE_ANTHRO2+SEX | 0 | 3167 | 1085 | 2082 | 84.409 | 13.43 | 30.536 | 29.352 | 7.899 |
| META_GWAS ILL_AMR | ILL | AMR | invn | AGE_ANTHRO+AGE_ANTHRO2+SEX | 3 | 3007 | 1148 | 1859 | 67.228 | 13.714 | 29.555 | 28.509 | 6.688 |
| META_GWAS ILL_EUR | ILL | EUR | invn | AGE_ANTHRO+AGE_ANTHRO2+SEX | 0 | 1355 | 846 | 509 | 52.389 | 12.053 | 26.855 | 26.046 | 5.281 |

## 9.2   Calibration
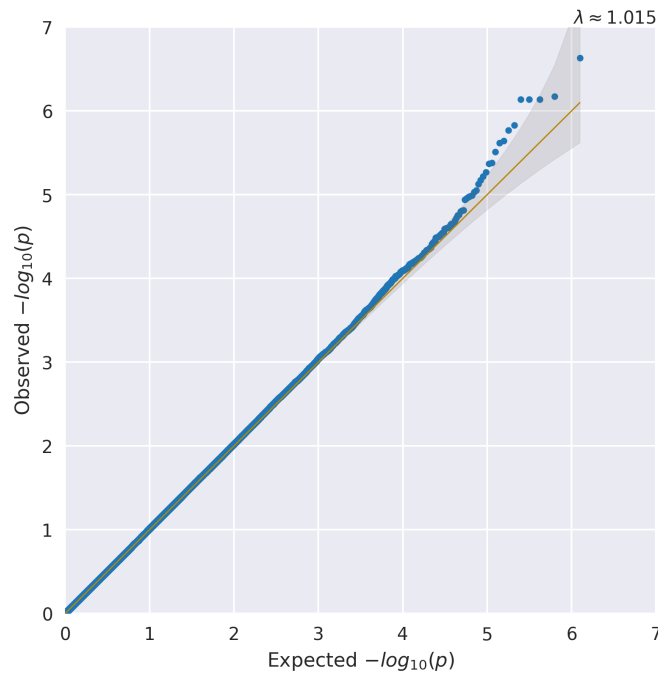


(a) invn Adjusted AGE_ANTHRO+AGE_ANTHRO2+SEX

Figure 33: QQ plots for BMI in the MERGE analysis
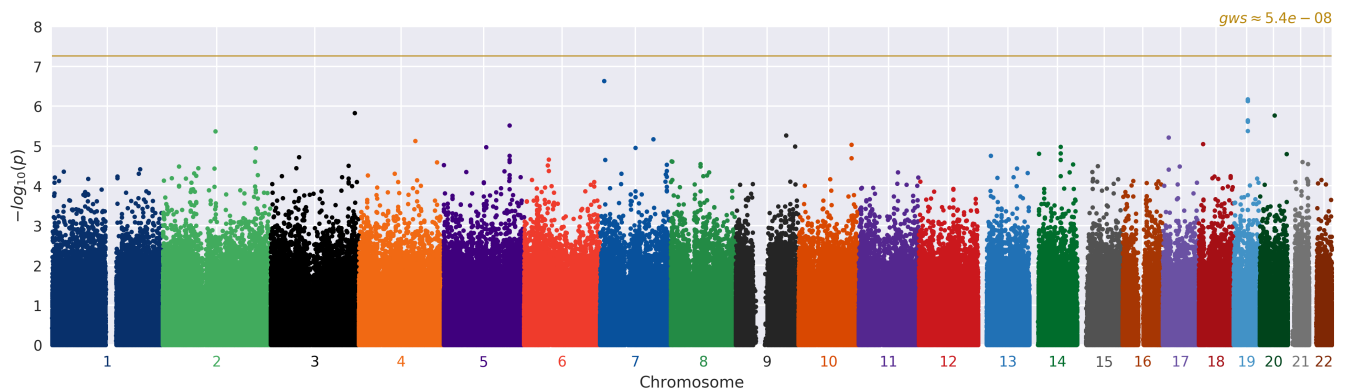


