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Genome-wide analysis in over 1 million individuals of European ancestry yields improved polygenic risk scores for blood pressure traits

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Supplementary Notes

Study Populations

UKB

UKB includes ~500,000 volunteers aged 40-69 years of age ascertained through NHS registers. Following informed consent participants completed a standardized questionnaire on life course exposures, medical history and treatments and underwent a standardized portfolio of phenotypic tests including two BP measurements taken seated after two minutes rest using an appropriate cuff and an Omron HEM-7015IT digital BP monitor. A manual sphygmomanometer was used if the standard automated device could not be employed. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2) with weight measured using an electronic weighing scale (Tanita BC-418). The participants undergo longitudinal life course linkage to electronic health data including Hospital Episode Statistics and Office for National Statistics cause of death data.

DNA extraction and genotyping for UKB has been previously described[47]. Briefly, UKB genetic data includes genotypes for 488,377 individuals. DNA was extracted from stored blood samples and genotyping was carried out by Affymetrix Research Services Laboratory. 49,950 participants involved in the UK Biobank Lung Exome Variant Evaluation (UK BiLEVE) study were genotyped at 807,411 markers using the Affymetrix UK BiLEVE Axiom Array and 438,427 participants were genotyped using the Affymetrix UK Biobank Axiom Array (825,927 markers), which shares 95% of marker content with the UK BiLEVE Axiom Array.

Variants were imputed centrally by UK Biobank using a reference panel that merged the UK10K and 1000 Genomes Phase 3 panel as well as the Haplotype Reference Consortium (HRC) panel[48]. For current analysis only SNPs imputed from the HRC panel were analyzed (N=39,235,157), of which ~7.1 million SNPs with minor allele frequency (MAF) >1% and imputation quality INFO >0.1 are analyzed here for GWAS.

For the UKB GWAS, we calculated the mean SBP and DBP values from two automated (N=418,755) or two manual (N=25,888) BP measurements. For individuals with one manual and one automated BP measurement (N=13,521), we used the mean of these two values. For individuals with only one available BP measurement (N=413), we used this single value. Following both genetic and phenotypic data QC and by excluding pregnant women (n=372) and those individuals who had withdrawn consent (N=36), the sample size for analysis

therefore included N=458,577 and N=458,575 self-reported European-ancestry individuals for SBP and DBP, respectively. For measures taken while a patient was on an antihypertensive medication, we added 15 mm Hg to SBP and 10 mm Hg to DBP. We performed linear mixed model (LMM) association testing under an additive genetic model of the three (untransformed) continuous, medication-adjusted BP traits (SBP, DBP, PP) for all measured and imputed genetic variants in dosage format using the BOLT-LMM (v2.3) software.

ICBP

ICBP GWAS is an international consortium to investigate BP genetics and has been previously described elsewhere[6,49]. All study participants were of European descent and were imputed to either the 1000 Genomes Project Phase 1 integrated release version 3 [March 2012] all ancestry reference panel or the HRC panel. The final ICBP GWAS dataset included 77 studies comprising data from 299,024 individuals. Three quantitative BP traits were analyzed: SBP, DBP, and PP. Within each study, BP measures were adjusted for medication use by adding 15 and 10 mm Hg to SBP and DBP, respectively.

Prior to meta-analysis of all 77 ICBP GWAS studies, we undertook central quality control checks across all studies. This included checks to ensure allele frequency consistency (across studies and with reference populations), checks of effect size and standard error distributions (i.e., to highlight phenotype issues) and generation of quantile-quantile (QQ) plots and genomic inflation factor lambdas to check for over- or under-inflation of test statistics. Genomic control was applied (if lambda>1) at study-level. Variants with imputation quality <0.1 were excluded prior to meta-analysis. EasyQC was used for the quality control process[50]. Finally, data were filtered to SNPs with MAF ≥1% and effective sample size (reflecting the quality of genotype imputation) >60% of the total effective sample size. Meta-analysis was performed using METAL software employing inverse variance weighted fixed-effects models[51]. Between-study heterogeneity was assessed using the Cochran's Q statistic and we performed additional filtering removing heterogeneous variants with Cochran's Q $p<1x10^{-4}$.

MVP Study

The MVP study is a large cohort of fully consented participants who were recruited from the patient populations of 63 Department of Veterans Affairs (VA) medical facilities. Summary statistics from the analysis of 220,501 self-reported non-Hispanic white participants were

included in our meta-analysis. These results have been previously reported by Giri et al[4]. Briefly, DNA was extracted from whole blood and genotyped using a custom Affymetrix array (Axiom Biobank; Thermo Fischer Scientific Inc, Waltham, MA, USA). Genotype calling and QC were performed centrally and genotypes were phased using EAGLE v2[52] and imputed from the 1000 Genomes Project phase 3 version 5 reference panel using Minimac3[53] software. Participants included adults (age ≥18 years) with non-Emergency Department outpatient SBP and DBP measures available in their electronic health record. For individuals with greater than or equal to three measures available, median SBP and corresponding DBP were used in analysis. For rare cases where fewer than three measures were available, the lowest available SBP and corresponding DBP were used. We observed an average of 220 measures across individuals. In individuals in whom the median SBP value was observed at multiple clinical encounters on distinct dates, we used the earliest of those measures to identify the DBP, age, BMI, and anti-hypertensive treatment status of the individual at that time. Measures were ineligible if they occurred at or after an International Classification of Diseases Ninth Revision (ICD-9) code from the groups 585 (chronic kidney disease), 405 (secondary hypertension), or 428 (heart failure). If pain scores were available, BP measures taken during encounters when a pain score ≥5 was recorded were also ineligible. BP measures were adjusted for medication use by adding 15 and 10 mm Hg to SBP and DBP, respectively. Linear regression association tests were conducted using additive models for untransformed medication-adjusted BP traits (SBP, DBP, PP) using SNPTEST-v2.5.4-beta[54].

BioVU

The BioVU DNA Repository is a deidentified database of electronic health records that are linked to patient DNA samples at Vanderbilt University Medical Center. Summary statistics from the analysis of 50,649 self-reported non-Hispanic white participants were included in our meta-analysis. A detailed description of the database and how it is maintained has been published elsewhere[13]. BioVU participant DNA samples were genotyped on a custom Illumina Multi-Ethnic Genotyping Array (MEGA-ex; Illumina Inc., San Diego, CA, USA). Quality control (QC) was conducted, excluding samples or variants with missingness rates above 2%. Samples were also excluded if consent had been revoked, sample was duplicated, or failed sex concordance checks. Imputation was performed on the Michigan Imputation Server v1.2.4[53] using Minimac4 and the Haplotype Reference Consortium panel v1.1[48].

Among BioVU participants, we selected unrelated self-reported adults of European ancestry (age ≥ 18 years) and used the earliest median eligible non-Emergency Department outpatient

measured SBP in the electronic health record, and the corresponding DBP. For individuals with fewer than three measurements available (N=2,933), the lowest available SBP and corresponding DBP were used. On average, there were 69 SBP measures per individual. Measures were considered ineligible if they occurred at or after an ICD-9/10 billing code from the groups 585/N18 (chronic kidney disease), 405/I15 (secondary hypertension), or 428/I50 (heart failure). For measures taken while a patient was on an antihypertensive medication, we added 15 mm Hg to SBP and 10 mm Hg to DBP. We performed linear regression association tests with additive models for untransformed medication-adjusted BP traits (SBP, DBP, PP) using SNPTEST-v2.5.4-beta[54].

Lifelines Cohort Study genotype and phenotype data

The Lifelines cohort is a large prospective population-based cohort study performed in 167,729 individuals living in the North of the Netherlands with a unique three generation design, aiming at investigating risk factors for multifactorial diseases[72]. It was approved by the medical ethics committee of the University Medical Center Groningen and conducted in accordance with Helsinki Declaration Guidelines. All participants signed an informed consent form prior to enrollment.

A subset of 38,030 volunteers were genotyped using the Infinium Global Screening Array MultiEthnic Disease Version, according to manufacturer's instructions, at the Human Genomics Facility of the Erasmus Medical Center, Rotterdam and the Department of Genetics, University Medical Center Groningen. Standard QC was performed on both samples and markers. Samples with a genotyping call rate<99%, outliers for heterozygosity and sex mismatches were excluded, as well as samples that did not show consistent information between reported familial information and observed identity-by-descent sharing with family members, and between genotypes available from this and previous studies. Variants with a genotyping call rate <99%, Hardy-Weinberg equilibrium P $<1\times10^{-6}$ or excess of Mendelian errors in families (>1% of the parent-offspring pairs) were removed. A total of 36,339 samples and 571,420 autosomal and X-chromosome markers passed quality checks. The genotyping dataset was then imputed at the Sanger imputation server1 using the HRC panel v1.1.

From the set of 36,339 samples, we selected 10,782 unrelated individuals who are also independent from Lifelines samples that were included in a previous ICBP meta-GWAS[5]. After excluding 552 children (age<18 years), 12 pregnant women, five individuals without

SBP or DBP, and three individuals without BMI, a final total number of 10,210 individuals were included for analyses that broadly represent the total Lifelines sample (see Supplementary Table 24b).

In Lifelines, BP was measured every minute during a period of ten minutes using an automated DINAMAP Monitor (GE Healthcare) and the average of the final three readings was recorded for SBP and DBP. Participants with a measured BP ≥140/90 mm Hg irrespective of treatment and those taking antihypertensive medication (ATC codes C02, C03, C07, C08, C09) irrespective of BP were defined as having hypertension. In continuous trait analyses, 15 mm Hg was added to SBP and 10 mm Hg was added to DBP for 1,236 individuals who were taking antihypertensive medication. PP was calculated using these medication-adjusted BP values.

African-American Cohort from the All of Us Research Program

The NIH All of Us Research Program is a deidentified database of electronic health records linked to participant genomic data from contributing medical centers nationwide. Analysis considered 24,718 predicted African-ancestry individuals (from PC clustering) before phenotyping, and for whom whole genome sequencing data was available. Briefly, we selected unrelated individuals over the age of 18 and extracted the earliest median eligible non-Emergency Department outpatient measured SBP in the electronic health record, and the corresponding DBP. For individuals with an even number of SBP measures in their record, the lower value was used to compute the median. For individuals with fewer than three measurements available, the lowest available SBP and corresponding DBP were used. Measures were considered ineligible if they occurred at or after an ICD-9/10 billing code from the groups 585/N18 (chronic kidney disease), 405/I15 (secondary hypertension), or 428/I50 (heart failure). For participants who had started an antihypertensive medication before the date of their median SBP measurement, 15 mm Hg was added to SBP and 10 mm Hg to DBP. Eligible SBP measures were restricted to a range of 30 to 300 mmHg. Eligible DBP measures were restricted to values over 30 mmHg. Sample size for SBP, DBP, and PP GWAS analysis included 21,843 individuals. Pulse pressure was defined as SBP minus DBP. Hypertension status was defined by phecodes 401* and/or antihypertensive medication use. Sample size for hypertension case/control GWAS included 21,843 individuals (n = 8,098 cases and 13,745 controls). See Supplementary Table 13 for demographics of the All-Of-Us cohort.

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UKB

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Lifelines Cohort Study

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CHARGE consortium

Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) is a consortium formed to facilitate meta-analyses of genome-wide association studies of aging and cardiovascular traits, and the replication of genotype – phenotype associations identified in such studies.

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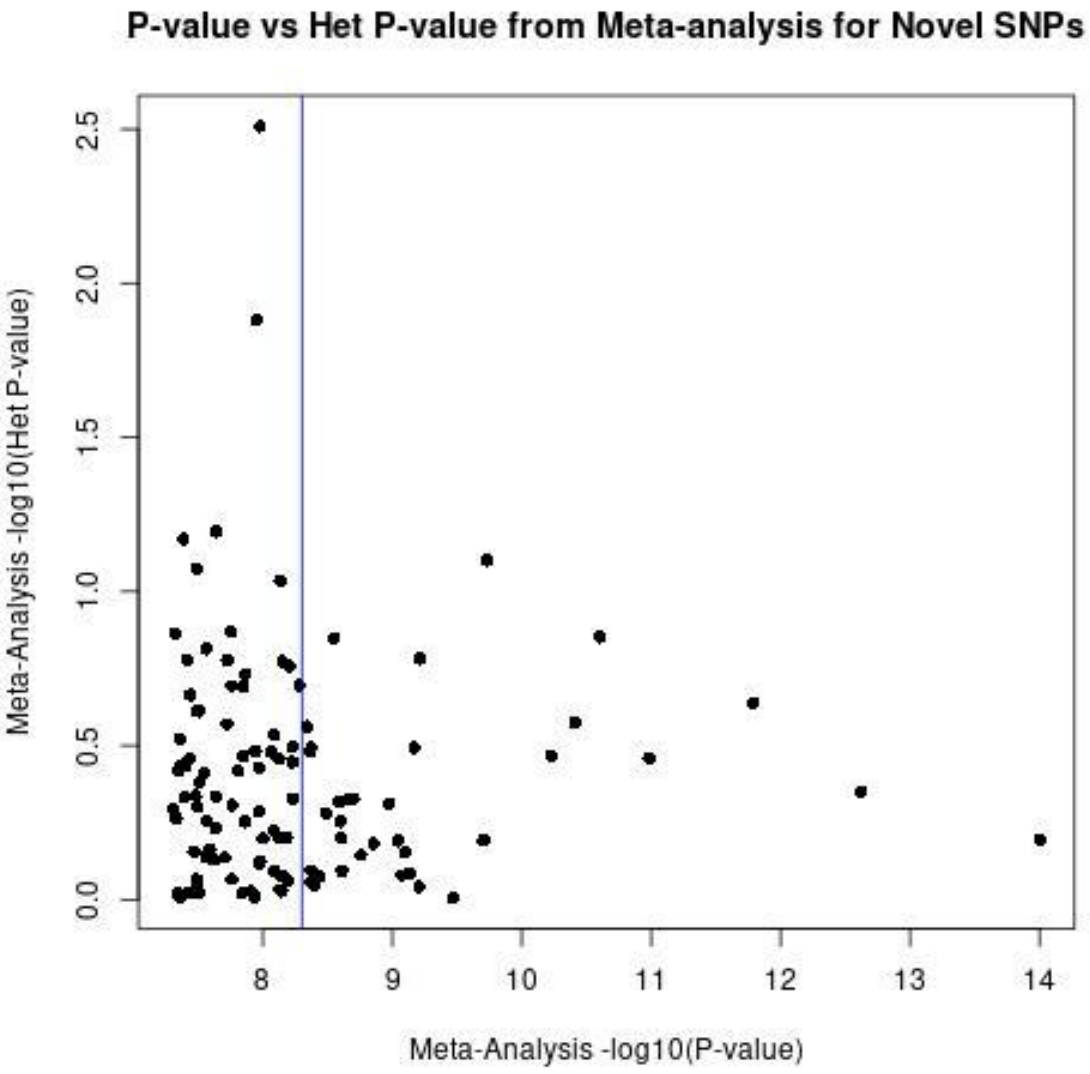
Supplementary Figures



Supplementary Figure 1: Meta-Analysis Heterogeneity P-values of 113 Novel Loci: Plotting the GWAS meta-analysis association p-values from inverse variance-weighted method on the x-axis vs the meta-analysis heterogeneity ("het") p-values from Q statistics on the y-axis, with all p-values on the -log10 scale. The blue vertical reference line indicates the stricter significance p-value threshold for the one-stage GWAS design ($P<5x10^{-9}$). "SNPs" = Single Nucleotide Polymorphisms.

a

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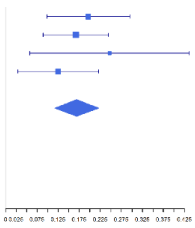
rs10991952

Cohort name	beta	95% CI
ICBP	0.196	(0.098 to 0.295)
UKBio	0.167	(0.089 to 0.244)
BioVu	0.247	(0.057 to 0.437)
MVP	0.125	(0.029 to 0.221)
Fixed effects meta	**0.169**	**(0.117 to 0.221)**
Meta p-value		**1.984E-10**
I2 Heterogeneity		**0**
Q statistic p-value		**0.641**
Number of samples		**1008680**



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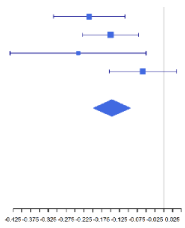
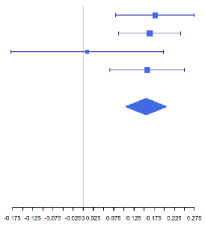
rs3861882

Cohort name	beta	95% CI
ICBP	-0.21	(-0.311 to -0.109)
UKBio	-0.15	(-0.229 to -0.071)
BioVu	-0.241	(-0.433 to -0.05)
MVP	-0.059	(-0.154 to 0.036)
Fixed effects meta	**-0.146**	**(-0.199 to -0.094)**
Meta p-value		**4.785E-8**
I2 Heterogeneity		**45.8**
Q statistic p-value		**0.1365**
Number of samples		**1007030**



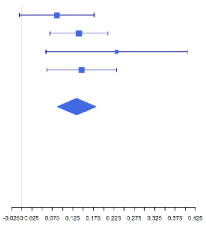
10:17266389
rs10904910

Cohort name	beta	95% CI
ICBP	0.178	(0.08 to 0.275)
UKBio	0.164	(0.087 to 0.241)
BioVu	0.009	(-0.18 to 0.198)
MVP	0.158	(0.066 to 0.25)
Fixed effects meta	**0.155**	**(0.104 to 0.206)**
Meta p-value		**2.559E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.4809**
Number of samples		**1009750**



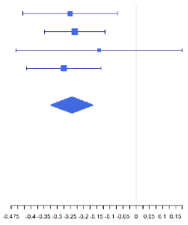
11:19736996
rs1319701

Cohort name	beta	95% CI
ICBP	0.086	(-0.006 to 0.177)
UKBio	0.14	(0.069 to 0.211)
BioVu	0.232	(0.059 to 0.405)
MVP	0.146	(0.061 to 0.232)
Fixed effects meta	**0.134**	**(0.087 to 0.182)**
Meta p-value		**3.194E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.4994**
Number of samples		**1008750**



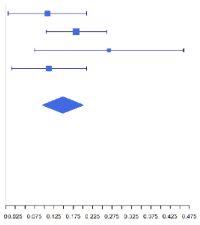
11:66325484
rs61890399

Cohort name	beta	95% CI
ICBP	-0.251	(-0.43 to -0.071)
UKBio	-0.233	(-0.348 to -0.119)
BioVu	-0.141	(-0.458 to 0.176)
MVP	-0.275	(-0.417 to -0.134)
Fixed effects meta	**-0.244**	**(-0.326 to -0.163)**
Meta p-value		**4.022E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.8955**
Number of samples		**1009760**



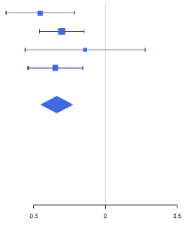
11:113655696
rs17542254

Cohort name	beta	95% CI
ICBP	0.108	(0.006 to 0.209)
UKBio	0.182	(0.104 to 0.261)
BioVu	0.267	(0.075 to 0.46)
MVP	0.112	(0.015 to 0.209)
Fixed effects meta	**0.148**	**(0.095 to 0.201)**
Meta p-value		**3.983E-8**
I2 Heterogeneity		**4.9**
Q statistic p-value		**0.3682**
Number of samples		**1008640**



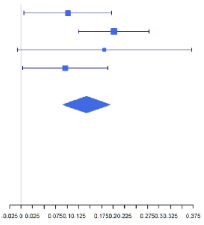
12:51355243
rs76637716

Cohort name	beta	95% CI
ICBP	-0.451	(-0.687 to -0.214)
UKBio	-0.303	(-0.456 to -0.149)
BioVu	-0.14	(-0.556 to 0.277)
MVP	-0.346	(-0.536 to -0.157)
Fixed effects meta	**-0.337**	**(-0.445 to -0.228)**
Meta p-value		**1.187E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.5943**
Number of samples		**1010530**



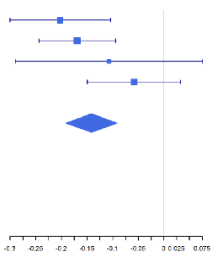
12:120124578
rs278123

Cohort name	beta	95% CI
ICBP	0.102	(0.006 to 0.197)
UKBio	0.202	(0.125 to 0.278)
BioVu	0.181	(-0.008 to 0.37)
MVP	0.096	(0.003 to 0.189)
Fixed effects meta	**0.142**	**(0.091 to 0.193)**
Meta p-value		**4.366E-8**
I2 Heterogeneity		**18.1**
Q statistic p-value		**0.3002**
Number of samples		**1017400**



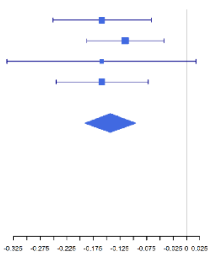
4:153006312
rs7665985

Cohort name	beta	95% CI
ICBP	-0.202	(-0.3 to -0.104)
UKBio	-0.169	(-0.243 to -0.094)
BioVu	-0.107	(-0.29 to 0.076)
MVP	-0.058	(-0.149 to 0.033)
Fixed effects meta	**-0.141**	**(-0.191 to -0.091)**
Meta p-value		**3.845E-8**
I2 Heterogeneity		**40.9**
Q statistic p-value		**0.1665**
Number of samples		**998915**



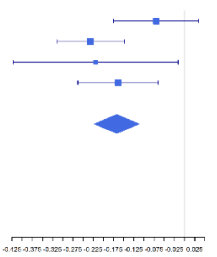
5:39444718
rs13162174

Cohort name	beta	95% CI
ICBP	-0.159	(-0.251 to -0.066)
UKBio	-0.115	(-0.187 to -0.042)
BioVu	-0.159	(-0.337 to 0.018)
MVP	-0.159	(-0.245 to -0.072)
Fixed effects meta	**-0.143**	**(-0.191 to -0.095)**
Meta p-value		**6.452E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.8628**
Number of samples		**1009750**



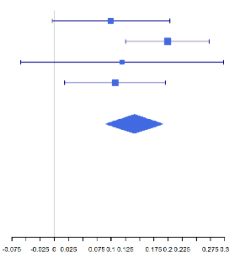
7:156990554
rs2286130

Cohort name	beta	95% CI
ICBP	-0.07	(-0.175 to 0.035)
UKBio	-0.232	(-0.315 to -0.149)
BioVu	-0.219	(-0.422 to -0.016)
MVP	-0.164	(-0.263 to -0.065)
Fixed effects meta	**-0.167**	**(-0.222 to -0.112)**
Meta p-value		**2.819E-9**
I2 Heterogeneity		**45**
Q statistic p-value		**0.1416**
Number of samples		**1008640**



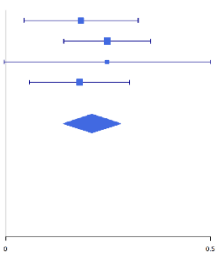
8:1212030
rs11136373

Cohort name	beta	95% CI
ICBP	0.099	(-0.004 to 0.203)
UKBio	0.199	(0.125 to 0.273)
BioVu	0.119	(-0.06 to 0.298)
MVP	0.107	(0.018 to 0.195)
Fixed effects meta	**0.141**	**(0.09 to 0.191)**
Meta p-value		**4.403E-8**
I2 Heterogeneity		**4.6**
Q statistic p-value		**0.3701**
Number of samples		**1003140**



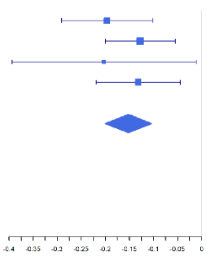
8:57153503
rs11988716

Cohort name	beta	95% CI
ICBP	0.184	(0.045 to 0.324)
UKBio	0.248	(0.142 to 0.354)
BioVu	0.248	(-0.004 to 0.501)
MVP	0.181	(0.059 to 0.303)
Fixed effects meta	**0.211**	**(0.141 to 0.281)**
Meta p-value		**3.624E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.8403**
Number of samples		**1009760**



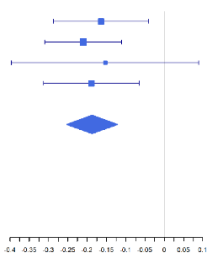
8:146130326
rs2978398

Cohort name	beta	95% CI
ICBP	-0.197	(-0.291 to -0.102)
UKBio	-0.128	(-0.2 to -0.055)
BioVu	-0.203	(-0.394 to -0.012)
MVP	-0.132	(-0.219 to -0.045)
Fixed effects meta	**-0.152**	**(-0.201 to -0.104)**
Meta p-value		**9.06E-10**
I2 Heterogeneity		**0**
Q statistic p-value		**0.6445**
Number of samples		**1006830**



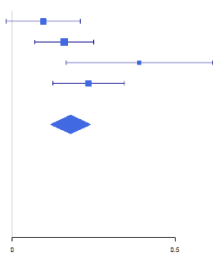
9:27230388
rs9886857

Cohort name	beta	95% CI
ICBP	-0.164	(-0.288 to -0.041)
UKBio	-0.21	(-0.31 to -0.111)
BioVu	-0.153	(-0.396 to 0.089)
MVP	-0.189	(-0.313 to -0.065)
Fixed effects meta	**-0.187**	**(-0.253 to -0.121)**
Meta p-value		**3.127E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.9442**
Number of samples		**1017400**



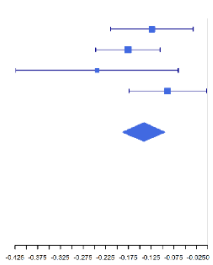
9:83432105
rs2224858

Cohort name	beta	95% CI
ICBP	0.095	(-0.02 to 0.209)
UKBio	0.159	(0.068 to 0.25)
BioVu	0.39	(0.165 to 0.616)
MVP	0.234	(0.124 to 0.344)
Fixed effects meta	**0.179**	**(0.118 to 0.239)**
Meta p-value		**7.374E-9**
I2 Heterogeneity		**53.4**
Q statistic p-value		**0.09224**
Number of samples		**1017400**



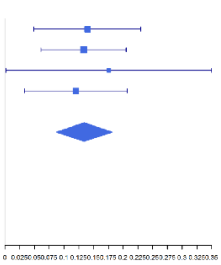
2:105205551
rs6729623

Cohort name	beta	95% CI
ICBP	-0.123	(-0.215 to -0.032)
UKBio	-0.176	(-0.247 to -0.105)
BioVu	-0.244	(-0.423 to -0.065)
MVP	-0.089	(-0.174 to -0.003)
Fixed effects meta	**-0.141**	**(-0.188 to -0.094)**
Meta p-value		**5.88E-9**
I2 Heterogeneity		**14.6**
Q statistic p-value		**0.3191**
Number of samples		**1009750**



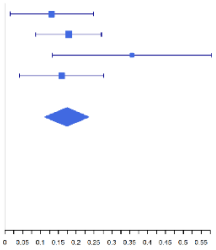
2:125429006
rs11123059

Cohort name	beta	95% CI
ICBP	0.14	(0.049 to 0.23)
UKBio	0.133	(0.061 to 0.205)
BioVu	0.176	(0.002 to 0.35)
MVP	0.12	(0.033 to 0.207)
Fixed effects meta	**0.134**	**(0.087 to 0.182)**
Meta p-value		**3.467E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.9544**
Number of samples		**1009750**



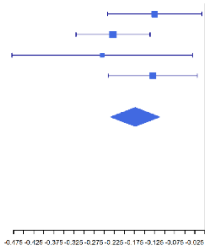
2:127839534
rs11690153

Cohort name	beta	95% CI
ICBP	0.131	(0.015 to 0.248)
UKBio	0.179	(0.087 to 0.271)
BioVu	0.356	(0.133 to 0.58)
MVP	0.159	(0.041 to 0.277)
Fixed effects meta	**0.174**	**(0.111 to 0.236)**
Meta p-value		**4.475E-8**
I2 Heterogeneity		**2.2**
Q statistic p-value		**0.3814**
Number of samples		**1009750**



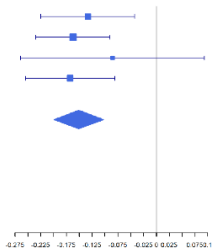
2:128822702
rs13022015

Cohort name	beta	95% CI
ICBP	-0.125	(-0.242 to -0.008)
UKBio	-0.228	(-0.32 to -0.136)
BioVu	-0.255	(-0.479 to -0.031)
MVP	-0.129	(-0.24 to -0.019)
Fixed effects meta	**-0.173**	**(-0.234 to -0.112)**
Meta p-value		**3.083E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.417**
Number of samples		**1000480**



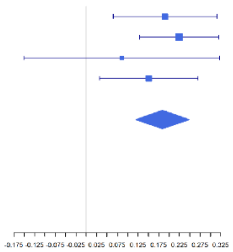
3:16363689
rs538180

Cohort name	beta	95% CI
ICBP	-0.133	(-0.225 to -0.042)
UKBio	-0.162	(-0.235 to -0.09)
BioVu	-0.085	(-0.264 to 0.093)
MVP	-0.168	(-0.255 to -0.081)
Fixed effects meta	**-0.151**	**(-0.199 to -0.103)**
Meta p-value		**8.467E-10**
I2 Heterogeneity		**0**
Q statistic p-value		**0.833**
Number of samples		**1008750**



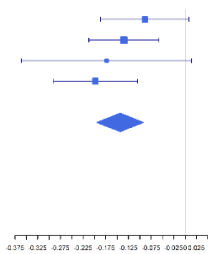
3:43992455
rs9877020

Cohort name	beta	95% CI
ICBP	0.19	(0.065 to 0.315)
UKBio	0.224	(0.128 to 0.319)
BioVu	0.086	(-0.151 to 0.322)
MVP	0.151	(0.032 to 0.27)
Fixed effects meta	**0.184**	**(0.119 to 0.249)**
Meta p-value		**2.57E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.6876**
Number of samples		**1009750**



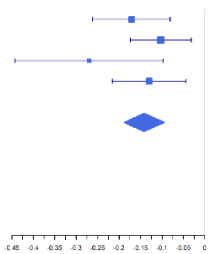
3:71607861
rs844218

Cohort name	beta	95% CI
ICBP	-0.089	(-0.187 to 0.008)
UKBio	-0.135	(-0.212 to -0.058)
BioVu	-0.173	(-0.361 to 0.014)
MVP	-0.198	(-0.29 to -0.105)
Fixed effects meta	**-0.143**	**(-0.195 to -0.092)**
Meta p-value		**4.027E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.4646**
Number of samples		**1009750**



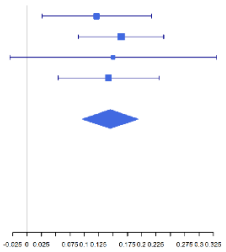
4:84452950
rs10018970

Cohort name	beta	95% CI
ICBP	-0.171	(-0.262 to -0.081)
UKBio	-0.103	(-0.174 to -0.032)
BioVu	-0.27	(-0.443 to -0.097)
MVP	-0.13	(-0.216 to -0.045)
Fixed effects meta	**-0.142**	**(-0.189 to -0.094)**
Meta p-value		**4.243E-9**
I2 Heterogeneity		**14.1**
Q statistic p-value		**0.3216**
Number of samples		**1006740**



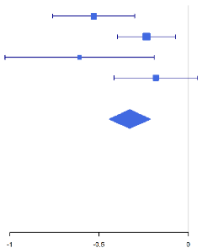
1:61877445
rs2092867

Cohort name	beta	95% CI
ICBP	0.121	(0.026 to 0.217)
UKBio	0.164	(0.09 to 0.238)
BioVu	0.15	(-0.03 to 0.331)
MVP	0.142	(0.054 to 0.23)
Fixed effects meta	**0.145**	**(0.096 to 0.194)**
Meta p-value		**7.403E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.9279**
Number of samples		**1001040**



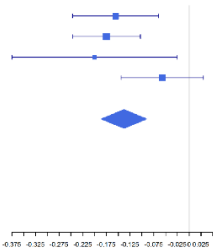
1:93524045
rs12145044

Cohort name	beta	95% CI
ICBP	-0.53	(-0.759 to -0.301)
UKBio	-0.235	(-0.397 to -0.072)
BioVu	-0.609	(-1.027 to -0.192)
MVP	-0.182	(-0.417 to 0.053)
Fixed effects meta	**-0.328**	**(-0.445 to -0.211)**
Meta p-value		**4.103E-8**
I2 Heterogeneity		**58**
Q statistic p-value		**0.06769**
Number of samples		**1009760**



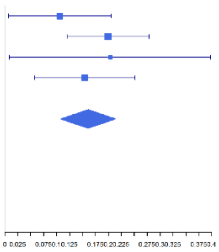
1:166023209
rs4573493

Cohort name	beta	95% CI
ICBP	-0.156	(-0.247 to -0.065)
UKBio	-0.175	(-0.246 to -0.103)
BioVu	-0.2	(-0.374 to -0.025)
MVP	-0.057	(-0.144 to 0.03)
Fixed effects meta	**-0.138**	**(-0.186 to -0.09)**
Meta p-value		**1.415E-8**
I2 Heterogeneity		**34.7**
Q statistic p-value		**0.2038**
Number of samples		**1007630**



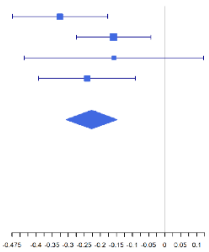
1:193271526
rs817140

Cohort name	beta	95% CI
ICBP	0.106	(0.007 to 0.206)
UKBio	0.199	(0.12 to 0.279)
BioVu	0.204	(0.009 to 0.398)
MVP	0.154	(0.058 to 0.251)
Fixed effects meta	**0.161**	**(0.108 to 0.214)**
Meta p-value		**2.523E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.5583**
Number of samples		**1009750**



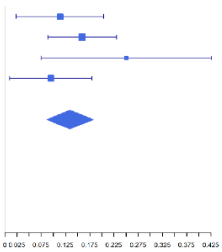
2:12994692
rs6723772

Cohort name	beta	95% CI
ICBP	-0.326	(-0.474 to -0.177)
UKBio	-0.159	(-0.274 to -0.043)
BioVu	-0.158	(-0.437 to 0.121)
MVP	-0.241	(-0.392 to -0.091)
Fixed effects meta	**-0.227**	**(-0.306 to -0.148)**
Meta p-value		**1.552E-8**
I2 Heterogeneity		**1.9**
Q statistic p-value		**0.3829**
Number of samples		**1009750**



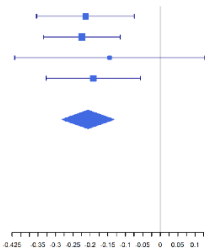
2:32620888
rs10172510

Cohort name	beta	95% CI
ICBP	0.114	(0.023 to 0.204)
UKBio	0.159	(0.088 to 0.231)
BioVu	0.251	(0.075 to 0.427)
MVP	0.095	(0.01 to 0.179)
Fixed effects meta	**0.134**	**(0.087 to 0.182)**
Meta p-value		**2.849E-8**
I2 Heterogeneity		**0.6**
Q statistic p-value		**0.3889**
Number of samples		**1009760**



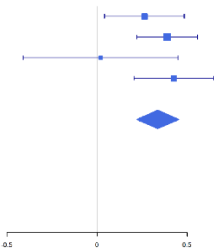
2:39061959
rs56350535

Cohort name	beta	95% CI
ICBP	-0.214	(-0.355 to -0.074)
UKBio	-0.225	(-0.335 to -0.115)
BioVu	-0.145	(-0.418 to 0.128)
MVP	-0.192	(-0.327 to -0.056)
Fixed effects meta	**-0.207**	**(-0.281 to -0.133)**
Meta p-value		**3.847E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.9534**
Number of samples		**1009760**



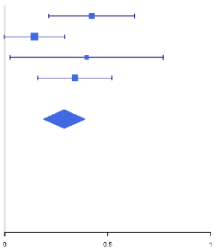
2:54738168
rs75243511

Cohort name	beta	95% CI
ICBP	0.264	(0.041 to 0.486)
UKBio	0.39	(0.22 to 0.559)
BioVu	0.021	(-0.409 to 0.451)
MVP	0.427	(0.205 to 0.649)
Fixed effects meta	**0.338**	**(0.221 to 0.455)**
Meta p-value		**1.417E-8**
I2 Heterogeneity		**10.1**
Q statistic p-value		**0.3426**
Number of samples		**1009760**



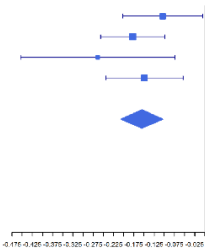
13:40671137
rs190533862

Cohort name	beta	95% CI
ICBP	0.422	(0.214 to 0.63)
UKBio	0.143	(-0.005 to 0.291)
BioVu	0.397	(0.026 to 0.768)
MVP	0.34	(0.16 to 0.519)
Fixed effects meta	**0.288**	**(0.186 to 0.389)**
Meta p-value		**2.754E-8**
I2 Heterogeneity		**43**
Q statistic p-value		**0.1538**
Number of samples		**1010960**



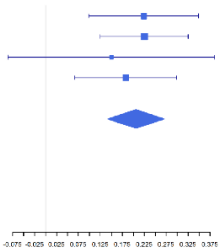
13:54264395
rs9596839

Cohort name	beta	95% CI
ICBP	-0.104	(-0.203 to -0.005)
UKBio	-0.178	(-0.257 to -0.099)
BioVu	-0.264	(-0.454 to -0.074)
MVP	-0.149	(-0.244 to -0.054)
Fixed effects meta	**-0.155**	**(-0.208 to -0.103)**
Meta p-value		**5.865E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.4706**
Number of samples		**1009140**



