Comparing different methods of estimating GWAS heritability with a new approach using only summary statistics

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Supplementary materials:

Part 1. Comparing Multiple $-R^2$ and Adjusted $-R^2$:

To compare Multiple R^2 and Adjusted R^2 we made a simulation to show the performance of these two estimators under different conditions. The purpose is to see if we knew the correct value of r^2 which one of the R^2's provides the more accurate estimate of the real value. For this reason, a series of simulations with different sample sizes and predefined r^2 was built.

So that, $y = a_1x_1 + a_2x_1 + \cdots + a_kx_k + \varepsilon$, $x_i \sim N(.)$; $x_i's\ are\ independent$, $a_i \sim N(.)$ and $\varepsilon \sim N(0, v)$.

$$Y = a_1X_1 + a_2X_1 + \cdots + a_kX_k + \varepsilon$$

$$E(Y) = 0 \qquad ; \qquad v(y) = {a_1}^2 + {a_2}^2 + \cdots + {a_k}^2 + v = \sum_{i=1}^{k} {a_i}^2 + v$$

$$as\ X_i's\ are\ independent, \qquad corr^2(Y, X) = r^2 = \frac{cov(y, \sum_{i=1}^{k} x_i)}{v(y)v(\sum_{i=1}^{k} x_i)} = \sum_{i=1}^{k} \frac{cov^2(y, x_i)}{v(y)v(x_i)} = \frac{\sum_{i=1}^{k} {a_i}^2}{\sum_{i=1}^{k} {a_i}^2 + v}$$

$$v = \sum_{i=1}^{k} {a_i}^2 \left(\frac{1 - r^2}{r^2}\right)$$

Therefore, v can be calculated, by simulating a_i's and choosing a desired r^2. In the final step, by placing the simulated parts, y can be obtained. The table below shows the results of Multiple_R^2 and adjusted_R^2 of regressing Y on $X_i's$.

Following simulation was done for n=2000 sample, (10,20,100) predictors and 1000 repeats. (R^2, adjusted-R^2, number of significant predictors, the percentage of being significant for rest of the predictors all together in the model.

The results of this simulation showed that the difference between R^2 and adjusted $-R^2$ gets larger when the ratio of predictors/sample size becomes larger and the correlation between predictors and dependent variable is small.

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n=2k	$r^2 = 0.2$	$r^2 = 0.5$	$r^2 = 0.9$	**Simulation number**
Number Of Predictors = 10		**Predictors/Sample size (0.005%)**		
R^2 / SE	(0.2046, 0.0155)	(0.5024, 0.0159)	(0.9005, 0.0043)	1k
$Adj - R^2$ / SE	(0.2006, 0.0156)	(0.4999, 0.0160)	(0.8999, 0.0043)	
NSP	7	8	9	
PSAT	0%	0%	0%	
Number Of Predictors = 20		**Predictors/Sample size (1%)**		
R^2	(0.2072,0.0005)	(0.5042,0.0005)	(0.9007,0.0001)	1k
$Adj - R^2$	(0.1992,0.0005)	(0.4992,0.0005)	(0.8997,0.0001)	
NSP	14	16	18	
PSAT	0.001%	0%	0.001%	
Number Of Predictors = 100		**Predictors/Sample size (5%)**		
R^2	(0.2404, 0.0005)	(0.5244, 0.0005)	(0.9050, 0.0041)	1k
$Adj - R^2$	(0.2004, 0.0005)	(0.4994, 0.0005)	(0.9000, 0.0043)	
NSP	41	66	87	
PSAT	0%	0%	0%	

Supplementary Table 1. NSP: number of significant predictors, PSAT: percentage of being significant for the rest of the predictors all together. To assesses whether other predictors are significant all together or not, Partial F test was used.

$$F_0 = \frac{(R^2_{\text{Full-Model}} - R^2_{\text{Reducted}})/r}{R^2_{\text{Full-Model}}/(n-k-1)} \quad ; \quad \text{reject } F_0 \text{: if } F_0 > F_{1-\alpha}(r, n-k-1)$$

Part 2.

Comparing clumping methods:

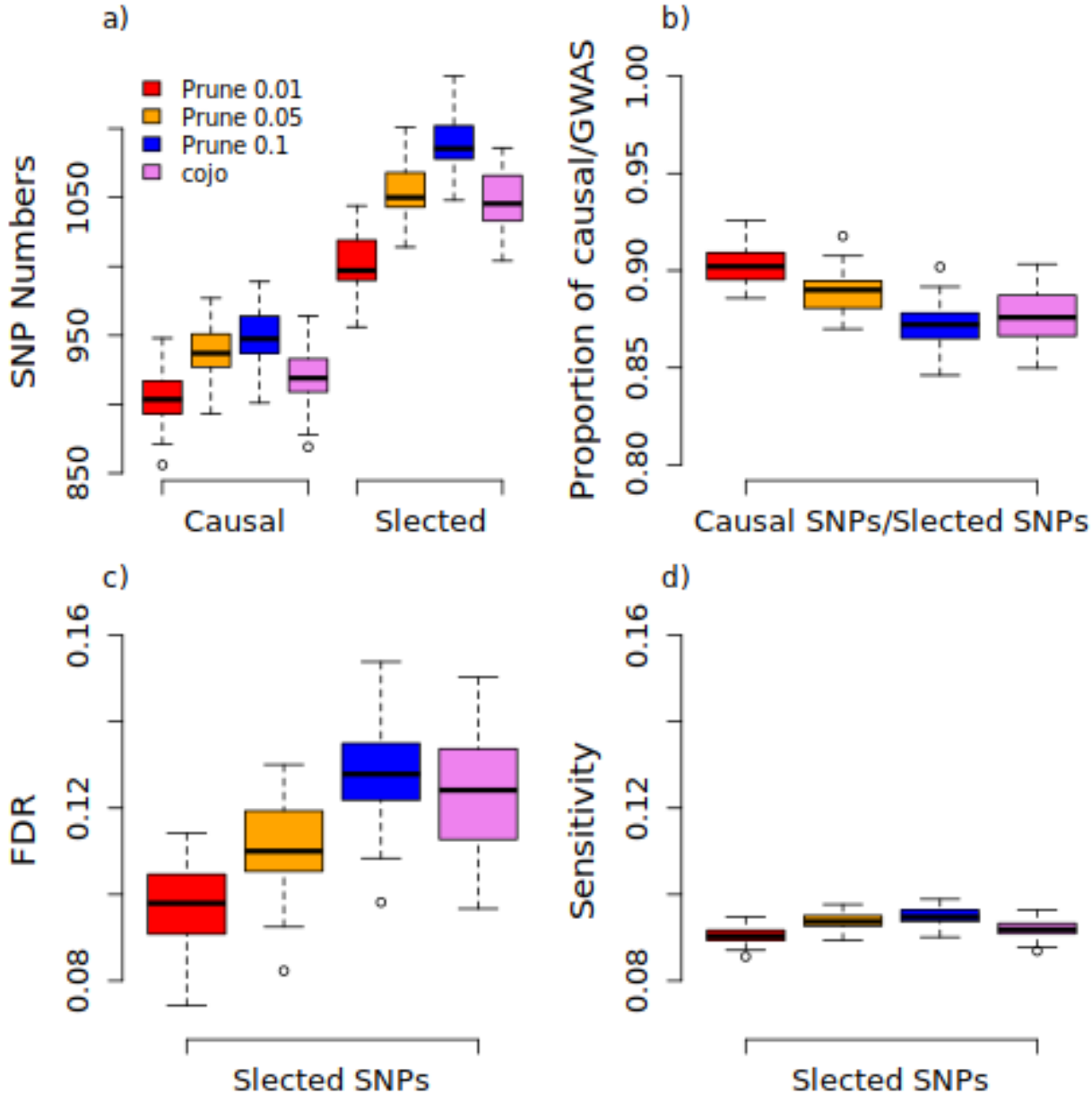
In our simulation, we demonstrated that the LD-pruning method by considering $r^2 = 0.05$ is more reliable than other LD levels or COJO analysis (Supplementary Fig.1). With LD-pruning ($r^2 = 0.05$), we observed a slight increase in sensitivity and a mild increase in the number of causal SNPs, although the proportion of causal/GWAS decreased and the false discovery rate increased slightly. When we increased the LD level to 0.1, we observed a mild increase in false discovery rate, while the increase in sensitivity and the number of causal SNPs was negligible and minor, respectively. Furthermore, the proportion of causal SNPs / selected SNPs decreased when LD level increased from $r^2 = 0.01$ to $r^2 = 0.05$. This indicates that entering more correlated SNPs into the study may not result in an accurate estimate of h^2_{GWAS}. (Supplementary Fig.1).

Under COJO analysis we found less causal SNPs than LD-pruning ($r^2 = 0.05$) while h^2_{GWAS} for both were relatively similar (Supplementary Fig.1 and Supplementary Fig.3). Supplementary Fig.2 showed that number of common causal SNPs found in both COJO and LD-pruning ($r^2 = 0.05$) is 96.5% on average across 50 simulation. While this number was 93% for non-causal SNPs. As the number of causals in COJO was less than LD-pruning ($r^2 = 0.05$) and most of the difference is because of non-casuals, the increase in h^2_{GWAS} in COJO cannot be because of adding more causal SNPs.

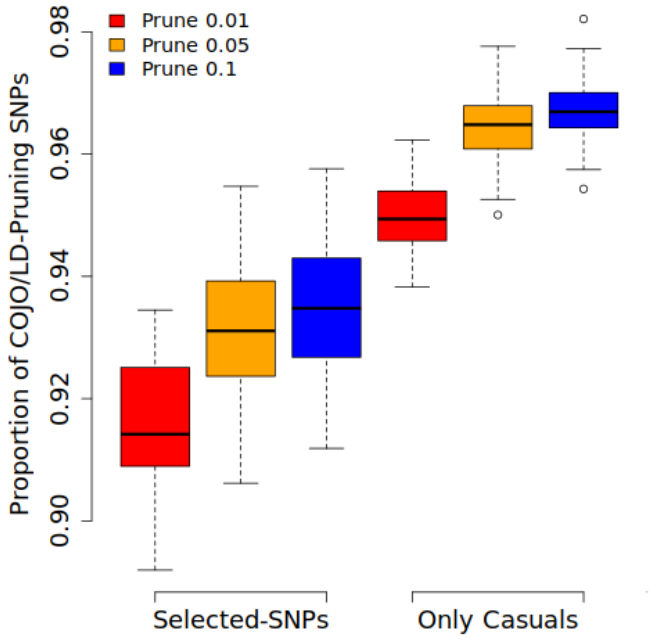
By considering all this information, we decided to consider LD-pruning ($r^2 = 0.05$) when calculating h^2_{GWAS} that can end with more reliable values for h^2_{GWAS} without a severe overestimation or underestimation.