(a) invn Adjusted AGE_ANTHRO+AGE_ANTHRO2+SEX

Figure 34: Manhattan plots for BMI in the MERGE analysis

## 9.3 Top associations

Table 31: Top variants in the MERGE invn Adjusted AGE_ANTHRO+AGE_ANTHRO2+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 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 7 | 9469697 | rs12111963 | C | T | NXPH1 | META_GWAS | xxx-++ | 1,561 | 834 | 727 | $5.22 \cdot 10^{-2}$ | $1.27 \cdot 10^{-3}$ | 0.104 | 0.419 | $8.11 \cdot 10^{-2}$ | 1.521 | $-5.171$ | $2.33 \cdot 10^{-7}$ |
| 19 | 32480688 | rs12610055 | G | A | ZNF507 | META_GWAS | xxx+++ | 1,561 | 834 | 727 | 0.429 | 0.334 | 0.547 | 0.179 | $3.6 \cdot 10^{-2}$ | 1.196 | 4.969 | $6.73 \cdot 10^{-7}$ |
| 3 | 189016395 | rs7644778 | G | T | TPRG1 | META_GWAS | ++++-+ | 9,090 | 3,913 | 5,177 | $9.18 \cdot 10^{-2}$ | $1.14 \cdot 10^{-2}$ | 0.179 | 0.125 | $2.6 \cdot 10^{-2}$ | 1.133 | $-4.813$ | $1.49 \cdot 10^{-6}$ |
| 20 | 33501958 | rs140958101 | A | C | ACSS2 | META_EX | +++ | 9,084 | 3,901 | 5,183 | $4.95 \cdot 10^{-4}$ | $2.83 \cdot 10^{-4}$ | $6.66 \cdot 10^{-4}$ | 1.593 | 0.333 | 4.918 | 4.787 | $1.7 \cdot 10^{-6}$ |
| 5 | 147880181 | rs6881498 | A | G | HTR4 | META_GWAS | xxx+++ | 1,560 | 834 | 726 | 0.602 | 0.415 | 0.796 | 0.172 | $3.69 \cdot 10^{-2}$ | 1.188 | $-4.666$ | $3.07 \cdot 10^{-6}$ |
| 2 | 118822403 | rs11687724 | C | T | INSIG2 | META_GWAS | +++xxx | 7,528 | 3,079 | 4,449 | $5.32 \cdot 10^{-2}$ | $4.67 \cdot 10^{-2}$ | $5.81 \cdot 10^{-2}$ | 0.167 | $3.63 \cdot 10^{-2}$ | 1.182 | $-4.598$ | $4.27 \cdot 10^{-6}$ |
| 9 | 113171262 | rs16914997 | G | A | SVEP1 | META_GWAS | ++++-+ | 9,088 | 3,912 | 5,176 | 0.213 | 0.194 | 0.242 | $8.19 \cdot 10^{-2}$ | $1.8 \cdot 10^{-2}$ | 1.085 | $-4.549$ | $5.39 \cdot 10^{-6}$ |
| 17 | 13023456 | rs2322788 | T | C | ELAC2 | META_GWAS | +++xxx | 7,524 | 3,076 | 4,448 | 0.638 | 0.589 | 0.688 | $7.73 \cdot 10^{-2}$ | $1.71 \cdot 10^{-2}$ | 1.08 | 4.524 | $6.07 \cdot 10^{-6}$ |
| 7 | 119915432 | exm652814 | T | C | KCND2 | META_EX | +++ | 9,083 | 3,900 | 5,183 | $2.75 \cdot 10^{-4}$ | $1.33 \cdot 10^{-4}$ | $8.51 \cdot 10^{-4}$ | 2.009 | 0.446 | 7.455 | 4.503 | $6.7 \cdot 10^{-6}$ |