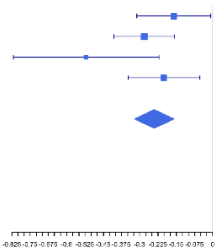
14:71352648
rs36563

Cohort name	beta	95% CI
ICBP	0.224	(0.098 to 0.349)
UKBio	0.225	(0.125 to 0.325)
BioVu	0.15	(-0.086 to 0.386)
MVP	0.183	(0.067 to 0.298)
Fixed effects meta	**0.206**	**(0.141 to 0.271)**
Meta p-value		**6.213E-10**
I2 Heterogeneity		**0**
Q statistic p-value		**0.908**
Number of samples		**1017410**



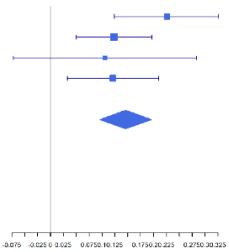
14:88825415
rs7160184

Cohort name	beta	95% CI
ICBP	-0.16	(-0.312 to -0.009)
UKBio	-0.282	(-0.407 to -0.158)
BioVu	-0.52	(-0.819 to -0.221)
MVP	-0.202	(-0.349 to -0.054)
Fixed effects meta	**-0.241**	**(-0.322 to -0.16)**
Meta p-value		**6.221E-9**
I2 Heterogeneity		**39.5**
Q statistic p-value		**0.1749**
Number of samples		**1017400**



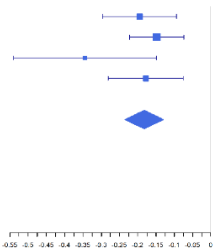
17:81036344
rs9675039

Cohort name	beta	95% CI
ICBP	0.226	(0.124 to 0.327)
UKBio	0.123	(0.049 to 0.197)
BioVu	0.106	(-0.072 to 0.284)
MVP	0.121	(0.033 to 0.21)
Fixed effects meta	**0.146**	**(0.096 to 0.196)**
Meta p-value		**1.067E-8**
I2 Heterogeneity		**4.1**
Q statistic p-value		**0.3721**
Number of samples		**985779**



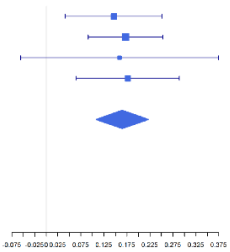
18:7131618
rs880132

Cohort name	beta	95% CI
ICBP	-0.195	(-0.297 to -0.094)
UKBio	-0.148	(-0.222 to -0.074)
BioVu	-0.345	(-0.54 to -0.149)
MVP	-0.178	(-0.281 to -0.076)
Fixed effects meta	**-0.182**	**(-0.235 to -0.13)**
Meta p-value		**1.036E-11**
I2 Heterogeneity		**9.2**
Q statistic p-value		**0.3469**
Number of samples		**1016400**



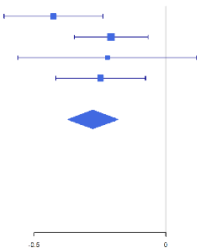
18:44040660
rs17766830

Cohort name	beta	95% CI
ICBP	0.147	(0.041 to 0.252)
UKBio	0.172	(0.091 to 0.253)
BioVu	0.159	(-0.056 to 0.374)
MVP	0.177	(0.065 to 0.289)
Fixed effects meta	**0.165**	**(0.108 to 0.222)**
Meta p-value		**1.158E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.9804**
Number of samples		**1016400**



18:46461487
rs72917789

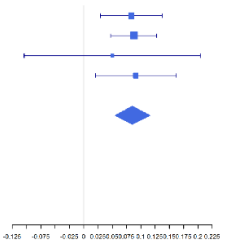
Cohort name	beta	95% CI
ICBP	-0.427	(-0.615 to -0.24)
UKBio	-0.208	(-0.349 to -0.067)
BioVu	-0.222	(-0.561 to 0.118)
MVP	-0.248	(-0.419 to -0.077)
Fixed effects meta	**-0.277**	**(-0.372 to -0.182)**
Meta p-value		**1.141E-8**
I2 Heterogeneity		**12.6**
Q statistic p-value		**0.3294**
Number of samples		**1002320**



b

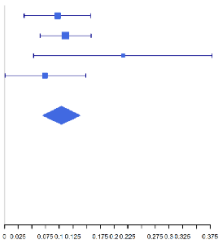
11:108350451
rs11212666

Cohort name	beta	95% CI
ICBP	0.083	(0.029 to 0.137)
UKBio	0.088	(0.047 to 0.128)
BioVu	0.05	(-0.104 to 0.204)
MVP	0.091	(0.021 to 0.162)
Fixed effects meta	**0.085**	**(0.055 to 0.116)**
Meta p-value		**4.39E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.9706**
Number of samples		**1027900**



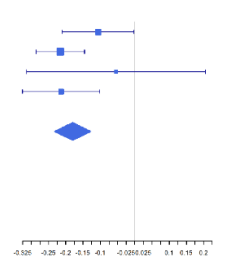
11:124619407
rs11604175

Cohort name	beta	95% CI
ICBP	0.097	(0.036 to 0.157)
UKBio	0.111	(0.065 to 0.158)
BioVu	0.216	(0.053 to 0.379)
MVP	0.074	(0.001 to 0.148)
Fixed effects meta	**0.104**	**(0.07 to 0.138)**
Meta p-value		**1.992E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.4698**
Number of samples		**1028900**



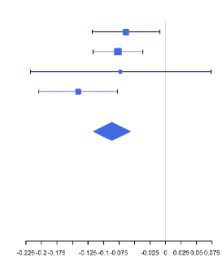
11:128769876
rs3765618

Cohort name	beta	95% CI
ICBP	-0.106	(-0.211 to -0.002)
UKBio	-0.216	(-0.286 to -0.146)
BioVu	-0.054	(-0.314 to 0.205)
MVP	-0.213	(-0.326 to -0.101)
Fixed effects meta	**-0.18**	**(-0.234 to -0.127)**
Meta p-value		**3.867E-11**
I2 Heterogeneity		**24.2**
Q statistic p-value		**0.2662**
Number of samples		**1025020**



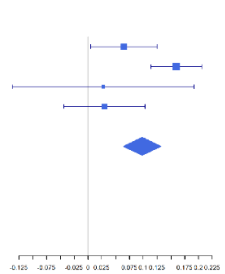
12:52418075
rs1732235

Cohort name	beta	95% CI
ICBP	-0.064	(-0.118 to -0.01)
UKBio	-0.077	(-0.117 to -0.037)
BioVu	-0.073	(-0.218 to 0.073)
MVP	-0.141	(-0.204 to -0.078)
Fixed effects meta	**-0.087**	**(-0.116 to -0.057)**
Meta p-value		**8.177E-9**
I2 Heterogeneity		**19.5**
Q statistic p-value		**0.2925**
Number of samples		**1027790**



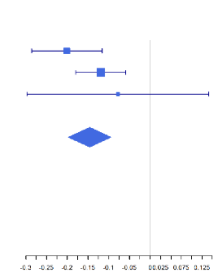
13:38249726
rs56312513

Cohort name	beta	95% CI
ICBP	0.065	(0.005 to 0.125)
UKBio	0.16	(0.114 to 0.206)
BioVu	0.028	(-0.137 to 0.192)
MVP	0.03	(-0.044 to 0.103)
Fixed effects meta	**0.098**	**(0.064 to 0.132)**
Meta p-value		**1.118E-8**
I2 Heterogeneity		**72.1**
Q statistic p-value		**0.01317**
Number of samples		**1028900**



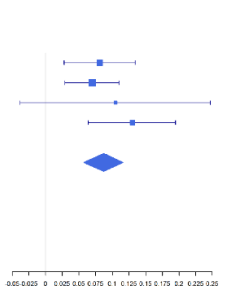
14:21841154
rs7350752

Cohort name	beta	95% CI
ICBP	-0.201	(-0.286 to -0.116)
UKBio	-0.119	(-0.18 to -0.059)
BioVu	-0.078	(-0.297 to 0.141)
Fixed effects meta	**-0.146**	**(-0.198 to -0.095)**
Meta p-value		**1.886E-8**
I2 Heterogeneity		**23.7**
Q statistic p-value		**0.2695**
Number of samples		**807694**



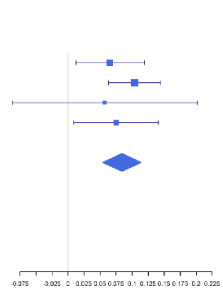
14:59900020
rs2774052

Cohort name	beta	95% CI
ICBP	0.081	(0.028 to 0.134)
UKBio	0.07	(0.029 to 0.11)
BioVu	0.105	(-0.038 to 0.247)
MVP	0.13	(0.064 to 0.195)
Fixed effects meta	**0.087**	**(0.057 to 0.116)**
Meta p-value		**1.065E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.5171**
Number of samples		**1027890**



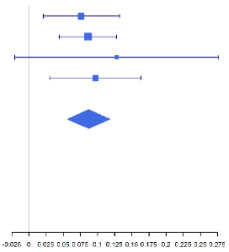
14:71874638
rs2041330

Cohort name	beta	95% CI
ICBP	0.065	(0.012 to 0.119)
UKBio	0.104	(0.063 to 0.144)
BioVu	0.057	(-0.087 to 0.201)
MVP	0.075	(0.009 to 0.141)
Fixed effects meta	**0.084**	**(0.054 to 0.114)**
Meta p-value		**3.419E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.6981**
Number of samples		**1027890**



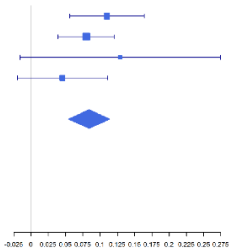
6:10034452
rs9477605

Cohort name	beta	95% CI
ICBP	0.076	(0.021 to 0.132)
UKBio	0.086	(0.044 to 0.128)
BioVu	0.128	(-0.021 to 0.277)
MVP	0.097	(0.03 to 0.163)
Fixed effects meta	**0.087**	**(0.056 to 0.118)**
Meta p-value		**3.219E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.9171**
Number of samples		**1027790**



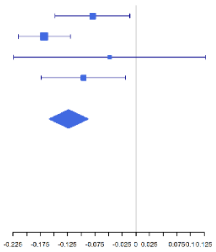
6:17477425
rs9370995

Cohort name	beta	95% CI
ICBP	0.11	(0.056 to 0.164)
UKBio	0.08	(0.039 to 0.12)
BioVu	0.129	(-0.016 to 0.274)
MVP	0.045	(-0.02 to 0.111)
Fixed effects meta	**0.084**	**(0.054 to 0.114)**
Meta p-value		**3.312E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.4601**
Number of samples		**1028900**



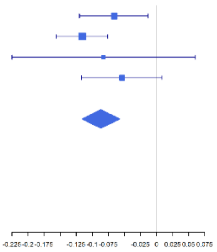
6:100629078
rs57989773

Cohort name	beta	95% CI
ICBP	-0.079	(-0.148 to -0.011)
UKBio	-0.168	(-0.215 to -0.12)
BioVu	-0.048	(-0.224 to 0.128)
MVP	-0.096	(-0.173 to -0.019)
Fixed effects meta	**-0.123**	**(-0.159 to -0.087)**
Meta p-value		**2.494E-11**
I2 Heterogeneity		**45.1**
Q statistic p-value		**0.1406**
Number of samples		**1026780**



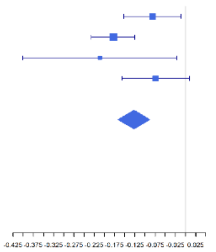
6:109625797
rs1546722

Cohort name	beta	95% CI
ICBP	-0.066	(-0.12 to -0.013)
UKBio	-0.116	(-0.156 to -0.076)
BioVu	-0.083	(-0.225 to 0.06)
MVP	-0.054	(-0.117 to 0.008)
Fixed effects meta	**-0.087**	**(-0.116 to -0.057)**
Meta p-value		**7.461E-9**
I2 Heterogeneity		**8.7**
Q statistic p-value		**0.3497**
Number of samples		**1028900**



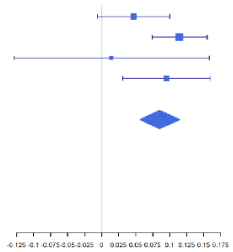
8:49391836
rs10087280

Cohort name	beta	95% CI
ICBP	-0.081	(-0.152 to -0.011)
UKBio	-0.178	(-0.232 to -0.125)
BioVu	-0.211	(-0.401 to -0.022)
MVP	-0.074	(-0.157 to 0.01)
Fixed effects meta	**-0.127**	**(-0.166 to -0.088)**
Meta p-value		**1.859E-10**
I2 Heterogeneity		**55.8**
Q statistic p-value		**0.07922**
Number of samples		**1028900**



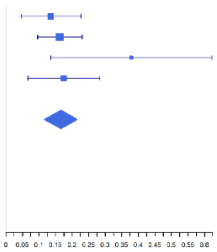
8:134229535
rs6982341

Cohort name	beta	95% CI
ICBP	0.047	(-0.006 to 0.1)
UKBio	0.114	(0.074 to 0.155)
BioVu	0.014	(-0.129 to 0.158)
MVP	0.095	(0.031 to 0.159)
Fixed effects meta	**0.085**	**(0.056 to 0.115)**
Meta p-value		**1.741E-8**
I2 Heterogeneity		**35**
Q statistic p-value		**0.2025**
Number of samples		**1028900**



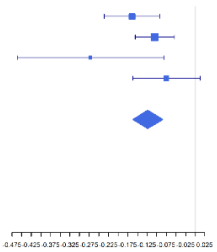
9:129643296
rs10819246

Cohort name	beta	95% CI
ICBP	0.136	(0.046 to 0.227)
UKBio	0.163	(0.096 to 0.23)
BioVu	0.379	(0.135 to 0.622)
MVP	0.175	(0.067 to 0.284)
Fixed effects meta	**0.166**	**(0.116 to 0.216)**
Meta p-value		**5.909E-11**
I2 Heterogeneity		**10.4**
Q statistic p-value		**0.3409**
Number of samples		**1020640**



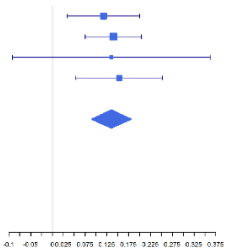
11:96151677
rs61909958

Cohort name	beta	95% CI
ICBP	-0.164	(-0.236 to -0.092)
UKBio	-0.105	(-0.156 to -0.053)
BioVu	-0.272	(-0.462 to -0.082)
MVP	-0.075	(-0.162 to 0.013)
Fixed effects meta	**-0.123**	**(-0.162 to -0.084)**
Meta p-value		**6.114E-10**
I2 Heterogeneity		**41.1**
Q statistic p-value		**0.1654**
Number of samples		**1027890**



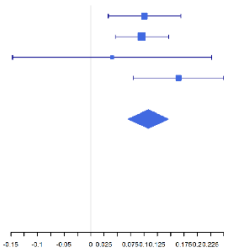
3:136692308
rs73231988

Cohort name	beta	95% CI
ICBP	0.117	(0.034 to 0.2)
UKBio	0.14	(0.075 to 0.204)
BioVu	0.135	(-0.092 to 0.362)
MVP	0.153	(0.054 to 0.252)
Fixed effects meta	**0.135**	**(0.089 to 0.182)**
Meta p-value		**1.448E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.9556**
Number of samples		**1028900**



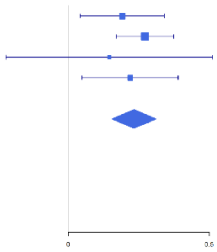
4:72002332
rs6822301

Cohort name	beta	95% CI
ICBP	0.101	(0.033 to 0.169)
UKBio	0.096	(0.046 to 0.146)
BioVu	0.04	(-0.147 to 0.227)
MVP	0.165	(0.08 to 0.25)
Fixed effects meta	**0.108**	**(0.07 to 0.146)**
Meta p-value		**1.728E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.4933**
Number of samples		**1027890**



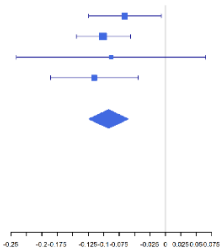
4:152163489
rs7671332

Cohort name	beta	95% CI
ICBP	0.191	(0.042 to 0.34)
UKBio	0.271	(0.17 to 0.373)
BioVu	0.145	(-0.221 to 0.512)
MVP	0.219	(0.048 to 0.389)
Fixed effects meta	**0.233**	**(0.155 to 0.311)**
Meta p-value		**4.265E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.8033**
Number of samples		**1027790**



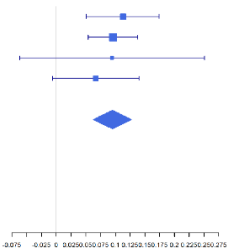
4:187818466
rs9685837

Cohort name	beta	95% CI
ICBP	-0.066	(-0.124 to -0.007)
UKBio	-0.101	(-0.144 to -0.057)
BioVu	-0.088	(-0.241 to 0.065)
MVP	-0.115	(-0.186 to -0.044)
Fixed effects meta	**-0.092**	**(-0.124 to -0.06)**
Meta p-value		**1.983E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.7305**
Number of samples		**1025880**



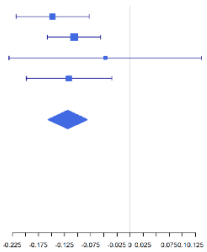
5:38616887
rs172906

Cohort name	beta	95% CI
ICBP	0.113	(0.051 to 0.174)
UKBio	0.096	(0.054 to 0.138)
BioVu	0.094	(-0.062 to 0.251)
MVP	0.067	(-0.006 to 0.14)
Fixed effects meta	**0.095**	**(0.063 to 0.127)**
Meta p-value		**7.125E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.8365**
Number of samples		**1027900**



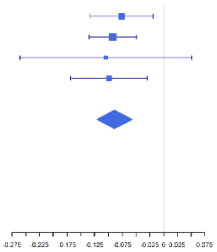
5:42515027
rs62370646

Cohort name	beta	95% CI
ICBP	-0.148	(-0.218 to -0.078)
UKBio	-0.107	(-0.158 to -0.056)
BioVu	-0.047	(-0.231 to 0.137)
MVP	-0.117	(-0.198 to -0.035)
Fixed effects meta	**-0.119**	**(-0.157 to -0.081)**
Meta p-value		**7.973E-10**
I2 Heterogeneity		**0**
Q statistic p-value		**0.7011**
Number of samples		**1027900**



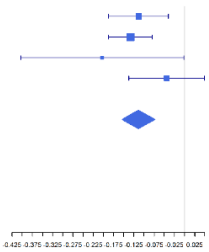
5:58352210
rs10061553

Cohort name	beta	95% CI
ICBP	-0.076	(-0.133 to -0.019)
UKBio	-0.092	(-0.135 to -0.049)
BioVu	-0.105	(-0.261 to 0.051)
MVP	-0.099	(-0.169 to -0.029)
Fixed effects meta	**-0.089**	**(-0.121 to -0.057)**
Meta p-value		**4.596E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.9528**
Number of samples		**1027890**



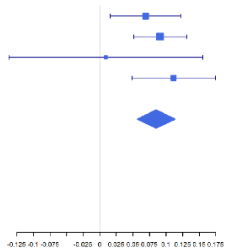
5:76884661
rs34237622

Cohort name	beta	95% CI
ICBP	-0.113	(-0.187 to -0.04)
UKBio	-0.133	(-0.187 to -0.08)
BioVu	-0.203	(-0.403 to -0.002)
MVP	-0.044	(-0.137 to 0.049)
Fixed effects meta	**-0.114**	**(-0.154 to -0.073)**
Meta p-value		**3.719E-8**
I2 Heterogeneity		**8.8**
Q statistic p-value		**0.3493**
Number of samples		**1027900**



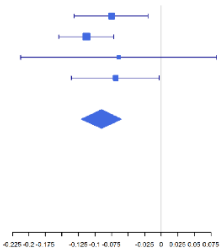
1:21155195
rs2320590

Cohort name	beta	95% CI
ICBP	0.069	(0.016 to 0.122)
UKBio	0.091	(0.051 to 0.131)
BioVu	0.009	(-0.137 to 0.155)
MVP	0.111	(0.048 to 0.174)
Fixed effects meta	**0.085**	**(0.056 to 0.114)**
Meta p-value		**1.384E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.5587**
Number of samples		**1027880**



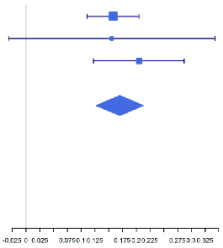
1:68143195
rs10889711

Cohort name	beta	95% CI
ICBP	-0.075	(-0.131 to -0.02)
UKBio	-0.113	(-0.155 to -0.072)
BioVu	-0.064	(-0.212 to 0.084)
MVP	-0.069	(-0.136 to -0.003)
Fixed effects meta	**-0.09**	**(-0.121 to -0.06)**
Meta p-value		**6.566E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.6282**
Number of samples		**1019060**



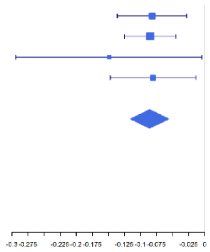
1:110229787
rs36209093

Cohort name	beta	95% CI
UKBio	0.158	(0.111 to 0.205)
BioVu	0.155	(-0.032 to 0.343)
MVP	0.205	(0.122 to 0.287)
Fixed effects meta	**0.17**	**(0.127 to 0.213)**
Meta p-value		**9.938E-15**
I2 Heterogeneity		**0**
Q statistic p-value		**0.6396**
Number of samples		**729874**



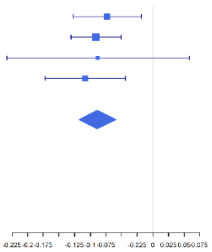
1:112261533
rs565522

Cohort name	beta	95% CI
ICBP	-0.082	(-0.136 to -0.028)
UKBio	-0.085	(-0.125 to -0.045)
BioVu	-0.149	(-0.294 to -0.005)
MVP	-0.081	(-0.147 to -0.014)
Fixed effects meta	**-0.086**	**(-0.116 to -0.056)**
Meta p-value		**1.739E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.8574**
Number of samples		**1020640**



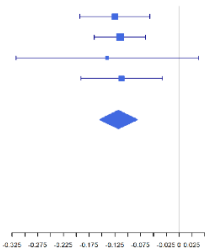
1:118223275
rs6669446

Cohort name	beta	95% CI
ICBP	-0.073	(-0.127 to -0.019)
UKBio	-0.091	(-0.131 to -0.051)
BioVu	-0.088	(-0.233 to 0.058)
MVP	-0.108	(-0.172 to -0.044)
Fixed effects meta	**-0.089**	**(-0.118 to -0.059)**
Meta p-value		**4.288E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.8761**
Number of samples		**1028900**



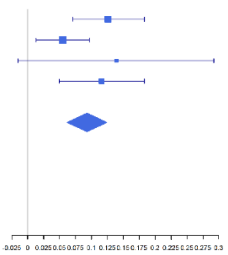
2:9803203
rs57503539

Cohort name	beta	95% CI
ICBP	-0.125	(-0.193 to -0.057)
UKBio	-0.115	(-0.165 to -0.065)
BioVu	-0.14	(-0.317 to 0.038)
MVP	-0.112	(-0.191 to -0.032)
Fixed effects meta	**-0.118**	**(-0.155 to -0.081)**
Meta p-value		**3.421E-10**
I2 Heterogeneity		**0**
Q statistic p-value		**0.9879**
Number of samples		**1026780**



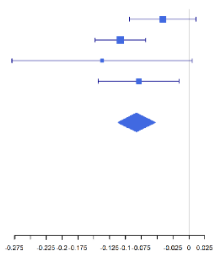
3:25424929
rs2306623

Cohort name	beta	95% CI
ICBP	0.126	(0.07 to 0.183)
UKBio	0.055	(0.013 to 0.097)
BioVu	0.139	(-0.015 to 0.292)
MVP	0.116	(0.049 to 0.183)
Fixed effects meta	**0.093**	**(0.062 to 0.124)**
Meta p-value		**5.22E-9**
I2 Heterogeneity		**35.1**
Q statistic p-value		**0.2017**
Number of samples		**1027780**



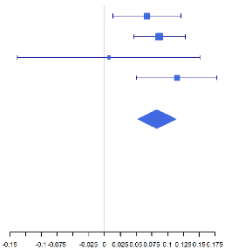
3:117492152
rs6805393

Cohort name	beta	95% CI
ICBP	-0.041	(-0.094 to 0.011)
UKBio	-0.108	(-0.148 to -0.068)
BioVu	-0.137	(-0.279 to 0.005)
MVP	-0.079	(-0.143 to -0.016)
Fixed effects meta	**-0.083**	**(-0.112 to -0.053)**
Meta p-value		**3.274E-8**
I2 Heterogeneity		**27.9**
Q statistic p-value		**0.2444**
Number of samples		**1028900**



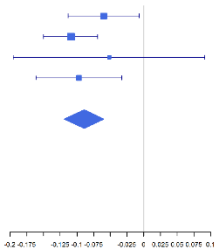
14:84911548
rs12883344

Cohort name	beta	95% CI
ICBP	0.067	(0.013 to 0.121)
UKBio	0.087	(0.046 to 0.128)
BioVu	0.007	(-0.138 to 0.151)
MVP	0.115	(0.051 to 0.178)
Fixed effects meta	**0.083**	**(0.053 to 0.113)**
Meta p-value		**4.944E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.5073**
Number of samples		**1028900**



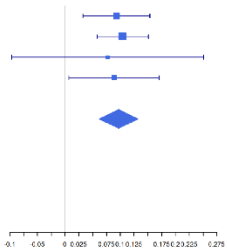
15:51559845
rs28490942

Cohort name	beta	95% CI
ICBP	-0.06	(-0.113 to -0.007)
UKBio	-0.109	(-0.15 to -0.069)
BioVu	-0.052	(-0.195 to 0.091)
MVP	-0.097	(-0.161 to -0.033)
Fixed effects meta	**-0.089**	**(-0.119 to -0.06)**
Meta p-value		**3.248E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.5244**
Number of samples		**1028900**



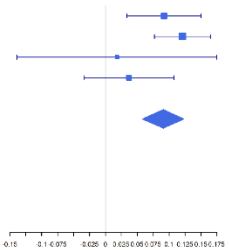
15:72429989
rs2034879

Cohort name	beta	95% CI
ICBP	0.093	(0.032 to 0.154)
UKBio	0.104	(0.058 to 0.151)
BioVu	0.077	(-0.097 to 0.251)
MVP	0.089	(0.007 to 0.171)
Fixed effects meta	**0.097**	**(0.062 to 0.132)**
Meta p-value		**4.392E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.9798**
Number of samples		**1028900**



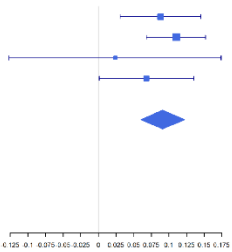
15:82186535
rs983353

Cohort name	beta	95% CI
ICBP	0.092	(0.034 to 0.15)
UKBio	0.121	(0.077 to 0.165)
BioVu	0.018	(-0.139 to 0.175)
MVP	0.037	(-0.034 to 0.108)
Fixed effects meta	**0.091**	**(0.058 to 0.123)**
Meta p-value		**3.653E-8**
I2 Heterogeneity		**32.6**
Q statistic p-value		**0.2167**
Number of samples		**1026790**



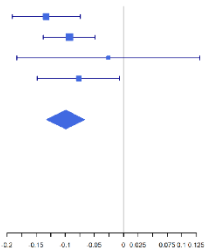
15:94214587
rs7174977

Cohort name	beta	95% CI
ICBP	0.088	(0.031 to 0.145)
UKBio	0.11	(0.068 to 0.152)
BioVu	0.024	(-0.127 to 0.174)
MVP	0.068	(0.001 to 0.135)
Fixed effects meta	**0.091**	**(0.06 to 0.122)**
Meta p-value		**8.152E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.5978**
Number of samples		**1022910**



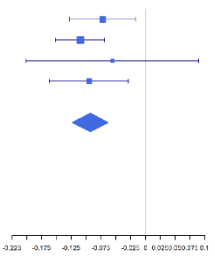
16:56859216
rs12919839

Cohort name	beta	95% CI
ICBP	-0.133	(-0.191 to -0.074)
UKBio	-0.093	(-0.138 to -0.049)
BioVu	-0.026	(-0.183 to 0.131)
MVP	-0.077	(-0.148 to -0.007)
Fixed effects meta	**-0.099**	**(-0.132 to -0.067)**
Meta p-value		**2.149E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.4709**
Number of samples		**1028900**



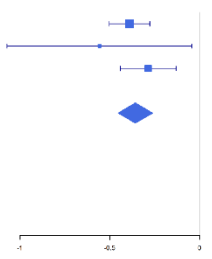
16:84082650
rs8056413

Cohort name	beta	95% CI
ICBP	-0.072	(-0.128 to -0.017)
UKBio	-0.11	(-0.152 to -0.069)
BioVu	-0.056	(-0.201 to 0.089)
MVP	-0.095	(-0.162 to -0.029)
Fixed effects meta	**-0.093**	**(-0.124 to -0.063)**
Meta p-value		**1.746E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.7176**
Number of samples		**1027890**



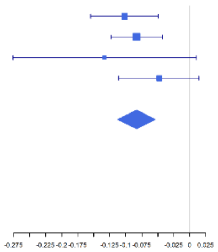
18:77161324
rs117777118

Cohort name	beta	95% CI
UKBio	-0.39	(-0.503 to -0.278)
BioVu	-0.558	(-1.072 to -0.045)
MVP	-0.287	(-0.443 to -0.13)
Fixed effects meta	**-0.358**	**(-0.454 to -0.262)**
Meta p-value		**2.398E-13**
I2 Heterogeneity		**0**
Q statistic p-value		**0.4463**
Number of samples		**729881**



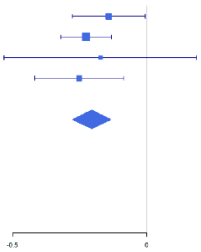
19:44746657
rs2125578

Cohort name	beta	95% CI
ICBP	-0.102	(-0.155 to -0.049)
UKBio	-0.083	(-0.123 to -0.043)
BioVu	-0.133	(-0.276 to 0.01)
MVP	-0.048	(-0.111 to 0.014)
Fixed effects meta	**-0.083**	**(-0.113 to -0.054)**
Meta p-value		**2.7E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.5558**
Number of samples		**1025680**



20:35169916
rs146827176

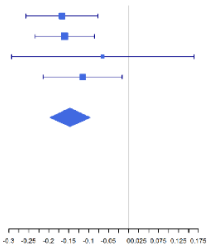
Cohort name	beta	95% CI
ICBP	-0.142	(-0.278 to -0.006)
UKBio	-0.226	(-0.319 to -0.132)
BioVu	-0.172	(-0.532 to 0.187)
MVP	-0.252	(-0.417 to -0.086)
Fixed effects meta	**-0.205**	**(-0.277 to -0.133)**
Meta p-value		**2.754E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.7265**
Number of samples		**1020700**



c

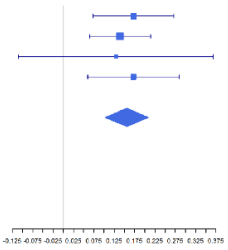
9:80751434
rs112324977

Cohort name	beta	95% CI
ICBP	-0.167	(-0.257 to -0.077)
UKBio	-0.16	(-0.234 to -0.086)
BioVu	-0.065	(-0.293 to 0.164)
MVP	-0.115	(-0.214 to -0.016)
Fixed effects meta	**-0.147**	**(-0.197 to -0.096)**
Meta p-value		**1.067E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.763**
Number of samples		**1017040**



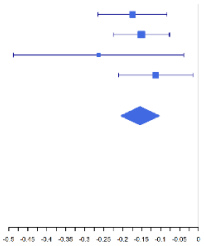
9:122890934
rs72751391

Cohort name	beta	95% CI
ICBP	0.172	(0.073 to 0.271)
UKBio	0.139	(0.065 to 0.214)
BioVu	0.129	(-0.111 to 0.368)
MVP	0.172	(0.06 to 0.284)
Fixed effects meta	**0.156**	**(0.102 to 0.209)**
Meta p-value		**1.226E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.9418**
Number of samples		**1016040**



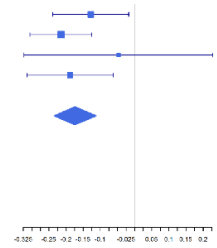
9:133711263
rs2987903

Cohort name	beta	95% CI
ICBP	-0.174	(-0.265 to -0.083)
UKBio	-0.151	(-0.225 to -0.076)
BioVu	-0.264	(-0.488 to -0.039)
MVP	-0.113	(-0.211 to -0.015)
Fixed effects meta	**-0.154**	**(-0.205 to -0.103)**
Meta p-value		**2.486E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.6305**
Number of samples		**1017040**



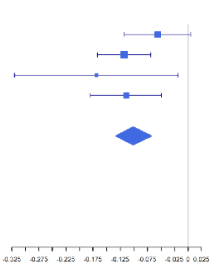
11:11793978
rs11022023

Cohort name	beta	95% CI
ICBP	-0.128	(-0.24 to -0.017)
UKBio	-0.215	(-0.306 to -0.125)
BioVu	-0.047	(-0.323 to 0.229)
MVP	-0.189	(-0.314 to -0.063)
Fixed effects meta	**-0.174**	**(-0.236 to -0.111)**
Meta p-value		**4.798E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.5385**
Number of samples		**1008280**



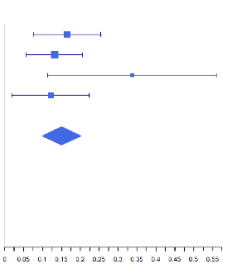
11:73783478
rs4944038

Cohort name	beta	95% CI
ICBP	-0.056	(-0.117 to 0.005)
UKBio	-0.118	(-0.167 to -0.069)
BioVu	-0.169	(-0.32 to -0.019)
MVP	-0.114	(-0.18 to -0.049)
Fixed effects meta	**-0.101**	**(-0.134 to -0.067)**
Meta p-value		**4.298E-9**
I2 Heterogeneity		**12.5**
Q statistic p-value		**0.3301**
Number of samples		**1009390**



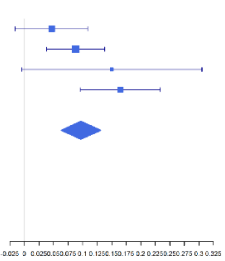
11:110657616
rs77759442

Cohort name	beta	95% CI
ICBP	0.165	(0.076 to 0.254)
UKBio	0.132	(0.057 to 0.206)
BioVu	0.337	(0.114 to 0.56)
MVP	0.122	(0.019 to 0.224)
Fixed effects meta	**0.15**	**(0.1 to 0.201)**
Meta p-value		**5.905E-9**
I2 Heterogeneity		**7.1**
Q statistic p-value		**0.3576**
Number of samples		**1009390**



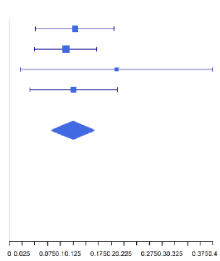
12:12045264
rs1062298

Cohort name	beta	95% CI
ICBP	0.047	(-0.016 to 0.109)
UKBio	0.088	(0.038 to 0.138)
BioVu	0.15	(-0.005 to 0.305)
MVP	0.165	(0.096 to 0.233)
Fixed effects meta	**0.097**	**(0.063 to 0.132)**
Meta p-value		**3.241E-8**
I2 Heterogeneity		**54.8**
Q statistic p-value		**0.08414**
Number of samples		**1015920**



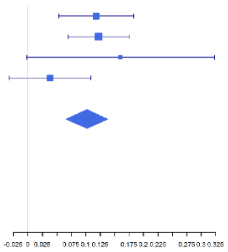
12:46385848
rs12828693

Cohort name	beta	95% CI
ICBP	0.129	(0.051 to 0.206)
UKBio	0.111	(0.05 to 0.171)
BioVu	0.211	(0.022 to 0.4)
MVP	0.126	(0.04 to 0.212)
Fixed effects meta	**0.125**	**(0.082 to 0.167)**
Meta p-value		**8.199E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.8063**
Number of samples		**1016040**



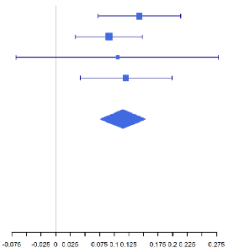
6:99548729
rs72943226

Cohort name	beta	95% CI
ICBP	0.118	(0.053 to 0.183)
UKBio	0.122	(0.069 to 0.175)
BioVu	0.16	(-0.002 to 0.323)
MVP	0.038	(-0.033 to 0.109)
Fixed effects meta	**0.102**	**(0.066 to 0.138)**
Meta p-value		**3.118E-8**
I2 Heterogeneity		**27.8**
Q statistic p-value		**0.245**
Number of samples		**1009390**



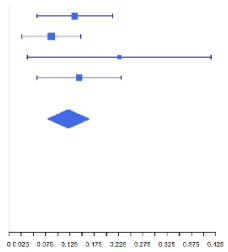
6:121258543
rs9320778

Cohort name	beta	95% CI
ICBP	0.143	(0.073 to 0.214)
UKBio	0.091	(0.034 to 0.148)
BioVu	0.106	(-0.068 to 0.279)
MVP	0.12	(0.042 to 0.199)
Fixed effects meta	**0.115**	**(0.076 to 0.154)**
Meta p-value		**1.046E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.7503**
Number of samples		**1009380**