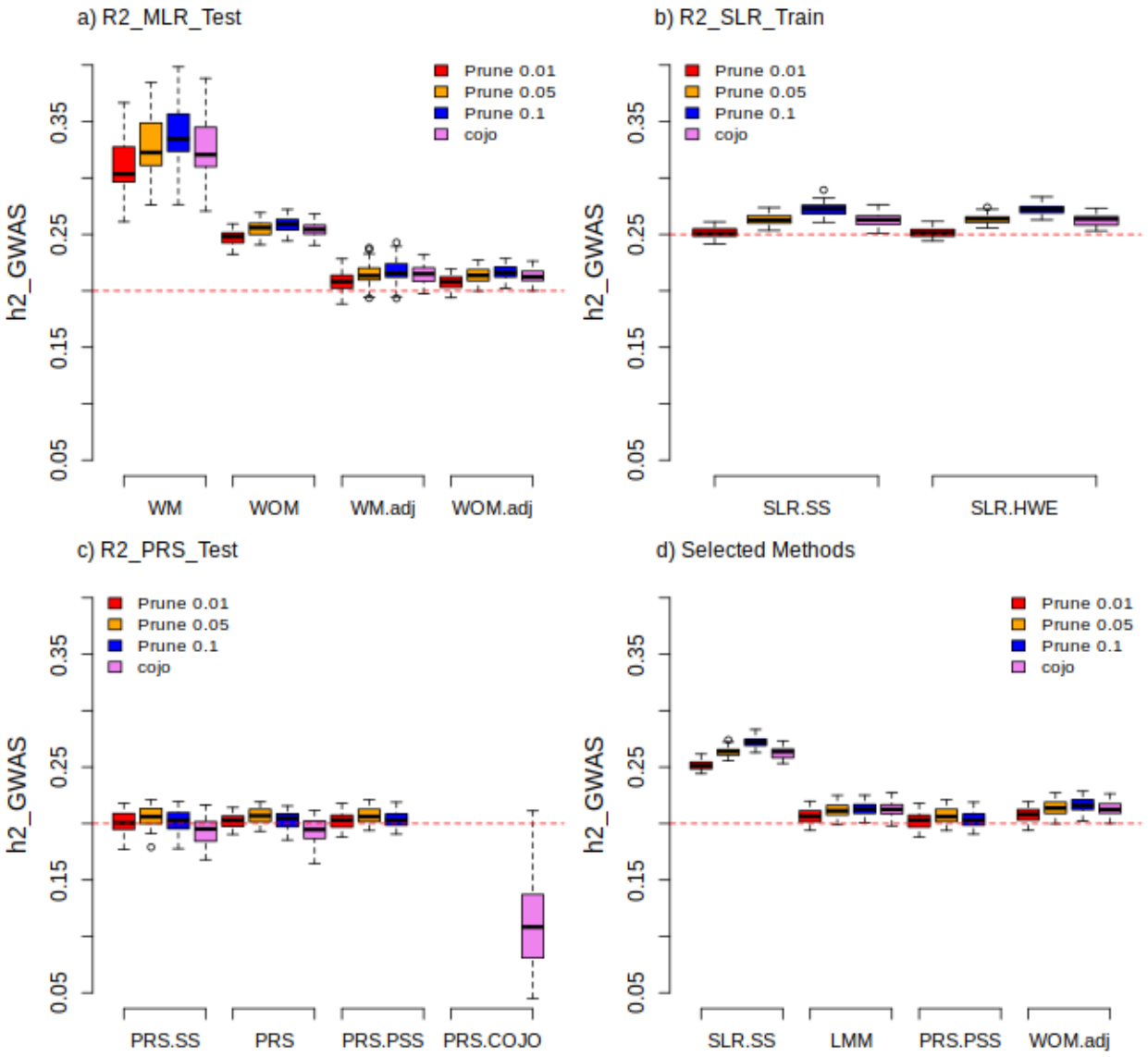
Part 3. Supplementary Figures:

Supplementary Fig. 1, provides information about the number of selected and causal SNPs extracted from different clumping methods. Part (a) shows the number of selected SNPs clumped after pruning and causal SNPs (we extracted causals from selected SNPs from simulated causal SNPs list). Part (b) represents, the creation of a gap between true causals and selected SNPs. It shows by adding more dependent SNPs the chance of being causal SNP decreases. Part (c) displays an ascending trend in false discovery rate when more correlated SNPs enter to the study. In part(d) the chance of finding true causal SNP under this sample size and Bonferroni test can be seen.

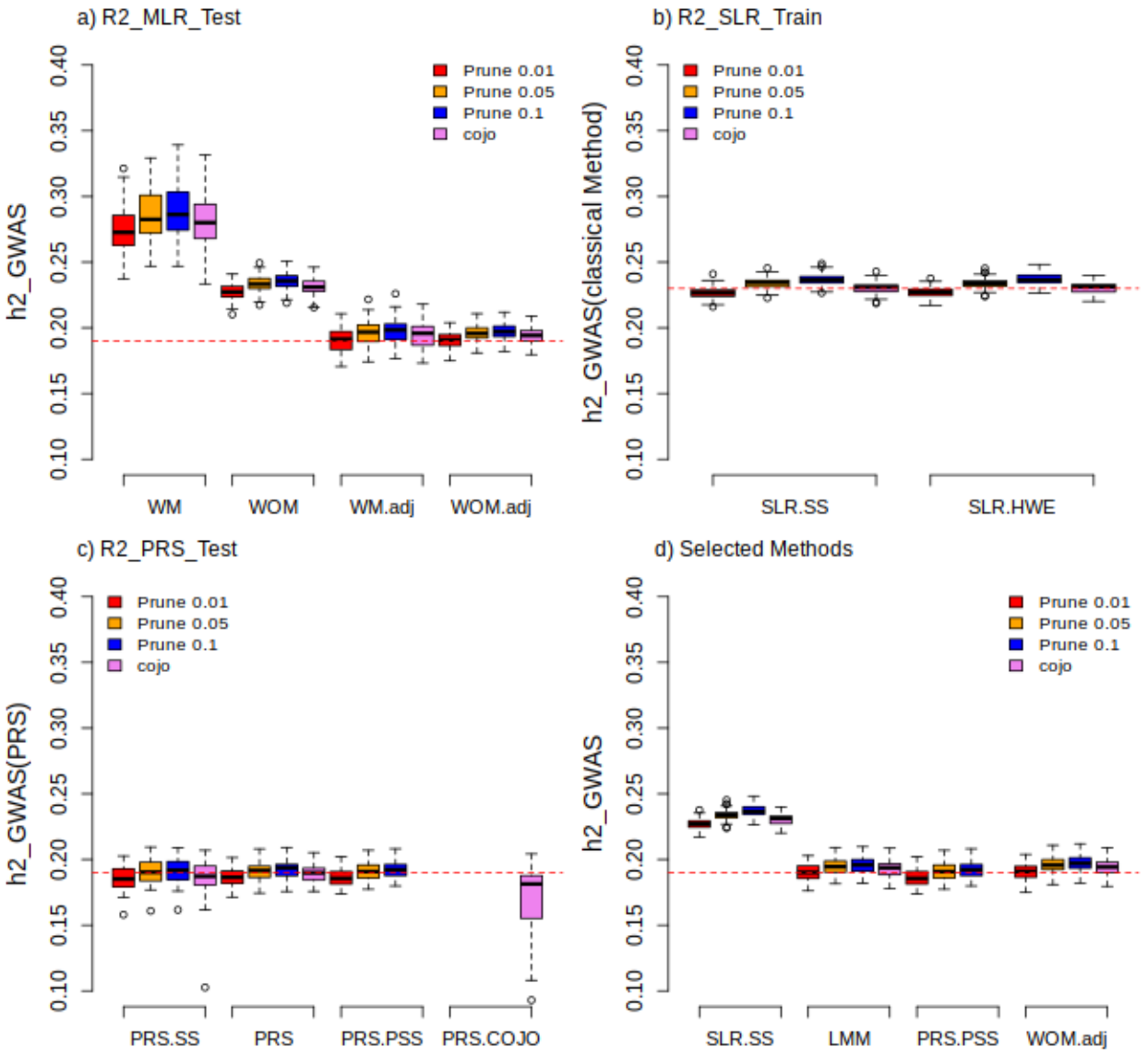


Supplementary Fig. 2. This figure shows the percentage of selected and only causal SNPs explored by COJO and LD-pruning under the titles of selected-SNPs and only causals in the figure. It can be seen that most of the differences are because of non-casuals than causal SNPs. In other words, with considering COJO analysis and LD-pruning ($r^2 = 0.05$) there are near 97% of causal SNPs but when considering selected SNPs the proportion of common SNPs decreases by 4% to 93%.

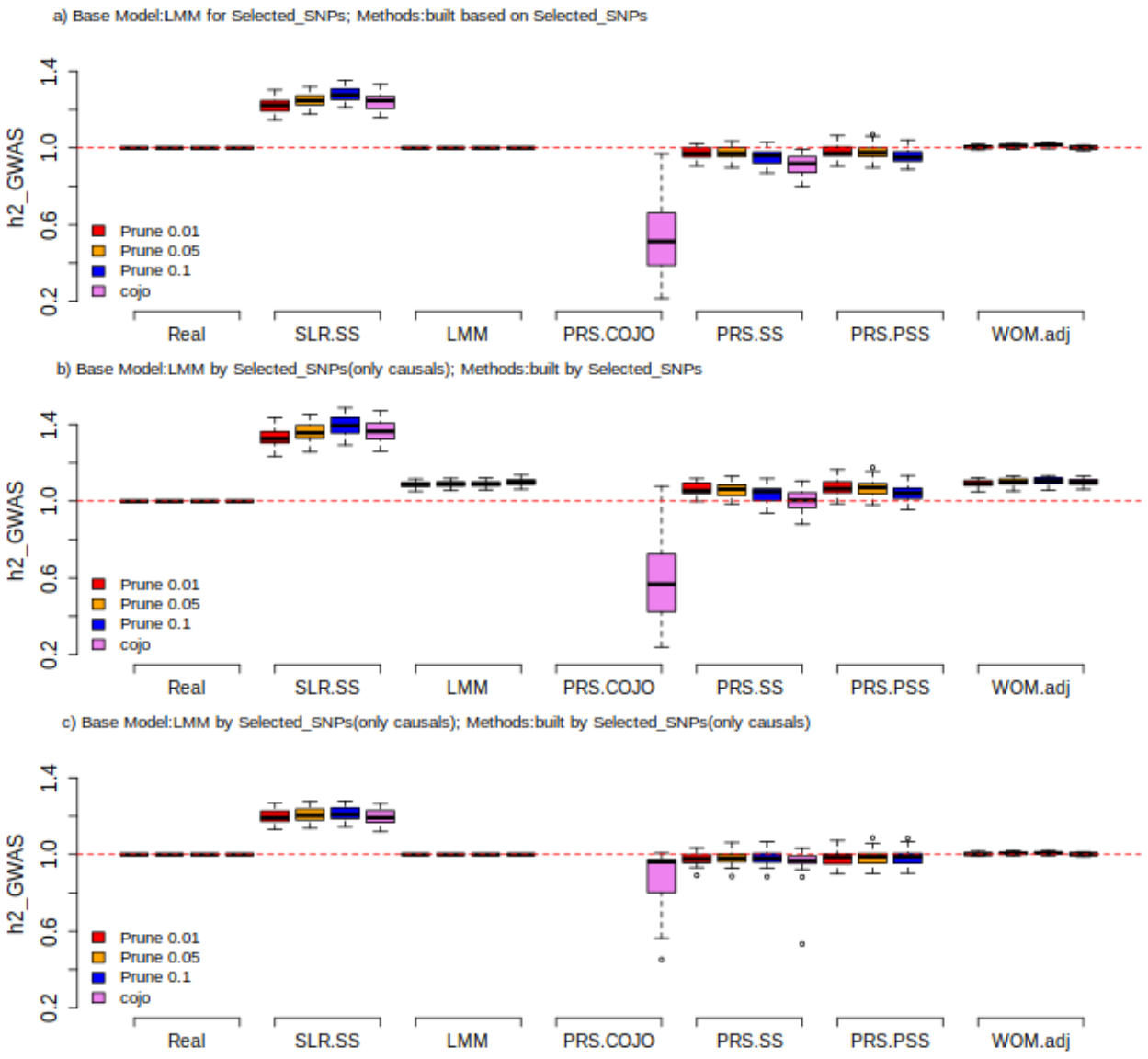




Supplementary Fig. 3. Comparing different methods of estimating h^2_{GWAS} explained in table 1of the paper for selected SNPs. In part (a), R^2 is prediction accuracy in $R^2\_MLR_{Test}$ method. WM: R^2 with missing SNPs, WOM: R^2 without missing SNPs (missing SNPs were replaced by their mean), WM.adj: $adjusted\ R^2$ with missing SNPs and WOM.adj: $adjusted\ R^2$ without missing SNPs, missing were replaced by their mean. **(b)**, $SLR.HWE$ and $SLR.SS$ are estimates of $R^2\_SLR_{Train}$, where variance of SNPs is obtained based on binomial distribution and the data respectively. **(c),** $PRS.COJO$, $PRS.SS$, PRS and $PRS.PSS$ are estimates of R^2_PRS_COJO$_{\text{Test}}$, R^2_PRS_SS$_{\text{Test}}$, R^2_PRS and R^2_PRS_PSS$_{\text{Test}}$ methods, respectively. **(d),** LMM is an estimate from LMM_{Test} method. Other than $SLR.HWE$ and $SLR.SS$ which was made based on information from train data set, the rest of models were built from a validation (test) data set. In this outputs, selected SNPs were applied in the calculations.