| 4 | 127336047 | rs12647099 | G | A | FAT4 | META_GWAS | +++xxx | 7,526 | 3,078 | 4,448 | 0.408 | 0.273 | 0.505 | $7.66 \cdot 10^{-2}$ | $1.71 \cdot 10^{-2}$ | 1.08 | $-4.481$ | $7.44 \cdot 10^{-6}$ |
| 18 | 9759714 | rs12970907 | A | C | RAB31 | META_GWAS | +++xxx | 7,527 | 3,077 | 4,450 | 0.174 | 0.15 | 0.203 | $9.56 \cdot 10^{-2}$ | $2.15 \cdot 10^{-2}$ | 1.1 | $-4.443$ | $8.89 \cdot 10^{-6}$ |
| 10 | 119233375 | rs242967 | A | G | EMX2 | META_GWAS | +++xxx | 7,529 | 3,079 | 4,450 | 0.705 | 0.625 | 0.792 | $8.03 \cdot 10^{-2}$ | $1.81 \cdot 10^{-2}$ | 1.084 | $-4.434$ | $9.27 \cdot 10^{-6}$ |
| 9 | 133552145 | rs10751506 | G | A | PRDM12 | META_GWAS | ++++-+ | 9,089 | 3,912 | 5,177 | 0.854 | 0.691 | 0.961 | $9.65 \cdot 10^{-2}$ | $2.19 \cdot 10^{-2}$ | 1.101 | 4.413 | $1.02 \cdot 10^{-5}$ |
| 14 | 70522684 | rs10142899 | A | C | SLC8A3 | META_GWAS | xxx+++ | 1,561 | 834 | 727 | 0.449 | 0.418 | 0.492 | 0.159 | $3.62 \cdot 10^{-2}$ | 1.173 | $-4.408$ | $1.04 \cdot 10^{-5}$ |
| 5 | 95849216 | rs261965 | G | A | PCSK1 | META_GWAS | xxx+++ | 1,561 | 834 | 727 | 0.974 | 0.945 | 0.999 | 0.506 | 0.115 | 1.658 | 4.402 | $1.07 \cdot 10^{-5}$ |
| 7 | 79678973 | rs7778622 | A | G | GNAI1 | META_GWAS | xxx+++ | 1,561 | 834 | 727 | 0.445 | 0.33 | 0.582 | 0.159 | $3.63 \cdot 10^{-2}$ | 1.173 | 4.394 | $1.11 \cdot 10^{-5}$ |
| 2 | 209185355 | rs10932260 | T | C | PIKFYVE | META_GWAS | +++xxx | 7,527 | 3,079 | 4,448 | 0.632 | 0.459 | 0.84 | $7.83 \cdot 10^{-2}$ | $1.78 \cdot 10^{-2}$ | 1.082 | 4.388 | $1.15 \cdot 10^{-5}$ |
| 14 | 21802579 | rs17103594 | A | T | RPGRIP1 | META_GWAS | xxx+++ | 1,561 | 834 | 727 | $4.04 \cdot 10^{-2}$ | $8.86 \cdot 10^{-3}$ | $8.18 \cdot 10^{-2}$ | 0.406 | $9.4 \cdot 10^{-2}$ | 1.501 | $-4.322$ | $1.55 \cdot 10^{-5}$ |
| 20 | 60685349 | rs6142952 | T | G | LSM14B | META_GWAS | xxx+++ | 1,559 | 833 | 726 | 0.596 | 0.302 | 0.832 | 0.178 | $4.12 \cdot 10^{-2}$ | 1.195 | 4.317 | $1.58 \cdot 10^{-5}$ |
| 13 | 28566951 | rs2504240 | G | A | URAD | META_GWAS | +++xxx | 7,529 | 3,079 | 4,450 | 0.303 | 0.198 | 0.416 | $7.78 \cdot 10^{-2}$ | $1.81 \cdot 10^{-2}$ | 1.081 | $-4.294$ | $1.75 \cdot 10^{-5}$ |