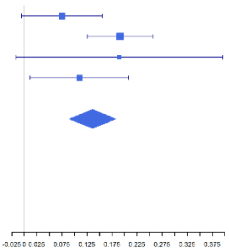
7:15421023
rs67615620

Cohort name	beta	95% CI
ICBP	0.135	(0.057 to 0.213)
UKBio	0.087	(0.026 to 0.148)
BioVu	0.227	(0.038 to 0.415)
MVP	0.144	(0.058 to 0.23)
Fixed effects meta	**0.122**	**(0.079 to 0.165)**
Meta p-value		**2.321E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.4625**
Number of samples		**1009390**



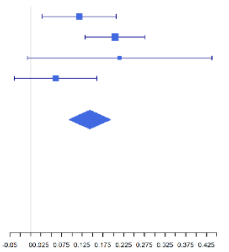
7:16117030
rs75177877

Cohort name	beta	95% CI
ICBP	0.075	(-0.006 to 0.155)
UKBio	0.191	(0.126 to 0.257)
BioVu	0.189	(-0.017 to 0.395)
MVP	0.11	(0.011 to 0.208)
Fixed effects meta	**0.136**	**(0.09 to 0.182)**
Meta p-value		**7.015E-9**
I2 Heterogeneity		**40.5**
Q statistic p-value		**0.1687**
Number of samples		**1009390**



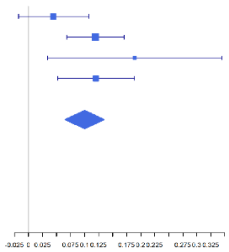
8:34164285
rs2953937

Cohort name	beta	95% CI
ICBP	0.118	(0.028 to 0.207)
UKBio	0.204	(0.132 to 0.277)
BioVu	0.215	(-0.008 to 0.438)
MVP	0.061	(-0.039 to 0.16)
Fixed effects meta	**0.143**	**(0.093 to 0.193)**
Meta p-value		**1.755E-8**
I2 Heterogeneity		**46**
Q statistic p-value		**0.1353**
Number of samples		**1009390**



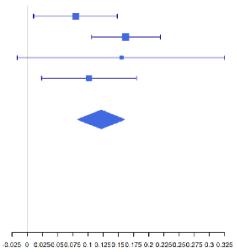
8:108319395
rs36036692

Cohort name	beta	95% CI
ICBP	0.044	(-0.018 to 0.107)
UKBio	0.119	(0.068 to 0.17)
BioVu	0.189	(0.034 to 0.345)
MVP	0.12	(0.052 to 0.189)
Fixed effects meta	**0.1**	**(0.065 to 0.135)**
Meta p-value		**1.888E-8**
I2 Heterogeneity		**40.9**
Q statistic p-value		**0.1666**
Number of samples		**1009390**



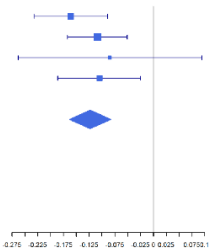
9:14535119
rs34361301

Cohort name	beta	95% CI
ICBP	0.08	(0.011 to 0.148)
UKBio	0.162	(0.106 to 0.219)
BioVu	0.155	(-0.016 to 0.325)
MVP	0.102	(0.024 to 0.18)
Fixed effects meta	**0.122**	**(0.083 to 0.16)**
Meta p-value		**6.762E-10**
I2 Heterogeneity		**14.1**
Q statistic p-value		**0.3215**
Number of samples		**1017040**



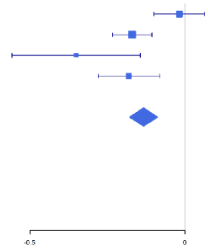
9:35191014
rs61241090

Cohort name	beta	95% CI
ICBP	-0.161	(-0.232 to -0.089)
UKBio	-0.109	(-0.167 to -0.051)
BioVu	-0.085	(-0.263 to 0.094)
MVP	-0.105	(-0.186 to -0.025)
Fixed effects meta	**-0.123**	**(-0.163 to -0.083)**
Meta p-value		**1.395E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.6579**
Number of samples		**1015830**



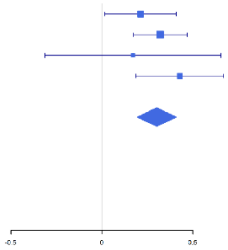
1:40763095
rs12134085

Cohort name	beta	95% CI
ICBP	-0.017	(-0.099 to 0.065)
UKBio	-0.17	(-0.233 to -0.106)
BioVu	-0.351	(-0.558 to -0.144)
MVP	-0.181	(-0.28 to -0.082)
Fixed effects meta	**-0.133**	**(-0.179 to -0.087)**
Meta p-value		**1.054E-8**
I2 Heterogeneity		**78.4**
Q statistic p-value		**0.003098**
Number of samples		**1008380**



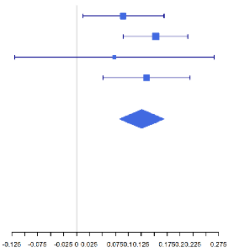
1:72229240
rs12084868

Cohort name	beta	95% CI
ICBP	0.213	(0.015 to 0.41)
UKBio	0.321	(0.174 to 0.469)
BioVu	0.171	(-0.313 to 0.655)
MVP	0.429	(0.187 to 0.671)
Fixed effects meta	**0.302**	**(0.194 to 0.41)**
Meta p-value		**4.665E-8**
I2 Heterogeneity		**0**
Q statistic p-value		**0.5455**
Number of samples		**1009390**



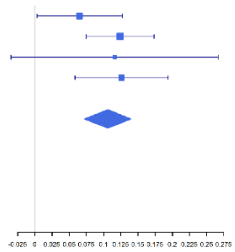
1:115019239
rs71664847

Cohort name	beta	95% CI
ICBP	0.09	(0.012 to 0.169)
UKBio	0.153	(0.09 to 0.215)
BioVu	0.073	(-0.119 to 0.266)
MVP	0.135	(0.051 to 0.219)
Fixed effects meta	**0.126**	**(0.083 to 0.169)**
Meta p-value		**9.987E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.633**
Number of samples		**1009390**



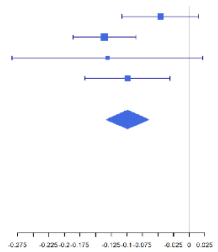
2:209622
rs300753

Cohort name	beta	95% CI
ICBP	0.065	(0.003 to 0.127)
UKBio	0.124	(0.075 to 0.173)
BioVu	0.116	(-0.035 to 0.267)
MVP	0.126	(0.058 to 0.194)
Fixed effects meta	**0.106**	**(0.072 to 0.14)**
Meta p-value		**1.055E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.4874**
Number of samples		**1007270**



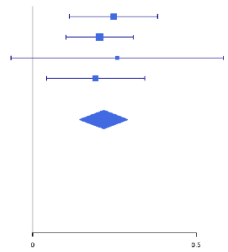
2:196590414
rs10208493

Cohort name	beta	95% CI
ICBP	-0.046	(-0.108 to 0.015)
UKBio	-0.136	(-0.186 to -0.086)
BioVu	-0.131	(-0.284 to 0.022)
MVP	-0.099	(-0.167 to -0.031)
Fixed effects meta	**-0.099**	**(-0.133 to -0.065)**
Meta p-value		**1.364E-8**
I2 Heterogeneity		**37.7**
Q statistic p-value		**0.1855**
Number of samples		**1009390**



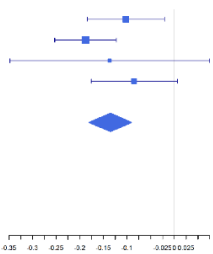
3:69919744
rs62253186

Cohort name	beta	95% CI
ICBP	0.247	(0.112 to 0.381)
UKBio	0.204	(0.101 to 0.308)
BioVu	0.258	(-0.067 to 0.584)
MVP	0.192	(0.042 to 0.342)
Fixed effects meta	**0.217**	**(0.143 to 0.29)**
Meta p-value		**7.138E-9**
I2 Heterogeneity		**0**
Q statistic p-value		**0.9397**
Number of samples		**1009390**



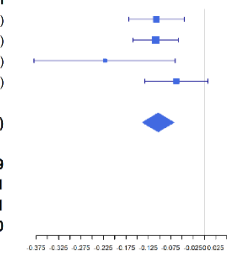
3:187456904
rs3821817

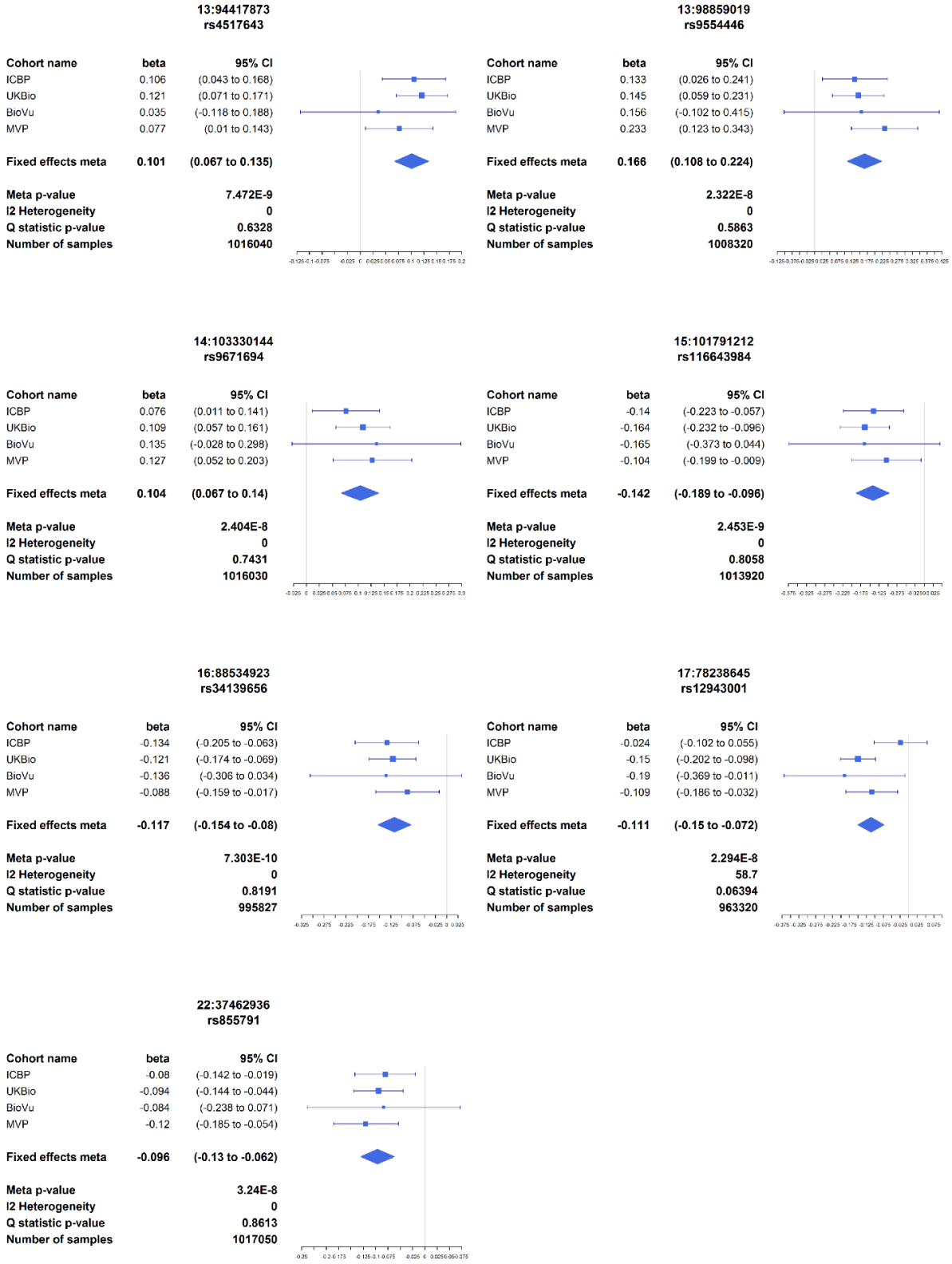
Cohort name	beta	95% CI
ICBP	-0.103	(-0.185 to -0.021)
UKBio	-0.188	(-0.253 to -0.123)
BioVu	-0.137	(-0.348 to 0.075)
MVP	-0.085	(-0.176 to 0.006)
Fixed effects meta	**-0.135**	**(-0.181 to -0.09)**
Meta p-value		**4.592E-9**
I2 Heterogeneity		**22.8**
Q statistic p-value		**0.2741**
Number of samples		**1007280**



6:85988429
rs4053778

Cohort name	beta	95% CI
ICBP	-0.107	(-0.169 to -0.045)
UKBio	-0.109	(-0.16 to -0.058)
BioVu	-0.222	(-0.38 to -0.065)
MVP	-0.063	(-0.133 to 0.008)
Fixed effects meta	**-0.103**	**(-0.138 to -0.068)**
Meta p-value		**8.672E-9**
I2 Heterogeneity		**12.1**
Q statistic p-value		**0.3321**
Number of samples		**1009390**

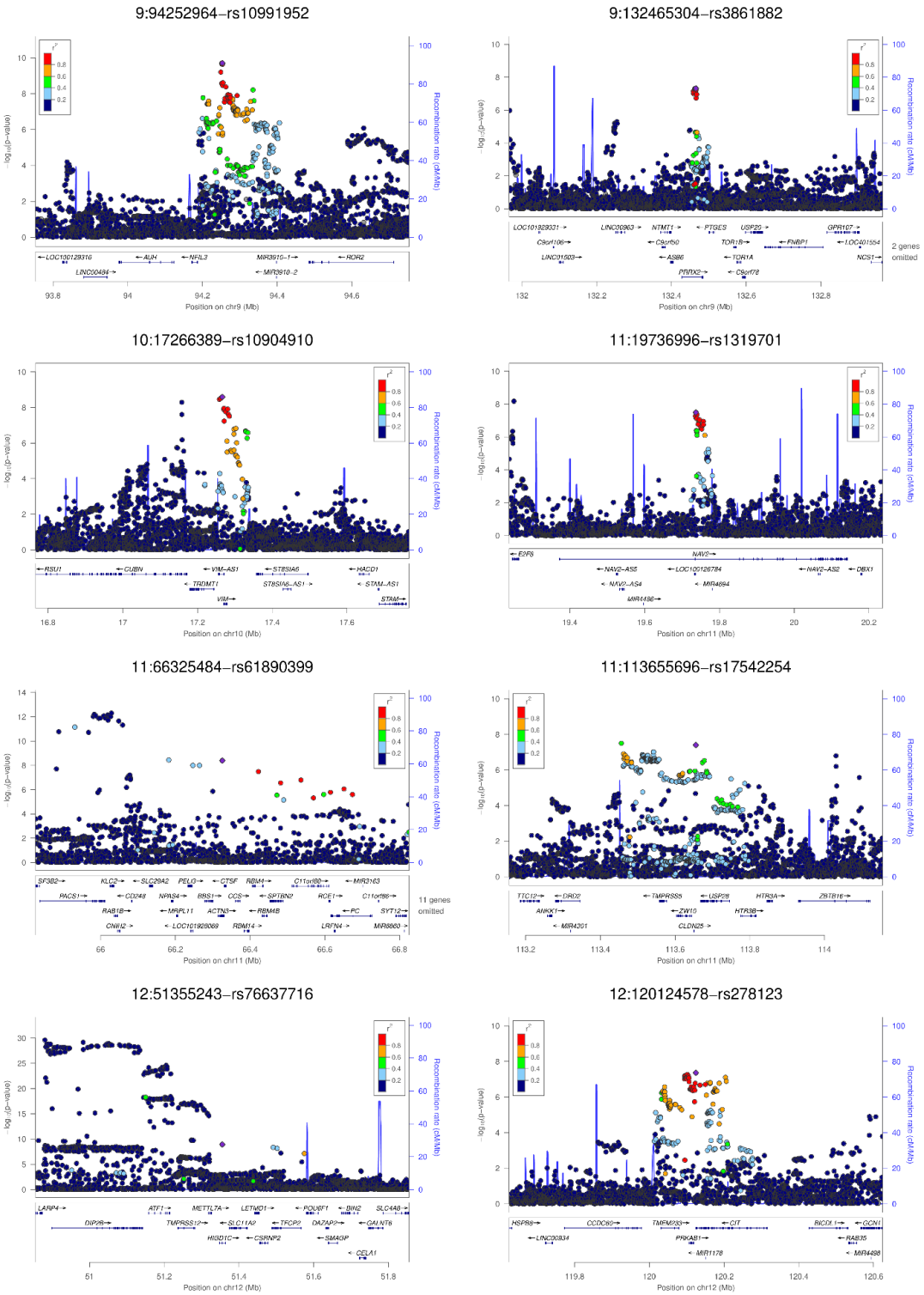




Supplementary Figure 2a-c. Forest plots for all novel loci for systolic (a), diastolic (b), and pulse pressure (c). ICBP = International Consortium of Blood Pressure meta-analysis (n=299,024); UKBio = UK Biobank (n=458,577); BioVU = Biobank Repository of the Vanderbilt University (n=50,649); MVP = Million Veterans Program (n=220,501); CI =

Confidence Interval. Meta-analysis p-values are calculated by inverse variance-weighted method, heterogeneity is calculated by I^2 statistic and Cochran's Q Test.

a



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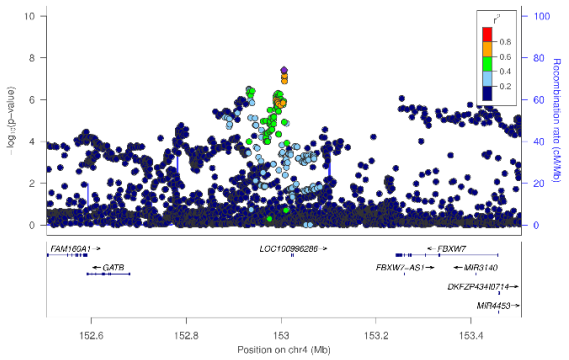

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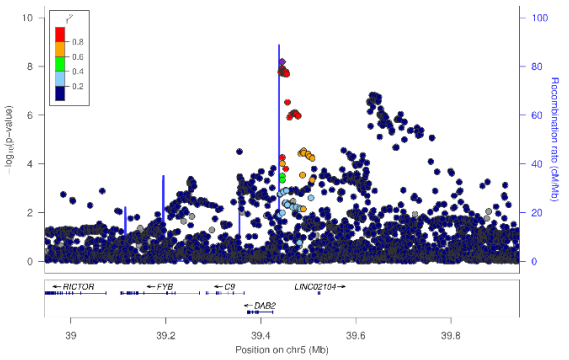

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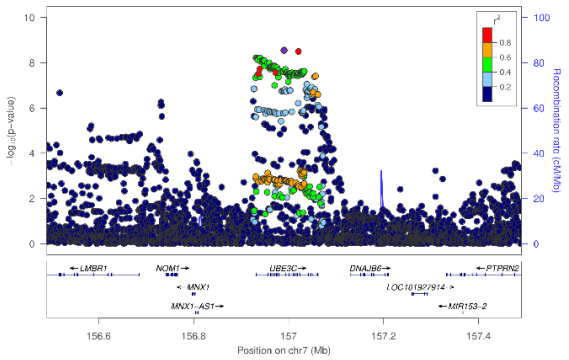

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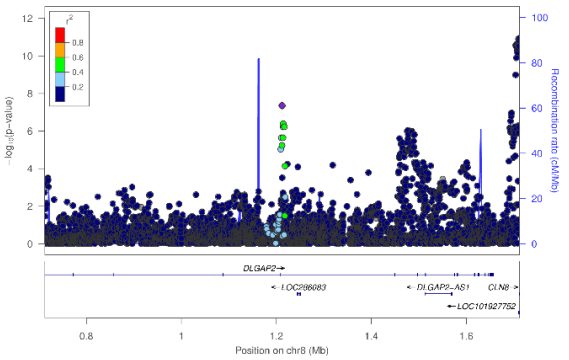

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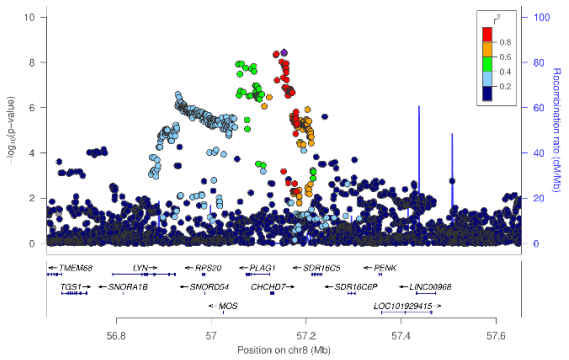

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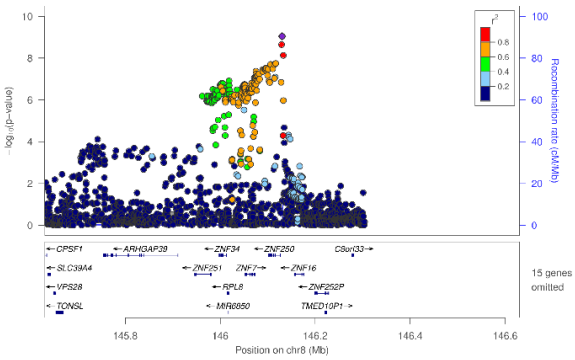

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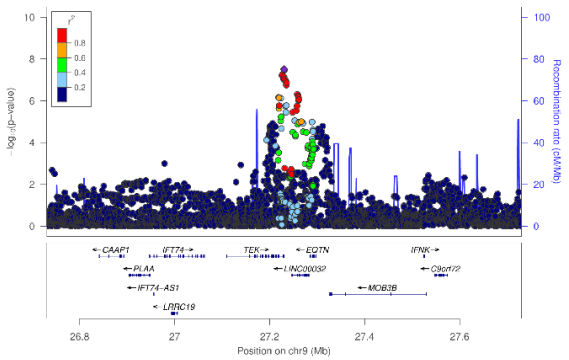

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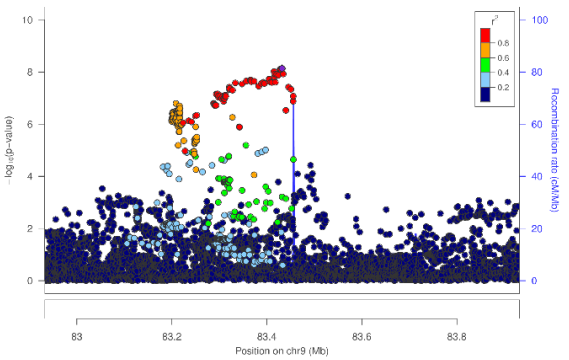

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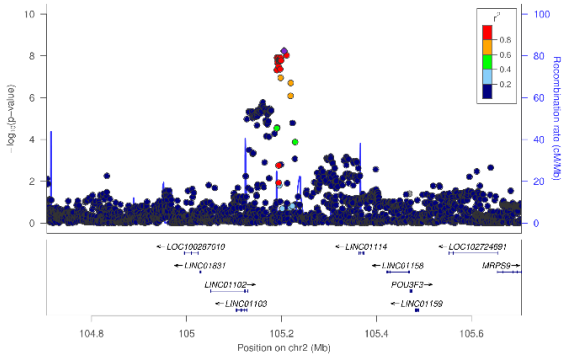

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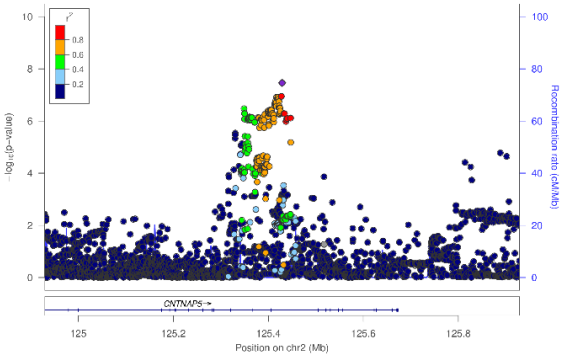

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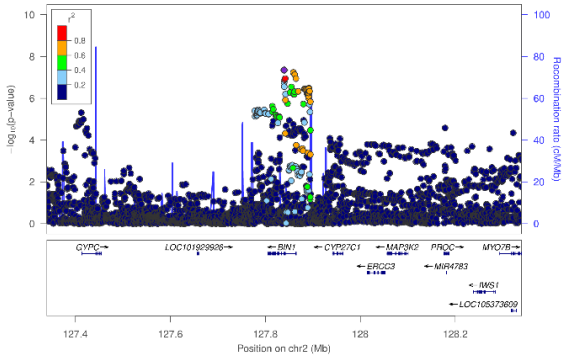

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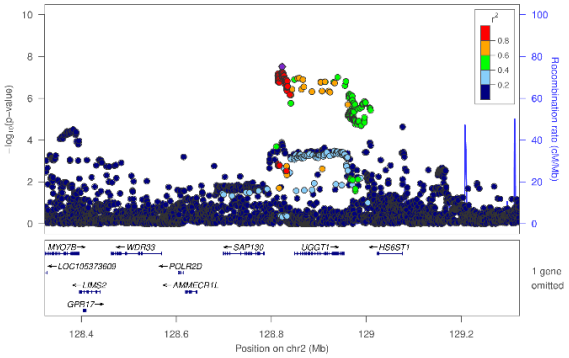

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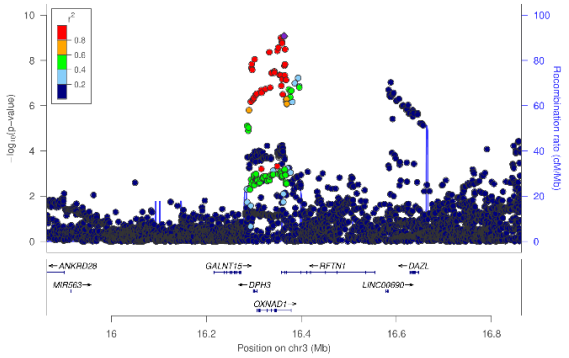

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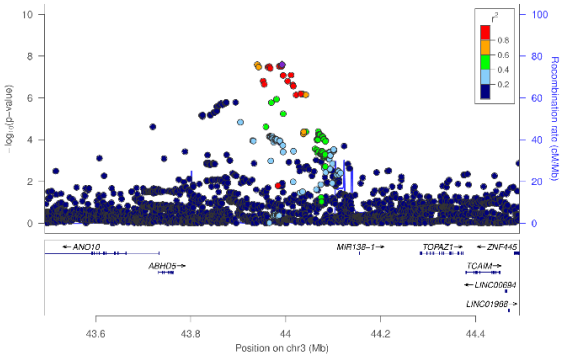

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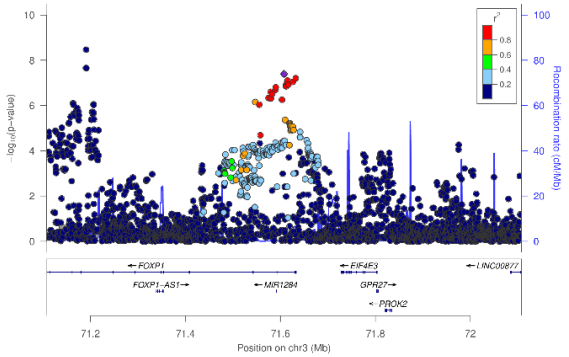

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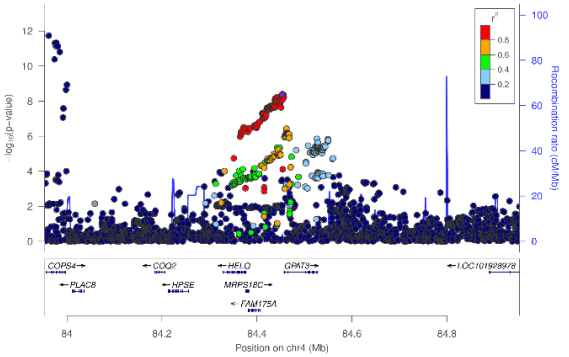

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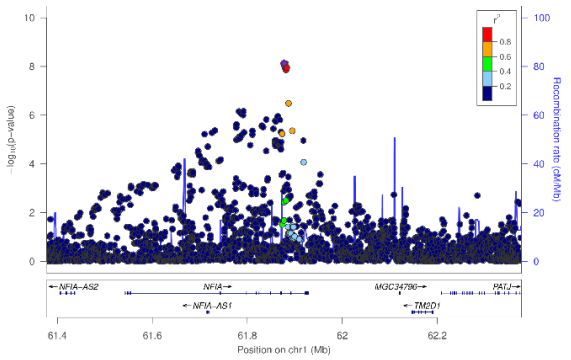

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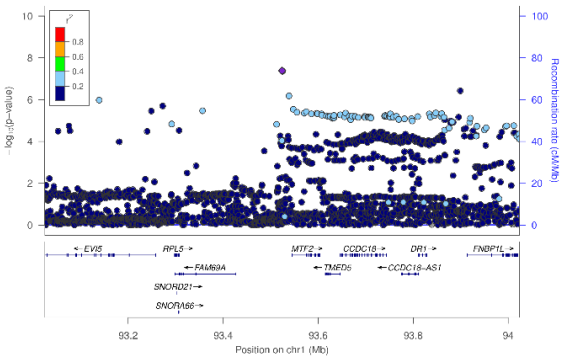

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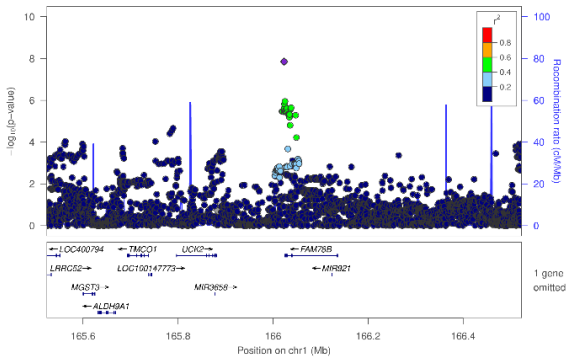

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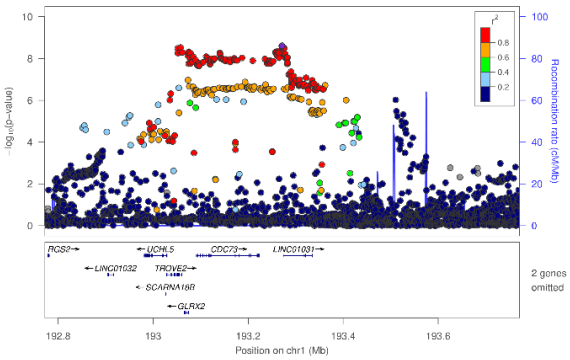

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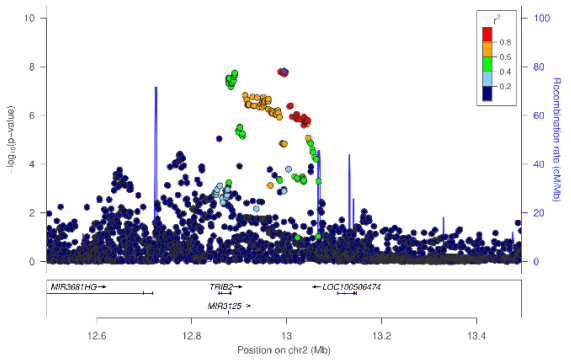

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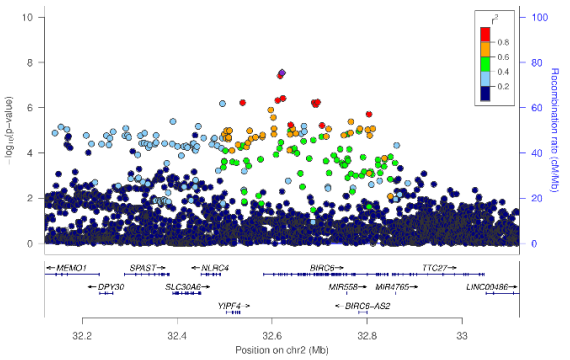

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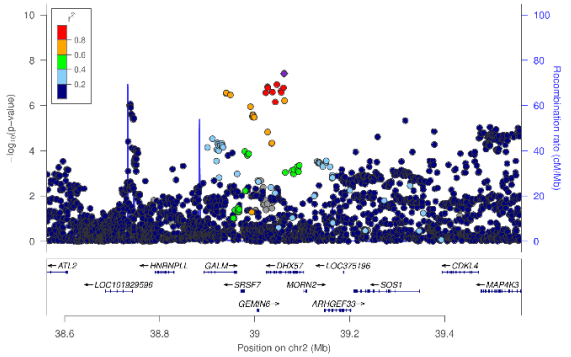

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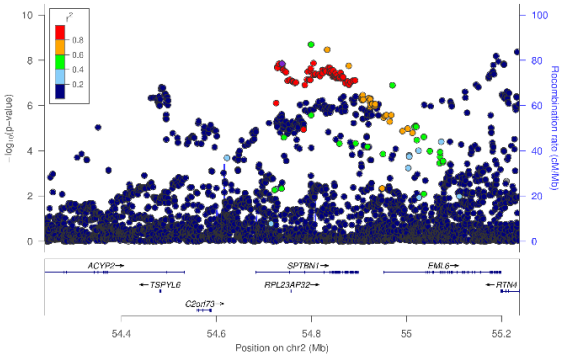

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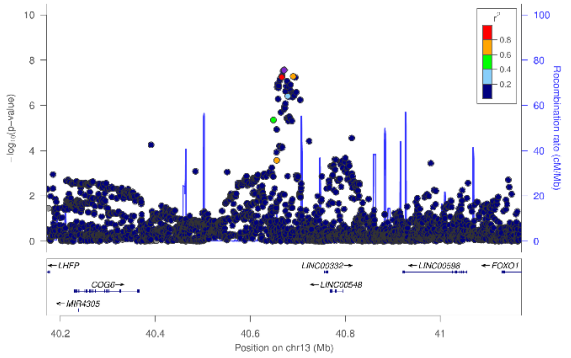

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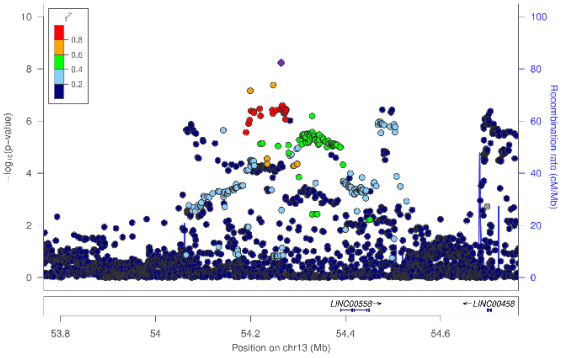

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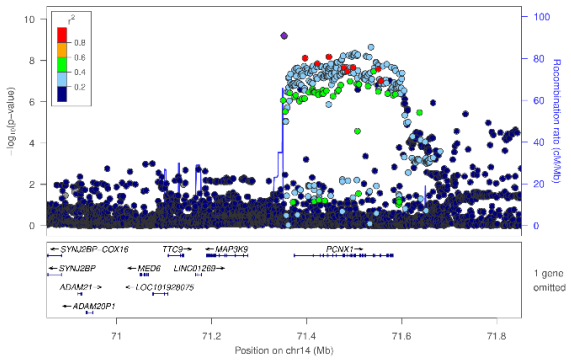

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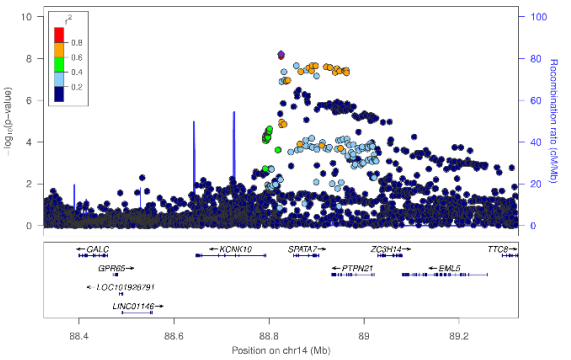

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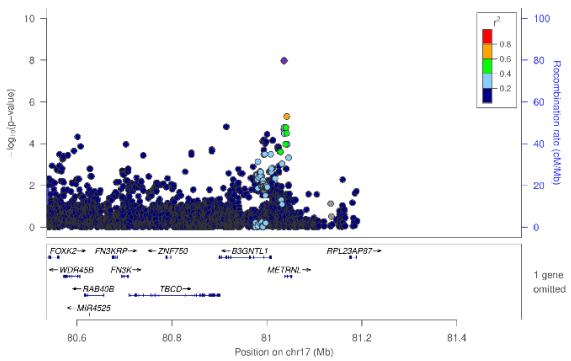

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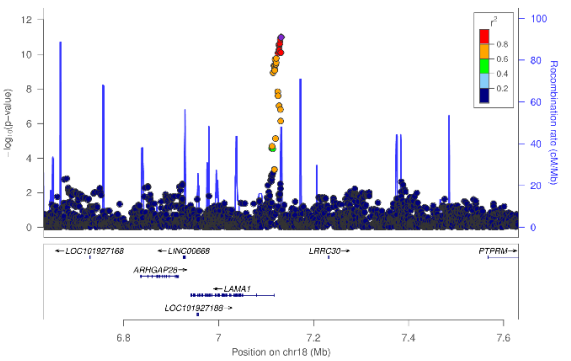