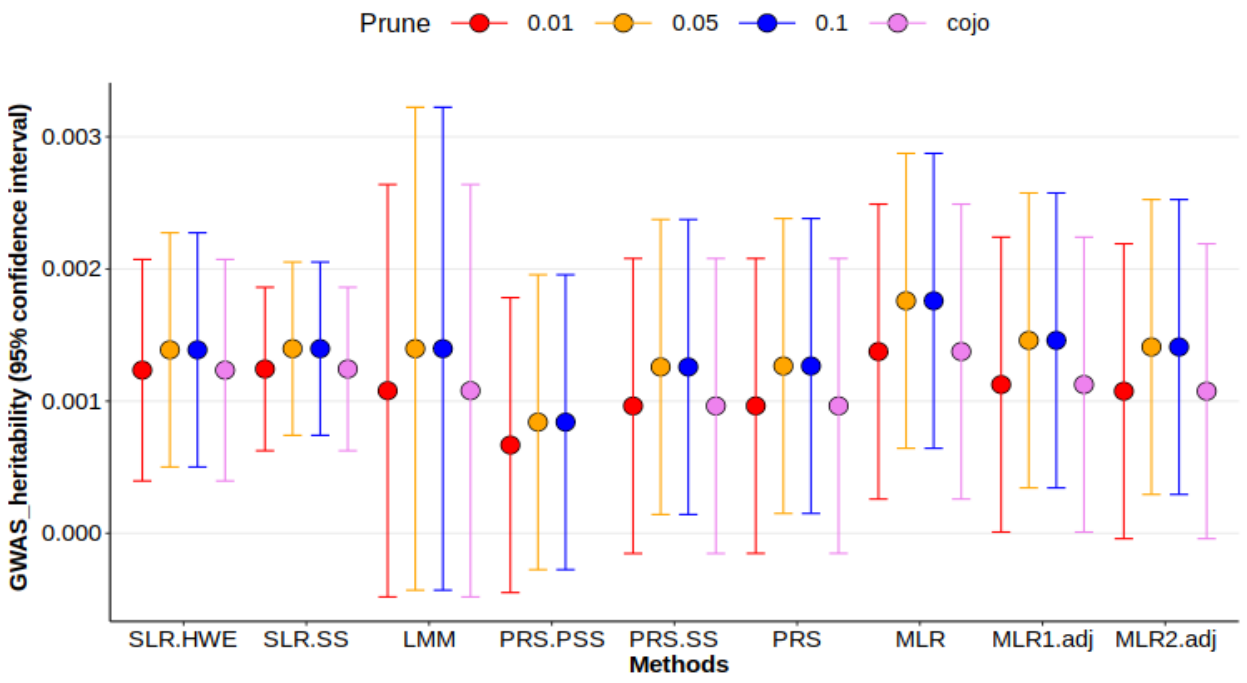
Supplementary Fig. 4. Comparing different methods of estimating h^2_{GWAS} clarified in table 1of the paper for only causal SNPs. Here causal SNPs extracted from selected SNPs in Supplementary Figure 4 and applied in the analysis. **In part (a),** R^2 is prediction accuracy in $R^2\_MLR_{Test}$ method. WM: R^2 with missing SNPs, WOM: R^2 without missing SNPs (missing SNPs were replaced by their mean), WM.adj: $adjusted\ R^2$ with missing SNPs and WOM.adj: $adjusted\ R^2$ without missing SNPs, missing were replaced by their mean. **(b)**, $SLR.HWE$ and $SLR.SS$ are estimates of $R^2\_SLR_{Train}$, where variance of SNPs is obtained based on binomial distribution and the data respectively. **(c),** $PRS.COJO$, $PRS.SS$, PRS and $PRS.PSS$ are estimates of R^2_PRS_COJO$_{\text{Test}}$, R^2_PRS_SS$_{\text{Test}}$, R^2_PRS and R^2_PRS_PSS$_{\text{Test}}$ methods, respectively. **(d),** LMM is an estimate from LMM_{Test} method. Other than $SLR.HWE$ and $SLR.SS$ which was made based on information from train data set, the rest of models were built from a validation (test) data set. In this results, selected SNPs were considered in the analysis.



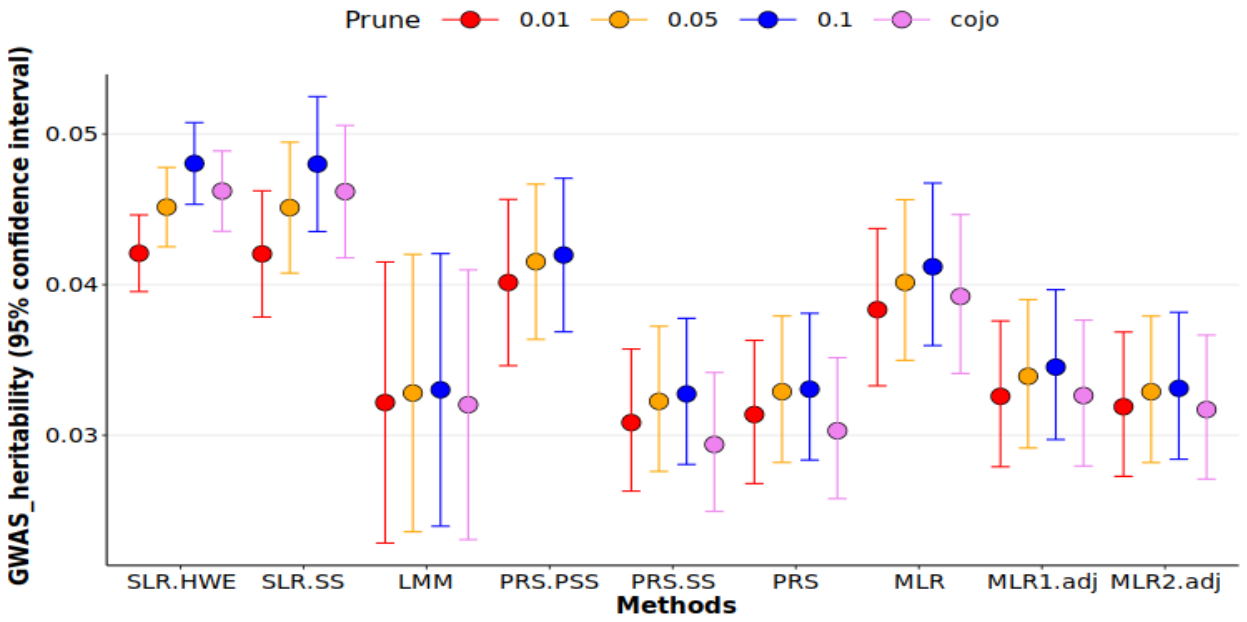
Supplementary Fig 5. Comparing different methods of estimating h^2_{GWAS} described in the paper (table 1) for both causal SNPs and selected SNPs by assuming LMM constructed from causal SNPs and selected SNPs. In part (a), selected SNPs were considered for constructing LMM as base model and other methods. We did the same analysis in part(c), by replacing selected SNPs with causal SNPs. In part (b), LMM constructed from causal SNPs (base model) while other methods were constructed from selected SNPs. Base model in each selection is shown by. R^2 is prediction accuracy in $R^2\_MLR_{Test}$ method. WOM.adj is $adjusted - R^2$ without missing SNPs, missing SNPs were replaced by their mean. $SLR.SS$ is an estimates from $R^2\_SLR_{Train}$ where variance of SNPs is calculated based on the data. $PRS.COJO$, $PRS.SS$ and $PRS.PSS$ are estimates of R^2_PRS_COJO$_{\text{Test}}$, R^2_PRS_SS_{Test} and R^2_PRS_PSS$_{\text{Test}}$ methosds respectively. LMM is an estimate of LMM_{Test} method. Other than $SLR.SS$ which was made based on information from train data set, the rest of models were built from a validation (test) data set.

In supplementary figures 6-13, Comparing different methods of estimating h^2_{GWAS} for 8 traits of UKBB. These traits are: ever smoked, forced vital capacity, hypertension, impedance, neuroticism score, pulse rate, reaction time and systolic blood pressure.

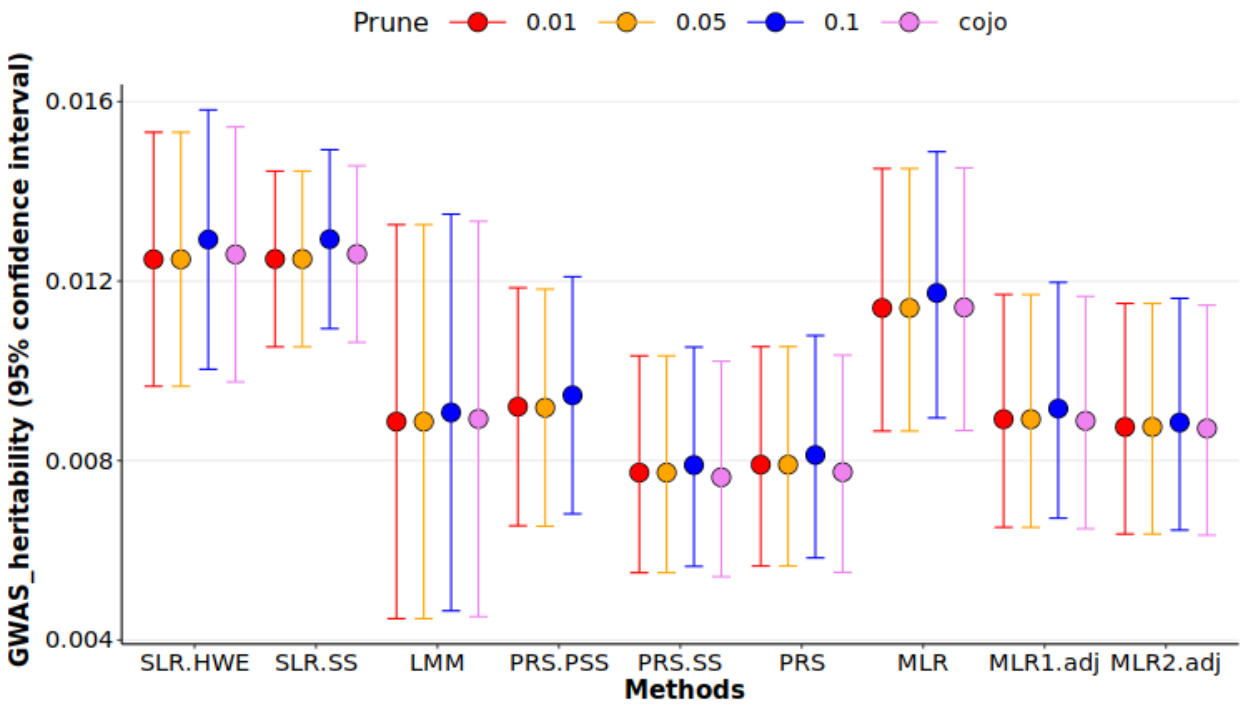
Supplementary Fig. 6. Comparing different methods of estimating h^2_{GWAS} for ever smoked trait. About methods: SLR_HWE and SLR_SS are estimates from R^2_SLR_{Train} method where variance of SNPs is calculated based on binomial distribution and the data itself respectively. PRS_PSS_{Test}, PRS_SS_{Test} and PRS_{Test} are estimates of correlation between y and $\hat{y}$(PRS) that PRS has been made from pseudo summary statistic, summary statistic and real phenotype. MLR is an estimate of R^2 from R^2_MLR_{Test} method. MLR1.adj and MLR2.adj are estimates of adjusted $-R^2$ via R^2_MLR_{Test} with filling missing SNPs with their mean and R^2 in R^2_MLR_{Test} with ignoring missing SNPs, respectively. LMM is an estimate of LMM_{Test} method. Other than SLR_HWE and SLR_SS which were made based on information from train data set, the rest of models were built from a validation (test) data set. In the figures, only selected SNPs were considered in the analysis. Also, LMM_{Test} considered as the base model.