## 9.4 Previously identified risk loci

Table 32 shows statistics from the MERGE cohort for 50 loci that were shown to be significantly associated with Body Mass Index in the 2015 Nature paper by Locke et al [14]. Where a previously reported variant was not genotyped in the study (indicated by $\bar{R}^2 < 1$), if available, a tagging variant in LD with the reported variant ($\bar{R}^2 >= 0.7$ and within 250kb) was provided. Tags were identified using 1000 Genomes data. There are 10 variants that show at least nominal significance ($p < 0.05$) in this study. Out of the 50 variants in both studies, 35 exhibit the same direction of effect with the known result (binomial test $p = 0.0033$).

Table 32: Top known loci in MERGE model invn Adjusted AGE_ANTHRO+AGE_ANTHRO2+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 | $GENE_{CLOSEST}$ | $R^2$ | $ID_{KNOWN}$ | $N_{KNOWN}$ | $EFFECT_{KNOWN}$ | $STDERR_{KNOWN}$ | $P_{KNOWN}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 16 | 53803574 | rs1558902 | A | T | 9,027 | 0.233 | $9.52 \cdot 10^{-2}$ | 0.455 | $7.05 \cdot 10^{-2}$ | $1.89 \cdot 10^{-2}$ | $1.96 \cdot 10^{-4}$ | +++ | META_EX | FTO | 1 | rs1558902 | $3.22 \cdot 10^5$ | $-8.18 \cdot 10^{-2}$ | $3.1 \cdot 10^{-3}$ | $7.51 \cdot 10^{-153}$ |
| 18 | 57829135 | **rs6567160** | C | T | 7,525 | 0.193 | 0.177 | 0.221 | $7.29 \cdot 10^{-2}$ | $2.05 \cdot 10^{-2}$ | $3.85 \cdot 10^{-4}$ | +++xxx | META_GWAS | MC4R | 1 | rs6567160 | $3.22 \cdot 10^5$ | $5.56 \cdot 10^{-2}$ | $3.6 \cdot 10^{-3}$ | $3.93 \cdot 10^{-53}$ |
| 2 | 651105 | **rs2867110** | G | C | 1,561 | 0.21 | 0.187 | 0.251 | $8.58 \cdot 10^{-2}$ | $4.42 \cdot 10^{-2}$ | $5.22 \cdot 10^{-2}$ | xxx+++ | META_GWAS | TMEM18 | 1 | rs2867110 | $3.22 \cdot 10^5$ | $5.98 \cdot 10^{-2}$ | $4 \cdot 10^{-3}$ | $3.4 \cdot 10^{-50}$ |
| 18 | 57766512 | **rs1539952** | G | A | 9,079 | 0.22 | 0.196 | 0.247 | $4.46 \cdot 10^{-2}$ | $1.79 \cdot 10^{-2}$ | $1.26 \cdot 10^{-2}$ | +++++-+ | META_GWAS | PMAIP1 | 1 | rs1539952 | $3.22 \cdot 10^5$ | $4.85 \cdot 10^{-2}$ | $3.6 \cdot 10^{-3}$ | $1.61 \cdot 10^{-42}$ |
| 4 | 45182527 | rs10938397 | A | G | 9,077 | 0.334 | 0.253 | 0.441 | $9.54 \cdot 10^{-3}$ | $1.57 \cdot 10^{-2}$ | 0.544 | --+ | META_EX | GNPDA2 | 1 | rs10938397 | $3.22 \cdot 10^5$ | $-4.02 \cdot 10^{-2}$ | $3.1 \cdot 10^{-3}$ | $3.21 \cdot 10^{-38}$ |
| 1 | 177889480 | **rs543874** | G | A | 9,077 | 0.218 | 0.152 | 0.262 | $4.23 \cdot 10^{-2}$ | $1.8 \cdot 10^{-2}$ | $1.89 \cdot 10^{-2}$ | +++ | META_EX | SEC16B | 1 | rs543874 | $3.22 \cdot 10^5$ | $4.82 \cdot 10^{-2}$ | $3.9 \cdot 10^{-3}$ | $2.62 \cdot 10^{-35}$ |
| 6 | 50865820 | **rs943005** | T | C | 7,529 | 0.153 | $9.03 \cdot 10^{-2}$ | 0.212 | $6.1 \cdot 10^{-2}$ | $2.31 \cdot 10^{-2}$ | $8.3 \cdot 10^{-3}$ | +++xxx | META_GWAS | TFAP2B | 1 | rs943005 | $3.22 \cdot 10^5$ | $4.43 \cdot 10^{-2}$ | $4 \cdot 10^{-3}$ | $1.39 \cdot 10^{-28}$ |