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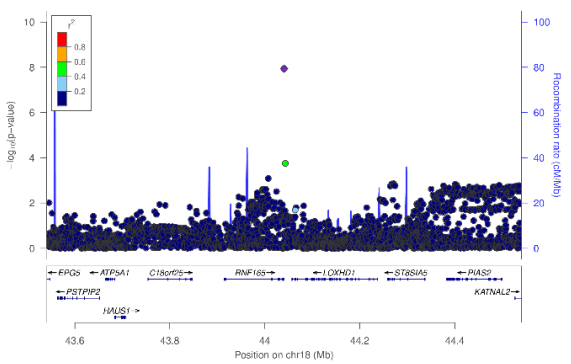

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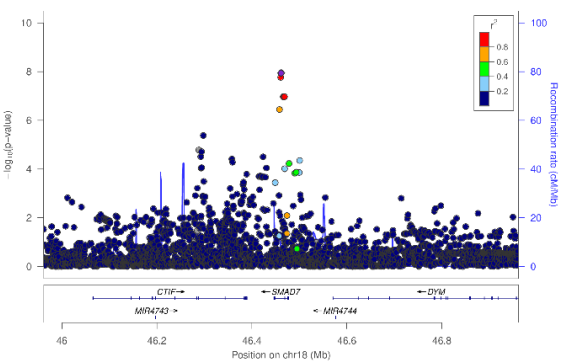

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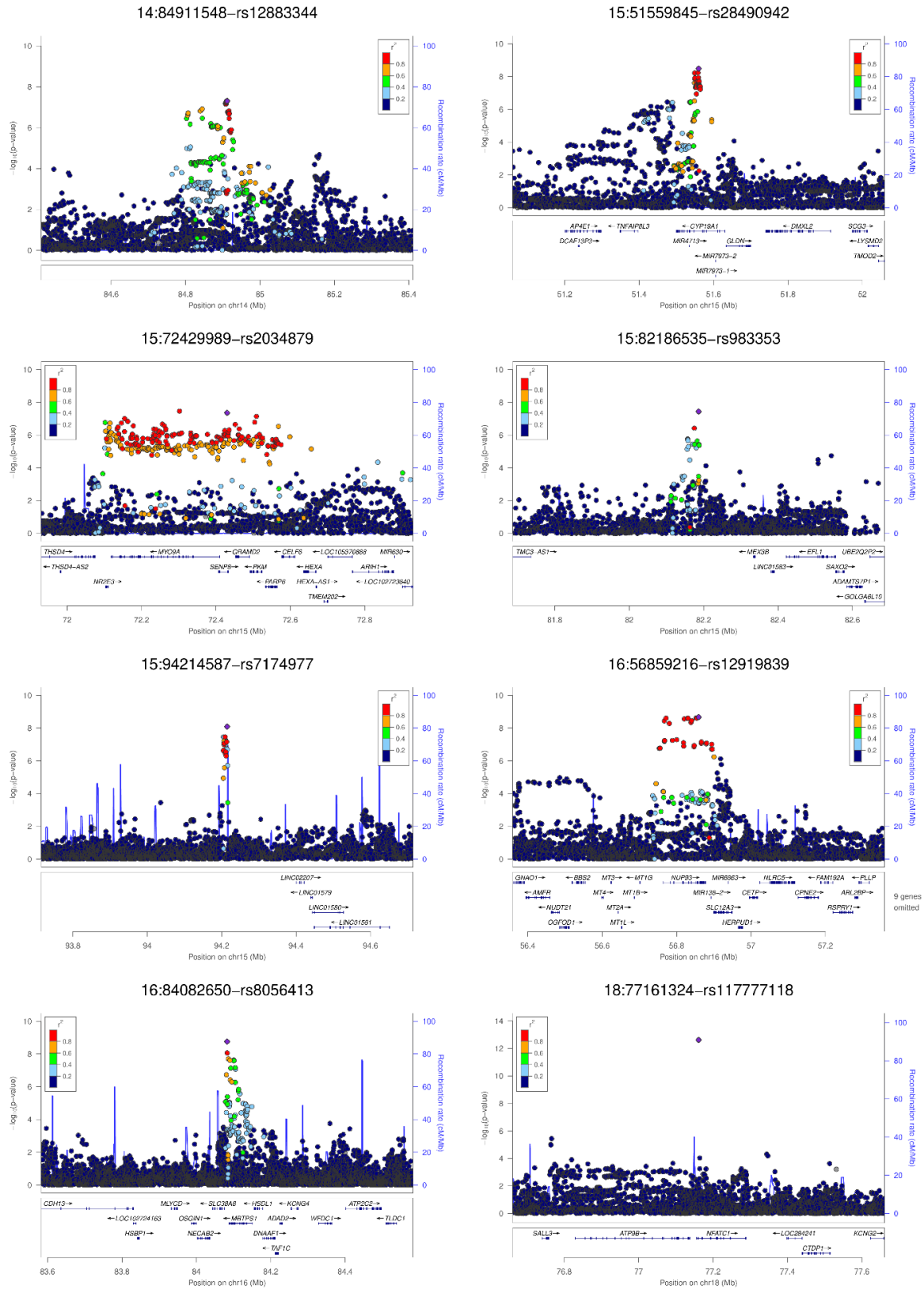
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16:56859216–rs12919839
16:84082650–rs8056413
18:77161324–rs117777118
Position on chr14 (Mb)
Position on chr15 (Mb)
Position on chr16 (Mb)
Position on chr18 (Mb)
Recombination rate (cM/Mb)
9 genes omitted

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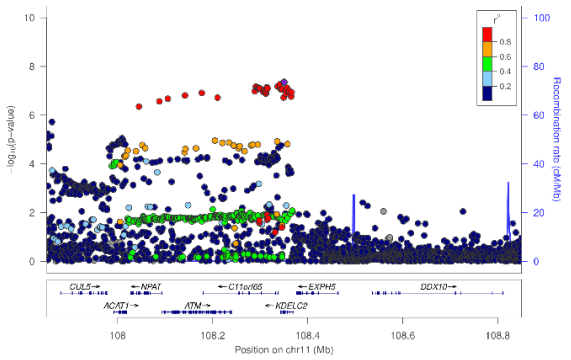

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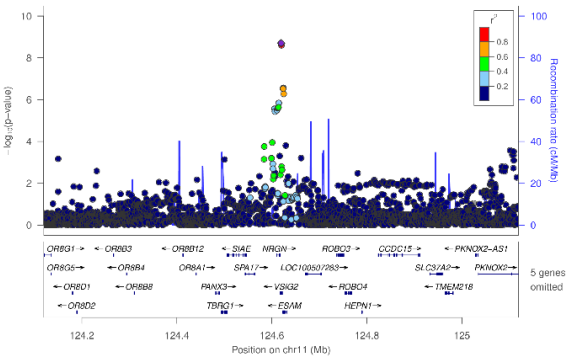

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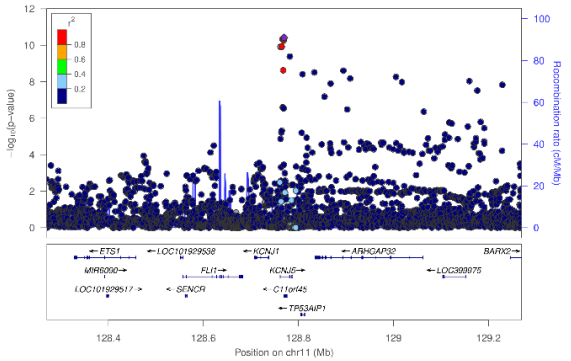

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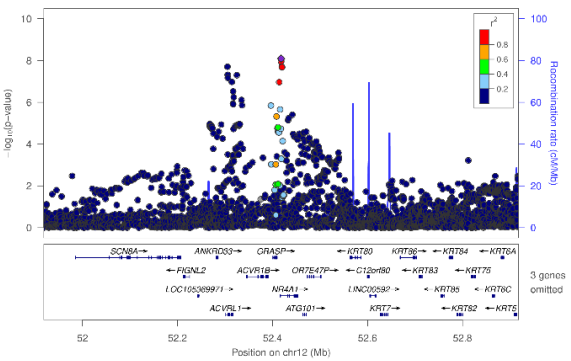

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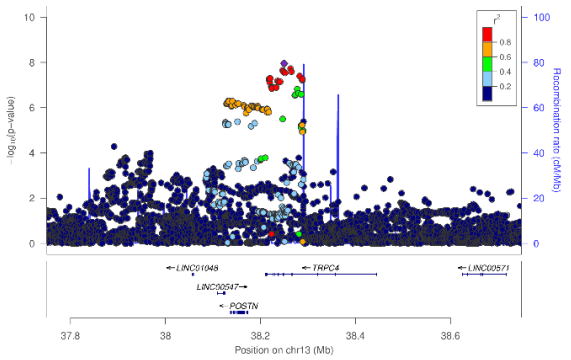

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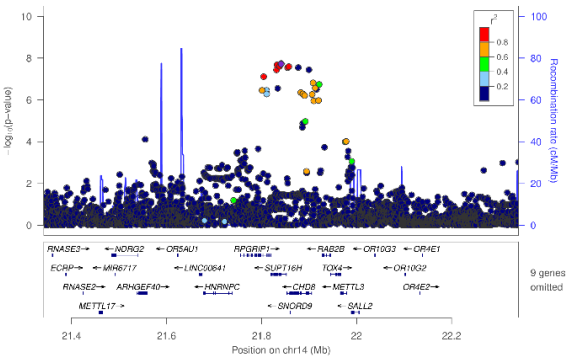

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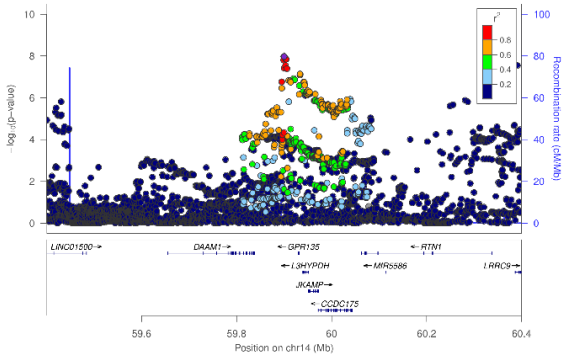

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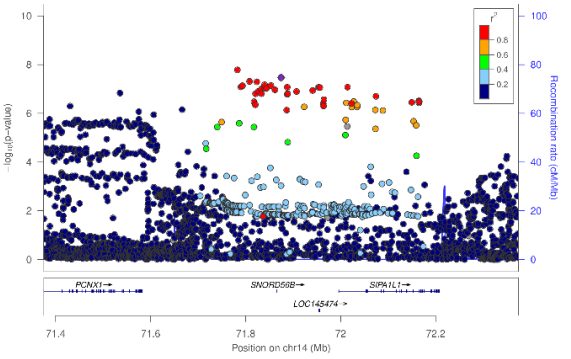

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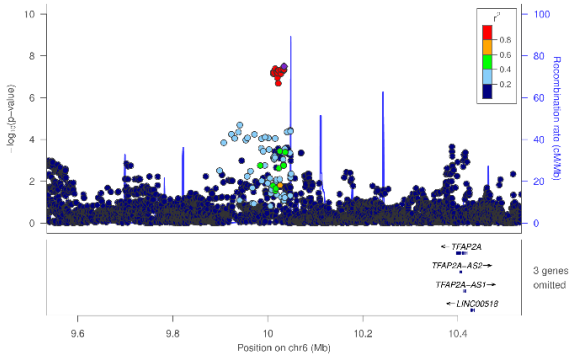

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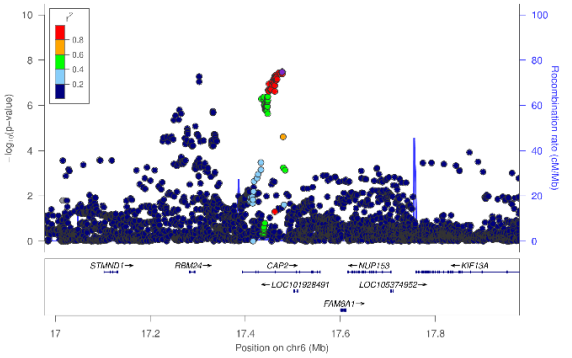

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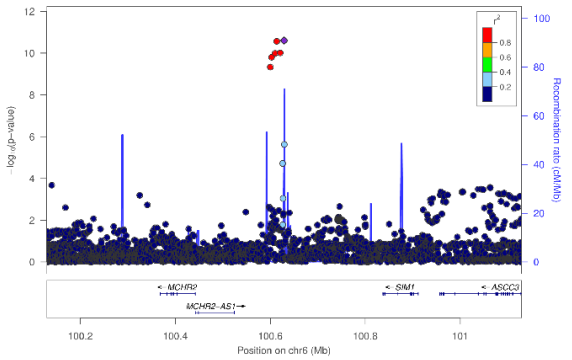

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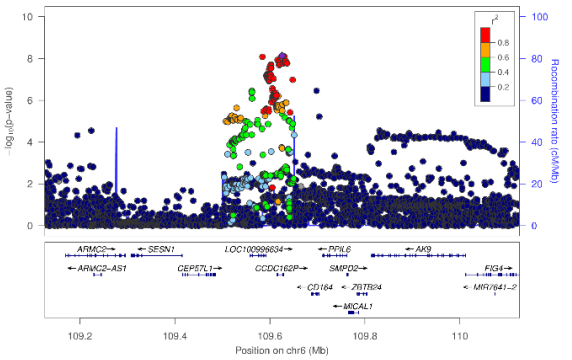

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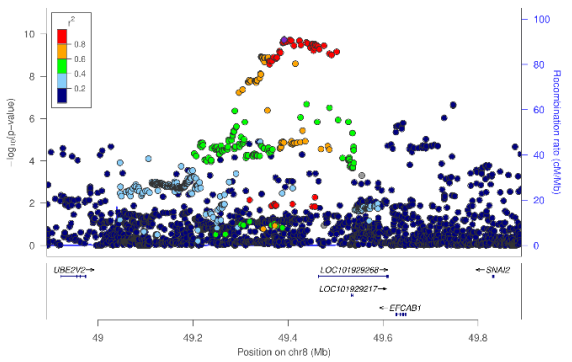

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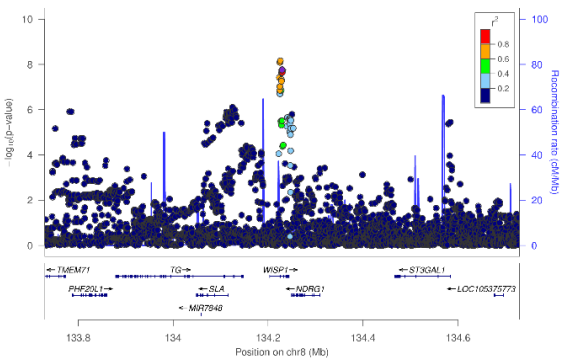

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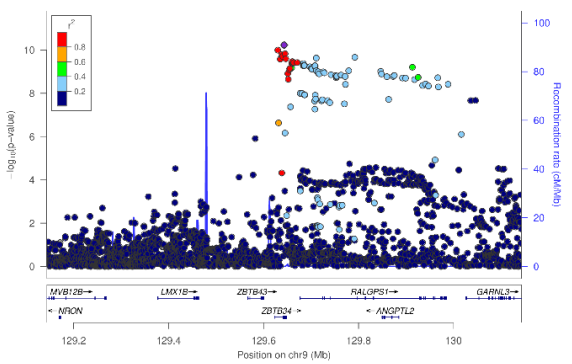

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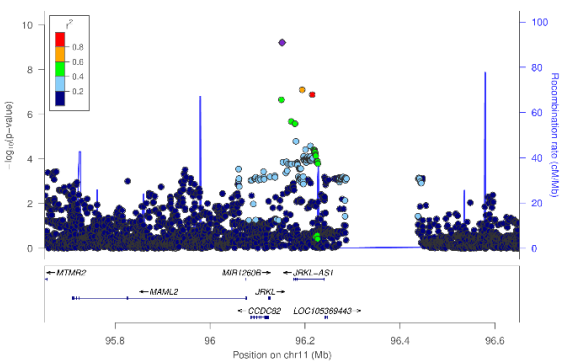

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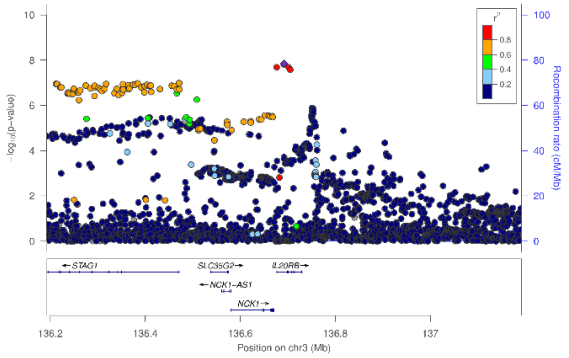

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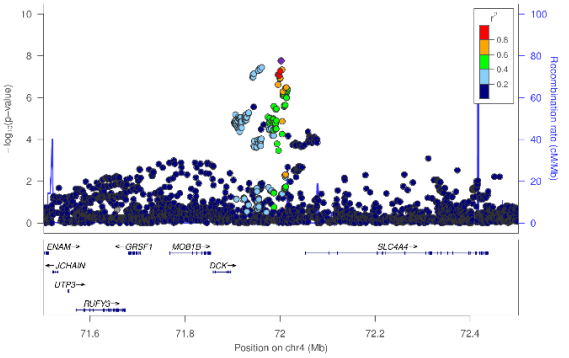

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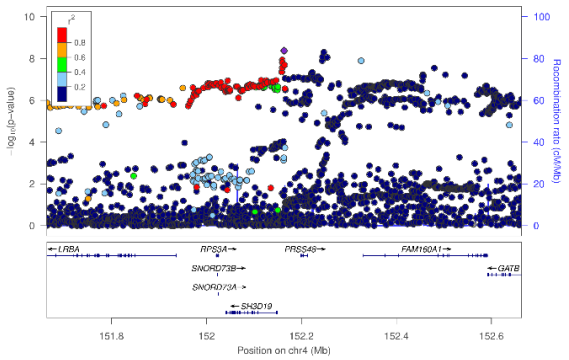

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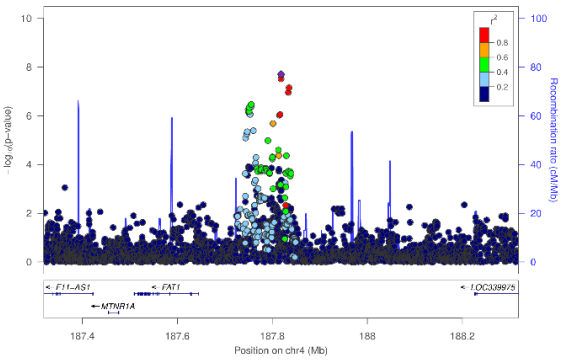

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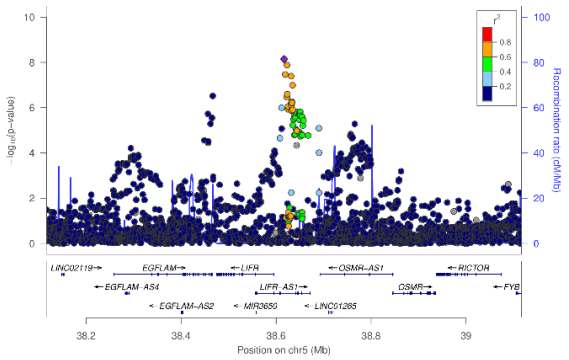

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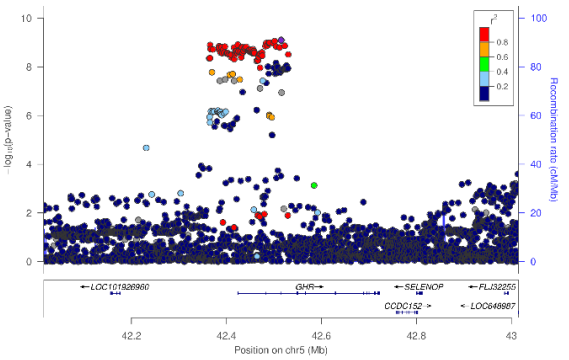

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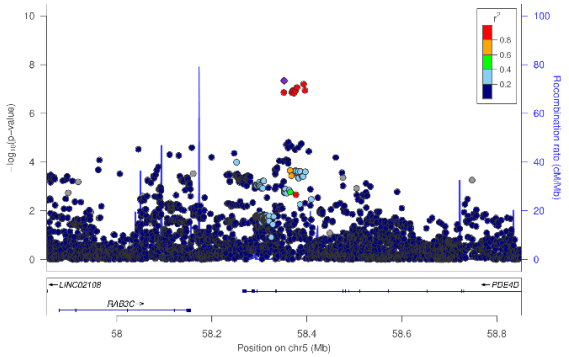

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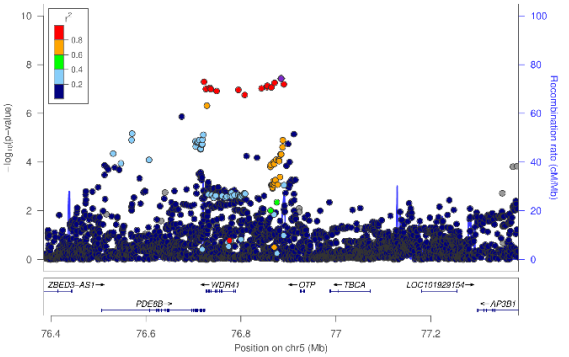

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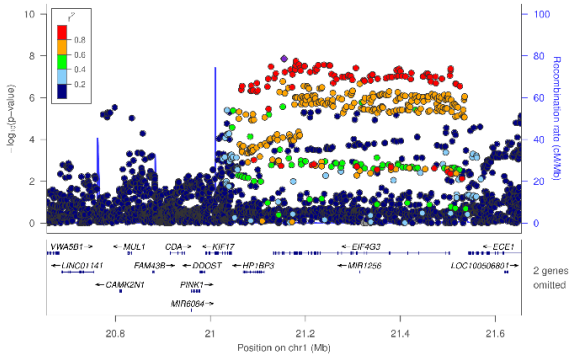

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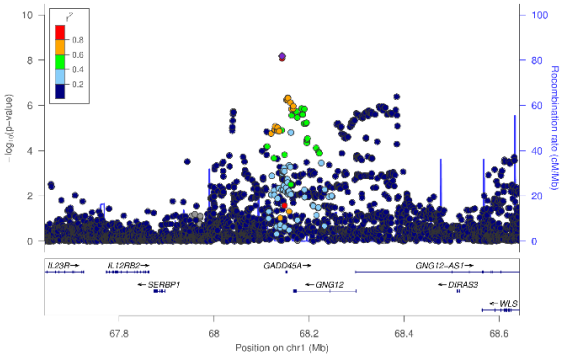

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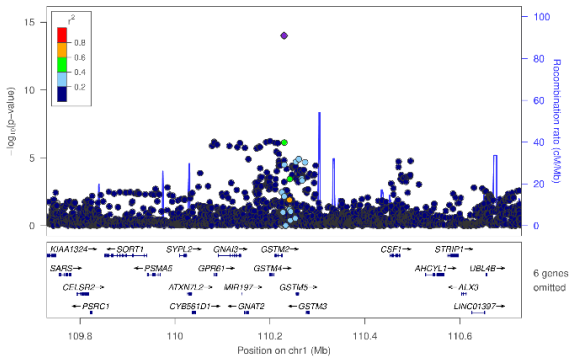

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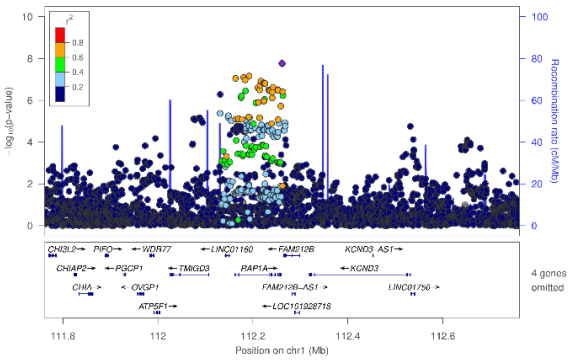

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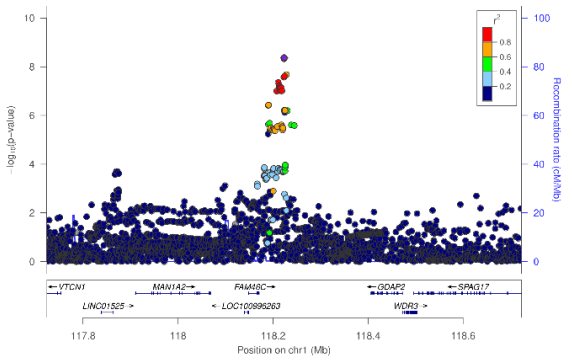

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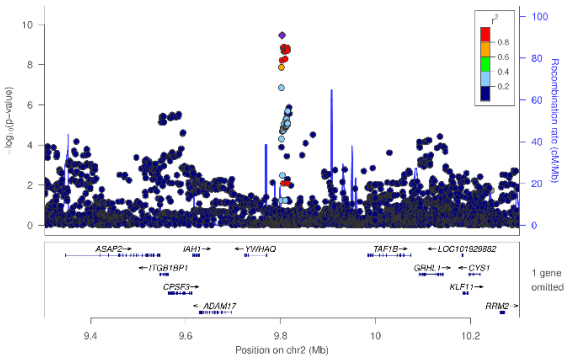

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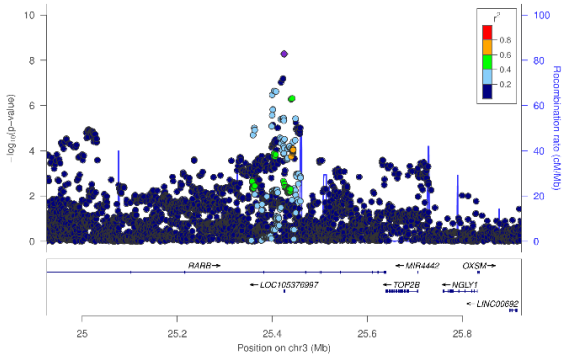

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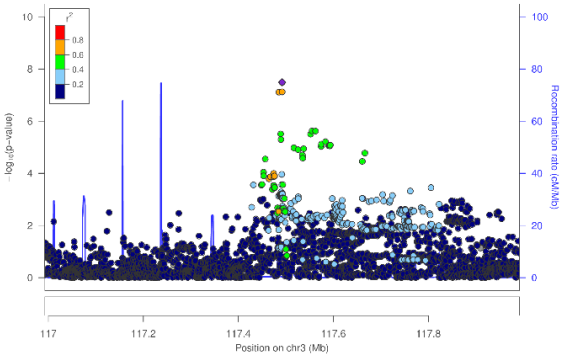

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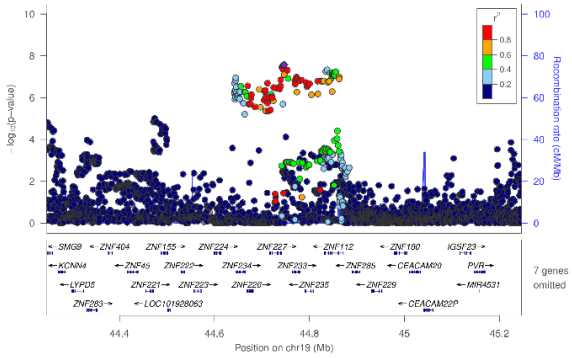

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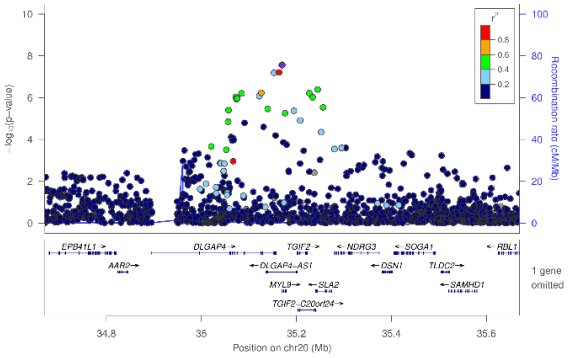
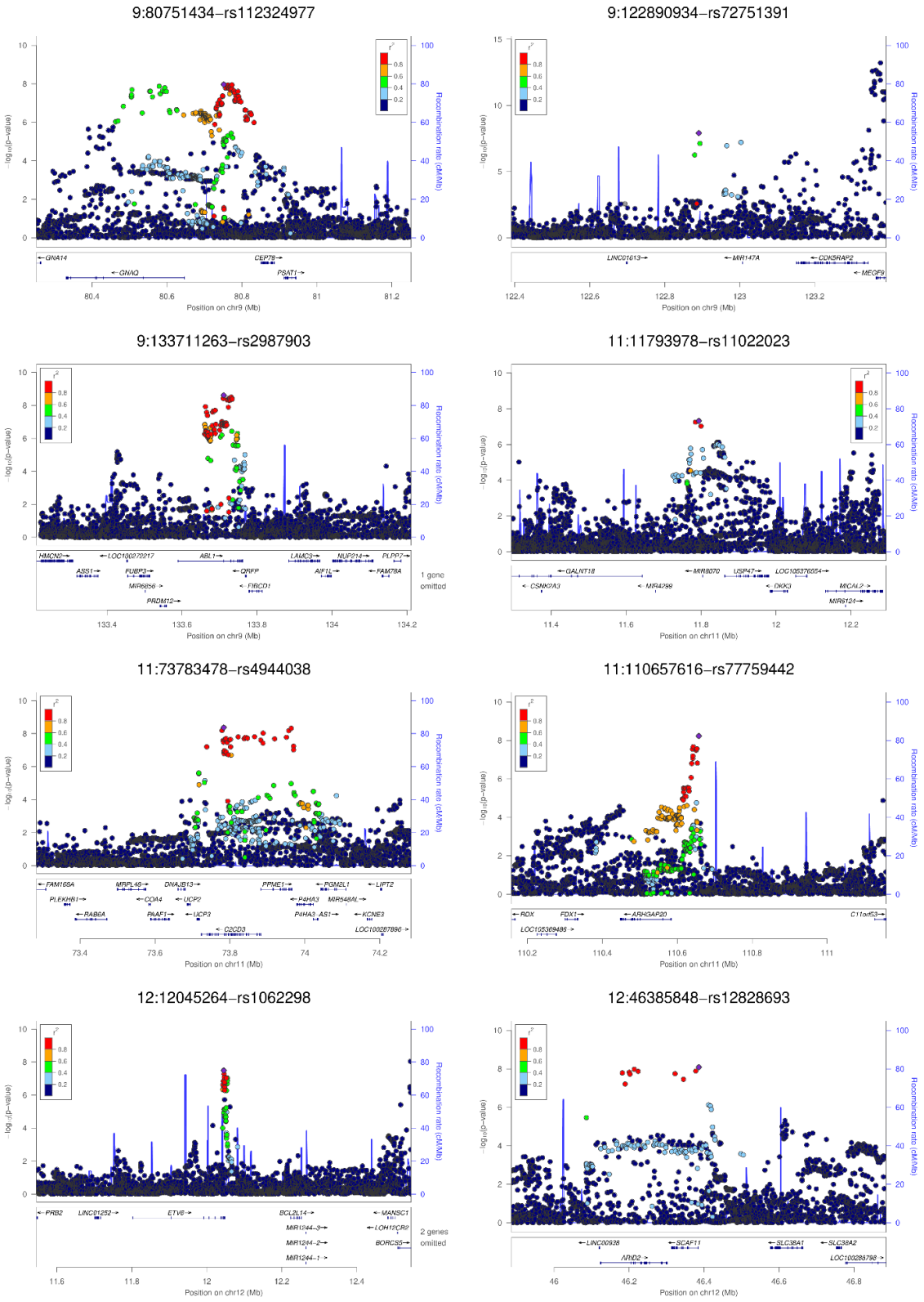
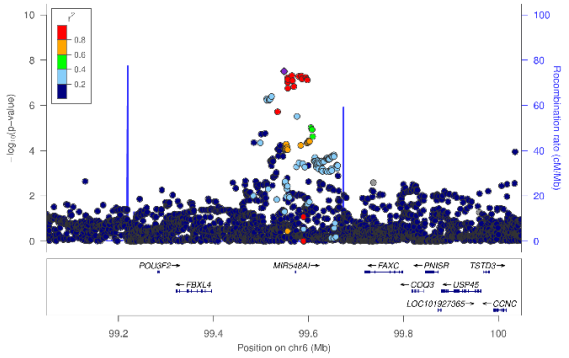


c


9:80751434–rs112324977
9:122890934–rs72751391
9:133711263–rs2987903
11:11793978–rs11022023
11:73783478–rs4944038
11:110657616–rs77759442
12:12045264–rs1062298
12:46385848–rs12828693
Position on chr9 (Mb)
Position on chr11 (Mb)
Position on chr12 (Mb)
Recombination rate (cM/Mb)
1 gene omitted
2 genes omitted

6:99548729–rs72943226



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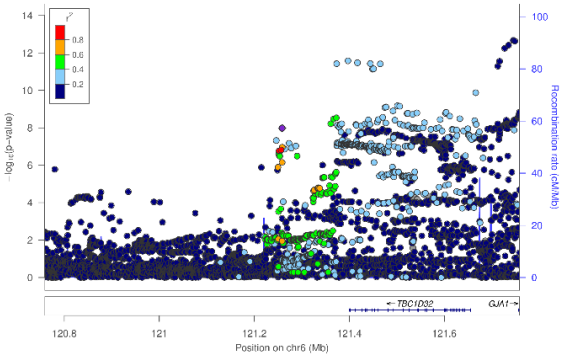

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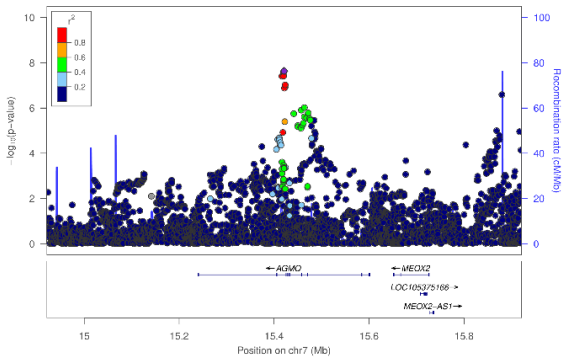

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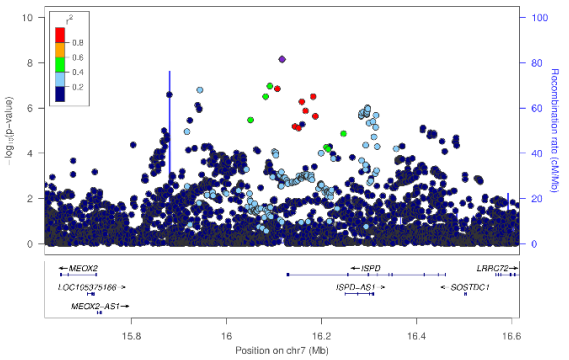

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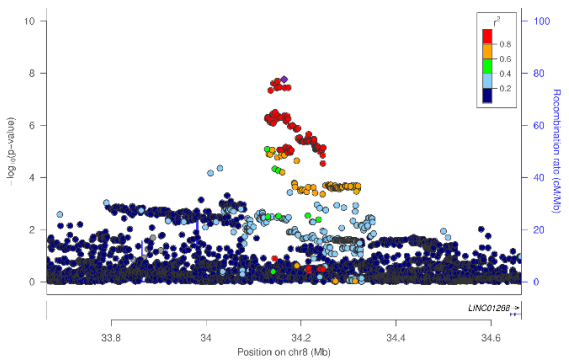

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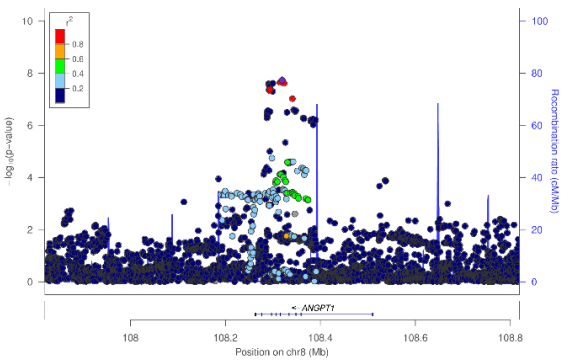

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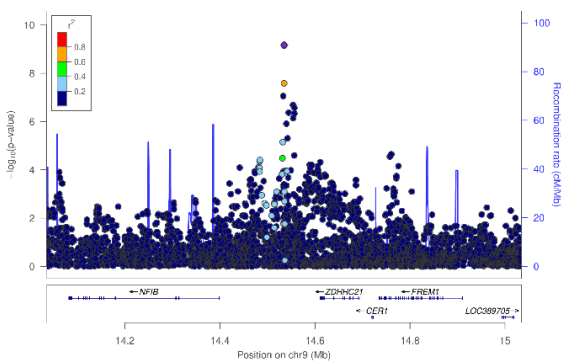