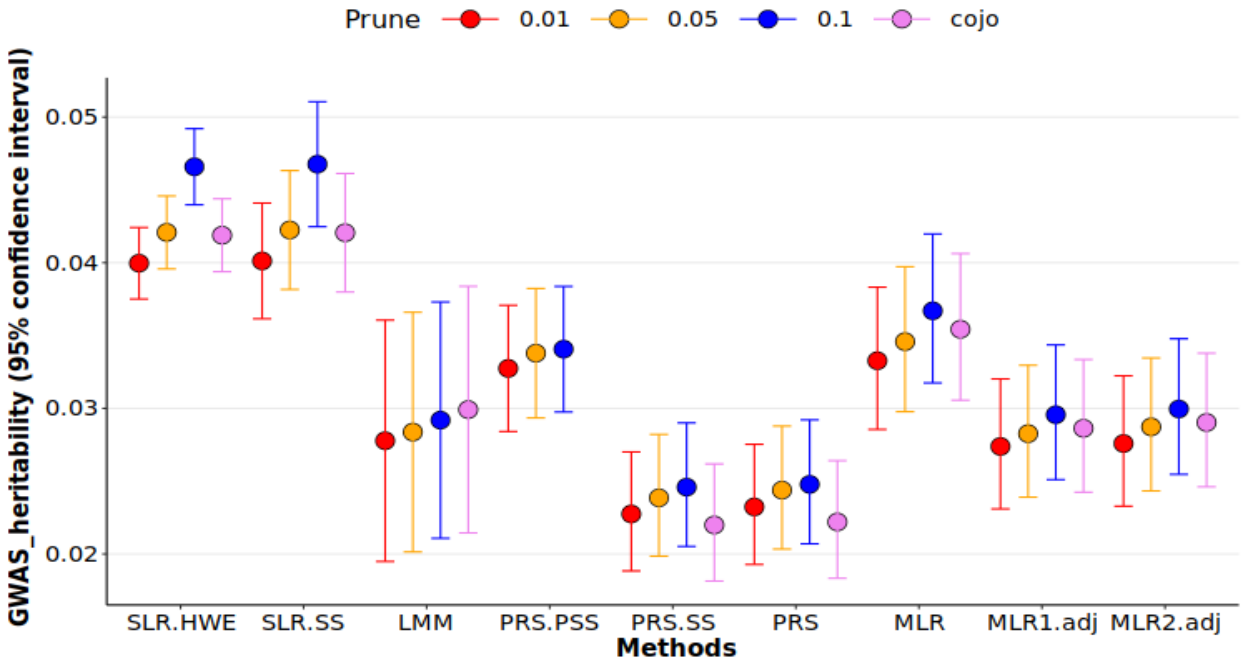
Supplementary Fig. 7. Comparing different methods of estimating h^2_{GWAS} for forced vital capacity trait. About methods: SLR_HWE and SLR_SS are estimates from R^2_SLR_{Train} method where variance of SNPs is calculated based on binomial distribution and the data itself respectively. PRS_PSS_{Test}, PRS_SS_{Test} and PRS_{Test} are estimates of correlation between y and $\hat{y}$(PRS) that PRS has been made from pseudo summary statistic, summary statistic and real phenotype. MLR is an estimate of R^2 from R^2_MLR_{Test} method. MLR1. adj and MLR2. adj are estimates of adjusted $-R^2$ via R^2_MLR_{Test} with filling missing SNPs with their mean and R^2 in R^2_MLR_{Test} with ignoring missing SNPs, respectively. LMM is an estimate of LMM_{Test} method. Other than SLR_HWE and SLR_SS which were made based on information from train data set, the rest of models were built from a validation (test) data set. In the figures, only selected SNPs were considered in the analysis. Also, LMM_{Test} considered as the base model.



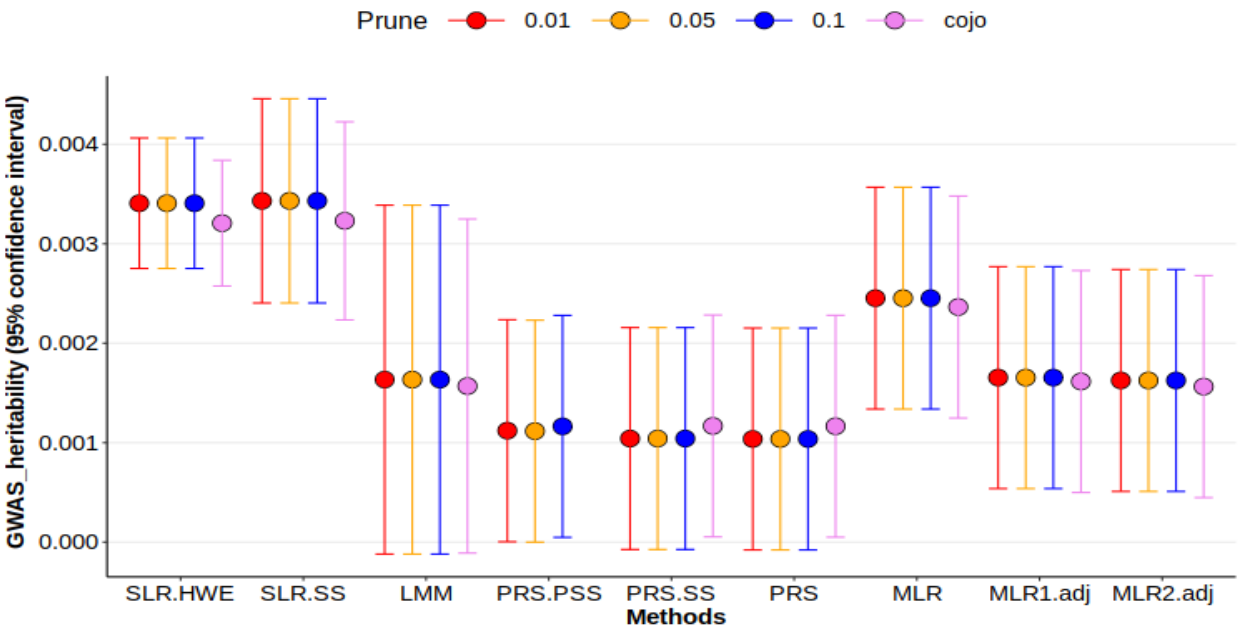
Supplementary Fig. 8. Comparing different methods of estimating h^2_{GWAS} for <u>hypertension</u> trait. <u>About methods:</u> SLR_HWE and SLR_SS are estimates from R^2_SLR_{Train} method where variance of SNPs is calculated based on binomial distribution and the data itself respectively. PRS_PSS_{Test}, PRS_SS_{Test} and PRS_{Test} are estimates of correlation between y and $\hat{y}$(PRS) that PRS has been made from pseudo summary statistic, summary statistic and real phenotype. MLR is an estimate of R^2 from R^2_MLR_{Test} method. MLR1. adj and MLR2. adj are estimates of adjusted $-R^2$ via R^2_MLR_{Test} with filling missing SNPs with their mean and R^2 in R^2_MLR_{Test} with ignoring missing SNPs, respectively. LMM is an estimate of LMM_{Test} method. Other than SLR_HWE and SLR_SS which were made based on information from train data set, the rest of models were built from a validation (test) data set. In the figures, only selected SNPs were considered in the analysis. Also, LMM_{Test} considered as the base model.



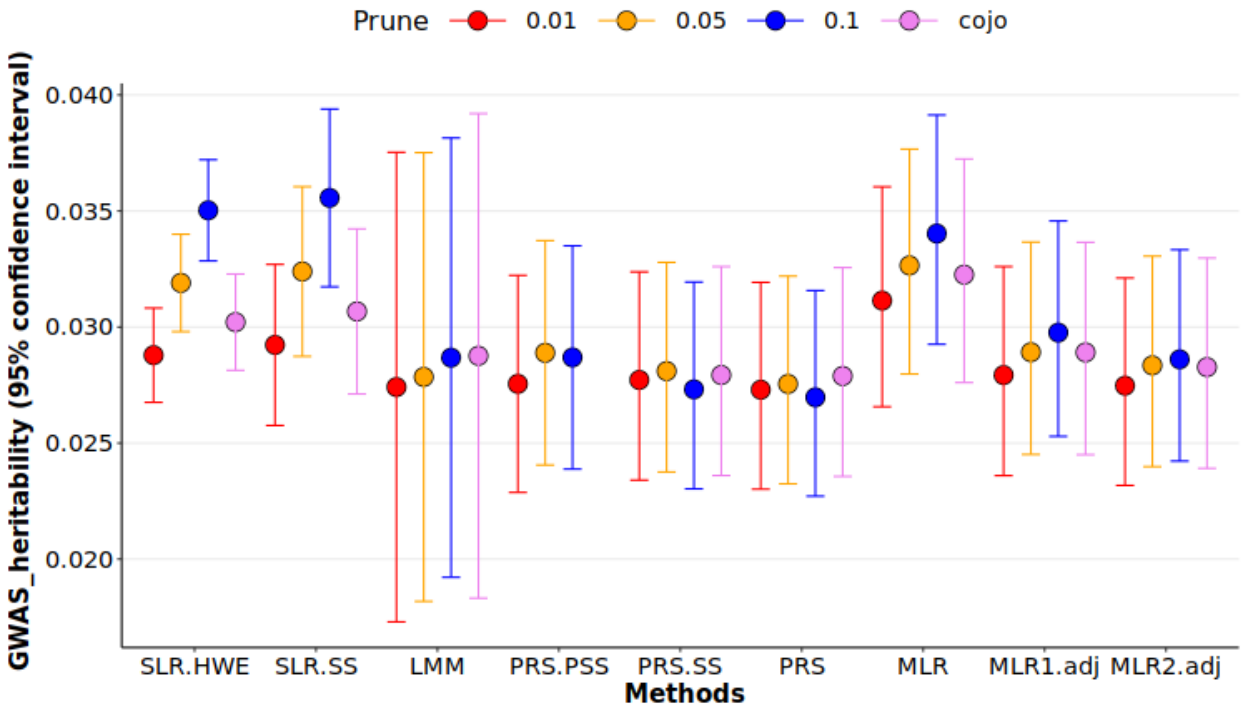
Supplementary Fig. 9. Comparing different methods of estimating h^2_{GWAS} for impedance trait. About methods: SLR_HWE and SLR_SS are estimates from R^2_SLR_{Train} method where variance of SNPs is calculated based on binomial distribution and the data itself respectively. PRS_PSS_{Test}, PRS_SS_{Test} and PRS_{Test} are estimates of correlation between y and $\hat{y}$(PRS) that PRS has been made from pseudo summary statistic, summary statistic and real phenotype. MLR is an estimate of R^2 from R^2_MLR_{Test} method. MLR1.adj and MLR2.adj are estimates of adjusted $-R^2$ via R^2_MLR_{Test} with filling missing SNPs with their mean and R^2 in R^2_MLR_{Test} with ignoring missing SNPs, respectively. LMM is an estimate of LMM_{Test} method. Other than SLR_HWE and SLR_SS which were made based on information from train data set, the rest of models were built from a validation (test) data set. In the figures, only selected SNPs were considered in the analysis. Also, LMM_{Test} considered as the base model.



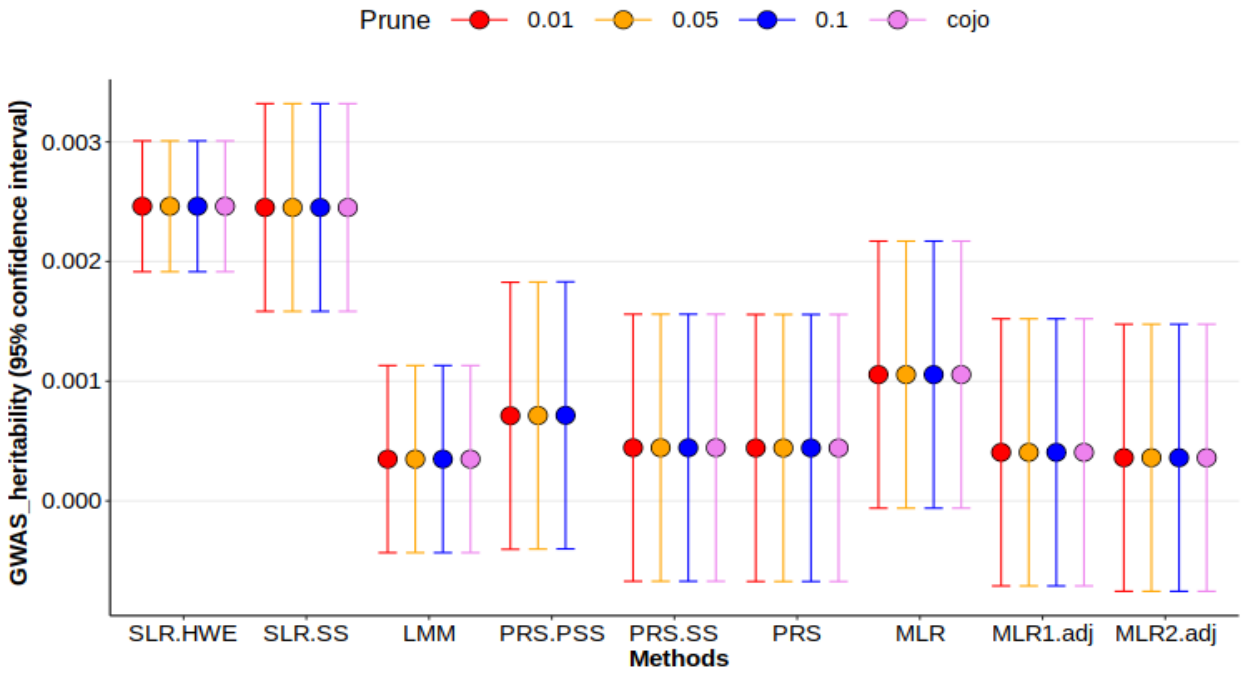
Supplementary Fig. 10. Comparing different methods of estimating h^2_{GWAS} for <u>neuroticism score</u> trait. <u>About methods:</u> SLR_HWE and SLR_SS are estimates from R^2_SLR_{Train} method where variance of SNPs is calculated based on binomial distribution and the data itself respectively. PRS_PSS_{Test}, PRS_SS_{Test} and PRS_{Test} are estimates of correlation between y and $\hat{y}$(PRS) that PRS has been made from pseudo summary statistic, summary statistic and real phenotype. MLR is an estimate of R^2 from R^2_MLR_{Test} method. MLR1. adj and MLR2. adj are estimates of adjusted $-R^2$ via R^2_MLR_{Test} with filling missing SNPs with their mean and R^2 in R^2_MLR_{Test} with ignoring missing SNPs, respectively. LMM is an estimate of LMM_{Test} method. Other than SLR_HWE and SLR_SS which were made based on information from train data set, the rest of models were built from a validation (test) data set. In the figures, only selected SNPs were considered in the analysis. Also, LMM_{Test} considered as the base model.