| 11 | 27684517 | **rs11030104** | A | G | 9,079 | 0.123 | $4.04 \cdot 10^{-2}$ | 0.245 | $5.26 \cdot 10^{-3}$ | $2.32 \cdot 10^{-2}$ | 0.82 | +--+++ | META_GWAS | BDNF | 1 | rs11030104 | $3.22 \cdot 10^5$ | $4.14 \cdot 10^{-2}$ | $3.8 \cdot 10^{-3}$ | $5.56 \cdot 10^{-28}$ |
| 1 | 72751185 | rs3101336 | C | T | 7,520 | 0.607 | 0.534 | 0.684 | $1.04 \cdot 10^{-2}$ | $1.66 \cdot 10^{-2}$ | 0.533 | +++xxx | META_GWAS | NEGR1 | 1 | rs3101336 | $3.22 \cdot 10^5$ | $3.34 \cdot 10^{-2}$ | $3.1 \cdot 10^{-3}$ | $2.66 \cdot 10^{-26}$ |
| 12 | 50247468 | rs7138803 | G | A | 9,077 | 0.246 | 0.167 | 0.397 | $4.07 \cdot 10^{-3}$ | $1.75 \cdot 10^{-2}$ | 0.816 | +-- | META_EX | BCDIN3D | 1 | rs7138803 | $3.22 \cdot 10^5$ | $-3.15 \cdot 10^{-2}$ | $3.1 \cdot 10^{-3}$ | $8.15 \cdot 10^{-24}$ |
| 2 | 25150296 | rs10182181 | A | G | 1,559 | 0.62 | 0.468 | 0.845 | $1.8 \cdot 10^{-2}$ | $4.06 \cdot 10^{-2}$ | 0.659 | xxx+-+ | META_GWAS | ADCY3 | 1 | rs10182181 | $3.22 \cdot 10^5$ | $-3.07 \cdot 10^{-2}$ | $3.1 \cdot 10^{-3}$ | $8.78 \cdot 10^{-24}$ |
| 16 | 28867804 | **rs4788101** | T | C | 7,528 | 0.314 | 0.264 | 0.363 | $2.09 \cdot 10^{-2}$ | $1.77 \cdot 10^{-2}$ | 0.236 | +-+xxx | META_GWAS | SH2B1 | 1 | rs4788101 | $3.22 \cdot 10^5$ | $3.07 \cdot 10^{-2}$ | $3.1 \cdot 10^{-3}$ | $4.82 \cdot 10^{-23}$ |
| 16 | 28855727 | **rs4788099** | G | A | 7,528 | 0.315 | 0.266 | 0.363 | $2.09 \cdot 10^{-2}$ | $1.77 \cdot 10^{-2}$ | 0.238 | +-+xxx | META_GWAS | TUFM | 1 | rs4788099 | $3.22 \cdot 10^5$ | $3.05 \cdot 10^{-2}$ | $3.1 \cdot 10^{-3}$ | $1.13 \cdot 10^{-22}$ |
| 16 | 28848668 | **rs12325113** | C | T | 7,523 | 0.205 | $6.91 \cdot 10^{-2}$ | 0.321 | $2.95 \cdot 10^{-2}$ | $2.14 \cdot 10^{-2}$ | 0.168 | +++xxx | META_GWAS | ATXN2L | 1 | rs12325113 | $3.22 \cdot 10^5$ | $3.04 \cdot 10^{-2}$ | $3.1 \cdot 10^{-3}$ | $1.26 \cdot 10^{-22}$ |
| 3 | 185822353 | **rs10513801** | T | G | 7,523 | $7.14 \cdot 10^{-2}$ | $2.7 \cdot 10^{-2}$ | 0.132 | $1.77 \cdot 10^{-2}$ | $3.23 \cdot 10^{-2}$ | 0.583 | -++xxx | META_GWAS | ETV5 | 1 | rs10513801 | $3.22 \cdot 10^5$ | $4.48 \cdot 10^{-2}$ | $4.7 \cdot 10^{-3}$ | $1.07 \cdot 10^{-21}$ |
| 11 | 27578946 | rs1013442 | A | T | 1,561 | 0.161 | $6.34 \cdot 10^{-2}$ | 0.238 | $3.32 \cdot 10^{-2}$ | $4.85 \cdot 10^{-2}$ | 0.494 | xxx+++ | META_GWAS | LIN7C | 1 | rs1013442 | $3.22 \cdot 10^5$ | $-3.32 \cdot 10^{-2}$ | $3.6 \cdot 10^{-3}$ | $3.36 \cdot 10^{-20}$ |
| 19 | 46202172 | rs2287019 | C | T | 9,079 | 0.149 | 0.114 | 0.223 | $5.42 \cdot 10^{-2}$ | $2.1 \cdot 10^{-2}$ | $1 \cdot 10^{-2}$ | +++ | META_EX | QPCTL | 1 | rs2287019 | $3.22 \cdot 10^5$ | $3.6 \cdot 10^{-2}$ | $4.2 \cdot 10^{-3}$ | $4.59 \cdot 10^{-18}$ |
| 16 | 19944363 | rs11639988 | G | A | 1,562 | 0.183 | 0.143 | 0.248 | $2.16 \cdot 10^{-2}$ | $4.62 \cdot 10^{-2}$ | 0.641 | xxx+-- | META_GWAS | GPRC5B | 1 | rs11639988 | $3.22 \cdot 10^5$ | $-3.97 \cdot 10^{-2}$ | $4.6 \cdot 10^{-3}$ | $5.36 \cdot 10^{-18}$ |