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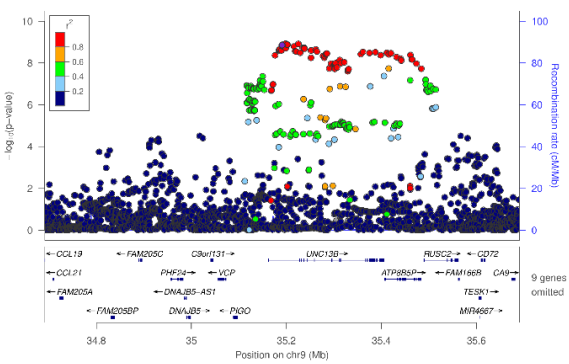

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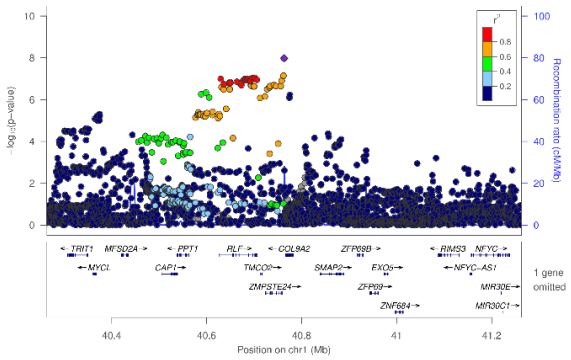

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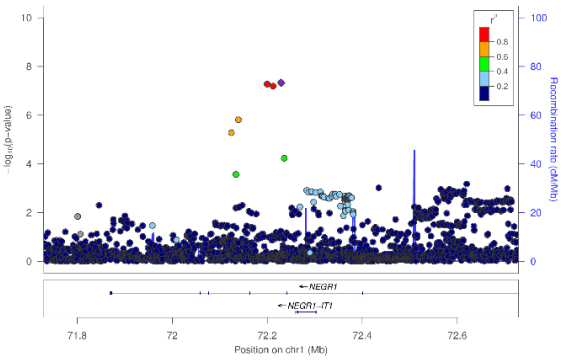

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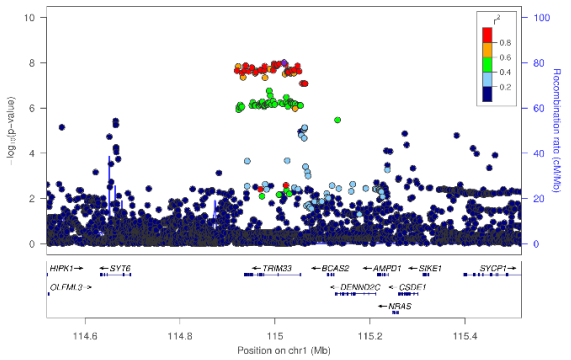

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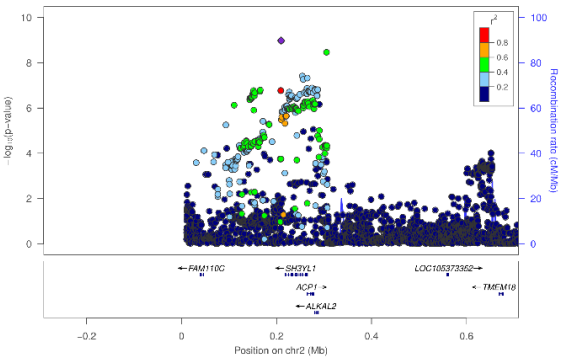

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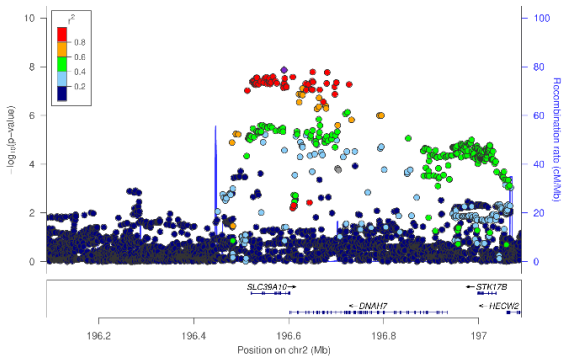

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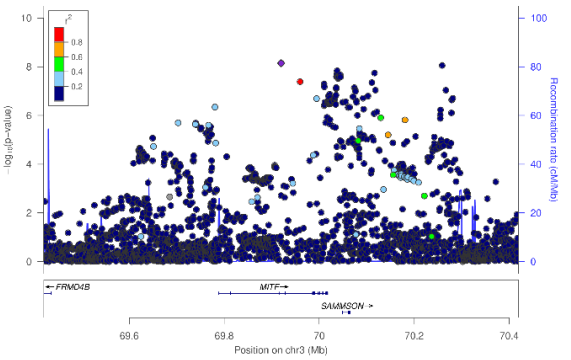

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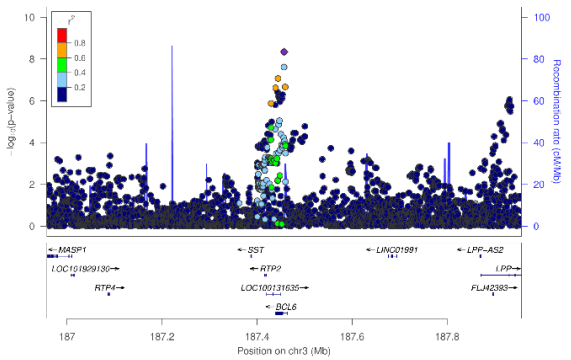
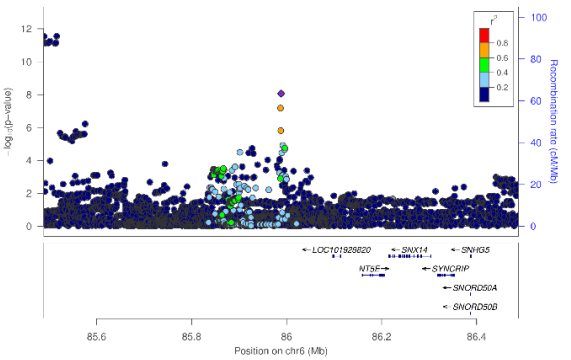
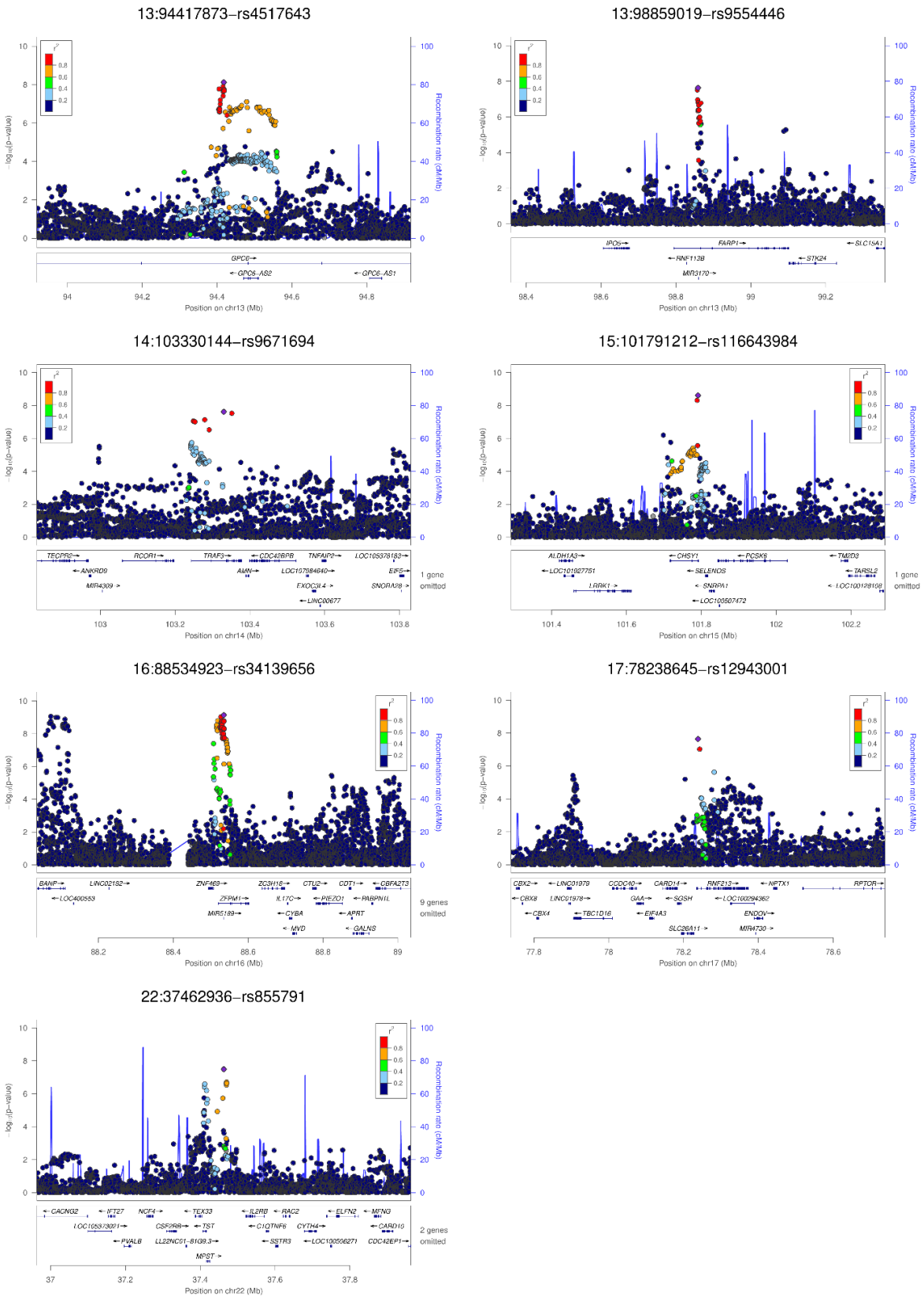
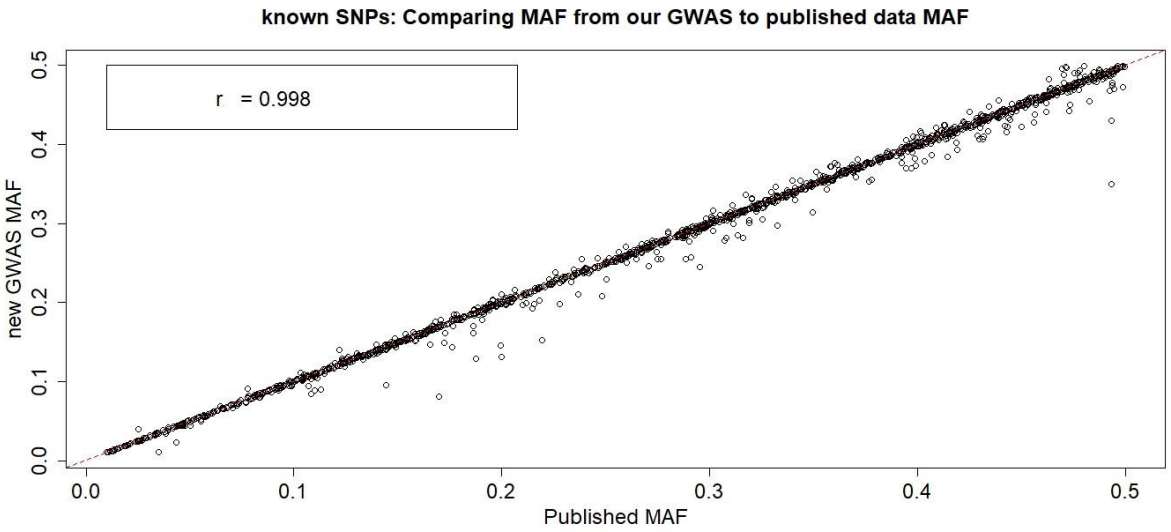


6:85988429–rs4053778

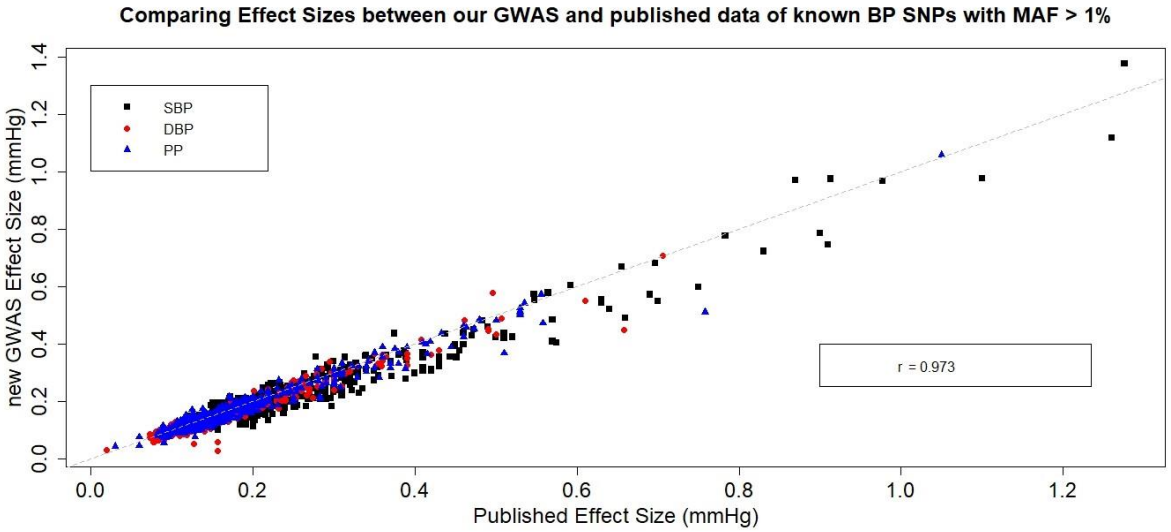




Supplementary Figure 3a-c. Locus Zoom plots for all novel loci for systolic (a), diastolic (b), and pulse pressure (c). P-values are from the inverse variance-weighted meta-analyses for each blood pressure trait and presented in logarithmic scale.

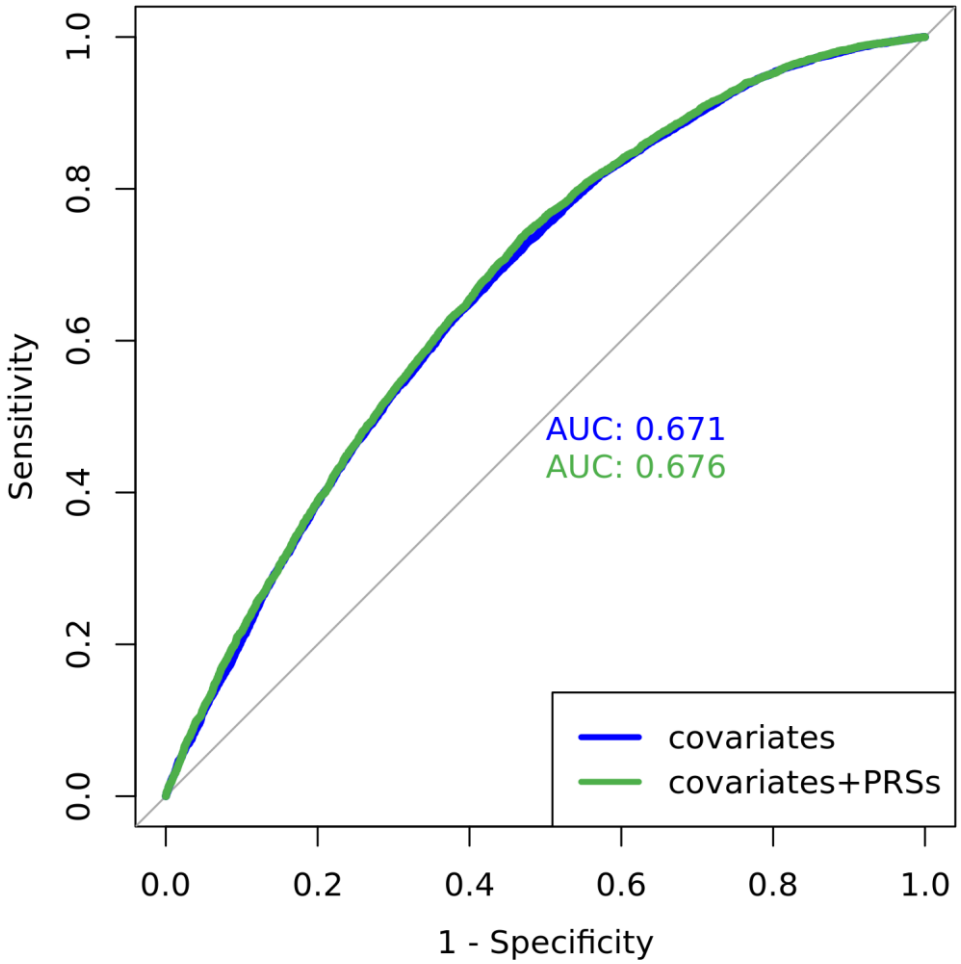


Supplementary Figure 4. Known SNPs: Comparing MAF from our GWAS to published data MAF. The x-axis shows the published MAF according to data taken from the publication where SNP is first reported (see PMID in Sup Table of all 3,800 known SNPs). The y-axis shows the MAF from our GWAS meta-analysis. The correlation between the published and observed MAF values is shown in the plot legend. For fair comparison, SNPs shown in this plot are restricted only to known SNPs published from main-effect primary GWAS analyses (i.e. excluding SNPs from conditional analyses, stratified or interaction analyses) in studies of predominantly European ancestry, with MAF > 1%, covered in our GWAS meta-analysis data, and with available data on both MAF and untransformed Effect Sizes on the mmHg scale reported in the original publication's published Tables, resulting in 1,483 SNPs plotted of the total 3,800 published SNPs. MAF: Minor Allele Frequency; GWAS: Genome-Wide Association Study; r: Pearson's Correlation Coefficient

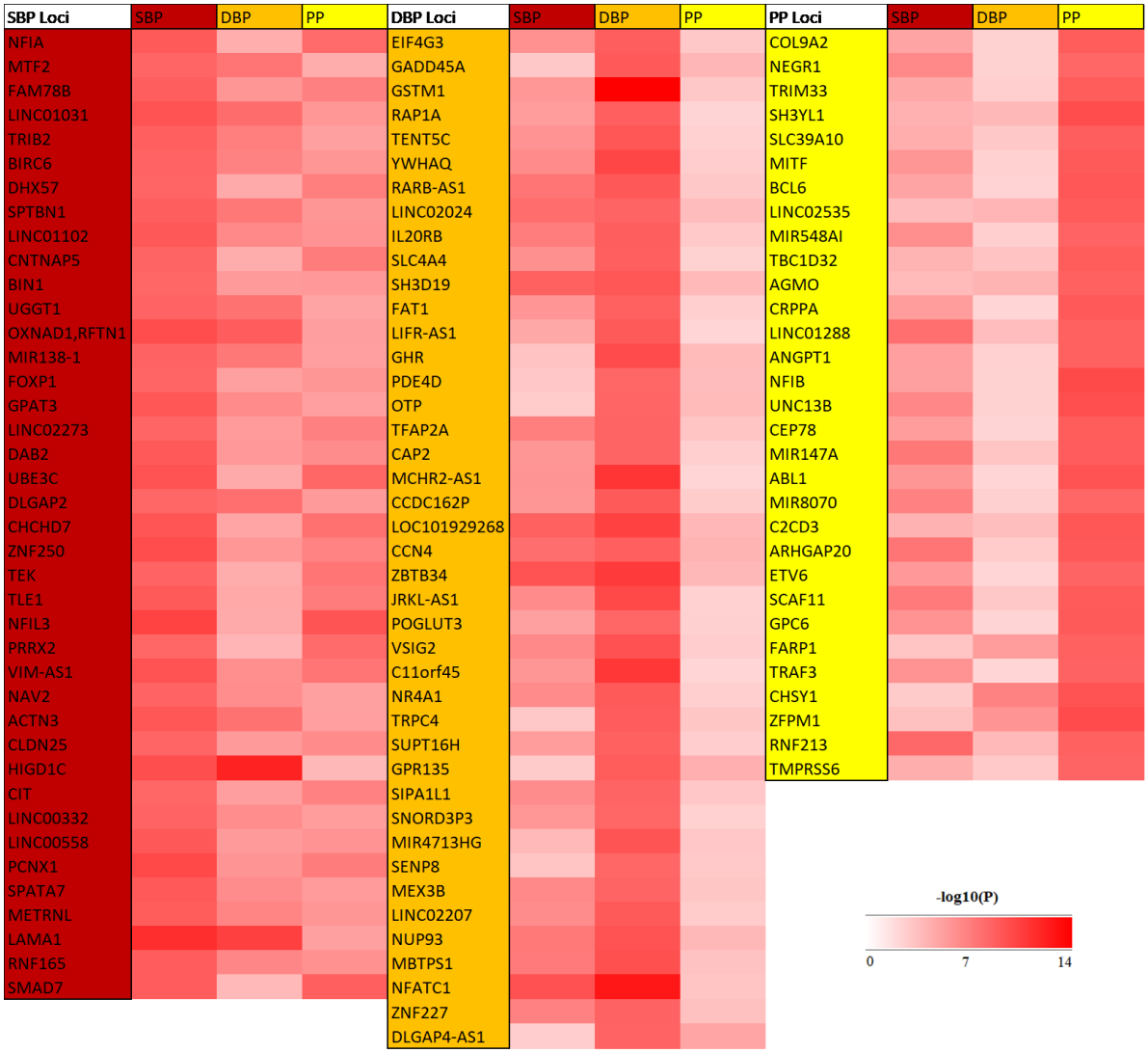


Supplementary Figure 5. Comparing Effect Sizes between our GWAS and published data of known BP SNPs. The x-axis shows the magnitude of the published effect size estimate (mmHg) according to data taken from the publication where SNP is first reported (see PMID

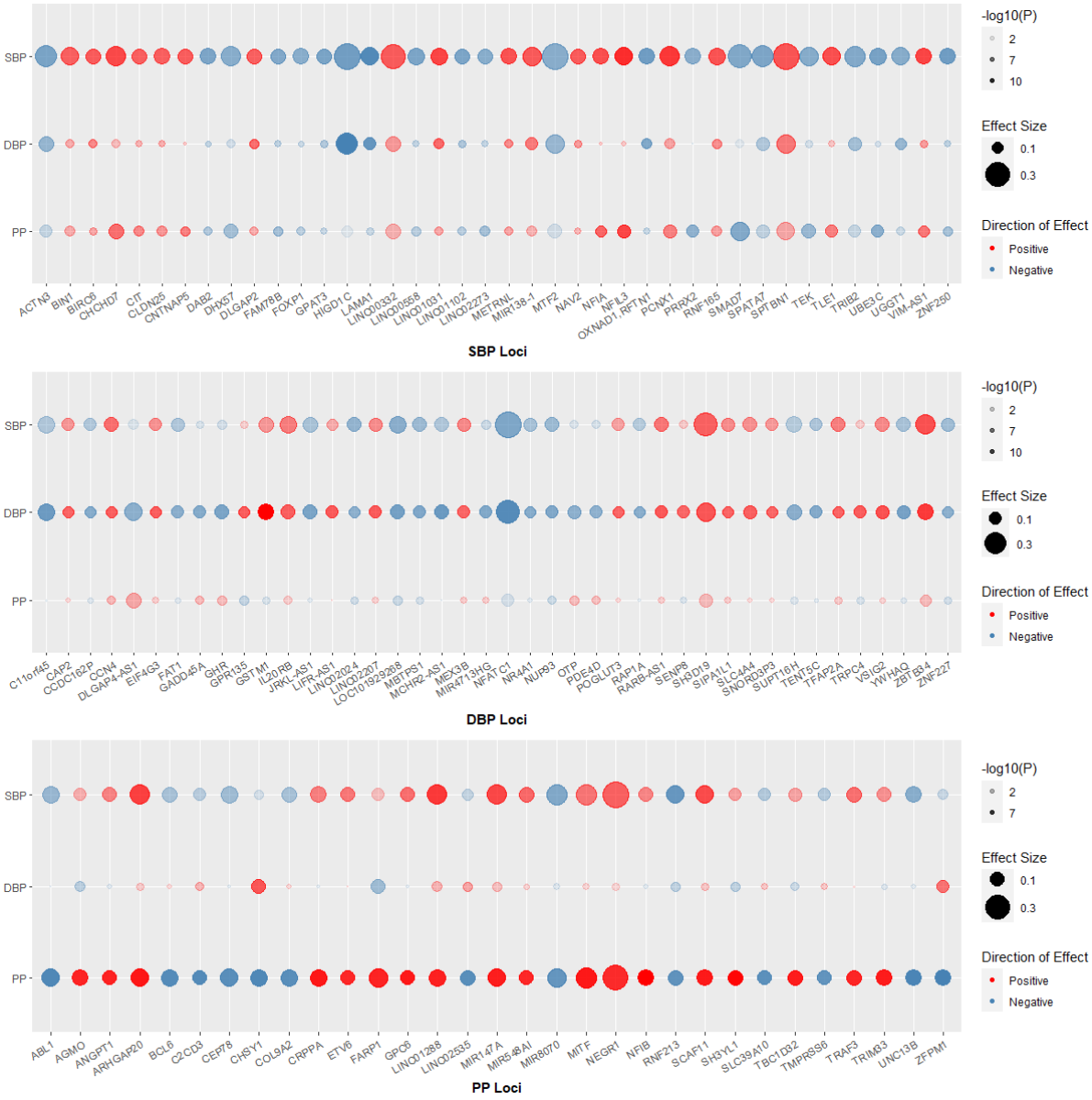
in Sup Table of all 3,800 known SNPs). The y-axis shows the magnitude of the effect size estimate (mmHg) from our GWAS meta-analysis. Each SNP is only plotted once according to the primary, most significant BP trait that the SNP was reported for from the original publication, as indicated by the differentiating colour-coded plot shapes per BP trait, explained in the plot legend. The correlation between the published and observed effect sizes is shown in the plot legend. For fair comparison, SNPs shown in this plot are restricted only to known SNPs published from main-effect primary GWAS analyses (i.e. excluding SNPs from conditional analyses, stratified or interaction analyses) in studies of predominantly European ancestry, with MAF > 1%, covered in our GWAS meta-analysis data, and with available data on both MAF and untransformed Effect Sizes on the mmHg scale reported in the original publication's published Tables, resulting in 1,483 SNPs plotted of the total 3,800 published SNPs. BP: blood pressure; MAF: Minor Allele Frequency; GWAS: Genome-Wide Association Study; r: Pearson's Correlation Coefficient



Supplementary Figure 6: PRS AUROC in AA: Area under the ROC curve (AUROC) of the two models (covariates only and covariates plus SBayesRC PRS) for HTN in African-American ancestry sub-sample of the All-Of-Us cohort (n=21,843).

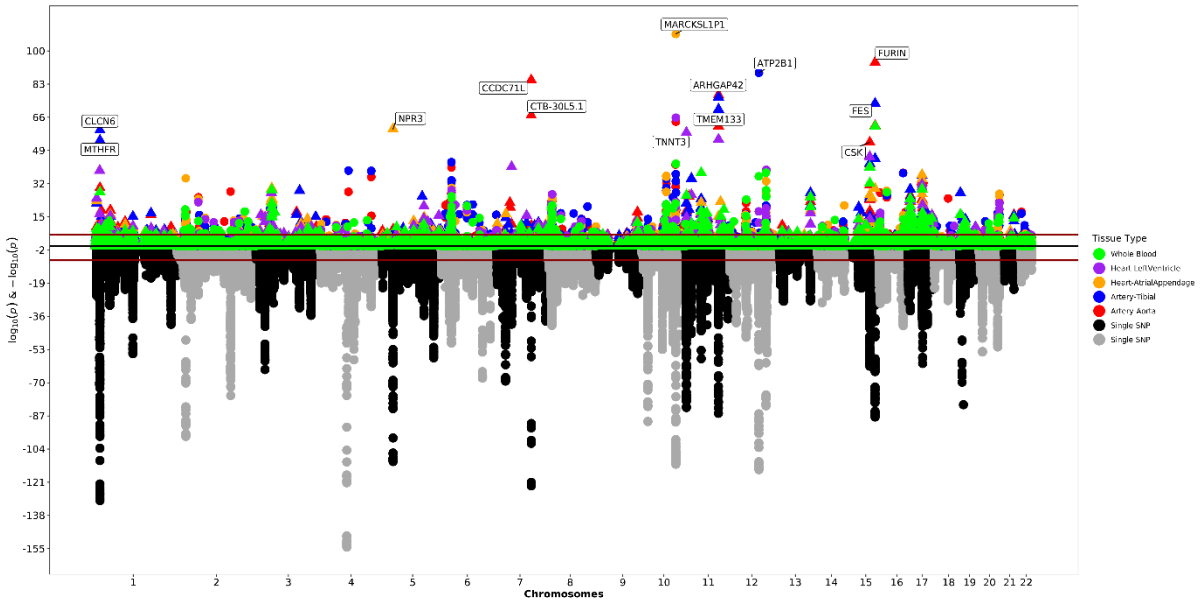


Supplementary Figure 7. Heatmap comparing significance of associations for 113 BP (Blood Pressure) novel loci across the other BP traits: SBP = systolic BP; DBP = diastolic BP; PP = Pulse Pressure. P-values are from the inverse variance-weighted meta-analyses for each blood pressure trait and presented in logarithmic scale.

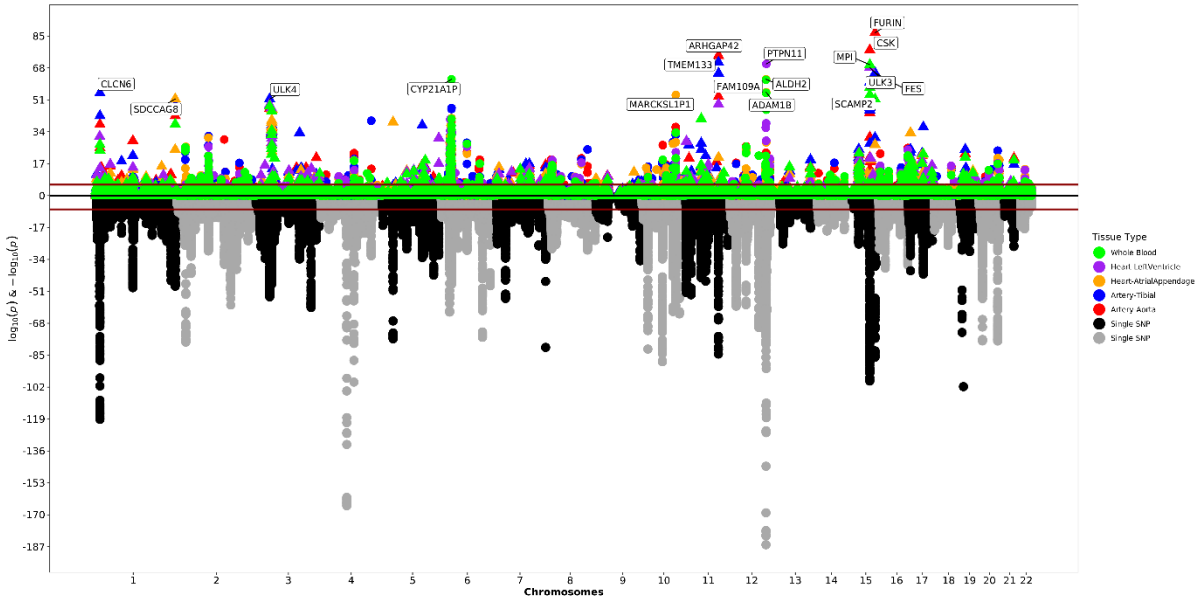


Supplementary Figure 8a-c. Bubble plots of associations for 113 Blood Pressure (BP) novel loci across other BP traits: SBP = systolic BP; DBP = diastolic BP; PP = Pulse Pressure. P-values are from the inverse variance-weighted meta-analyses for each blood pressure trait and presented in logarithmic scale.