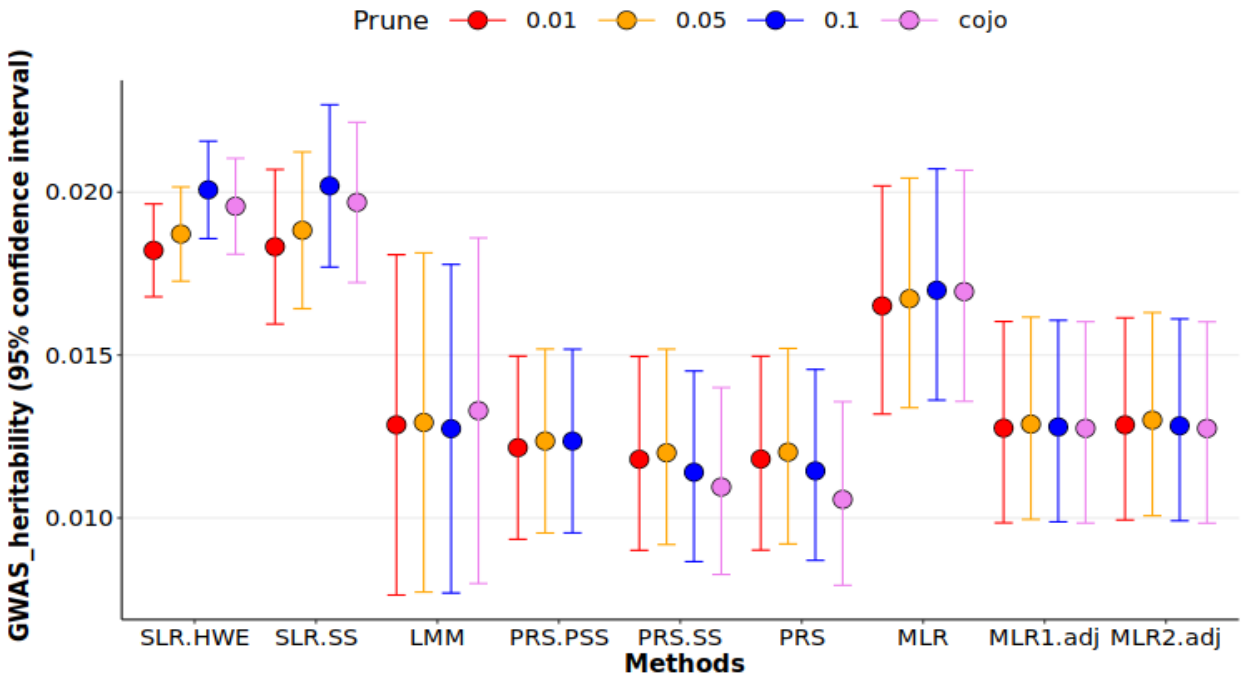
Supplementary Fig. 11. Comparing different methods of estimating h^2_{GWAS} for <u>pulse rate</u> trait. <u>About methods:</u> SLR_HWE and SLR_SS are estimates from R^2_SLR_{Train} method where variance of SNPs is calculated based on binomial distribution and the data itself respectively. PRS_PSS_{Test}, PRS_SS_{Test} and PRS_{Test} are estimates of correlation between y and $\hat{y}$(PRS) that PRS has been made from pseudo summary statistic, summary statistic and real phenotype. MLR is an estimate of R^2 from R^2_MLR_{Test} method. MLR1. adj and MLR2. adj are estimates of adjusted $-R^2$ via R^2_MLR_{Test} with filling missing SNPs with their mean and R^2 in R^2_MLR_{Test} with ignoring missing SNPs, respectively. LMM is an estimate of LMM_{Test} method. Other than SLR_HWE and SLR_SS which were made based on information from train data set, the rest of models were built from a validation (test) data set. In the figures, only selected SNPs were considered in the analysis. Also, LMM_{Test} considered as the base model.



Supplementary Fig. 12. Comparing different methods of estimating h^2_{GWAS} for reaction time trait. About methods: SLR_HWE and SLR_SS are estimates from R^2_SLR_{Train} method where variance of SNPs is calculated based on binomial distribution and the data itself respectively. PRS_PSS_{Test}, PRS_SS_{Test} and PRS_{Test} are estimates of correlation between y and $\hat{y}$(PRS) that PRS has been made from pseudo summary statistic, summary statistic and real phenotype. MLR is an estimate of R^2 from R^2_MLR_{Test} method. MLR1.adj and MLR2.adj are estimates of adjusted $-R^2$ via R^2_MLR_{Test} with filling missing SNPs with their mean and R^2 in R^2_MLR_{Test} with ignoring missing SNPs, respectively. LMM is an estimate of LMM_{Test} method. Other than SLR_HWE and SLR_SS which were made based on information from train data set, the rest of models were built from a validation (test) data set. In the figures, only selected SNPs were considered in the analysis. Also, LMM_{Test} considered as the base model.

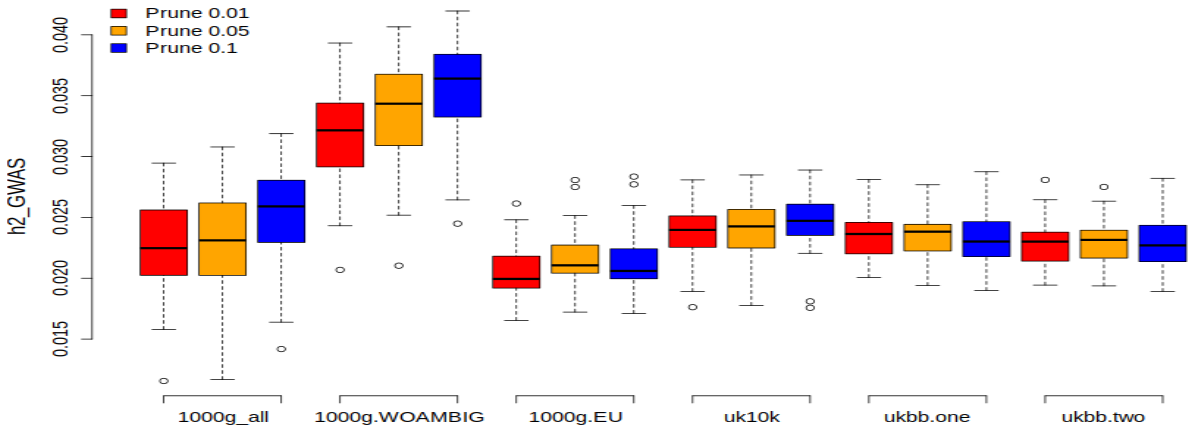


Supplementary Fig. 13. Comparing different methods of estimating h^2_{GWAS} for systolic blood pressure trait. About methods: SLR_HWE and SLR_SS are estimates from R^2_SLR_{Train} method where variance of SNPs is calculated based on binomial distribution and the data itself respectively. PRS_PSS_{Test}, PRS_SS_{Test} and PRS_{Test} are estimates of correlation between y and $\hat{y}$(PRS) that PRS has been made from pseudo summary statistic, summary statistic and real phenotype. MLR is an estimate of R^2 from R^2_MLR_{Test} method. MLR1.adj and MLR2.adj are estimates of adjusted $-R^2$ via R^2_MLR_{Test} with filling missing SNPs with their mean and R^2 in R^2_MLR_{Test} with ignoring missing SNPs, respectively. LMM is an estimate of LMM_{Test} method. Other than SLR_HWE and SLR_SS which were made based on information from train data set, the rest of models were built from a validation (test) data set. In the figures, only selected SNPs were considered in the analysis. Also, LMM_{Test} considered as the base model.

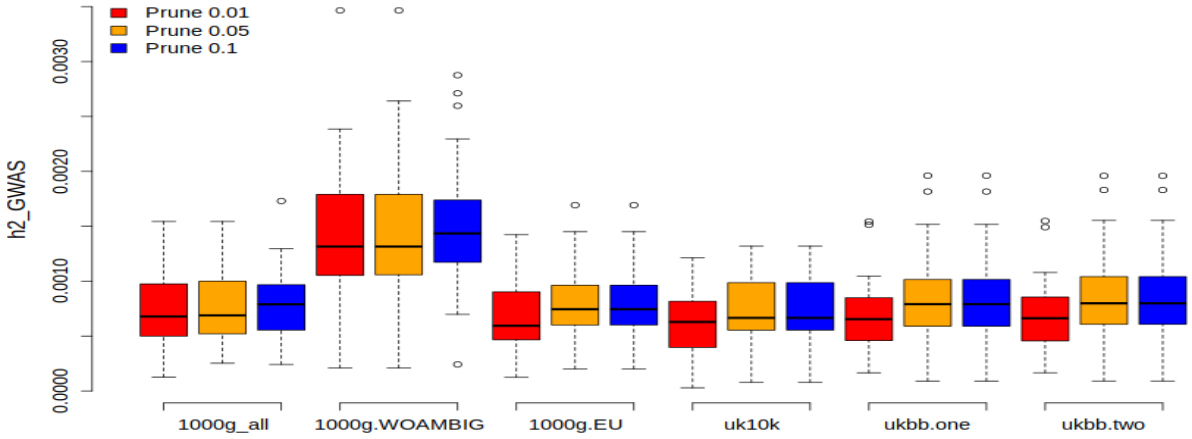


In figures 14-22, h^2_{GWAS} was estimated through PRS-PSS for 9 traits of UKBB (Body mass index (BMI) ever smoked, forced vital capacity, hypertension, impedance, neuroticism score, pulse rate, reaction time and systolic blood pressure) for 6 reference panels.

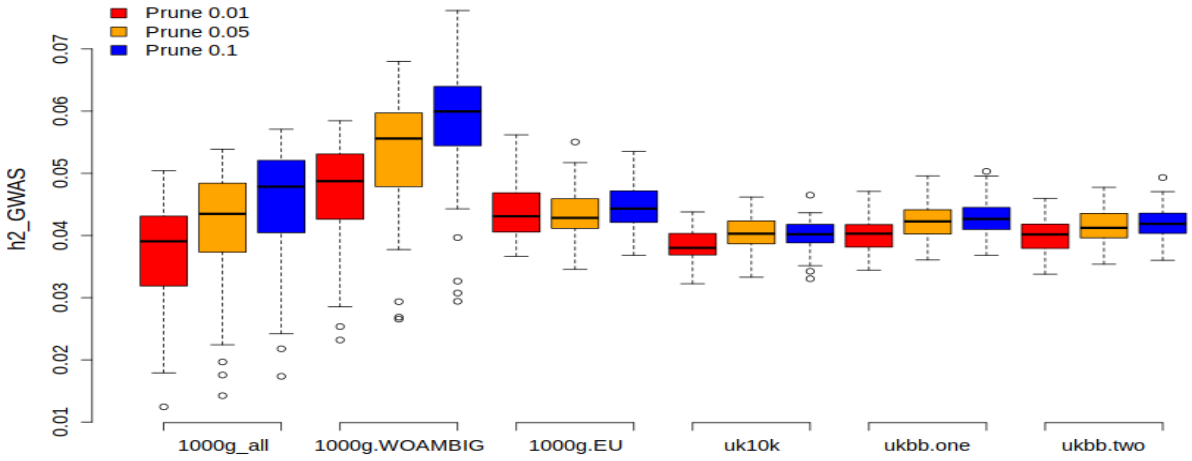
Supplementary Fig. 14. Calculating h^2_{GWAS} through R^2_PRS_PSS_{Test} for BMI for the 6 reference panels. The first three reference panels were extracted from 1000_genome study so that 1) all ancestries with 2504 individuals (1000g_all). 2) all ancestries with removing ambiguous alleles with 2504 individuals (1000g_WOAMBIG). 3) only European ancestry with 404 individuals (1000g.EU). 4) UK10K with 3708 individuals. For UKBB, two scenarios were considered, 5) Making both pseudo summary statistics and PRS based on one independent sample from UKBB for 5000 individuals. 6) Using two independent sample of size 5000 from UKBB, one for making pseudo summary statistics and another one for constructing PRSs.