| 19 | 46180184 | **rs11672660** | C | T | 7,528 | 0.152 | 0.111 | 0.239 | $5.46 \cdot 10^{-2}$ | $2.31 \cdot 10^{-2}$ | $1.8 \cdot 10^{-2}$ | +++xxx | META_GWAS | GIPR | 1 | rs11672660 | $3.22 \cdot 10^5$ | $3.45 \cdot 10^{-2}$ | $4 \cdot 10^{-3}$ | $8.49 \cdot 10^{-18}$ |
| 16 | 28490517 | **rs151181** | C | T | 9,077 | 0.262 | 0.158 | 0.336 | $1.23 \cdot 10^{-2}$ | $1.74 \cdot 10^{-2}$ | 0.478 | +-- | META_EX | CLN3 | 1 | rs151181 | $3.22 \cdot 10^5$ | $2.69 \cdot 10^{-2}$ | $3.1 \cdot 10^{-3}$ | $8.51 \cdot 10^{-18}$ |
| 16 | 28543381 | **rs12446550** | A | G | 7,527 | 0.311 | 0.236 | 0.372 | $2.88 \cdot 10^{-2}$ | $1.78 \cdot 10^{-2}$ | 0.106 | +++xxx | META_GWAS | NUPR1 | 1 | rs12446550 | $3.22 \cdot 10^5$ | $2.6 \cdot 10^{-2}$ | $3.1 \cdot 10^{-3}$ | $1.46 \cdot 10^{-17}$ |
| 15 | 68086838 | **rs2241423** | G | A | 9,078 | 0.342 | 0.277 | 0.374 | $1.86 \cdot 10^{-2}$ | $1.58 \cdot 10^{-2}$ | 0.237 | +++ | META_EX | MAP2K5 | 1 | rs2241423 | $3.22 \cdot 10^5$ | $3.1 \cdot 10^{-2}$ | $3.7 \cdot 10^{-3}$ | $2.37 \cdot 10^{-17}$ |
| 12 | 50251910 | **rs4898539** | T | G | 1,562 | 0.734 | 0.63 | 0.784 | $2.75 \cdot 10^{-2}$ | $4.04 \cdot 10^{-2}$ | 0.496 | xxx+++ | META_GWAS | FAIM2 | 1 | rs4898539 | $3.22 \cdot 10^5$ | $2.76 \cdot 10^{-2}$ | $3.3 \cdot 10^{-3}$ | $3.26 \cdot 10^{-17}$ |
| 11 | 47650993 | **rs3817334** | T | C | 9,078 | 0.329 | 0.256 | 0.398 | $4.01 \cdot 10^{-2}$ | $1.58 \cdot 10^{-2}$ | $1.09 \cdot 10^{-2}$ | +++ | META_EX | MTCH2 | 1 | rs3817334 | $3.22 \cdot 10^5$ | $2.62 \cdot 10^{-2}$ | $3.1 \cdot 10^{-3}$ | $5.15 \cdot 10^{-17}$ |
| 5 | 75015242 | **rs2112347** | T | G | 9,075 | 0.437 | 0.379 | 0.509 | $2.48 \cdot 10^{-2}$ | $1.51 \cdot 10^{-2}$ | 0.101 | +++ | META_EX | POC5 | 1 | rs2112347 | $3.22 \cdot 10^5$ | $2.61 \cdot 10^{-2}$ | $3.1 \cdot 10^{-3}$ | $6.19 \cdot 10^{-17}$ |
| 12 | 50223013 | **rs11169170** | T | C | 1,562 | 0.354 | 0.291 | 0.449 | $3.9 \cdot 10^{-3}$ | $3.85 \cdot 10^{-2}$ | 0.919 | xxx-+- | META_GWAS | NCKAP5L | 1 | rs11169170 | $3.22 \cdot 10^5$ | $2.54 \cdot 10^{-2}$ | $3 \cdot 10^{-3}$ | $6.35 \cdot 10^{-17}$ |
| 16 | 28898793 | **rs6565259** | C | T | 7,529 | 0.437 | 0.301 | 0.515 | $4.64 \cdot 10^{-3}$ | $1.67 \cdot 10^{-2}$ | 0.781 | +--+xxx | META_GWAS | ATP2A1 | 1 | rs6565259 | $3.22 \cdot 10^5$ | $2.69 \cdot 10^{-2}$ | $3.2 \cdot 10^{-3}$ | $8.11 \cdot 10^{-17}$ |
| 16 | 28631585 | rs1968752 | G | T | 1,558 | 0.587 | 0.49 | 0.683 | $2.4 \cdot 10^{-2}$ | $3.62 \cdot 10^{-2}$ | 0.507 | xxx-++ | META_GWAS | SULT1A1 | 1 | rs1968752 | $3.22 \cdot 10^5$ | $-2.72 \cdot 10^{-2}$ | $3.3 \cdot 10^{-3}$ | $9.06 \cdot 10^{-17}$ |
| 11 | 47529947 | **rs7124681** | A | C | 7,527 | 0.331 | 0.259 | 0.393 | $4.94 \cdot 10^{-2}$ | $1.74 \cdot 10^{-2}$ | $4.61 \cdot 10^{-3}$ | +-+xxx | META_GWAS | CELF1 | 1 | rs7124681 | $3.22 \cdot 10^5$ | $2.59 \cdot 10^{-2}$ | $3.1 \cdot 10^{-3}$ | $1.16 \cdot 10^{-16}$ |