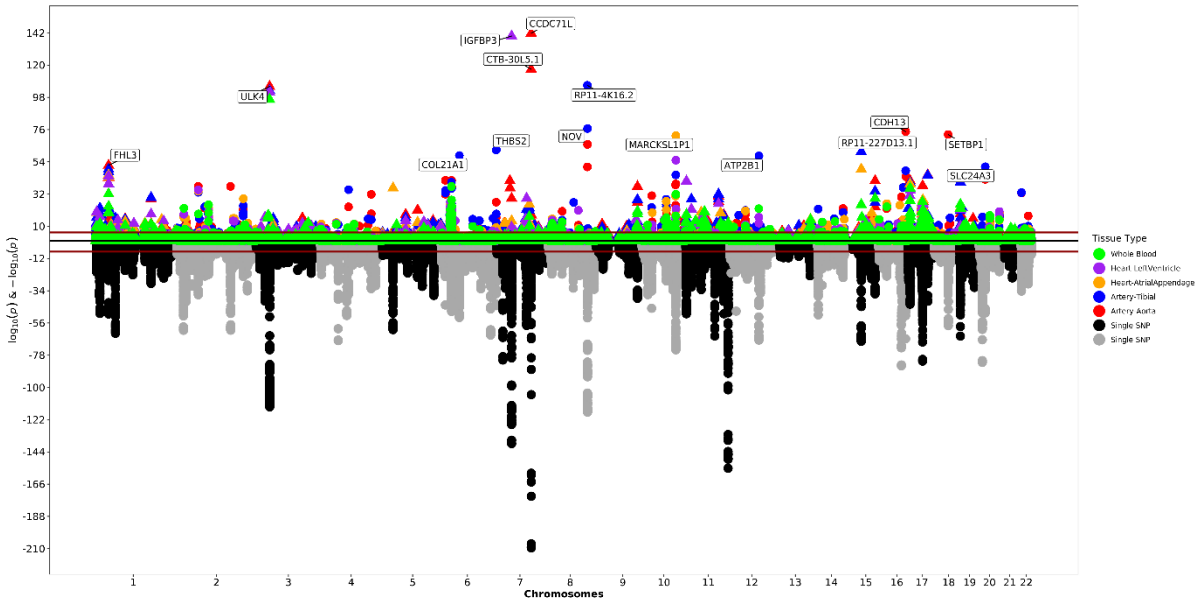
a


MARCKSL1P1
ATP2B1
FURIN
CCDC71L
ARHGAP42
CTB-30L5.1
FES
CLCN6
NPR3
TMEM133
MTHFR
TNNT3
CSK
Tissue Type
Whole Blood
Heart-AtrialAppendage
Artery-Tibial
Artery Aorta
Single SNP
Chromosomes

b

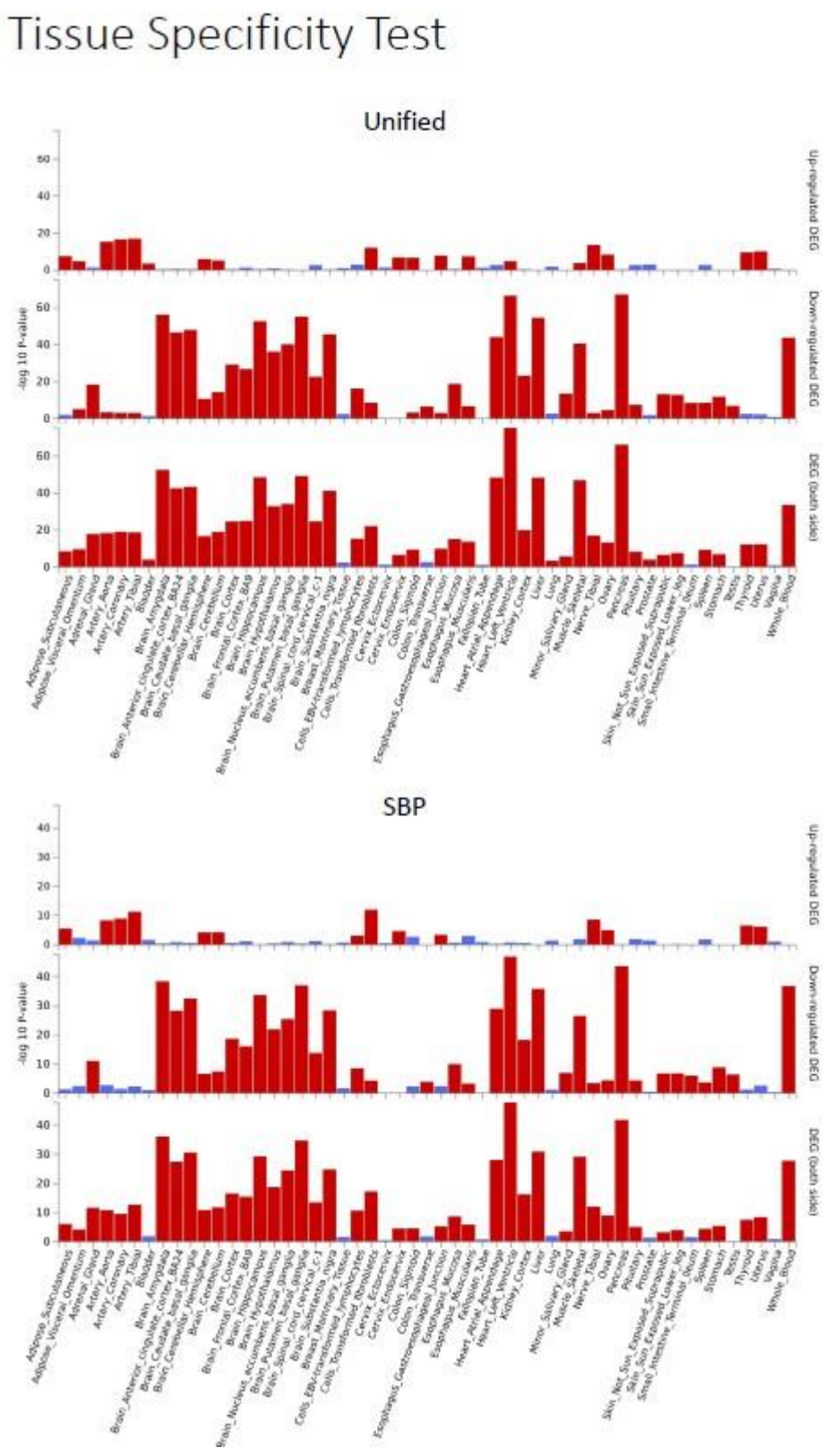

FURIN
CSK
ARHGAP42
PTPN11
TMEM133
MPI
CLCN6
ULK4
CYP21A1P
FAM109A
ALDH2
ULK3
FES
SDCCAG8
MARCKSL1P1
ADAM1B
SCAMP2
Tissue Type
Whole Blood
Heart-AtrialAppendage
Artery-Tibial
Artery Aorta
Single SNP
Chromosomes

c

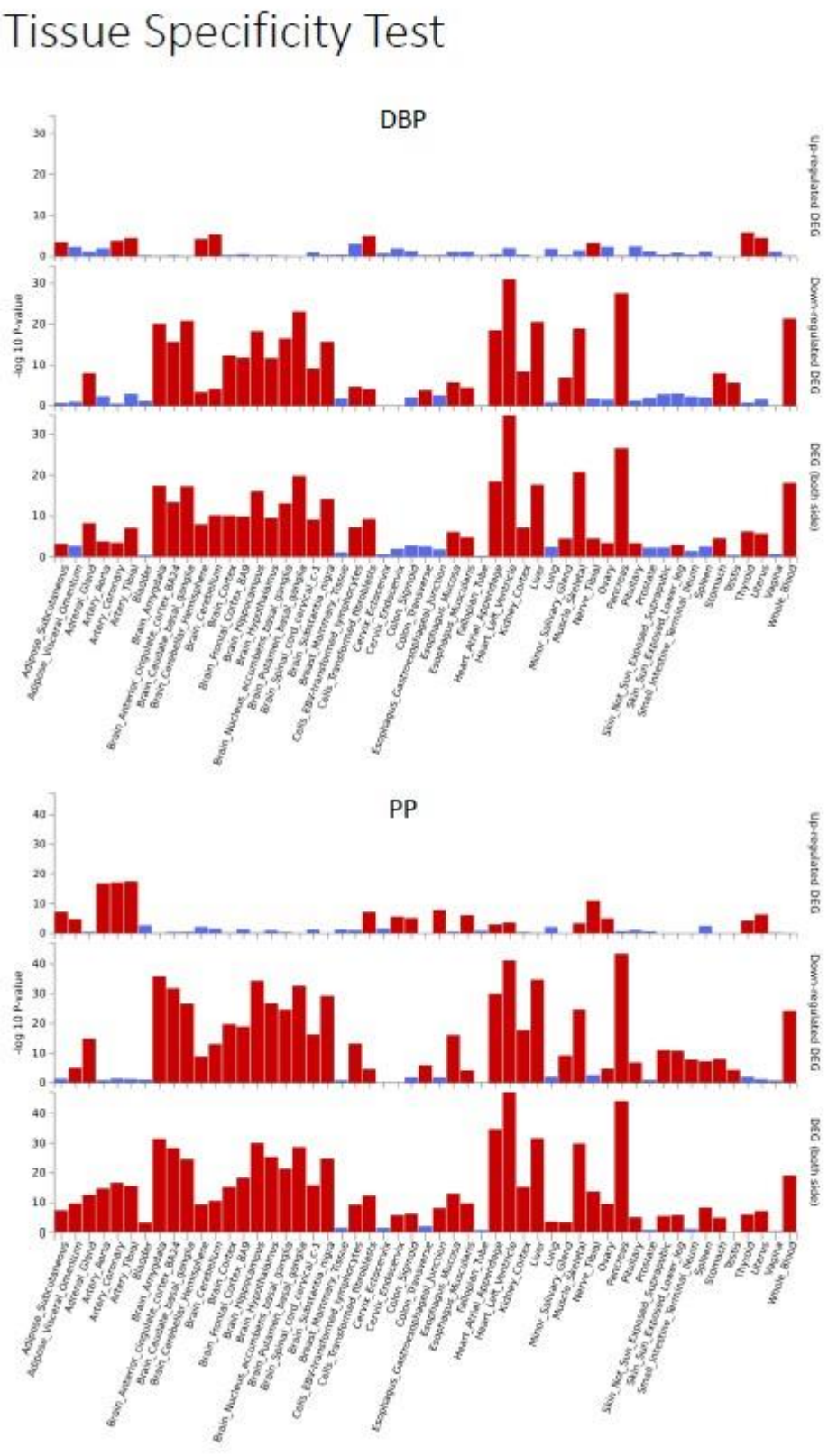


Supplementary Figure 9a-c. Opposed Manhattan plots for S-PrediXcan (–log10p) and GWAS (log10p) for BP-traits. $-Log_{10}$ p-values for associations between genetically predicted gene expression analyses with BP-traits in 5 tissues are juxtaposed with log_{10} p-values from the inverse variance-weighted GWAS meta-analyses for SBP (a); DBP (b) and PP (c).

a

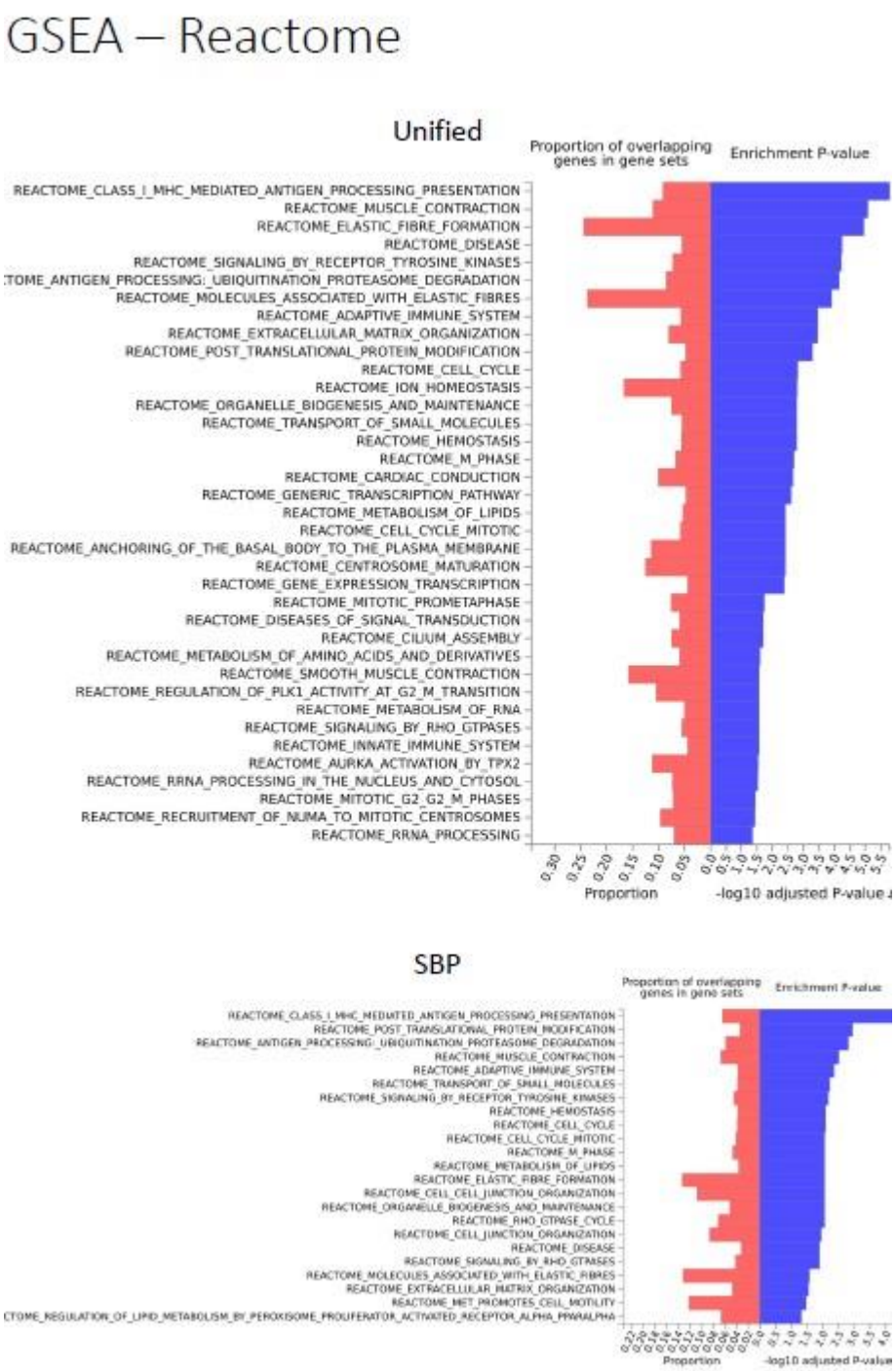

Tissue Specificity Test
Unified
SBP
-log 10 P-value
Up-regulated DEG
Down-regulated DEG
DEG (both side)
Adipose_Subcutaneous
Adipose_Visceral_Omentum
Adrenal_Gland
Artery_Aorta
Artery_Coronary
Artery_Tibial
Bladder
Brain_Amygdala
Brain_Anterior_cingulate_cortex_BA24
Brain_Caudate_basal_ganglia
Brain_Cerebellar_Hemisphere
Brain_Cerebellum
Brain_Cortex
Brain_Frontal_Cortex_BA9
Brain_Hippocampus
Brain_Hypothalamus
Brain_Nucleus_accumbens_basal_ganglia
Brain_Putamen_basal_ganglia
Brain_Spinal_cord_cervical_c-1
Brain_Substantia_nigra
Breast_Mammary_Tissue
Cells_EBV-transformed_lymphocytes
Cells_Transformed_fibroblasts
Cervix_Ectocervix
Cervix_Endocervix
Colon_Sigmoid
Colon_Transverse
Esophagus_Gastroesophageal_Junction
Esophagus_Mucosa
Esophagus_Muscularis
Fallopian_Tube
Heart_Atrial_Appendage
Heart_Left_Ventricle
Kidney_Cortex
Liver
Lung
Minor_Salivary_Gland
Muscle_Skeletal
Nerve_Tibial
Ovary
Pancreas
Pituitary
Prostate
Skin_Not_Sun_Exposed_Suprapubic
Skin_Sun_Exposed_Lower_leg
Small_Intestine_Terminal_Ileum
Spleen
Stomach
Testis
Thyroid
Uterus
Vagina
Whole_Blood

b

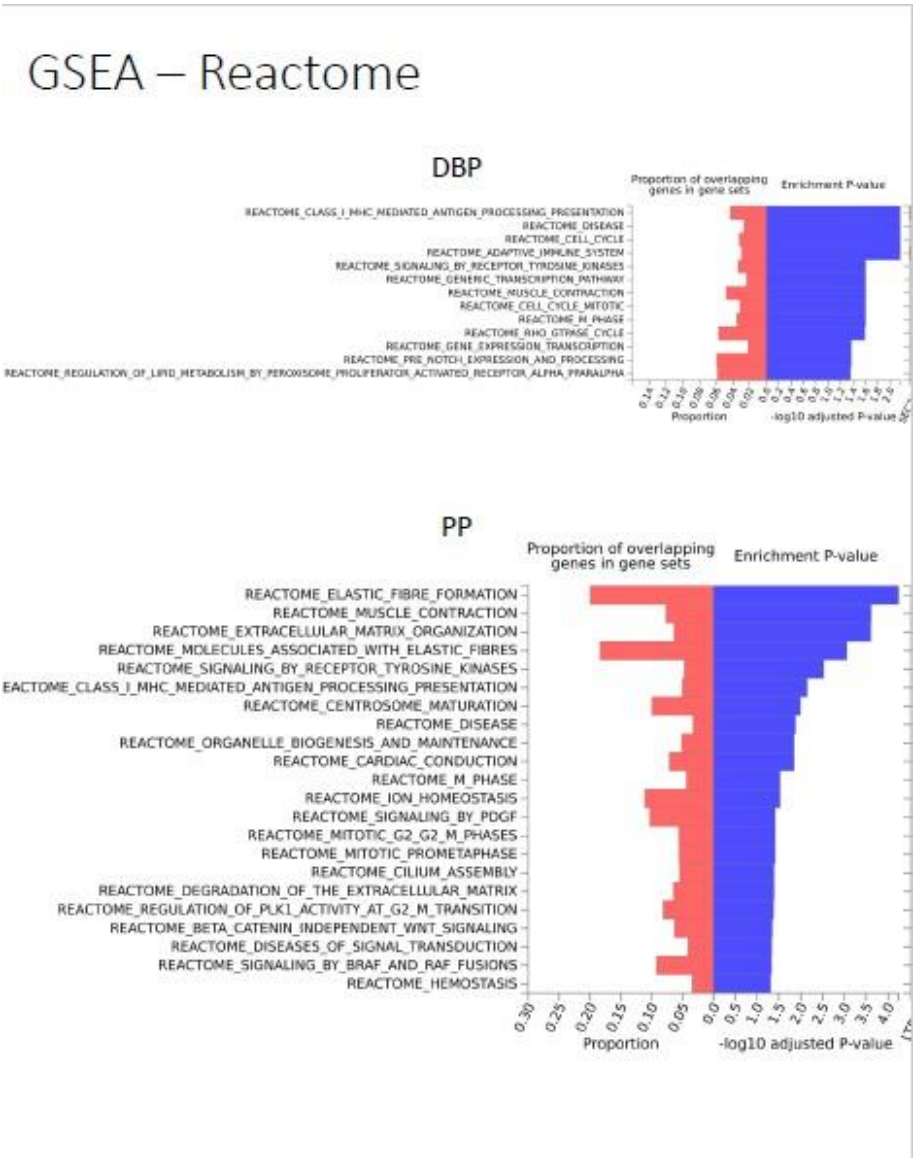

Tissue Specificity Test
DBP
PP
-log 10 P-value
Up-regulated DEG
Down-regulated DEG
DEG (both side)
Adipose_Subcutaneous
Adipose_Visceral_Omentum
Adrenal_Gland
Artery_Aorta
Artery_Coronary
Artery_Tibial
Bladder
Brain_Amygdala
Brain_Anterior_cingulate_cortex_BA24
Brain_Caudate_basal_ganglia
Brain_Cerebellar_Hemisphere
Brain_Cerebellum
Brain_Cortex
Brain_Frontal_Cortex_BA9
Brain_Hippocampus
Brain_Hypothalamus
Brain_Nucleus_accumbens_basal_ganglia
Brain_Putamen_basal_ganglia
Brain_Spinal_cord_cervical_c-1
Brain_Substantia_nigra
Breast_Mammary_Tissue
Cells_EBV-transformed_lymphocytes
Cells_Transformed_fibroblasts
Cervix_Ectocervix
Cervix_Endocervix
Colon_Sigmoid
Colon_Transverse
Esophagus_Gastroesophageal_Junction
Esophagus_Mucosa
Esophagus_Muscularis
Fallopian_Tube
Heart_Atrial_Appendage
Heart_Left_Ventricle
Kidney_Cortex
Liver
Lung
Minor_Salivary_Gland
Muscle_Skeletal
Nerve_Tibial
Ovary
Pancreas
Pituitary
Prostate
Skin_Not_Sun_Exposed_Suprapubic
Skin_Sun_Exposed_Lower_leg
Small_Intestine_Terminal_Ileum
Spleen
Stomach
Testis
Thyroid
Uterus
Vagina
Whole_Blood

Supplementary Figure 10: Results Output from FUMA Pathway Analyses: Tissue Specificity Test: (a) Unified Blood Pressure (BP) and Systolic BP (SBP); (b) Diastolic BP (DBP) and Pulse Pressure (PP). P-values of enrichment tests in different tissues are given on the y-axis in logarithmic scale.

a

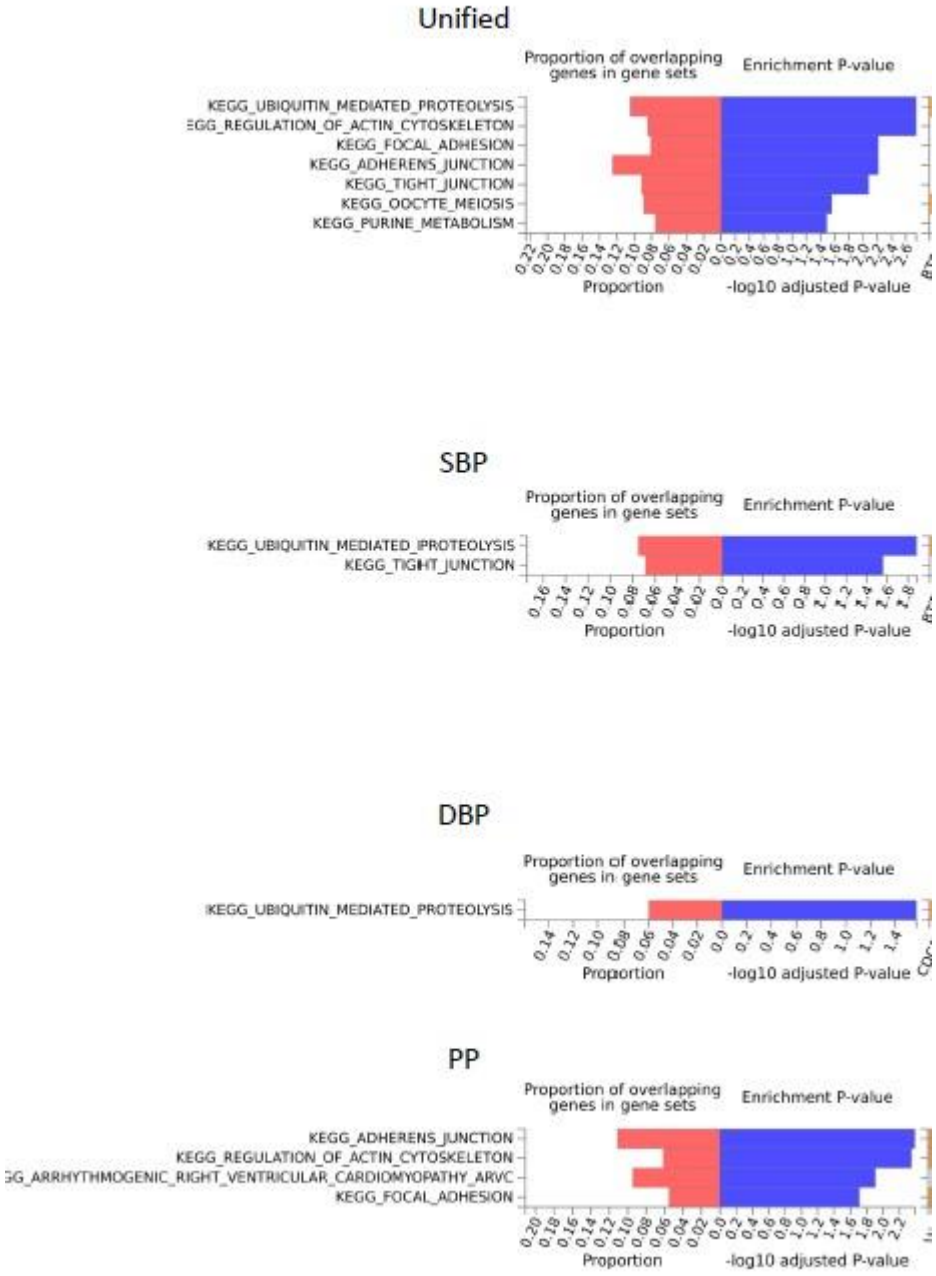


b



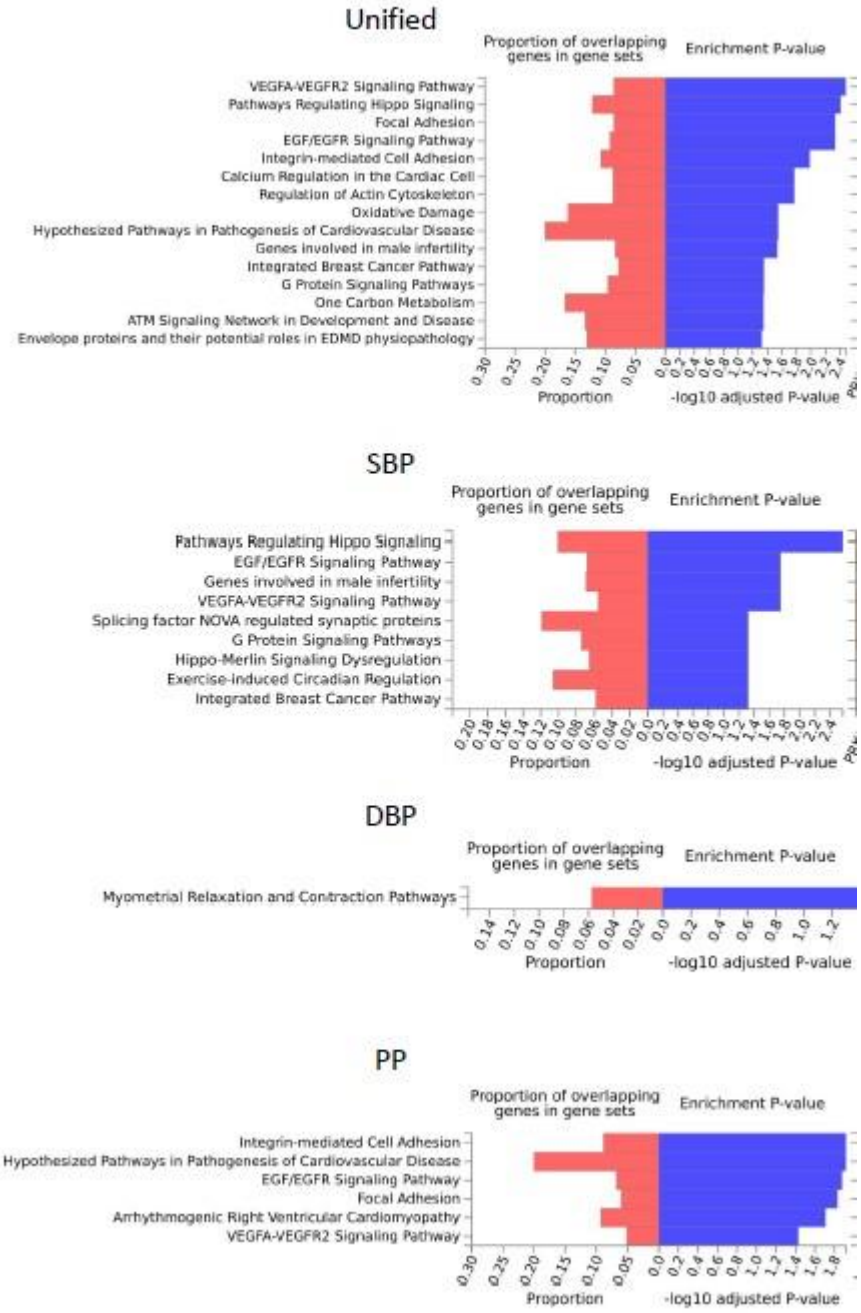
Supplementary Figure 11: Results Output from FUMA Pathway Analyses: GSEA Reactome: (a) Unified Blood Pressure (BP) and Systolic BP (SBP); (b) Diastolic BP (DBP) and Pulse Pressure (PP). P-values of enrichment tests in Reactome pathways are given on the x-axis in logarithmic scale as blue bars, together with the proportion of overlapping genes in gene sets as red bars.

GSEA – KEGG



Supplementary Figure 12: Results Output from FUMA Pathway Analyses: KEGG Pathways database: Unified Blood Pressure (BP); Systolic BP (SBP); Diastolic BP (DBP); Pulse Pressure (PP). P-values of enrichment tests in KEGG pathways are given on the x-axis in logarithmic scale as blue bars, together with the proportion of overlapping genes in gene sets as red bars.

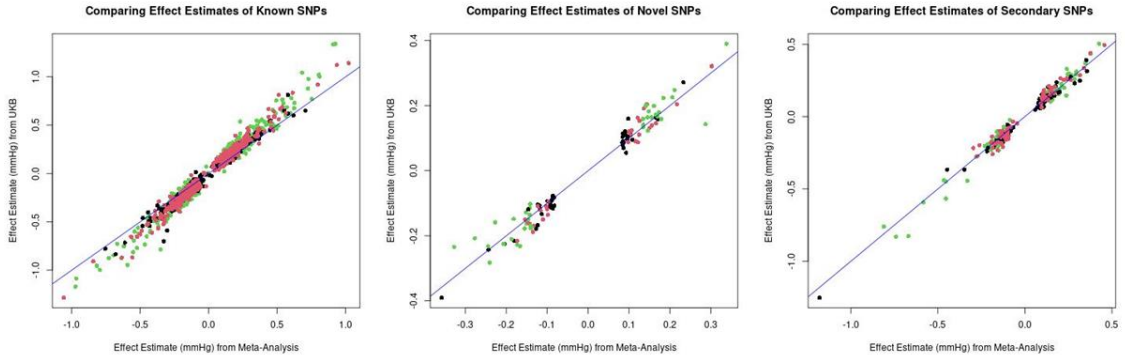
GSEA – WikiPathways



Supplementary Figure 13: Results Output from FUMA Pathway Analyses: Wiki Pathways: Unified Blood Pressure (BP); Systolic BP (SBP); Diastolic BP (DBP); Pulse Pressure (PP). P-values of enrichment tests in WikiPathways are given on the x-axis in logarithmic scale as blue bars, together with the proportion of overlapping genes in gene sets as red bars.

a

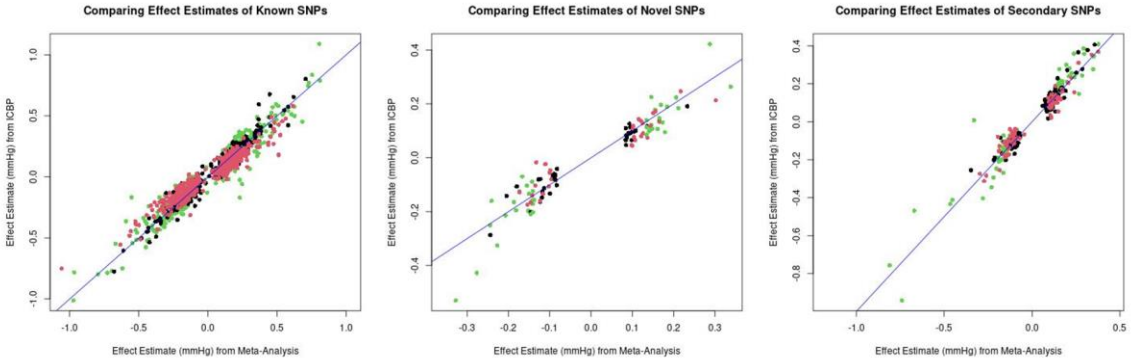
BETA plots: meta vs UKB: known / novel / sec



r = 0.987 r = 0.980 r = 0.989

b

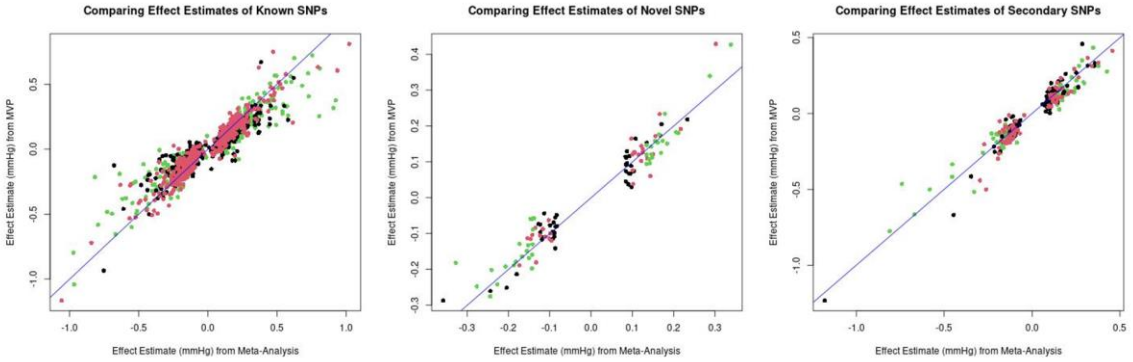
BETA plots: meta vs ICBP: known / novel / sec



r = 0.964 r = 0.951 r = 0.965

c

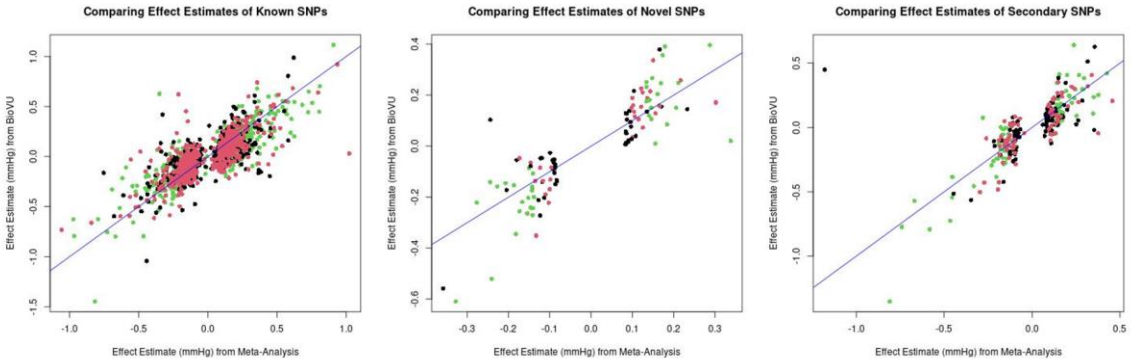
BETA plots: meta vs MVP: known / novel / sec



r = 0.935 r = 0.967 r = 0.962

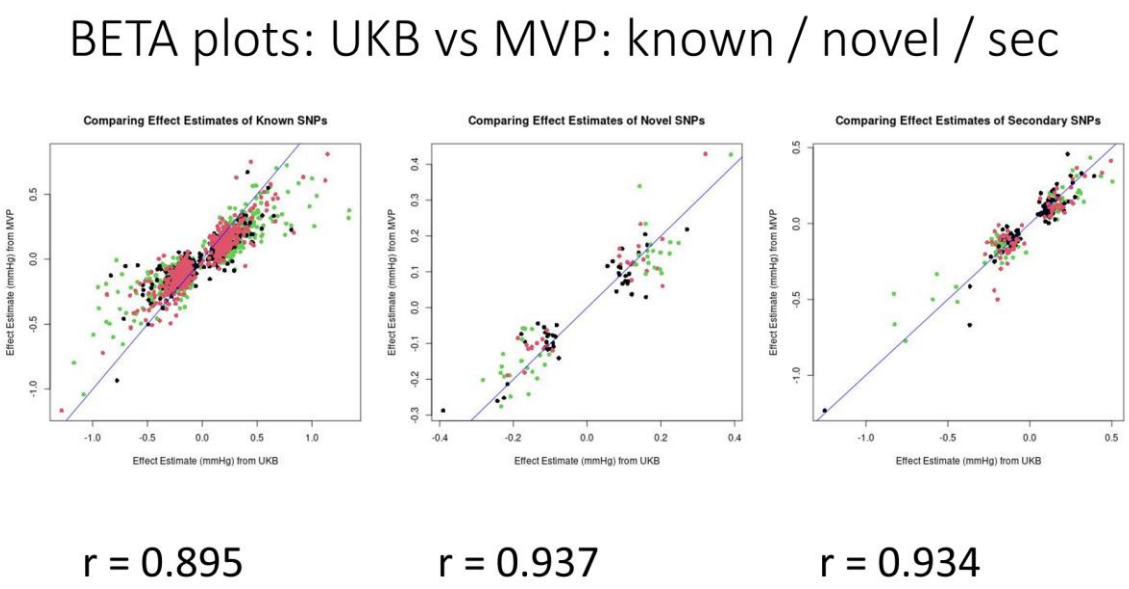
d

BETA plots: meta vs BioVU: known / novel / sec



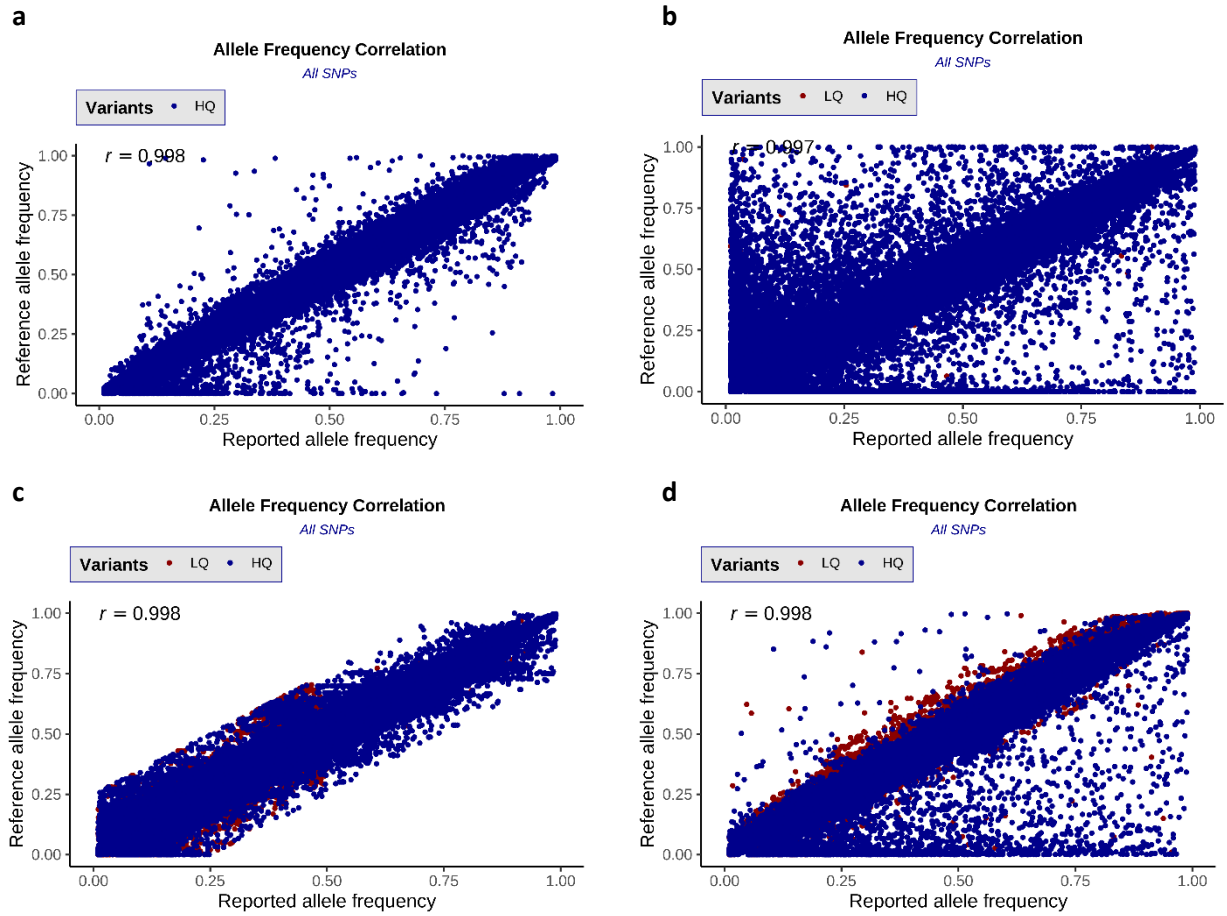
r = 0.796 r = 0.865 r = 0.756

e

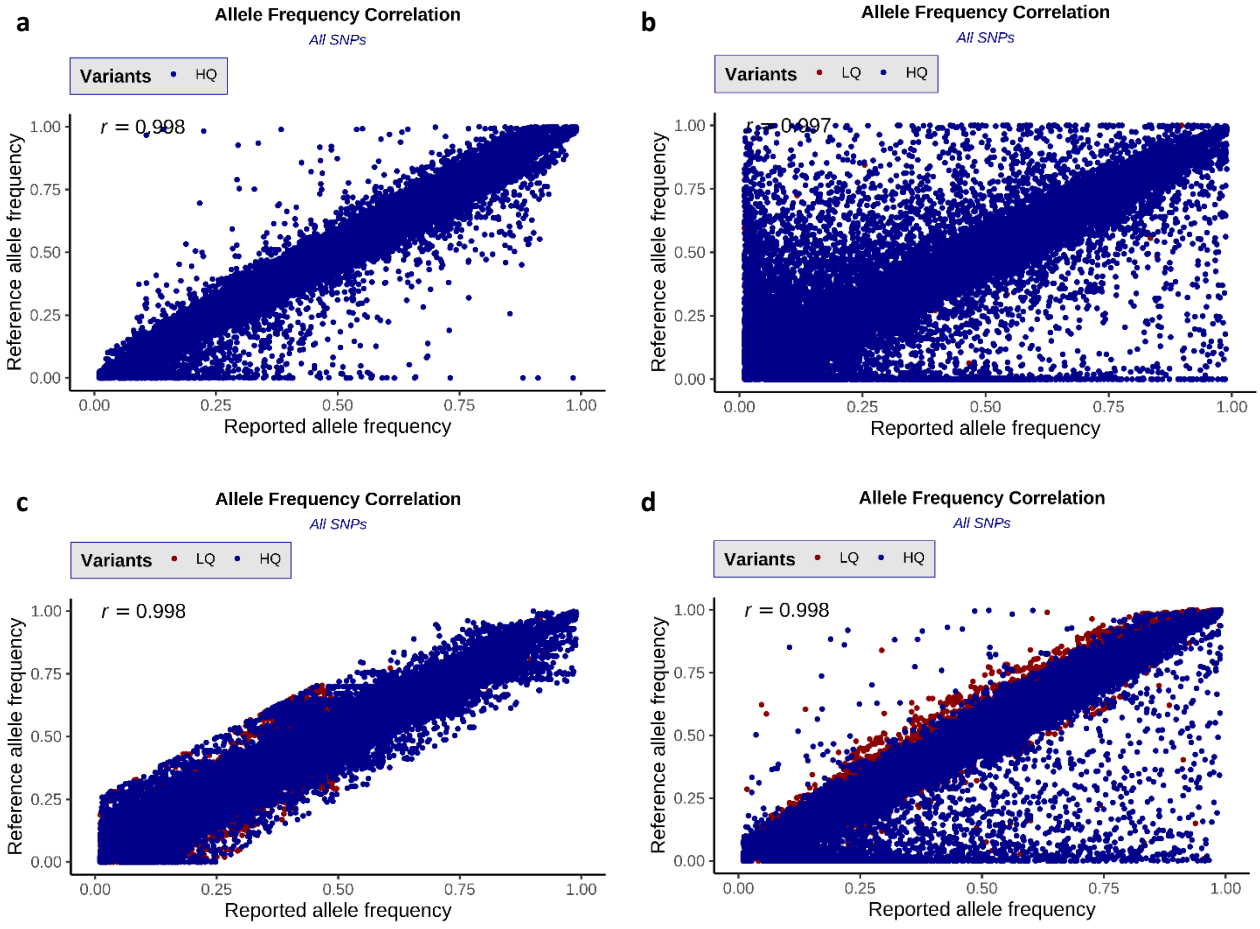


Supplementary Figure 14: Comparison of Beta Effect Estimates for the 113 Novel Loci: (a) meta-analysis vs UKB; (b) meta-analysis vs ICBP; (c) meta-analysis vs MVP; (d) meta-analysis vs BioVU; (e) UKB vs MVP. UKB = UK Biobank; ICBP = International Consortium of Blood Pressure; MVP = Million Veterans Program; BioVU = Biobank Repository of Vanderbilt University; "sec" = secondary variants; r = Pearson correlation coefficient. Points are colour coded to differentiate between SBP, DBP, PP.