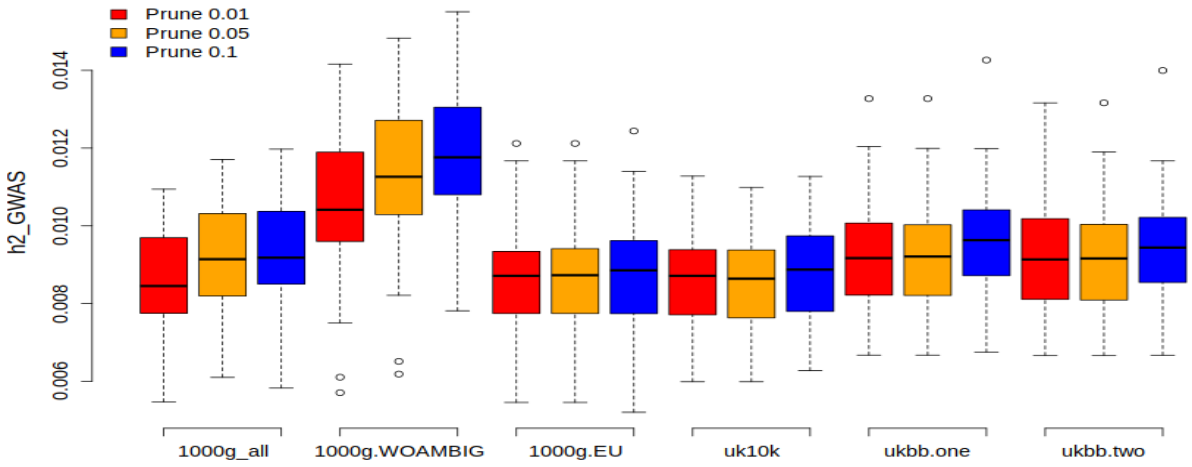
Supplementary Fig. 15. Calculating h^2_{GWAS} for <u>ever smoked</u> through R^2_PRS_PSS_{Test} for the 6 reference panels. The first three reference panels were extracted from 1000_genome study so that 1) all ancestries with 2504 individuals (1000g_all). 2) all ancestries with removing ambiguous alleles with 2504 individuals (1000g_WOAMBIG). 3) only European ancestry with 404 individuals (1000g.EU). 4) UK10K with 3708 individuals. For UKBB, two scenarios were considered, 5) Making both pseudo summary statistics and PRS based on one independent sample from UKBB for 5000 individuals. 6) Using two independent sample of size 5000 from UKBB, one for making pseudo summary statistics and another one for constructing PRSs.



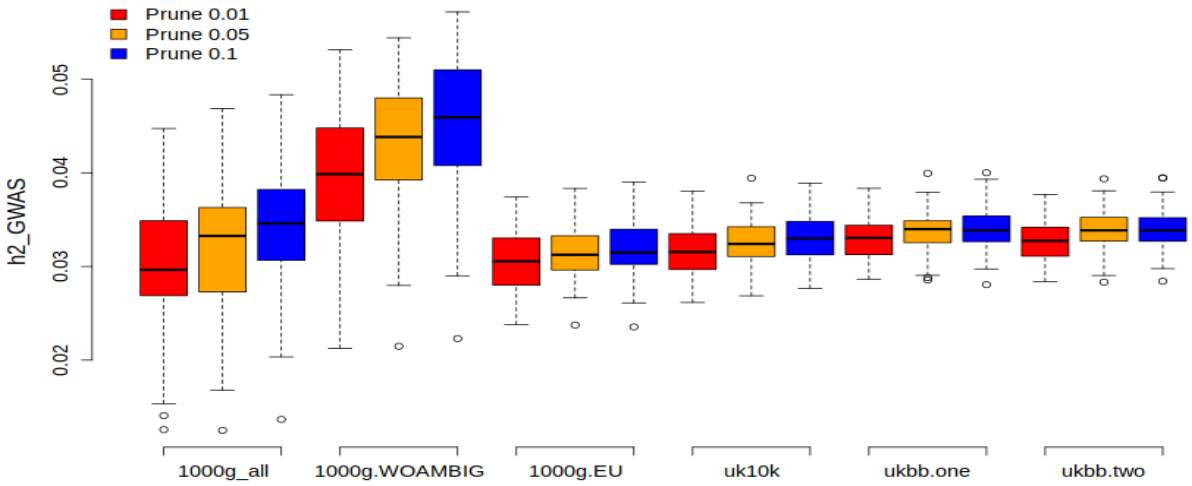
Supplementary Figure 16. Calculating h^2_{GWAS} for <u>forced vital capacity</u> through R^2_PRS_PSS_{Test} for the 6 reference panels. The first three reference panels were extracted from 1000_genome study so that 1) all ancestries with 2504 individuals (1000g_all). 2) all ancestries with removing ambiguous alleles with 2504 individuals (1000g_WOAMBIG). 3) only European ancestry with 404 individuals (1000g.EU). 4) UK10K with 3708 individuals. For UKBB, two scenarios were considered, 5) Making both pseudo summary statistics and PRS based on one independent sample from UKBB for 5000 individuals. 6) Using two independent sample of size 5000 from UKBB, one for making pseudo summary statistics and another one for constructing PRSs.



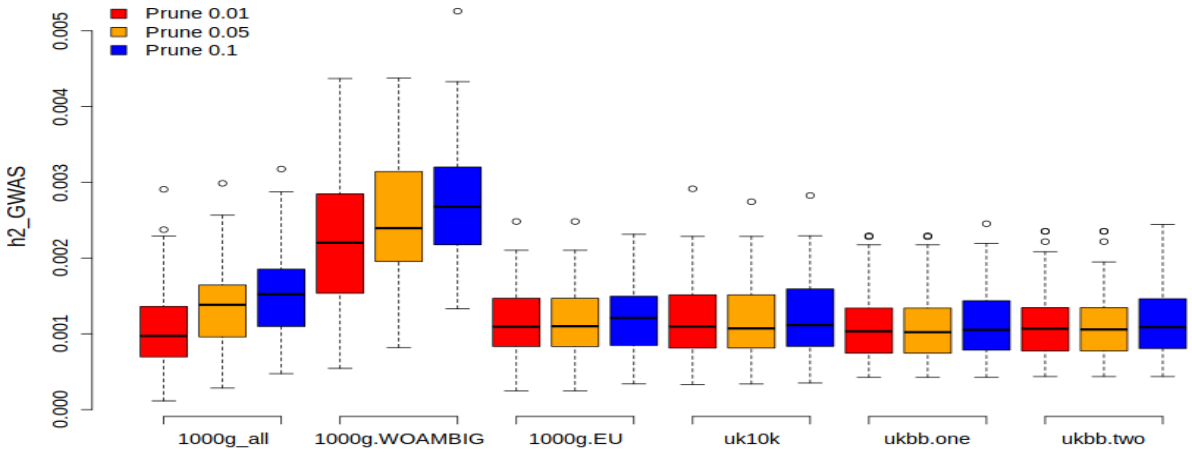
Supplementary Fig. 17. Calculating h^2_{GWAS} for <u>hypertension</u> through R^2_PRS_PSS_{Test} for the 6 reference panels. The first three reference panels were extracted from 1000_genome study so that 1) all ancestries with 2504 individuals (1000g_all). 2) all ancestries with removing ambiguous alleles with 2504 individuals (1000g_WOAMBIG). 3) only European ancestry with 404 individuals (1000g.EU). 4) UK10K with 3708 individuals. For UKBB, two scenarios were considered, 5) Making both pseudo summary statistics and PRS based on one independent sample from UKBB for 5000 individuals. 6) Using two independent sample of size 5000 from UKBB, one for making pseudo summary statistics and another one for constructing PRSs.



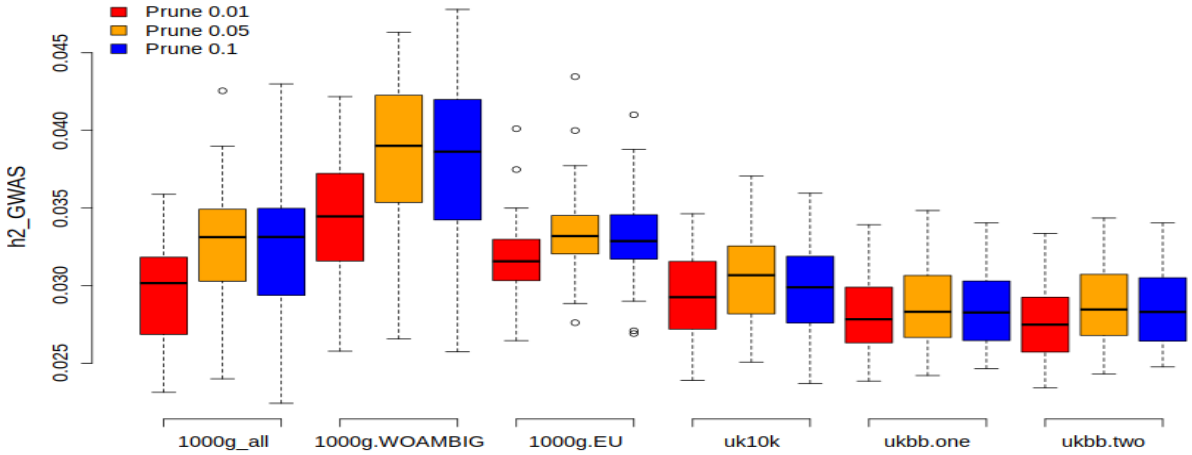
Supplementary Fig. 18. Calculating h^2_{GWAS} for <u>impedance</u> through R^2_PRS_PSS_{Test} for the 6 reference panels. The first three reference panels were extracted from 1000_genome study so that 1) all ancestries with 2504 individuals (1000g_all). 2) all ancestries with removing ambiguous alleles with 2504 individuals (1000g_WOAMBIG). 3) only European ancestry with 404 individuals (1000g.EU). 4) UK10K with 3708 individuals. For UKBB, two scenarios were considered, 5) Making both pseudo summary statistics and PRS based on one independent sample from UKBB for 5000 individuals. 6) Using two independent sample of size 5000 from UKBB, one for making pseudo summary statistics and another one for constructing PRSs.



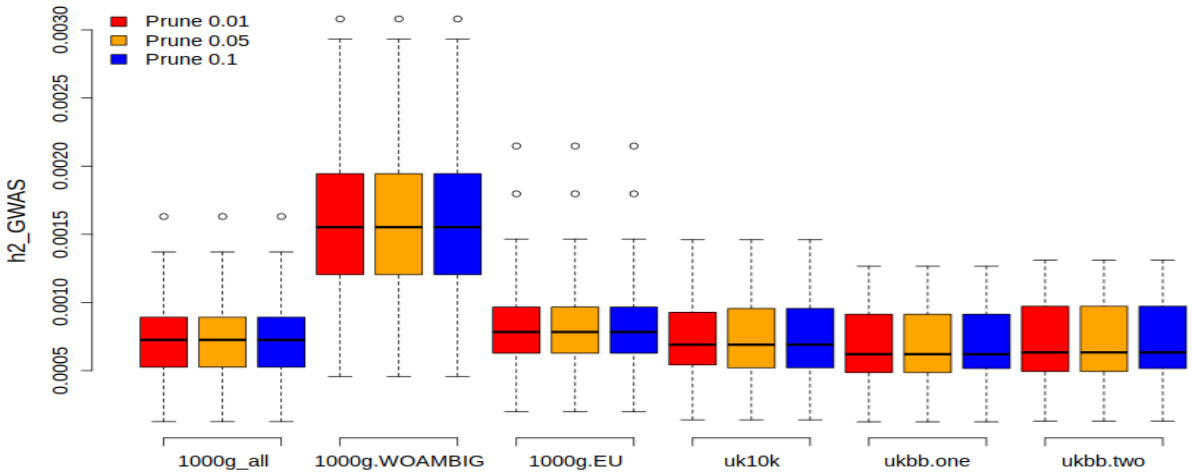
Supplementary Fig. 19. Calculating h^2_{GWAS} for <u>neuroticism score</u> through R^2_PRS_PSS_{Test} for the 6 reference panels. The first three reference panels were extracted from 1000_genome study so that 1) all ancestries with 2504 individuals (1000g_all). 2) all ancestries with removing ambiguous alleles with 2504 individuals (1000g_WOAMBIG). 3) only European ancestry with 404 individuals (1000g.EU). 4) UK10K with 3708 individuals. For UKBB, two scenarios were considered, 5) Making both pseudo summary statistics and PRS based on one independent sample from UKBB for 5000 individuals. 6) Using two independent sample of size 5000 from UKBB, one for making pseudo summary statistics and another one for constructing PRSs.