| 15 | 68114974 | **rs4776982** | A | G | 9,091 | 0.323 | 0.254 | 0.345 | $1.31 \cdot 10^{-2}$ | $1.59 \cdot 10^{-2}$ | 0.408 | +++-- | META_EX | SKOR1 | 1 | rs4776982 | $3.22 \cdot 10^5$ | $3.11 \cdot 10^{-2}$ | $3.8 \cdot 10^{-3}$ | $2.61 \cdot 10^{-16}$ |
| 16 | 28595700 | **rs17640009** | G | A | 7,528 | 0.287 | 0.235 | 0.329 | $3.29 \cdot 10^{-2}$ | $1.81 \cdot 10^{-2}$ | $6.91 \cdot 10^{-2}$ | +++xxx | META_GWAS | SGF29 | 1 | rs17640009 | $3.22 \cdot 10^5$ | $2.53 \cdot 10^{-2}$ | $3.1 \cdot 10^{-3}$ | $5.46 \cdot 10^{-16}$ |
| 16 | 28922149 | **rs11646653** | C | T | 9,089 | 0.707 | 0.659 | 0.745 | $7.58 \cdot 10^{-3}$ | $1.64 \cdot 10^{-2}$ | 0.643 | +-++- | META_GWAS | RABEP2 | 1 | rs11646653 | $3.22 \cdot 10^5$ | $2.68 \cdot 10^{-2}$ | $3.3 \cdot 10^{-3}$ | $5.57 \cdot 10^{-16}$ |
| 2 | 25158008 | rs713586 | T | C | 1,560 | 0.634 | 0.482 | 0.861 | $2.74 \cdot 10^{-2}$ | $4.11 \cdot 10^{-2}$ | 0.505 | xxx+-+ | META_GWAS | DNAJC27 | 1 | rs713586 | $3.22 \cdot 10^5$ | $-3.02 \cdot 10^{-2}$ | $3.8 \cdot 10^{-3}$ | $1.91 \cdot 10^{-15}$ |
| 19 | 47569003 | **rs3810291** | A | G | 9,074 | 0.382 | 0.178 | 0.658 | $1.25 \cdot 10^{-2}$ | $1.65 \cdot 10^{-2}$ | 0.449 | +++ | META_EX | ZC3H4 | 1 | rs3810291 | $3.22 \cdot 10^5$ | $2.83 \cdot 10^{-2}$ | $3.6 \cdot 10^{-3}$ | $4.81 \cdot 10^{-15}$ |
| 3 | 185847441 | rs16860471 | T | G | 9,090 | 0.133 | 0.12 | 0.156 | $7.39 \cdot 10^{-3}$ | $2.2 \cdot 10^{-2}$ | 0.737 | +-++- | META_GWAS | DGKG | 1 | rs16860471 | $3.22 \cdot 10^5$ | $-3.7 \cdot 10^{-2}$ | $4.7 \cdot 10^{-3}$ | $5.56 \cdot 10^{-15}$ |
| 1 | 74995225 | rs7551507 | T | C | 1,562 | 0.354 | 0.142 | 0.565 | $2.71 \cdot 10^{-2}$ | $4.04 \cdot 10^{-2}$ | 0.502 | xxx+-+ | META_GWAS | FPGT-TNNI3K | 1 | rs7551507 | $3.22 \cdot 10^5$ | $-2.41 \cdot 10^{-2}$ | $3.1 \cdot 10^{-3}$ | $8.86 \cdot 10^{-15}$ |
| 14 | 79899454 | rs7141420 | C | T | 9,090 | 0.593 | 0.53 | 0.623 | $1.57 \cdot 10^{-2}$ | $1.52 \cdot 10^{-2}$ | 0.918 | +++ | META_GWAS | NRXN3 | 1 | rs7141420 | $3.22 \cdot 10^5$ | $2.35 \cdot 10^{-2}$ | $3.1 \cdot 10^{-3}$ | $1.23 \cdot 10^{-14}$ |
| 3 | 85820181 | **rs13098327** | A | G | 1,558 | 0.139 | $5.52 \cdot 10^{-2}$ | 0.246 | $4.18 \cdot 10^{-2}$ | $5.21 \cdot 10^{-2}$ | 0.422 | xxx+-+ | META_GWAS | CADM2 | 1 | rs13098327 | $3.22 \cdot 10^5$ | $2.95 \cdot 10^{-2}$ | $3.9 \cdot 10^{-3}$ | $2.53 \cdot 10^{-14}$ |
| 5 | 74956517 | **rs253414** | T | C | 9,091 | 0.524 | 0.402 | 0.635 | $1.22 \cdot 10^{-2}$ | $1.51 \cdot 10^{-2}$ | 0.421 | +-+-++ | META_GWAS | ANKDD1B | 1 | rs253414 | $3.22 \cdot 10^5$ | $2.68 \cdot 10^{-2}$ | $3.5 \cdot 10^{-3}$ | $2.86 \cdot 10^{-14}$ |
| 11 | 47624714 | **rs12419692** | A | C | 1,560 | 0.227 | $8.73 \cdot 10^{-2}$ | 0.343 | $2.05 \cdot 10^{-2}$ | $4.23 \cdot 10^{-2}$ | 0.628 | xxx+-+ | META_GWAS | C1QTNF4 | 1 | rs12419692 | $3.22 \cdot 10^5$ | $2.37 \cdot 10^{-2}$ | $3.2 \cdot 10^{-3}$ | $6.12 \cdot 10^{-14}$ |