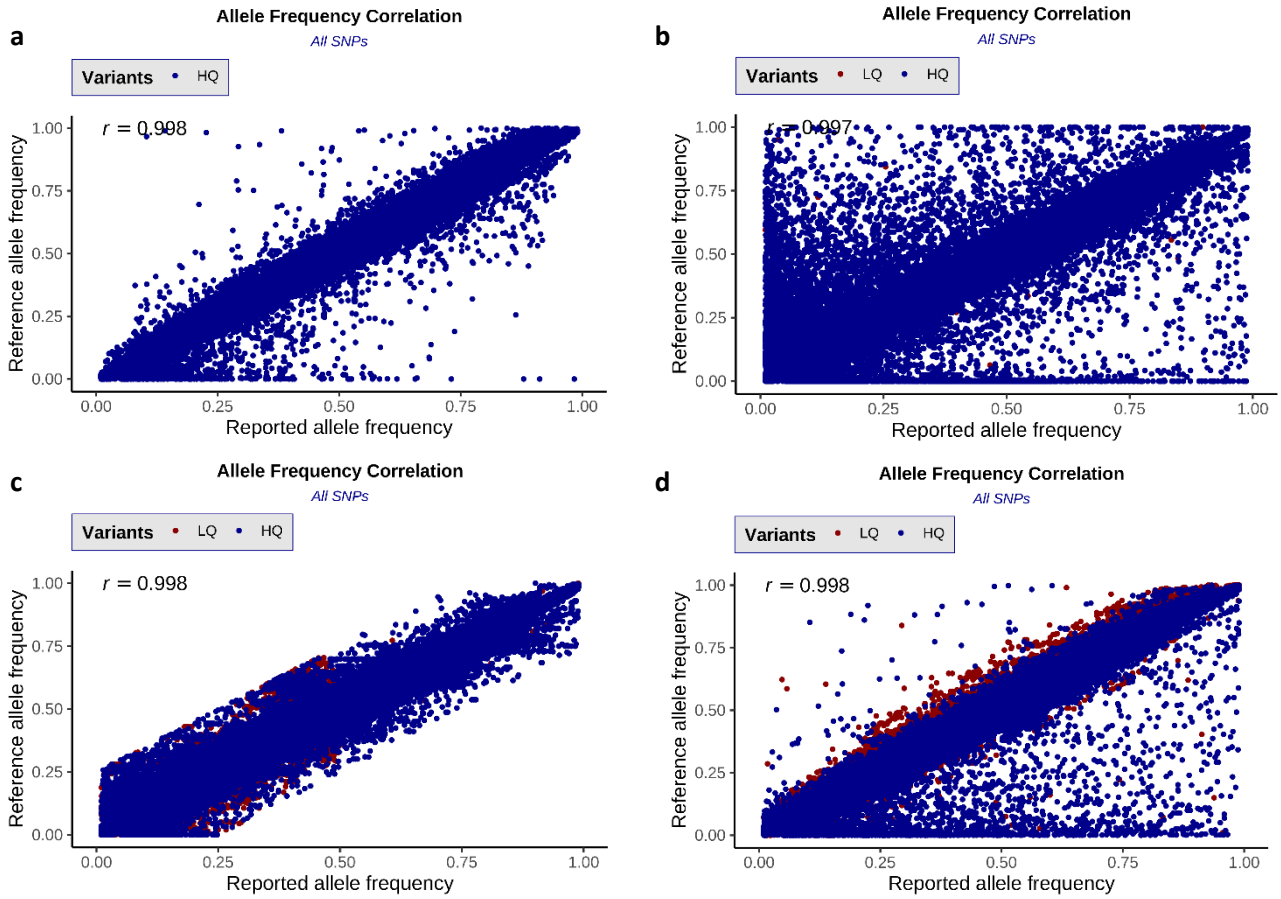
SBP:


a
Allele Frequency Correlation
All SNPs
Variants HQ
r = 0.998
Reference allele frequency
Reported allele frequency
b
Allele Frequency Correlation
All SNPs
Variants LQ HQ
r = 0.997
Reference allele frequency
Reported allele frequency
c
Allele Frequency Correlation
All SNPs
Variants LQ HQ
r = 0.998
Reference allele frequency
Reported allele frequency
d
Allele Frequency Correlation
All SNPs
Variants LQ HQ
r = 0.998
Reference allele frequency
Reported allele frequency

DBP:

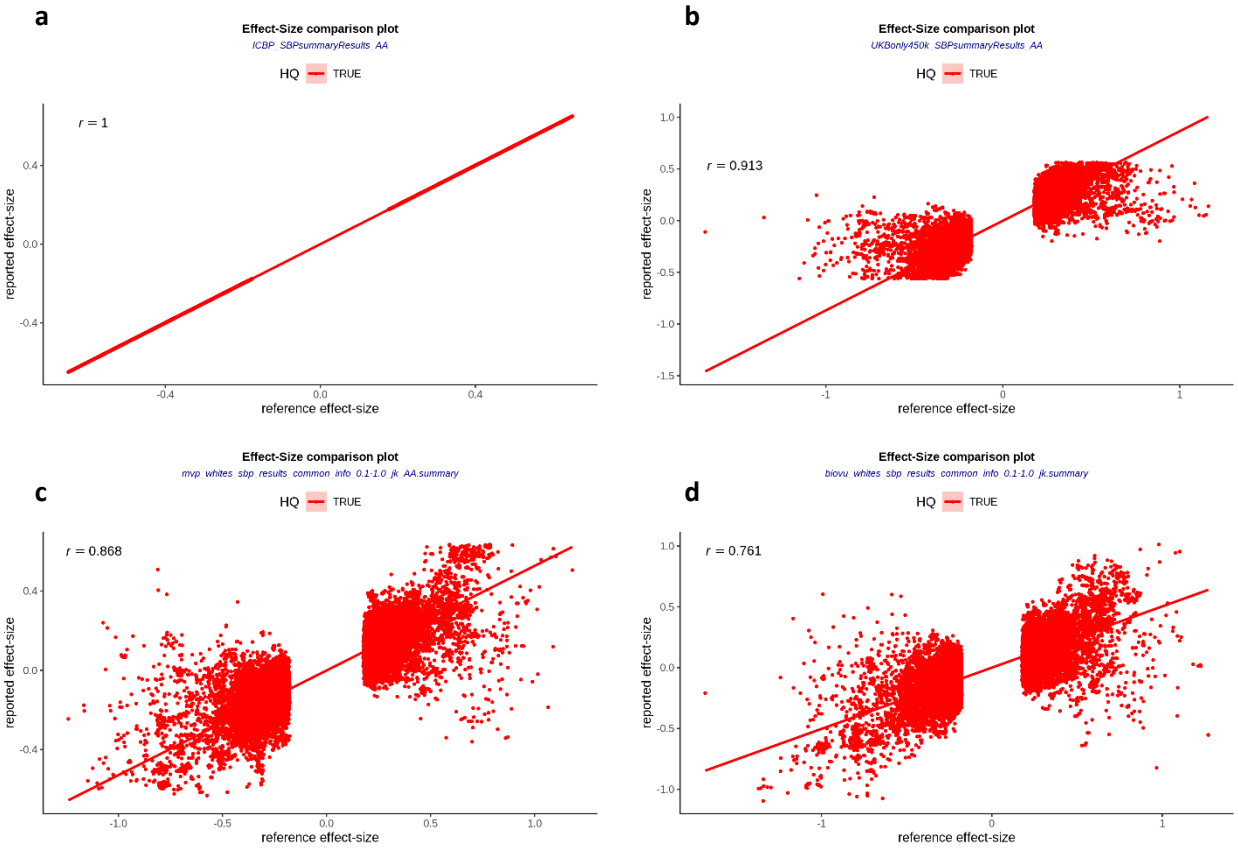

a
Allele Frequency Correlation
All SNPs
Variants HQ
r = 0.998
Reference allele frequency
Reported allele frequency
b
Allele Frequency Correlation
All SNPs
Variants LQ HQ
r = 0.997
Reference allele frequency
Reported allele frequency
c
Allele Frequency Correlation
All SNPs
Variants LQ HQ
r = 0.998
Reference allele frequency
Reported allele frequency
d
Allele Frequency Correlation
All SNPs
Variants LQ HQ
r = 0.998
Reference allele frequency
Reported allele frequency

PP:

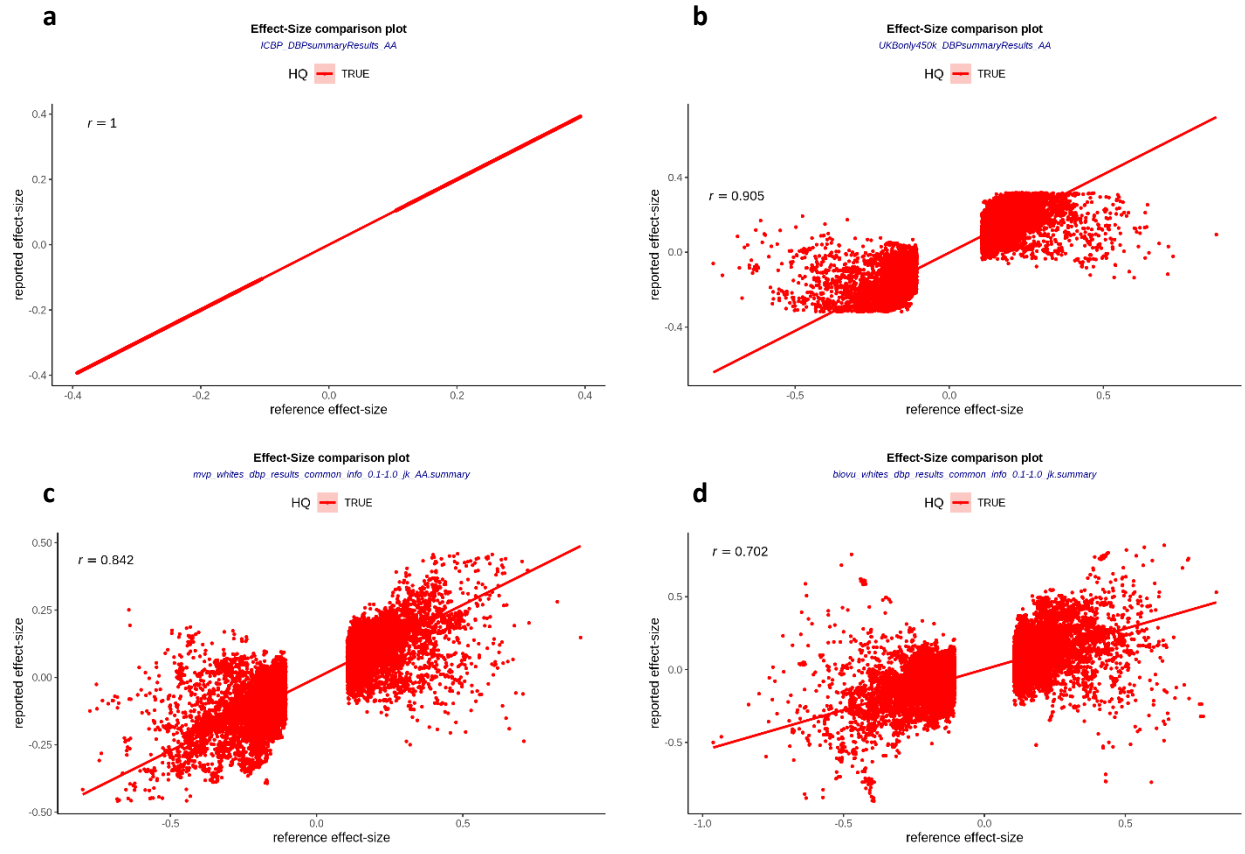


Supplementary Figures 15a-d. Allele frequency correlation of ICBP (a), UKB (b), MVP (c), and BioVU (d) datasets with the 1000 Genomes reference panel of European individuals in study-level QC for systolic-, diastolic-, and pulse pressure (SBP, DBP, and PP respectively). HQ: high-quality SNPs, LQ: low-quality SNPs. Filters for selecting high-quality SNPs include MAF ≥ 0.01, two-sided Hardy–Weinberg p-value ≥$1x10^{-6}$, and imputation quality > 0.3, where available.

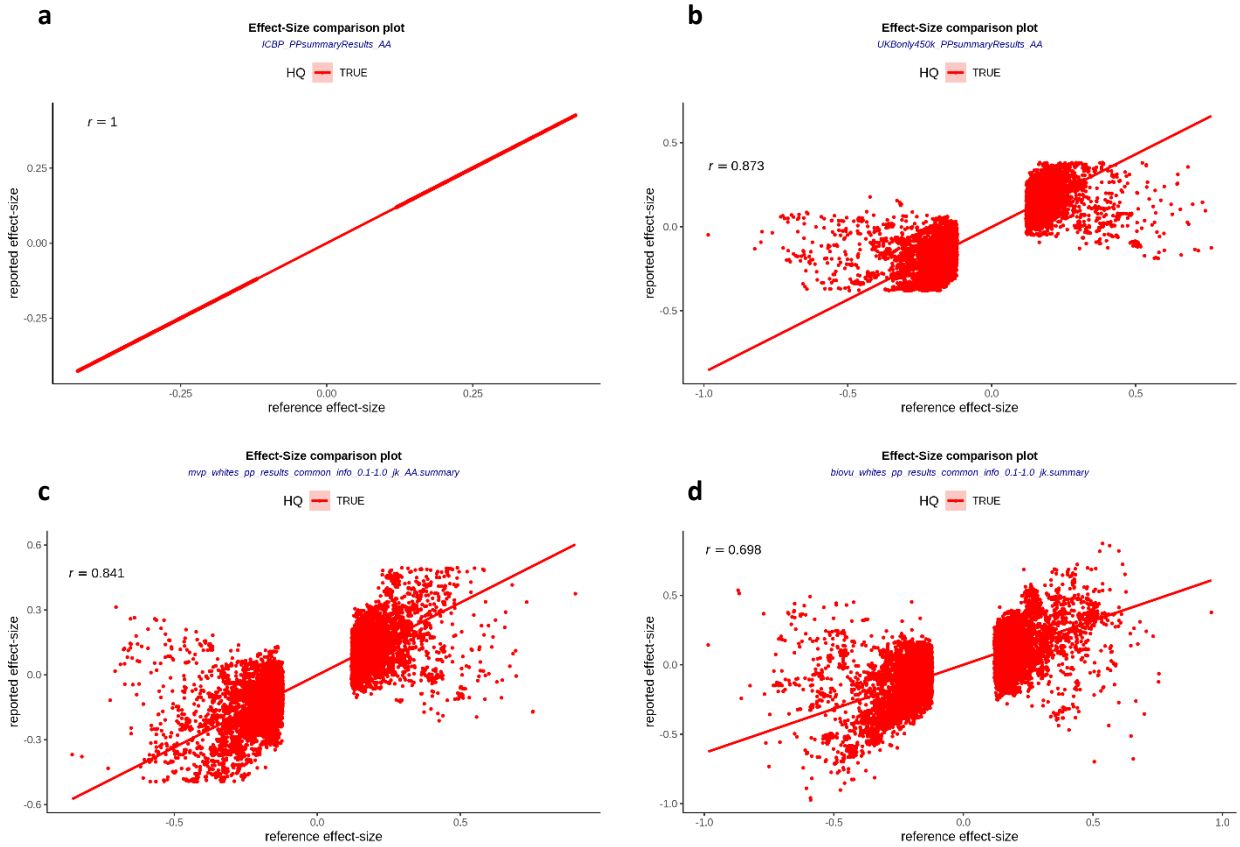
SBP:


a
Effect-Size comparison plot
ICBP_SBPsummaryResults_AA
HQ TRUE
r = 1
reported effect-size
reference effect-size
b
Effect-Size comparison plot
UKBonly450k_SBPsummaryResults_AA
HQ TRUE
r = 0.913
reported effect-size
reference effect-size
c
Effect-Size comparison plot
mvp_whites_sbp_results_common_info_0.1-1.0_jk_AA.summary
HQ TRUE
r = 0.868
reported effect-size
reference effect-size
d
Effect-Size comparison plot
biovu_whites_sbp_results_common_info_0.1-1.0_jk.summary
HQ TRUE
r = 0.761
reported effect-size
reference effect-size

DBP:

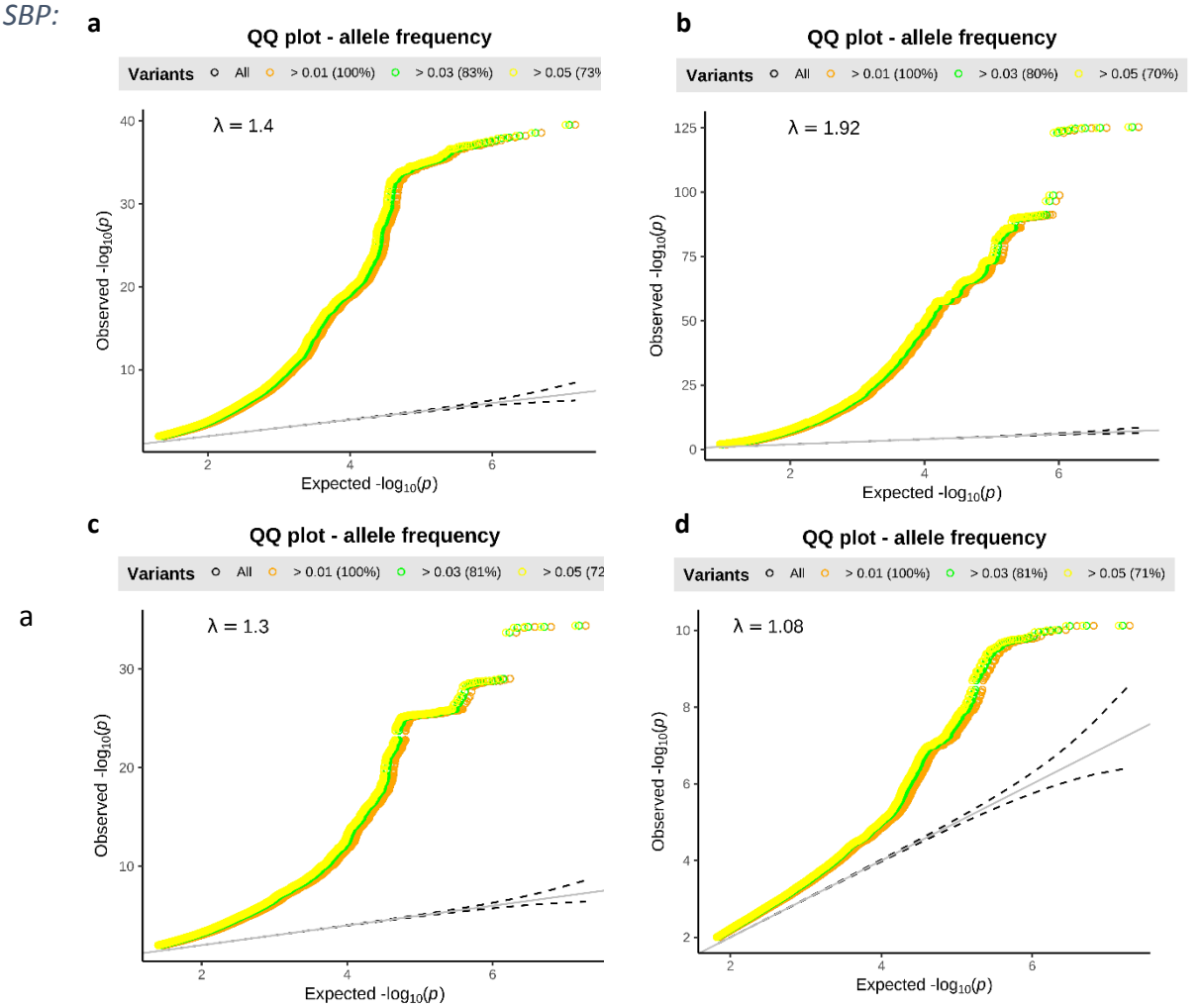

a
Effect-Size comparison plot
ICBP_DBPsummaryResults_AA
HQ TRUE
r = 1
reported effect-size
reference effect-size
b
Effect-Size comparison plot
UKBonly450k_DBPsummaryResults_AA
HQ TRUE
r = 0.905
reported effect-size
reference effect-size
c
Effect-Size comparison plot
mvp_whites_dbp_results_common_info_0.1-1.0_jk_AA.summary
HQ TRUE
r = 0.842
reported effect-size
reference effect-size
d
Effect-Size comparison plot
biovu_whites_dbp_results_common_info_0.1-1.0_jk.summary
HQ TRUE
r = 0.702
reported effect-size
reference effect-size

PP:



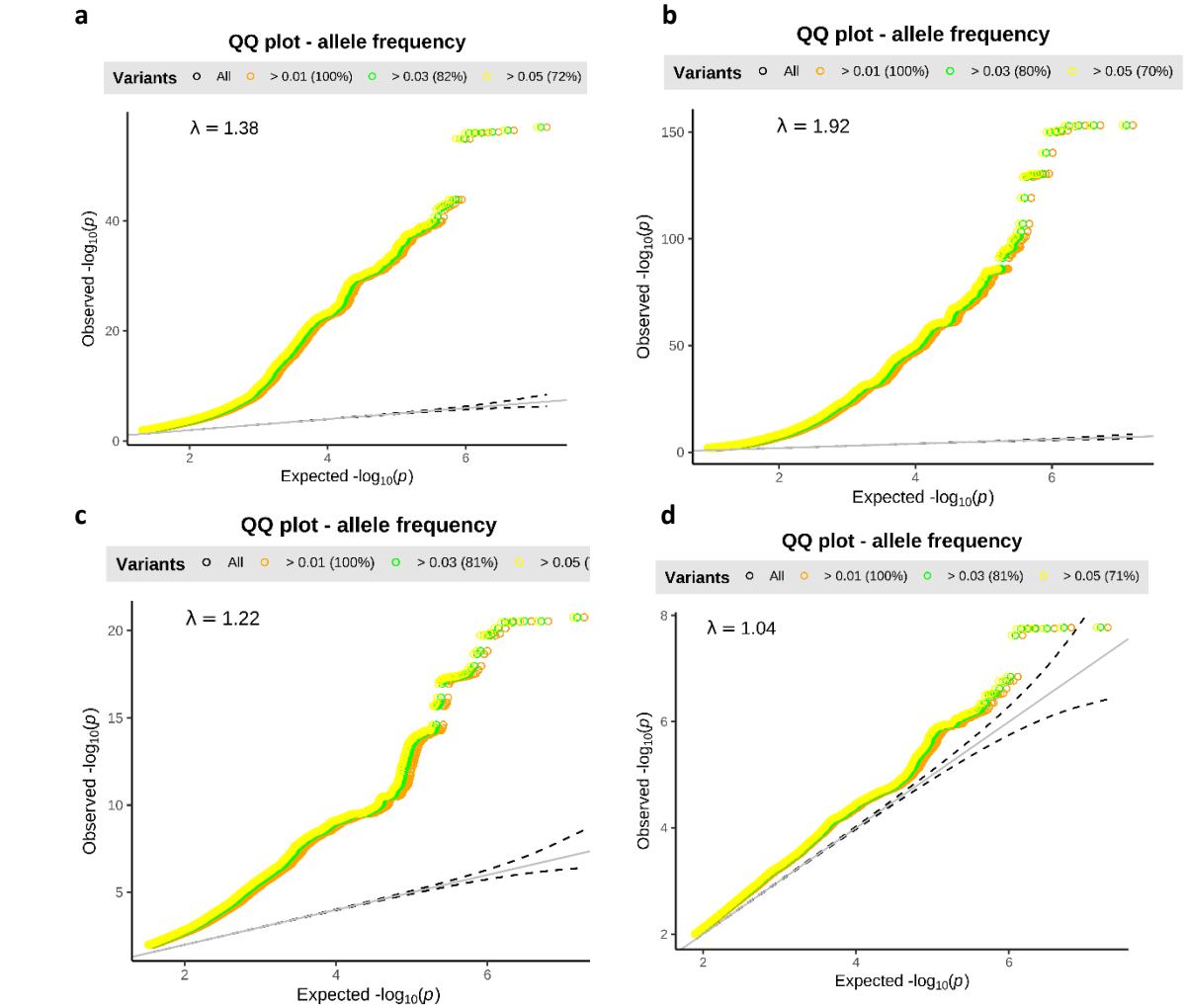
Supplementary Figures 16a-d. Effect size correlation of the ICBP (a), UKB (b), MVP (c), and BioVU (d) GWAS datasets of systolic-, diastolic-, and pulse pressure (SBP, DBP, and PP respectively) with the ICBP GWAS results as reference. HQ: high-quality SNPs, LQ: low-quality SNPs. Filters for selecting high-quality SNPs include MAF ≥ 0.01, two-sided Hardy–Weinberg p-value ≥1x10^{-6}, and imputation quality > 0.3, where available.

SBP:

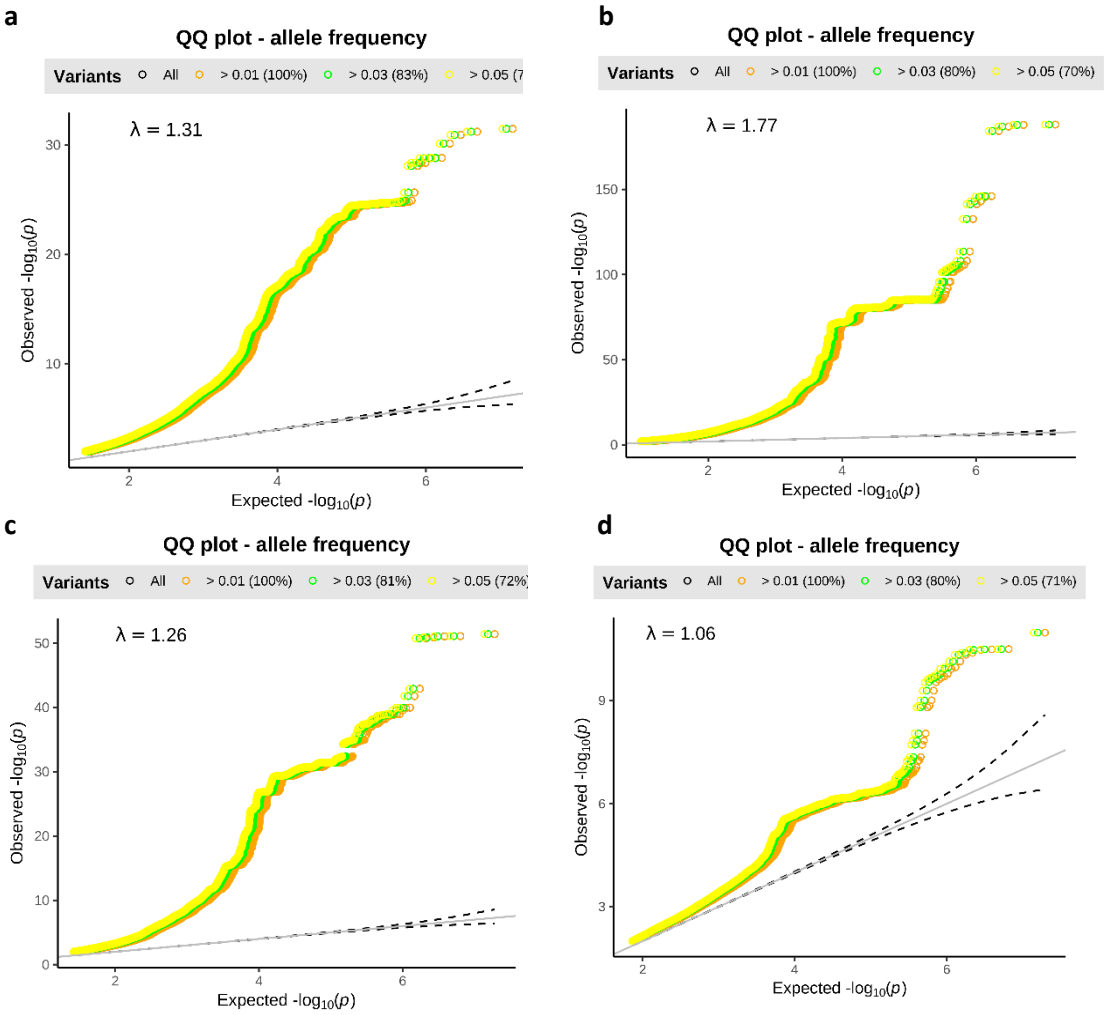

a
QQ plot - allele frequency
Variants All > 0.01 (100%) > 0.03 (83%) > 0.05 (73%
λ = 1.4
Observed -log10(p)
Expected -log10(p)
b
QQ plot - allele frequency
Variants All > 0.01 (100%) > 0.03 (80%) > 0.05 (70%)
λ = 1.92
Observed -log10(p)
Expected -log10(p)
c
QQ plot - allele frequency
Variants All > 0.01 (100%) > 0.03 (81%) > 0.05 (72
λ = 1.3
Observed -log10(p)
Expected -log10(p)
d
QQ plot - allele frequency
Variants All > 0.01 (100%) > 0.03 (81%) > 0.05 (71%)
λ = 1.08
Observed -log10(p)
Expected -log10(p)

a

DBP:

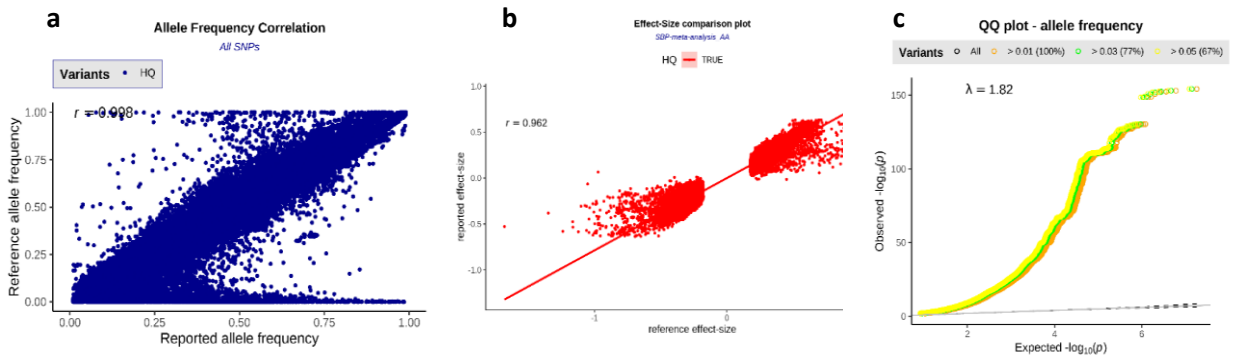

a
QQ plot - allele frequency
Variants All > 0.01 (100%) > 0.03 (82%) > 0.05 (72%)
λ = 1.38
Observed -log10(p)
Expected -log10(p)
b
QQ plot - allele frequency
Variants All > 0.01 (100%) > 0.03 (80%) > 0.05 (70%)
λ = 1.92
Observed -log10(p)
Expected -log10(p)
c
QQ plot - allele frequency
Variants All > 0.01 (100%) > 0.03 (81%) > 0.05 (
λ = 1.22
Observed -log10(p)
Expected -log10(p)
d
QQ plot - allele frequency
Variants All > 0.01 (100%) > 0.03 (81%) > 0.05 (71%)
λ = 1.04
Observed -log10(p)
Expected -log10(p)

PP:

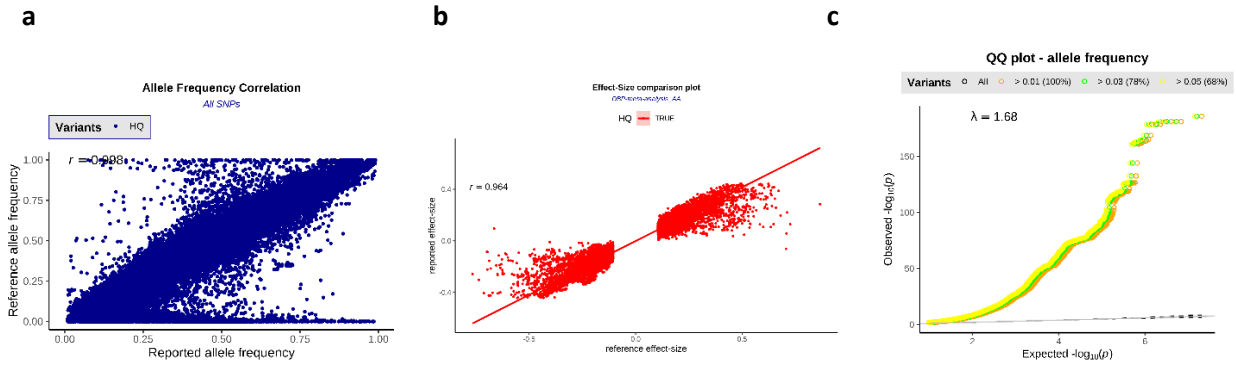


Supplementary Figure 17. QQ plots of the ICBP (a), UKB (b), MVP (c), and BioVU (d) GWAS datasets of systolic-, diastolic-, and pulse pressure (SBP, DBP, and PP, respectively). Observed p-values are from individual linear regression analyses and expected p-values are calculated under the null hypothesis that p-values are uniformly distributed between 0 and 1. QQ plot lines are presented according to different Minor Allele Frequency ranges.