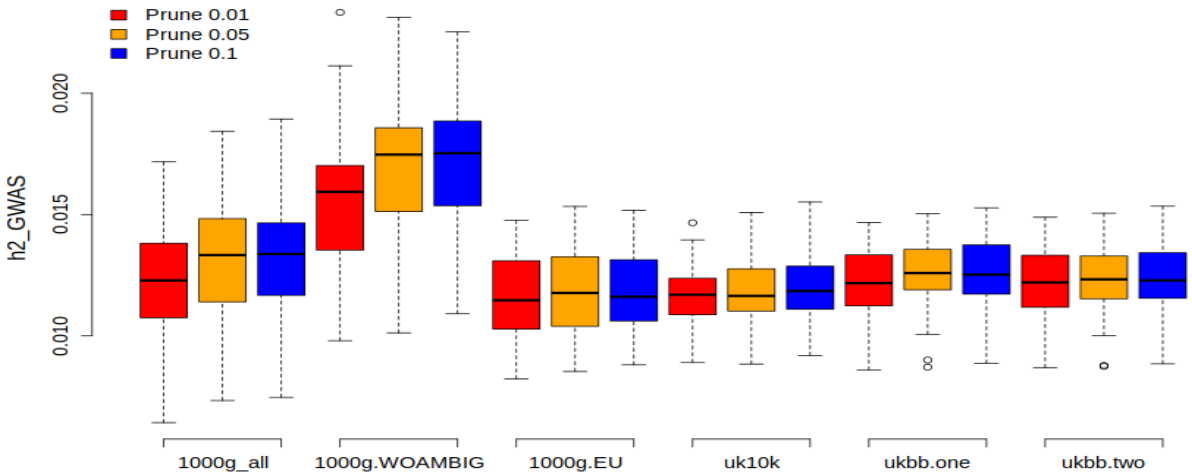
Supplementary Fig. 20. Calculating h^2_{GWAS} for <u>pulse rate</u> through R^2_PRS_PSS_{Test} for the 6 reference panels. The first three reference panels were extracted from 1000_genome study so that 1) all ancestries with 2504 individuals (1000g_all). 2) all ancestries with removing ambiguous alleles with 2504 individuals (1000g_WOAMBIG). 3) only European ancestry with 404 individuals (1000g.EU). 4) UK10K with 3708 individuals. For UKBB, two scenarios were considered, 5) Making both pseudo summary statistics and PRS based on one independent sample from UKBB for 5000 individuals. 6) Using two independent sample of size 5000 from UKBB, one for making pseudo summary statistics and another one for constructing PRSs.



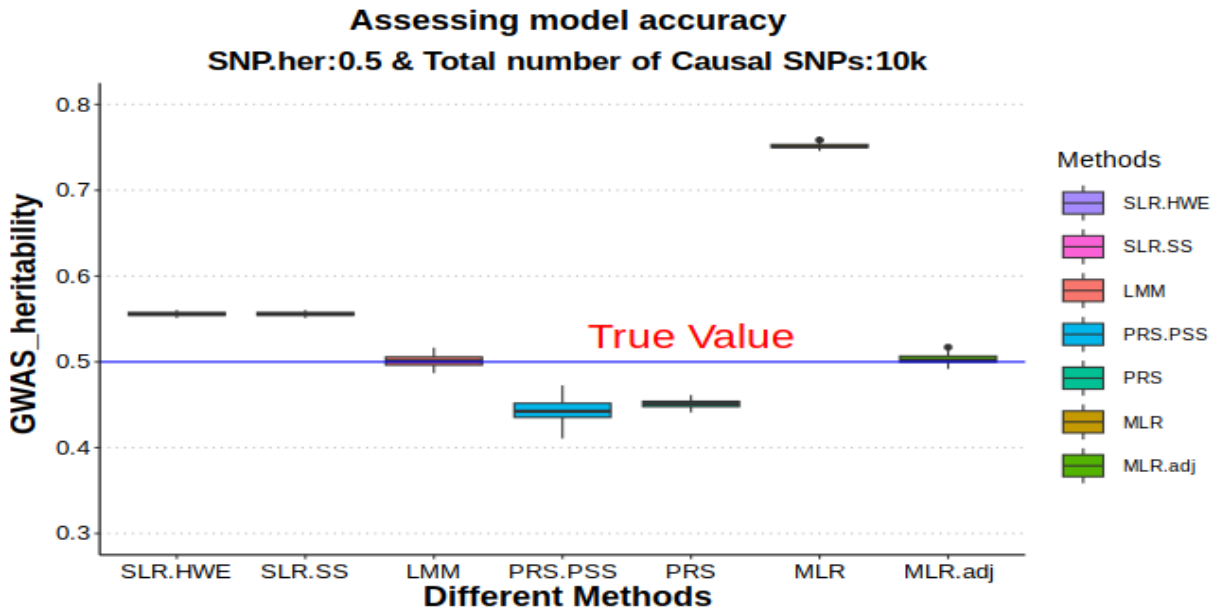
Supplementary Fig. 21. Calculating h^2_{GWAS} for reaction time through R^2_PRS_PSS_{Test} for the 6 reference panels. The first three reference panels were extracted from 1000_genome study so that 1) all ancestries with 2504 individuals (1000g_all). 2) all ancestries with removing ambiguous alleles with 2504 individuals (1000g_WOAMBIG). 3) only European ancestry with 404 individuals (1000g.EU). 4) UK10K with 3708 individuals. For UKBB, two scenarios were considered, 5) Making both pseudo summary statistics and PRS based on one independent sample from UKBB for 5000 individuals. 6) Using two independent sample of size 5000 from UKBB, one for making pseudo summary statistics and another one for constructing PRSs.



Supplementary Fig. 22. Calculating h^2_{GWAS} for systolic blood pressure through R^2_PRS_PSS_{Test} for the 6 reference panels. The first three reference panels were extracted from 1000_genome study so that 1) all ancestries with 2504 individuals (1000g_all). 2) all ancestries with removing ambiguous alleles with 2504 individuals (1000g_WOAMBIG). 3) only European ancestry with 404 individuals (1000g.EU). 4) UK10K with 3708 individuals. For UKBB, two scenarios were considered, 5) Making both pseudo summary statistics and PRS based on one independent sample from UKBB for 5000 individuals. 6) Using two independent sample of size 5000 from UKBB, one for making pseudo summary statistics and another one for constructing PRSs.



Supplementary Fig. 23. Comparing different methods of estimating h^2_{GWAS} applying simulated phenotypes for all causal SNPs (Simulated genotypes in LE and HWE). 50,000 SNPs were generated for 220,000 samples, using LDAK software which takes Hardy-Weinberg equilibrium and linkage equilibrium into account. The MAF (minor allele frequency) of randomly selected SNPs ranges from 0 to 0.5. Then I used similar numbers of training and test samples, 200k and 20k respectively, to perform the analysis for different methods. About methods: SLR_HWE and SLR_SS are estimates from R^2_SLR_{Train} method where variance of SNPs is calculated based on binomial distribution and the data itself respectively. PRS_SS_{Test} and PRS_{Test} are estimates of correlation between y and $\hat{y}$(PRS) that PRS has been made from summary statistic and real phenotype, respectively. MLR and adjusted-MLR are estimates of R^2 from R^2_MLR_{Test} method. Finally, LMM is an estimate of LMM_{Test} method. Other than SLR_HWE and SLR_SS which were made based on information from train data set, the rest of models were built from a validation (test) data set. In the figure, only selected SNPs (SNPs in LD level of 0.05 in window size of 1 CM) considered in the analysis. Also, LMM_{Test} with selected SNPs considered as base model.



Part 4. This part demonstrates estimates of h^2_{GWAS} and their 95% confidence intervals using different methods for 10 traits of UKBB. These traits are: body mass index (BMI), height, impedance, neuroticism score, pulse rate, reaction time, ever smoked, hypertension, systolic blood pressure and forced vital capacity.

Supplementary Table 2: Shows h^2_{GWAS} estimates and their 95% confidence intervals using different methods for <u>height</u> trait.

Group	Prune	her	Lower band	Upper band
SLR.HWE	**0.01**	0.2241	0.2192	0.2290
SLR.HWE	**0.05**	0.2636	0.2583	0.2688
SLR.HWE	**0.1**	0.3038	0.2983	0.3094
SLR.HWE	**COJO**	0.2588	0.2535	0.2641
SLR.SS	**0.01**	0.2252	0.2169	0.2336
SLR.SS	**0.05**	0.2650	0.2560	0.2740
SLR.SS	**0.1**	0.3054	0.2958	0.3151
SLR.SS	**COJO**	0.2602	0.2512	0.2691
LMM	**0.01**	0.1854	0.1659	0.2050
LMM	**0.05**	0.1963	0.1777	0.2149
LMM	**0.1**	0.1977	0.1801	0.2153
LMM	**COJO**	0.2076	0.1878	0.2275
PRS.PSS	**0.01**	0.1823	0.1716	0.1929
PRS.PSS	**0.05**	0.1878	0.1772	0.1984
PRS.PSS	**0.1**	0.1891	0.1778	0.2005
PRS.PSS	**COJO**	NA	NA	NA
PRS.SS	**0.01**	0.1976	0.1877	0.2075
PRS.SS	**0.05**	0.2023	0.1924	0.2123
PRS.SS	**0.1**	0.2056	0.1956	0.2156
PRS.SS	**COJO**	0.2026	0.1927	0.2126
PRS	**0.01**	0.1920	0.1822	0.2019
PRS	**0.05**	0.2009	0.1910	0.2108
PRS	**0.1**	0.2010	0.1911	0.2109
PRS	**COJO**	0.1987	0.1889	0.2087
MLR	**0.01**	0.2181	0.2080	0.2283
MLR	**0.05**	0.2394	0.2291	0.2498
MLR	**0.1**	0.2530	0.2426	0.2635
MLR	**COJO**	0.2430	0.2327	0.2534
MLR1.adj	**0.01**	0.1937	0.1839	0.2036
MLR1.adj	**0.05**	0.2089	0.1989	0.2189
MLR1.adj	**0.1**	0.2167	0.2067	0.2269
MLR1.adj	**COJO**	0.2150	0.2050	0.2252
MLR2.adj	**0.01**	0.1914	0.1817	0.2013
MLR2.adj	**0.05**	0.2002	0.1903	0.2101
MLR2.adj	**0.1**	0.2049	0.1949	0.2149
MLR2.adj	**COJO**	0.2069	0.1970	0.2170

Supplementary Table 3: Shows h^2_{GWAS} estimates and their 95% confidence intervals using different methods for body mass index (BMI).