| 9 | 28414339 | **rs10968576** | G | A | 9,079 | 0.217 | 0.168 | 0.276 | $1.18 \cdot 10^{-2}$ | $1.79 \cdot 10^{-2}$ | 0.511 | -++ | META_EX | LINGO2 | 1 | rs10968576 | $3.22 \cdot 10^5$ | $2.49 \cdot 10^{-2}$ | $3.3 \cdot 10^{-3}$ | $6.61 \cdot 10^{-14}$ |
| 1 | 110154688 | rs17024393 | C | T | 7,522 | $5.48 \cdot 10^{-2}$ | $1.77 \cdot 10^{-2}$ | $9.34 \cdot 10^{-2}$ | $8.78 \cdot 10^{-3}$ | $3.6 \cdot 10^{-2}$ | 0.807 | --++xxx | META_GWAS | GNAT2 | 1 | rs17024393 | $3.22 \cdot 10^5$ | $-6.58 \cdot 10^{-2}$ | $8.8 \cdot 10^{-3}$ | $7.03 \cdot 10^{-14}$ |
| 11 | 47432303 | **rs755553** | G | A | 7,528 | 0.623 | 0.604 | 0.669 | $3.3 \cdot 10^{-2}$ | $1.67 \cdot 10^{-2}$ | $4.85 \cdot 10^{-2}$ | +++xxx | META_GWAS | SLC39A13 | 1 | rs755553 | $3.22 \cdot 10^5$ | $2.45 \cdot 10^{-2}$ | $3.3 \cdot 10^{-3}$ | $7.31 \cdot 10^{-14}$ |
| 16 | 19867021 | rs4782294 | T | C | 7,524 | 0.122 | $9.98 \cdot 10^{-2}$ | 0.14 | $2.23 \cdot 10^{-2}$ | $2.5 \cdot 10^{-2}$ | 0.373 | ++xxx | META_GWAS | IQCK | 1 | rs4782294 | $3.22 \cdot 10^5$ | $-3.52 \cdot 10^{-2}$ | $4.7 \cdot 10^{-3}$ | $7.35 \cdot 10^{-14}$ |
| 1 | 110082886 | **rs7550711** | T | C | 9,078 | $1.61 \cdot 10^{-2}$ | $1.43 \cdot 10^{-2}$ | $1.79 \cdot 10^{-2}$ | $5.59 \cdot 10^{-2}$ | $5.89 \cdot 10^{-2}$ | 0.343 | ++- | META_EX | GPR61 | 1 | rs7550711 | $3.22 \cdot 10^5$ | $6.62 \cdot 10^{-2}$ | $9 \cdot 10^{-3}$ | $1.56 \cdot 10^{-13}$ |
| 11 | 47393638 | **rs4992357** | T | C | 1,562 | 0.709 | 0.67 | 0.778 | $1.96 \cdot 10^{-2}$ | $3.82 \cdot 10^{-2}$ | 0.607 | xxx+-+ | META_GWAS | SPI1 | 1 | rs4992357 | $3.22 \cdot 10^5$ | $2.41 \cdot 10^{-2}$ | $3.3 \cdot 10^{-3}$ | $1.7 \cdot 10^{-13}$ |
| 16 | 28980531 | rs11150675 | T | C | 7,528 | 0.224 | $9.84 \cdot 10^{-2}$ | 0.379 | $1.63 \cdot 10^{-2}$ | $2.04 \cdot 10^{-2}$ | 0.936 | --++xxx | META_GWAS | NFATC2IP | 1 | rs11150675 | $3.22 \cdot 10^5$ | $-2.38 \cdot 10^{-2}$ | $3.2 \cdot 10^{-3}$ | $2.03 \cdot 10^{-13}$ |
| 11 | 27480827 | **rs11030014** | T | C | 9,090 | 0.323 | 0.209 | 0.412 | $2.24 \cdot 10^{-2}$ | $1.6 \cdot 10^{-2}$ | 0.161 | -+++++ | META_GWAS | LGR4 | 1 | rs11030014 | $3.22 \cdot 10^5$ | $2.75 \cdot 10^{-2}$ | $3.8 \cdot 10^{-3}$ | $5.01 \cdot 10^{-13}$ |
| 1 | 49589847 | **rs657452** | A | G | 9,079 | 0.51 | 0.426 | 0.608 | $1.29 \cdot 10^{-2}$ | $1.49 \cdot 10^{-2}$ | 0.387 | -++ | META_EX | AGBL4 | 1 | rs657452 | $3.22 \cdot 10^5$ | $2.27 \cdot 10^{-2}$ | $3.1 \cdot 10^{-3}$ | $5.48 \cdot 10^{-13}$ |
| 16 | 28992646 | rs3922668 | A | G | 7,528 | 0.572 | 0.409 | 0.721 | $1.58 \cdot 10^{-2}$ | $1.71 \cdot 10^{-2}$ | 0.355 | -++xxx | META_GWAS | SPNS1 | 1 | rs3922668 | $3.22 \cdot 10^5$ | $-2.35 \cdot 10^{-2}$ | $3.3 \cdot 10^{-3}$ | $9.6 \cdot 10^{-13}$ |

# 10 Acknowledgements

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

Ryan Koesterer

Maria Costanzo

Lizz Caulkins

Noel Burtt

Jason Flannick

Miriam Udler

Alisa Manning

Jose Florez

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