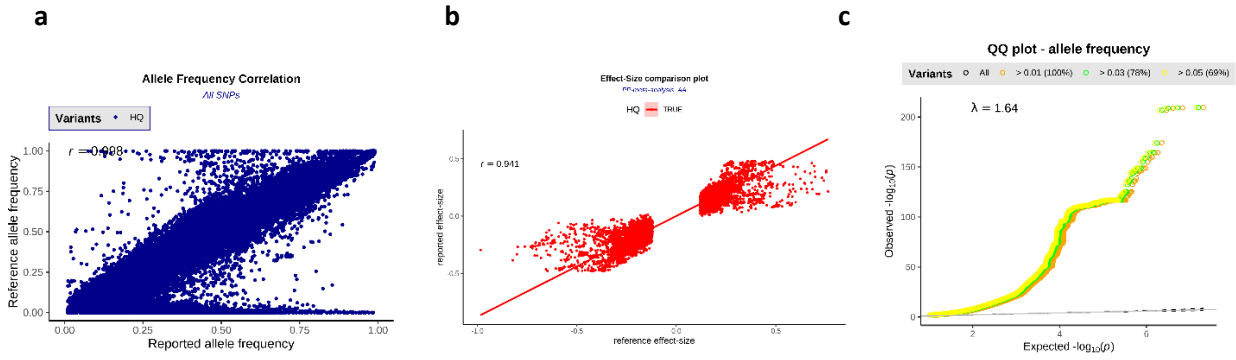
SBP:



DBP:

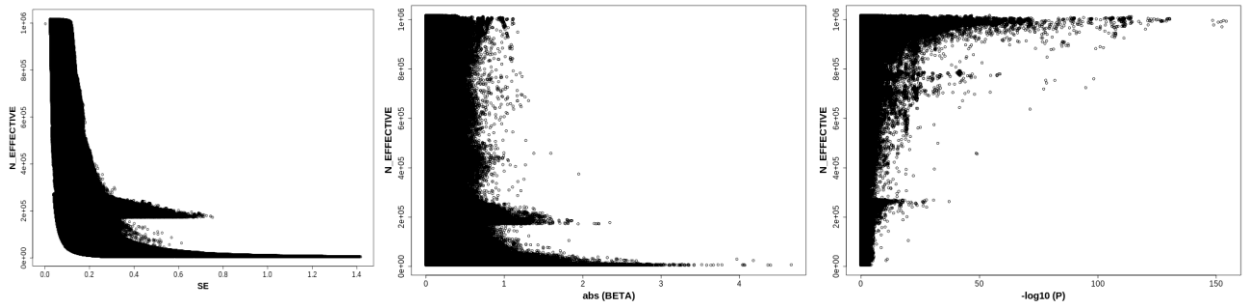


PP:

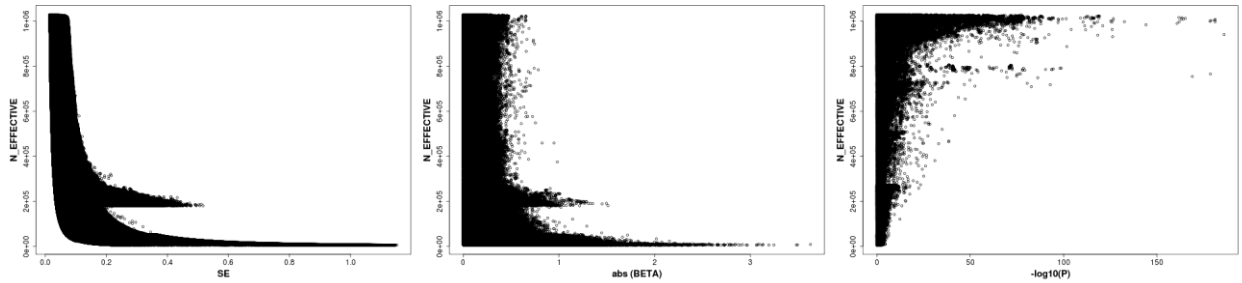


Supplementary Figures 18a-c. Quality checks of the meta-analysis results for systolic-, diastolic-, and pulse pressure (SBP, DBP, and PP respectively). a) Weighted allele frequency correlation with 1KG reference panel; b) correlation of Meta effect sizes with ICBP data, the same reference as for study-level QC; c) QQ plot of the meta-analysis results. Observed p-values are from the inverse variance-weighted GWAS meta-analysis results and expected p-values are calculated under the null hypothesis that p-values are uniformly distributed between 0 and 1. QQ plot lines are presented according to different Minor Allele Frequency ranges.

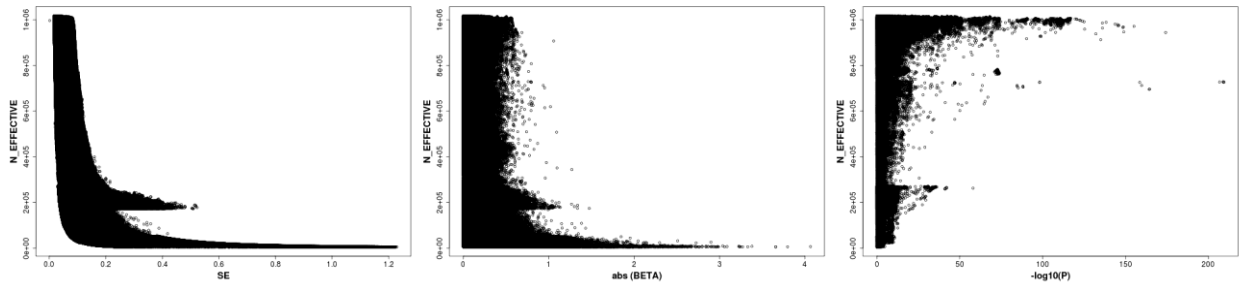
SBP:



DBP:

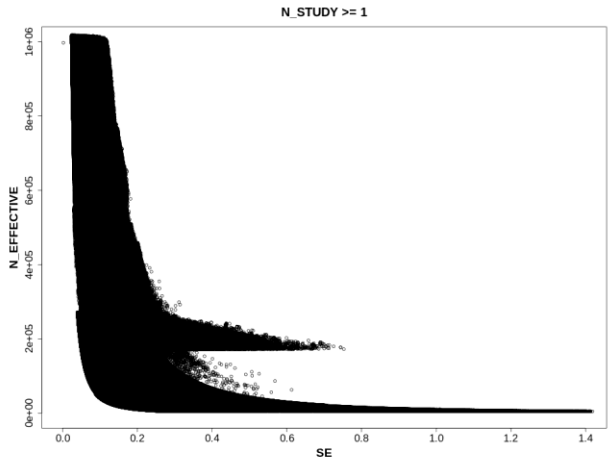


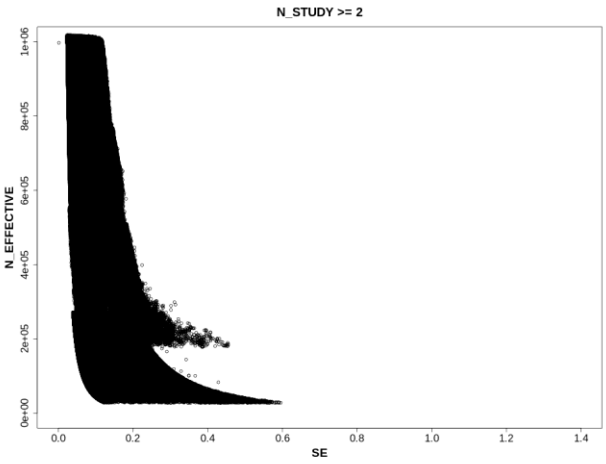
PP:

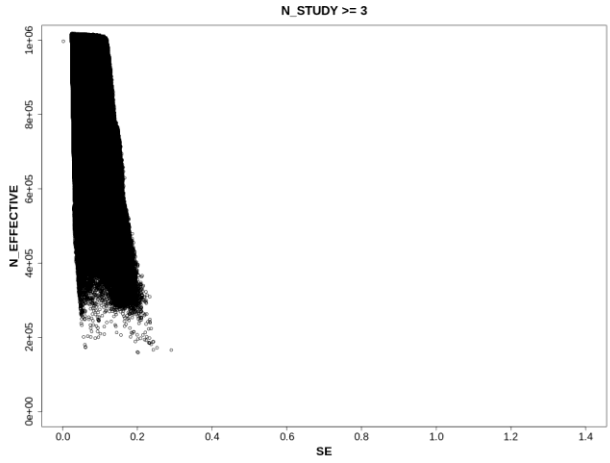


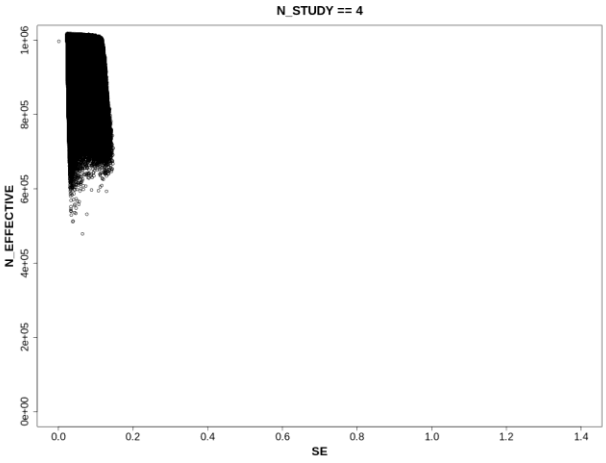
Supplementary Figure 19. Bivariate scatter plots of the key summary statistics in inverse variance-weighted GWAS meta-analysis results of systolic-, diastolic-, and pulse pressure (SBP, DBP, and PP respectively). N_EFFECTIVE = effective sample size; SE = standard error of estimates; abs(BETA) = absolute effect estimate; -log10(P) = minus of meta-GWAS p-values in logarithmic scale.

SBP:

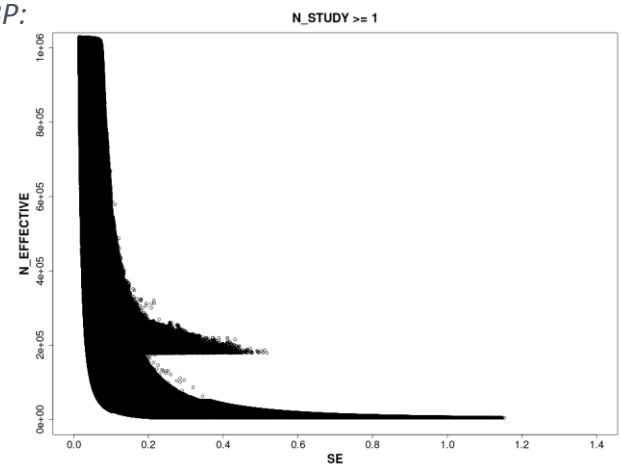

N_STUDY >= 1
N_EFFECTIVE
SE

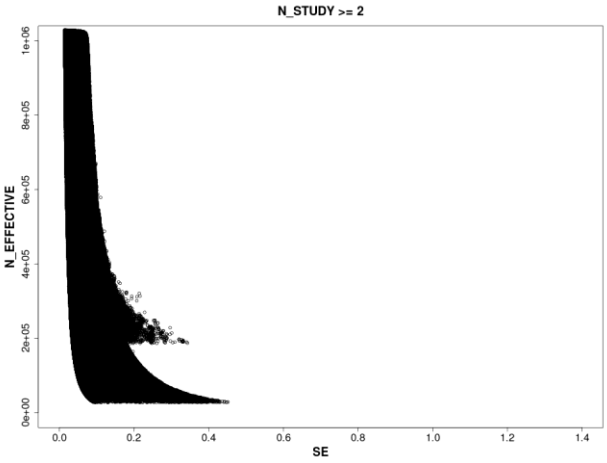

N_STUDY >= 2
N_EFFECTIVE
SE

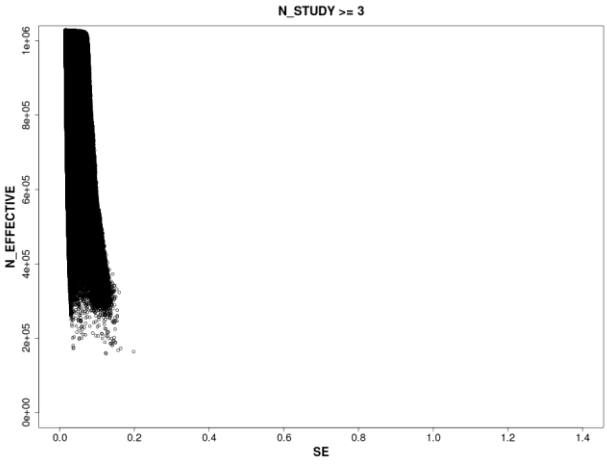

N_STUDY >= 3
N_EFFECTIVE
SE

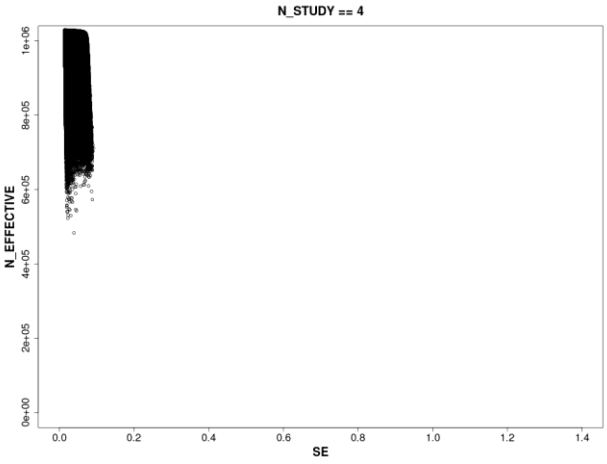

N_STUDY == 4
N_EFFECTIVE
SE

DBP:

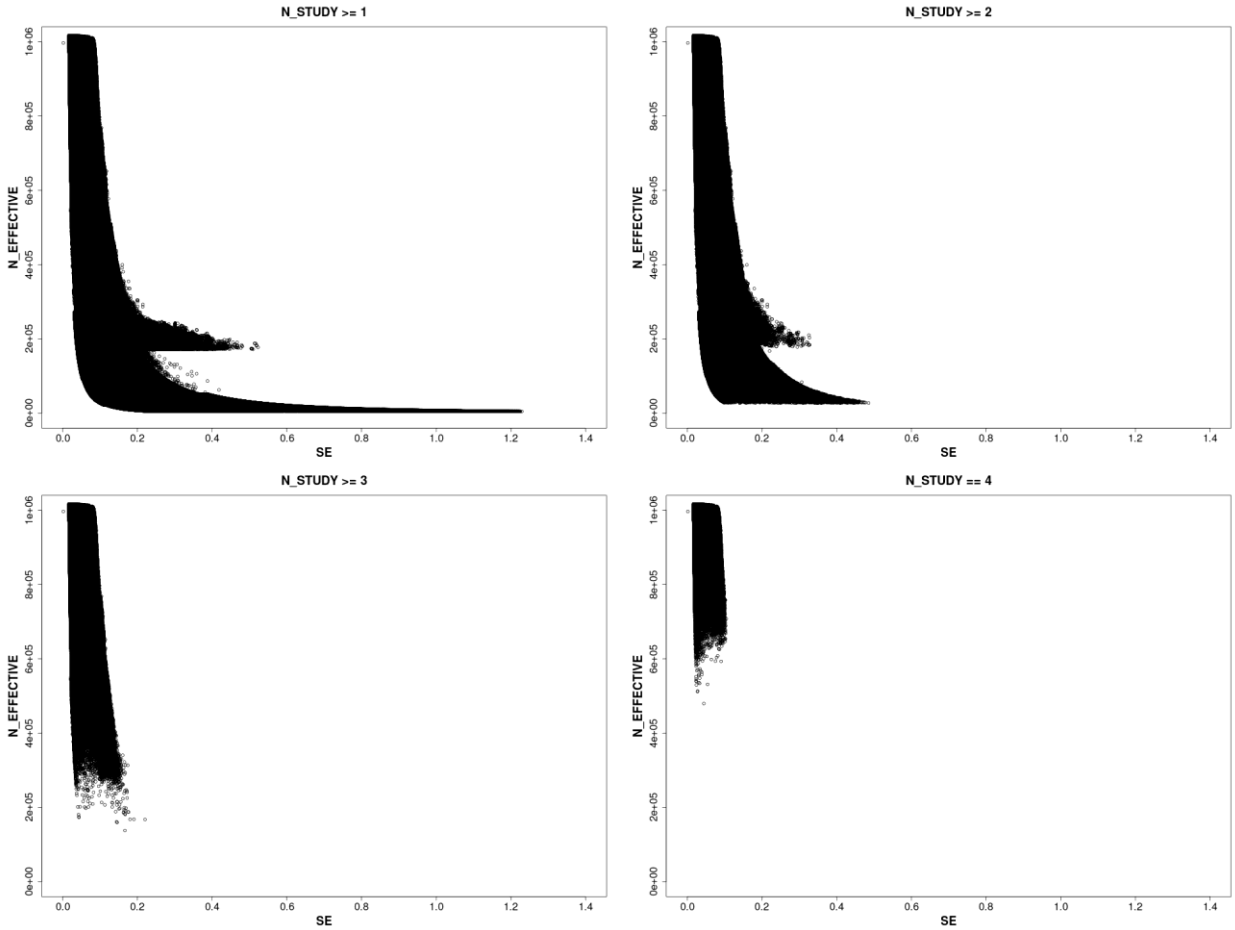

N_STUDY >= 1
N_EFFECTIVE
SE


N_STUDY >= 2
N_EFFECTIVE
SE

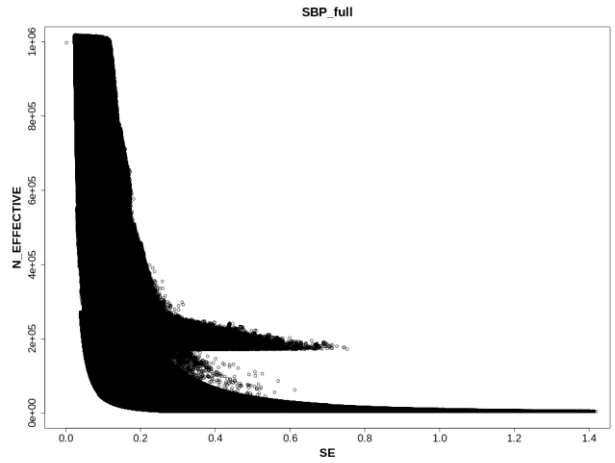

N_STUDY >= 3
N_EFFECTIVE
SE

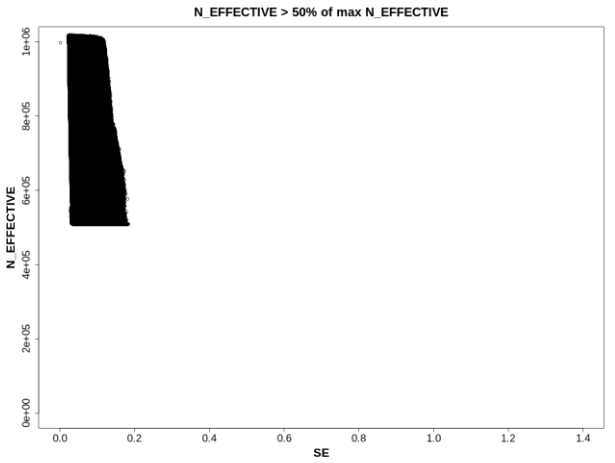

N_STUDY == 4
N_EFFECTIVE
SE

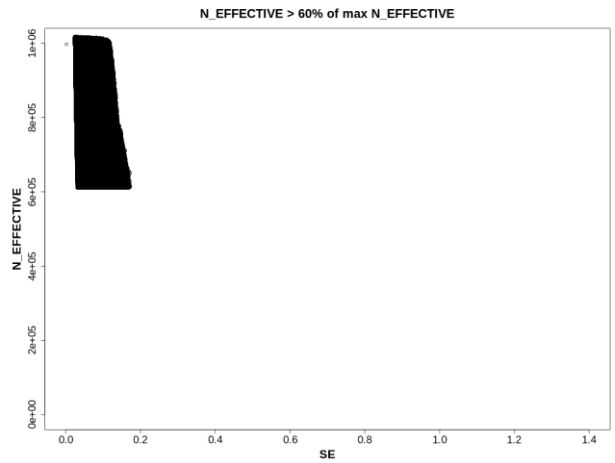
PP:

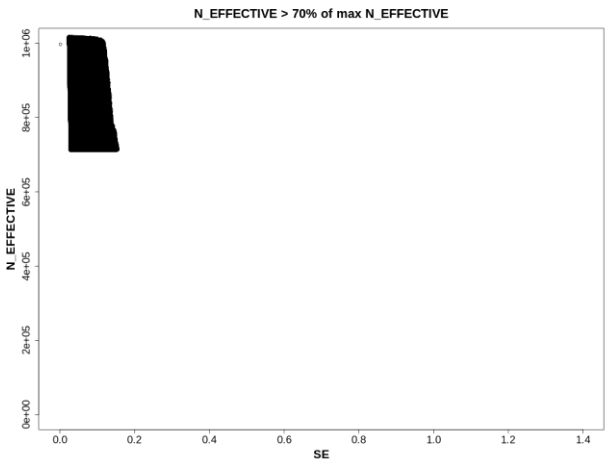


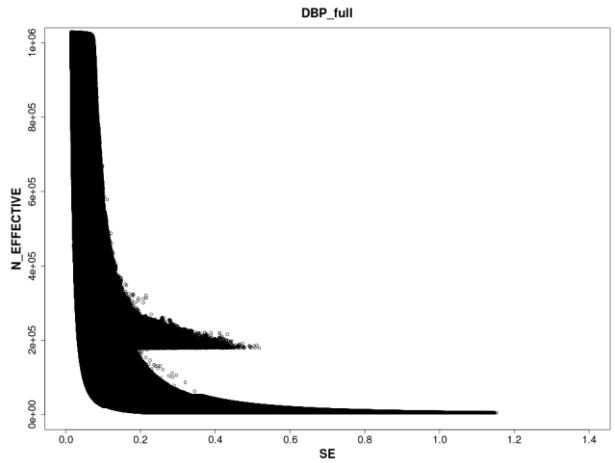
Supplementary Figure 20. Selection of filtering criteria based on N_STUDY (the number of study sub-datasets within the meta-analysis (up to 4) with available data for each variant. Data shown is for meta-analysis results of systolic-, diastolic-, and pulse pressure (SBP, DBP, and PP respectively).

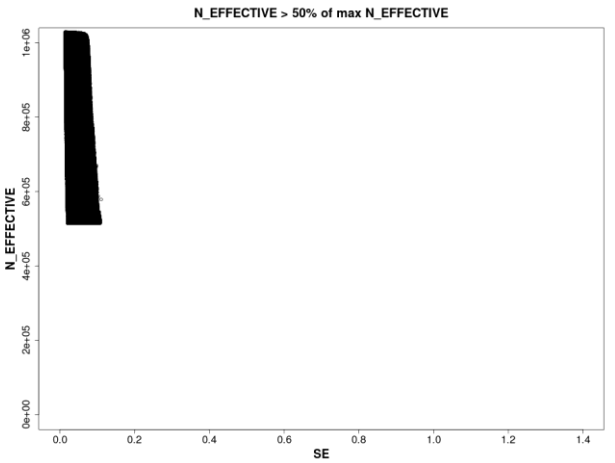

SBP_full
N_EFFECTIVE
SE
0e+00
2e+05
4e+05
6e+05
8e+05
1e+06
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4

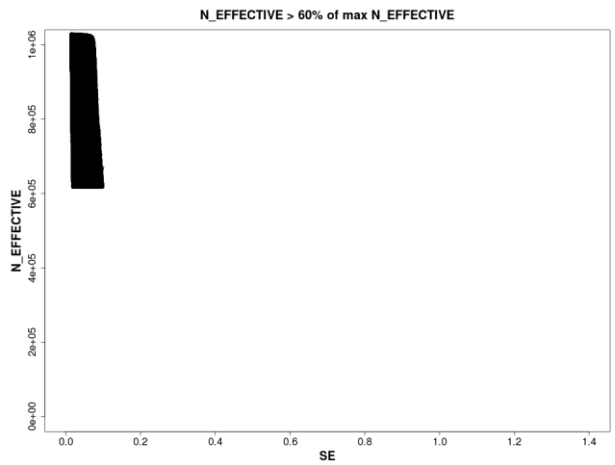

N_EFFECTIVE > 50% of max N_EFFECTIVE
N_EFFECTIVE
SE
0e+00
2e+05
4e+05
6e+05
8e+05
1e+06
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4

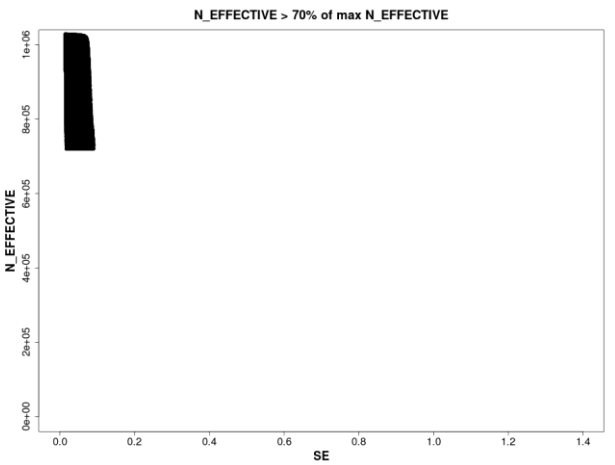

N_EFFECTIVE > 60% of max N_EFFECTIVE
N_EFFECTIVE
SE
0e+00
2e+05
4e+05
6e+05
8e+05
1e+06
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4

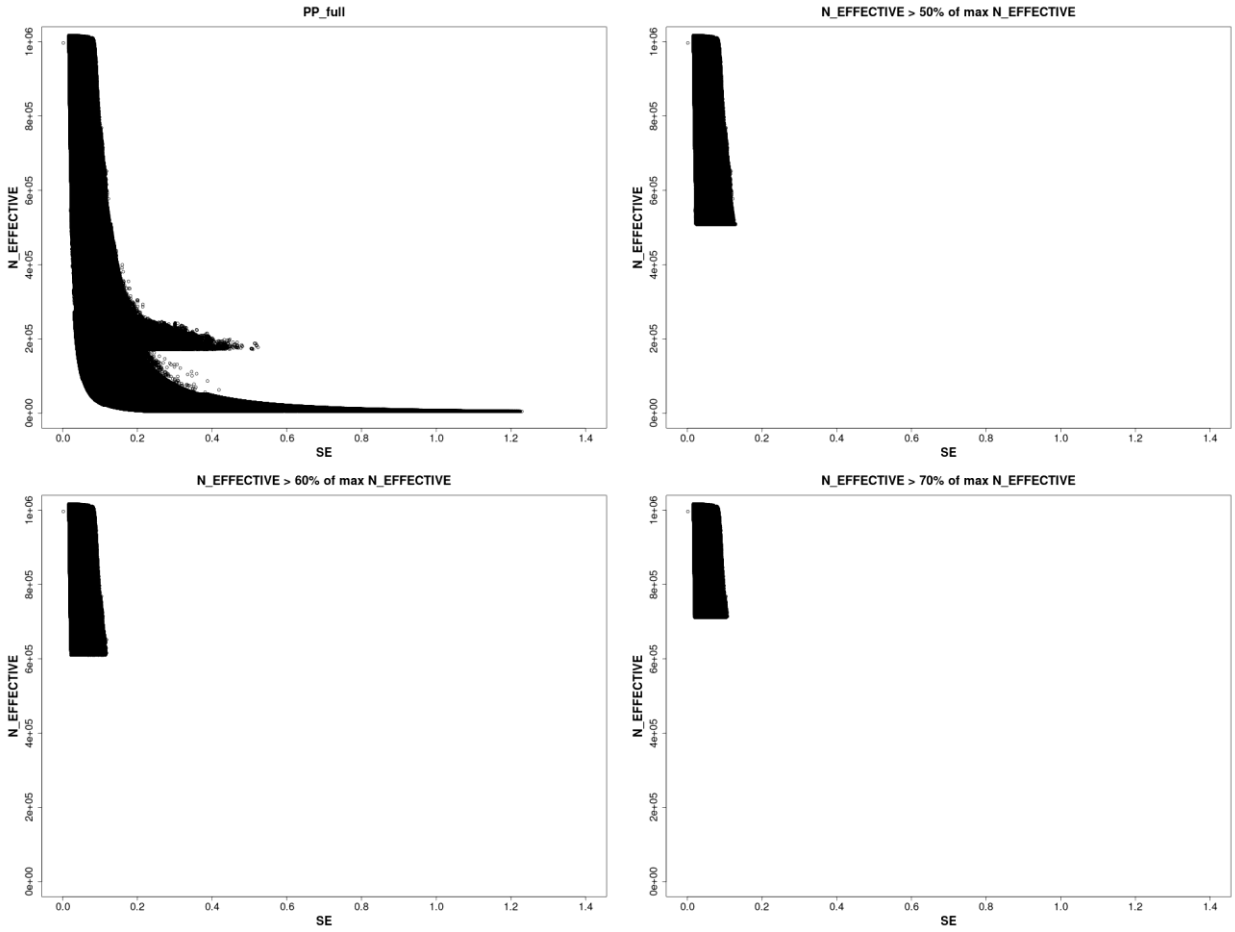

N_EFFECTIVE > 70% of max N_EFFECTIVE
N_EFFECTIVE
SE
0e+00
2e+05
4e+05
6e+05
8e+05
1e+06
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4


DBP_full
N_EFFECTIVE
SE
0e+00
2e+05
4e+05
6e+05
8e+05
1e+06
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4


N_EFFECTIVE > 50% of max N_EFFECTIVE
N_EFFECTIVE
SE
0e+00
2e+05
4e+05
6e+05
8e+05
1e+06
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4

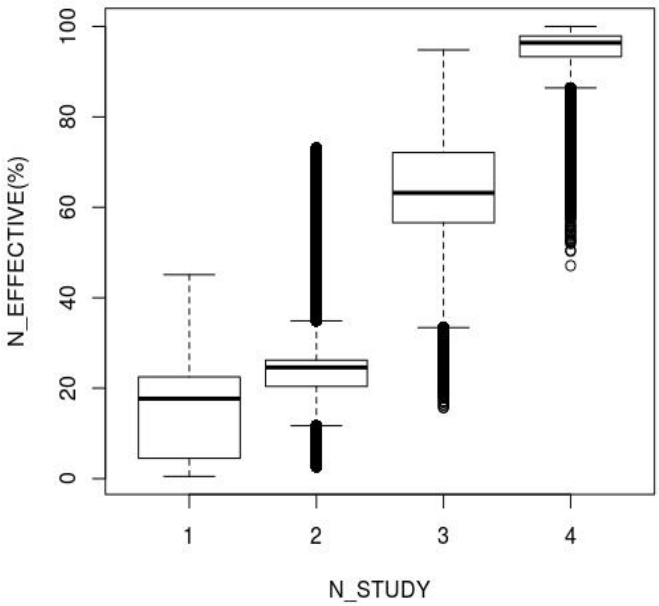

N_EFFECTIVE > 60% of max N_EFFECTIVE
N_EFFECTIVE
SE
0e+00
2e+05
4e+05
6e+05
8e+05
1e+06
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4


N_EFFECTIVE > 70% of max N_EFFECTIVE
N_EFFECTIVE
SE
0e+00
2e+05
4e+05
6e+05
8e+05
1e+06
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4

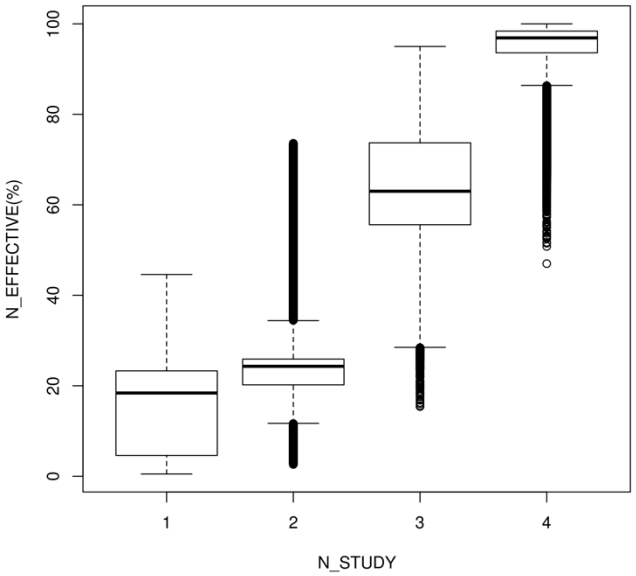


Supplementary Figure 21. Selection of filtering criteria based on N_EFFECTIVE. Data shown is for meta-analysis results of systolic-, diastolic-, and pulse pressure (SBP, DBP, and PP respectively).

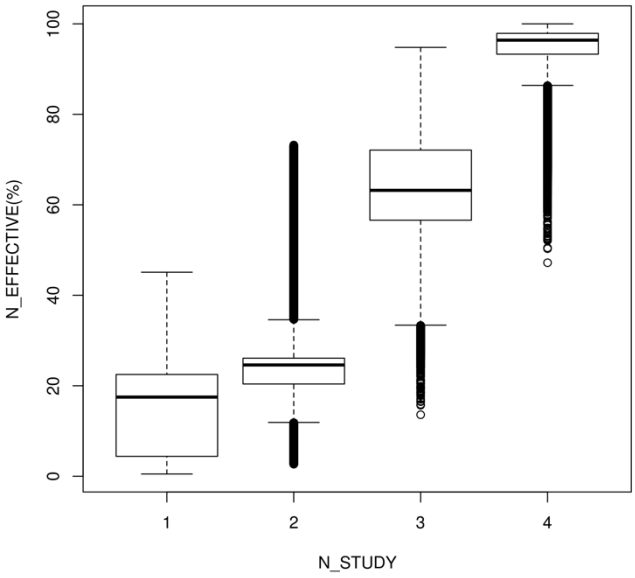
SBP:



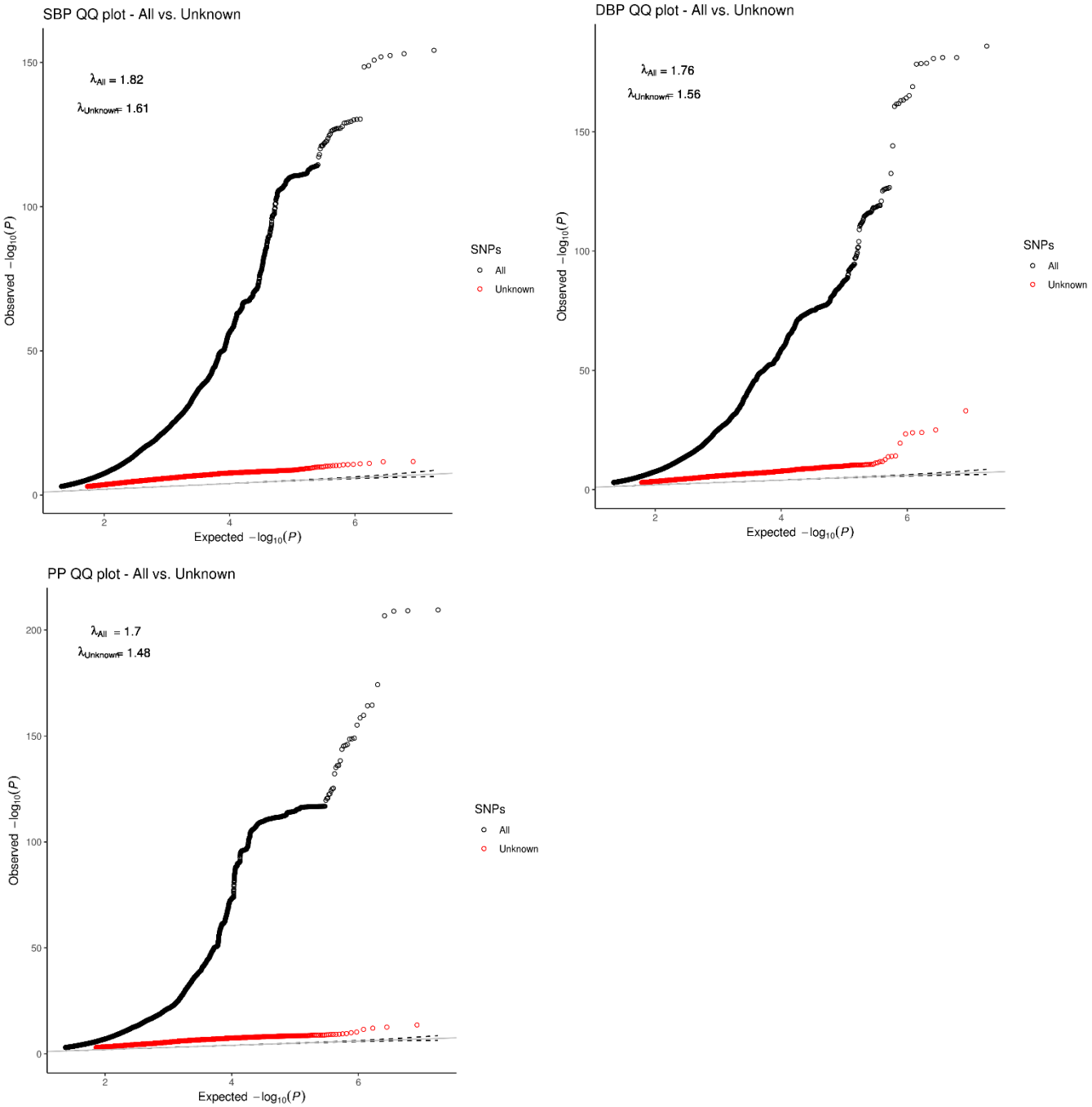
DBP:



PP:



Supplementary Figure 22. The distribution of N_EFFECTIVE/max(N_EFFECTIVE) in percent, for SNPs present in different number of studies (N_STUDY) in meta-analysis results *of* systolic-, diastolic-, and pulse pressure (SBP, DBP, and PP respectively). These studies are ICBP (n=299,024), UKB (n=458,577), BioVU (n= 50,649), and MVP (n= 220,501). Each box represents the interquartile range (IQR) of the data, with the median value shown as a horizontal line in the middle of the box. Whiskers show the 1.5 IQR range, with outlier values drawn as individual points outside.



Supplementary Figure 23a-c. QQ plots of meta-analysis results for all variants versus novel variants in the "unknown" subset of the GWAS data, for systolic-, diastolic-, and pulse pressure (SBP, DBP, and PP respectively). Genomic Inflation values λ are provided for both GWAS subsets.