Group	Prune	her	Lower band	Upper band
SLR.HWE	**0.01**	0.0269	0.0248	0.0289
SLR.HWE	**0.05**	0.0281	0.0260	0.0301
SLR.HWE	**0.1**	0.0313	0.0291	0.0334
SLR.HWE	**COJO**	0.0281	0.0261	0.0302
SLR.SS	**0.01**	0.0269	0.0236	0.0301
SLR.SS	**0.05**	0.0281	0.0248	0.0314
SLR.SS	**0.1**	0.0313	0.0278	0.0348
SLR.SS	**COJO**	0.0281	0.0248	0.0314
LMM	**0.01**	0.0202	0.0127	0.0276
LMM	**0.05**	0.0204	0.0130	0.0277
LMM	**0.1**	0.0212	0.0139	0.0285
LMM	**COJO**	0.0206	0.0132	0.0281
PRS.PSS	**0.01**	0.0223	0.0184	0.0265
PRS.PSS	**0.05**	0.0225	0.0186	0.0267
PRS.PSS	**0.1**	0.0222	0.0183	0.0264
PRS.PSS	**COJO**	NA	NA	NA
PRS.SS	**0.01**	0.0186	0.0151	0.0225
PRS.SS	**0.05**	0.0186	0.0151	0.0225
PRS.SS	**0.1**	0.0179	0.0144	0.0217
PRS.SS	**COJO**	0.0188	0.0153	0.0227
PRS	**0.01**	0.0189	0.0153	0.0228
PRS	**0.05**	0.0191	0.0155	0.0230
PRS	**0.1**	0.0187	0.0151	0.0226
PRS	**COJO**	0.0188	0.0153	0.0227
MLR	**0.01**	0.0235	0.0196	0.0279
MLR	**0.05**	0.0242	0.0201	0.0285
MLR	**0.1**	0.0257	0.0215	0.0302
MLR	**COJO**	0.0240	0.0200	0.0284
MLR1.adj	**0.01**	0.0199	0.0162	0.0239
MLR1.adj	**0.05**	0.0202	0.0165	0.0242
MLR1.adj	**0.1**	0.0211	0.0174	0.0253
MLR1.adj	**COJO**	0.0200	0.0164	0.0241
MLR2.adj	**0.01**	0.0201	0.0165	0.0242
MLR2.adj	**0.05**	0.0204	0.0167	0.0244
MLR2.adj	**0.1**	0.0215	0.0177	0.0256
MLR2.adj	**COJO**	0.0205	0.0168	0.0246

Supplementary Table 4: Shows h^2_{GWAS} estimates and their 95% confidence intervals using different methods for ever smoked trait.

Group	Prune	her	Lower band	Upper band
SLR.HWE	**0.01**	0.0012	0.0004	0.0021
SLR.HWE	**0.05**	0.0014	0.0005	0.0023
SLR.HWE	**0.1**	0.0014	0.0005	0.0023
SLR.HWE	**COJO**	0.0012	0.0004	0.0021
SLR.SS	**0.01**	0.0012	0.0006	0.0019
SLR.SS	**0.05**	0.0014	0.0007	0.0021
SLR.SS	**0.1**	0.0014	0.0007	0.0021
SLR.SS	**COJO**	0.0012	0.0006	0.0019
LMM	**0.01**	0.0011	-0.0005	0.0026
LMM	**0.05**	0.0014	-0.0004	0.0032
LMM	**0.1**	0.0014	-0.0004	0.0032
LMM	**COJO**	0.0011	-0.0005	0.0026
PRS.PSS	**0.01**	0.0007	-0.0004	0.0018
PRS.PSS	**0.05**	0.0008	-0.0003	0.0020
PRS.PSS	**0.1**	0.0008	-0.0003	0.0020
PRS.PSS	**COJO**	NA	NA	NA
PRS.SS	**0.01**	0.0010	-0.0002	0.0021
PRS.SS	**0.05**	0.0013	0.0001	0.0024
PRS.SS	**0.1**	0.0013	0.0001	0.0024
PRS.SS	**COJO**	0.0010	-0.0002	0.0021
PRS	**0.01**	0.0010	-0.0002	0.0021
PRS	**0.05**	0.0013	0.0002	0.0024
PRS	**0.1**	0.0013	0.0002	0.0024
PRS	**COJO**	0.0010	-0.0002	0.0021
MLR	**0.01**	0.0014	0.0003	0.0025
MLR	**0.05**	0.0018	0.0006	0.0029
MLR	**0.1**	0.0018	0.0006	0.0029
MLR	**COJO**	0.0014	0.0003	0.0025
MLR1.adj	**0.01**	0.0011	0.0000	0.0022
MLR1.adj	**0.05**	0.0015	0.0003	0.0026
MLR1.adj	**0.1**	0.0015	0.0003	0.0026
MLR1.adj	**COJO**	0.0011	0.0000	0.0022
MLR2.adj	**0.01**	0.0011	0.0000	0.0022
MLR2.adj	**0.05**	0.0014	0.0003	0.0025
MLR2.adj	**0.1**	0.0014	0.0003	0.0025
MLR2.adj	**COJO**	0.0011	0.0000	0.0022

Supplementary Table 5: Shows h^2_{GWAS} estimates and their 95% confidence intervals using different methods for forced vital capacity trait.

Group	Prune	her	Lower band	Upper band
SLR.HWE	**0.01**	0.0421	0.0395	0.0446
SLR.HWE	**0.05**	0.0451	0.0425	0.0478
SLR.HWE	**0.1**	0.0480	0.0453	0.0508
SLR.HWE	**COJO**	0.0462	0.0435	0.0489
SLR.SS	**0.01**	0.0420	0.0378	0.0462
SLR.SS	**0.05**	0.0451	0.0408	0.0495
SLR.SS	**0.1**	0.0480	0.0435	0.0525
SLR.SS	**COJO**	0.0462	0.0418	0.0506
LMM	**0.01**	0.0322	0.0228	0.0415
LMM	**0.05**	0.0328	0.0236	0.0420
LMM	**0.1**	0.0330	0.0240	0.0421
LMM	**COJO**	0.0320	0.0231	0.0410
PRS.PSS	**0.01**	0.0401	0.0346	0.0457
PRS.PSS	**0.05**	0.0415	0.0364	0.0467
PRS.PSS	**0.1**	0.0420	0.0369	0.0471
PRS.PSS	**COJO**	NA	NA	NA
PRS.SS	**0.01**	0.0308	0.0263	0.0357
PRS.SS	**0.05**	0.0323	0.0276	0.0372
PRS.SS	**0.1**	0.0327	0.0281	0.0378
PRS.SS	**COJO**	0.0294	0.0249	0.0342
PRS	**0.01**	0.0314	0.0268	0.0363
PRS	**0.05**	0.0329	0.0282	0.0379
PRS	**0.1**	0.0331	0.0284	0.0381
PRS	**COJO**	0.0303	0.0258	0.0351
MLR	**0.01**	0.0383	0.0333	0.0437
MLR	**0.05**	0.0401	0.0350	0.0456
MLR	**0.1**	0.0412	0.0360	0.0467
MLR	**COJO**	0.0392	0.0341	0.0447
MLR1.adj	**0.01**	0.0326	0.0279	0.0376
MLR1.adj	**0.05**	0.0339	0.0292	0.0390
MLR1.adj	**0.1**	0.0345	0.0297	0.0397
MLR1.adj	**COJO**	0.0326	0.0280	0.0376
MLR2.adj	**0.01**	0.0319	0.0273	0.0369
MLR2.adj	**0.05**	0.0329	0.0282	0.0379
MLR2.adj	**0.1**	0.0331	0.0284	0.0382
MLR2.adj	**COJO**	0.0317	0.0271	0.0367

Supplementary Table 6: Shows h^2_{GWAS} estimates and their 95% confidence intervals using different methods for hypertension trait.

Group	Prune	her	Lower band	Upper band
SLR.HWE	**0.01**	0.0125	0.0097	0.0153
SLR.HWE	**0.05**	0.0125	0.0097	0.0153
SLR.HWE	**0.1**	0.0129	0.0100	0.0158
SLR.HWE	**COJO**	0.0126	0.0098	0.0154
SLR.SS	**0.01**	0.0125	0.0105	0.0145
SLR.SS	**0.05**	0.0125	0.0105	0.0145
SLR.SS	**0.1**	0.0129	0.0109	0.0149
SLR.SS	**COJO**	0.0126	0.0106	0.0146
LMM	**0.01**	0.0089	0.0045	0.0133
LMM	**0.05**	0.0089	0.0045	0.0133
LMM	**0.1**	0.0091	0.0047	0.0135
LMM	**COJO**	0.0089	0.0045	0.0133
PRS.PSS	**0.01**	0.0092	0.0065	0.0119
PRS.PSS	**0.05**	0.0092	0.0065	0.0118
PRS.PSS	**0.1**	0.0095	0.0068	0.0121
PRS.PSS	**COJO**	NA	NA	NA
PRS.SS	**0.01**	0.0077	0.0055	0.0103
PRS.SS	**0.05**	0.0077	0.0055	0.0103
PRS.SS	**0.1**	0.0079	0.0056	0.0105
PRS.SS	**COJO**	0.0076	0.0054	0.0102
PRS	**0.01**	0.0079	0.0056	0.0105
PRS	**0.05**	0.0079	0.0056	0.0105
PRS	**0.1**	0.0081	0.0058	0.0108
PRS	**COJO**	0.0077	0.0055	0.0103
MLR	**0.01**	0.0114	0.0087	0.0145
MLR	**0.05**	0.0114	0.0087	0.0145
MLR	**0.1**	0.0117	0.0090	0.0149
MLR	**COJO**	0.0114	0.0087	0.0145
MLR1.adj	**0.01**	0.0089	0.0065	0.0117
MLR1.adj	**0.05**	0.0089	0.0065	0.0117
MLR1.adj	**0.1**	0.0092	0.0067	0.0120
MLR1.adj	**COJO**	0.0089	0.0065	0.0117
MLR2.adj	**0.01**	0.0087	0.0064	0.0115
MLR2.adj	**0.05**	0.0087	0.0064	0.0115
MLR2.adj	**0.1**	0.0088	0.0064	0.0116
MLR2.adj	**COJO**	0.0087	0.0063	0.0115

Supplementary Table 7: Shows h^2_{GWAS} estimates and their 95% confidence intervals using different methods for impedance trait.

Group	Prune	her	Lower band	Upper band
SLR.HWE	**0.01**	0.0400	0.0375	0.0424
SLR.HWE	**0.05**	0.0421	0.0396	0.0446
SLR.HWE	**0.1**	0.0466	0.0440	0.0492
SLR.HWE	**COJO**	0.0419	0.0394	0.0444
SLR.SS	**0.01**	0.0401	0.0361	0.0441
SLR.SS	**0.05**	0.0422	0.0382	0.0463
SLR.SS	**0.1**	0.0468	0.0425	0.0511
SLR.SS	**COJO**	0.0421	0.0380	0.0461
LMM	**0.01**	0.0278	0.0195	0.0361
LMM	**0.05**	0.0284	0.0201	0.0366
LMM	**0.1**	0.0292	0.0211	0.0373
LMM	**COJO**	0.0299	0.0214	0.0384
PRS.PSS	**0.01**	0.0327	0.0284	0.0371
PRS.PSS	**0.05**	0.0338	0.0293	0.0382
PRS.PSS	**0.1**	0.0341	0.0298	0.0384
PRS.PSS	**COJO**	NA	NA	NA
PRS.SS	**0.01**	0.0227	0.0188	0.0270
PRS.SS	**0.05**	0.0239	0.0199	0.0282
PRS.SS	**0.1**	0.0246	0.0205	0.0290
PRS.SS	**COJO**	0.0220	0.0181	0.0262
PRS	**0.01**	0.0232	0.0193	0.0275
PRS	**0.05**	0.0244	0.0203	0.0288
PRS	**0.1**	0.0248	0.0207	0.0292
PRS	**COJO**	0.0222	0.0183	0.0264
MLR	**0.01**	0.0333	0.0286	0.0383
MLR	**0.05**	0.0346	0.0298	0.0397
MLR	**0.1**	0.0367	0.0317	0.0420
MLR	**COJO**	0.0354	0.0306	0.0406
MLR1.adj	**0.01**	0.0274	0.0231	0.0320
MLR1.adj	**0.05**	0.0283	0.0239	0.0330
MLR1.adj	**0.1**	0.0296	0.0251	0.0344
MLR1.adj	**COJO**	0.0286	0.0242	0.0334
MLR2.adj	**0.01**	0.0276	0.0233	0.0322
MLR2.adj	**0.05**	0.0287	0.0243	0.0335
MLR2.adj	**0.1**	0.0300	0.0255	0.0348
MLR2.adj	**COJO**	0.0290	0.0246	0.0338

Supplementary Table 8: Shows h^2_{GWAS} estimates and their 95% confidence intervals using different methods for neuroticism score trait.

Group	Prune	her	Lower band	Upper band
SLR.HWE	**0.01**	0.0034	0.0028	0.0041
SLR.HWE	**0.05**	0.0034	0.0028	0.0041
SLR.HWE	**0.1**	0.0034	0.0028	0.0041
SLR.HWE	**COJO**	0.0032	0.0026	0.0038
SLR.SS	**0.01**	0.0034	0.0024	0.0045
SLR.SS	**0.05**	0.0034	0.0024	0.0045
SLR.SS	**0.1**	0.0034	0.0024	0.0045
SLR.SS	**COJO**	0.0032	0.0022	0.0042
LMM	**0.01**	0.0016	-0.0001	0.0034
LMM	**0.05**	0.0016	-0.0001	0.0034
LMM	**0.1**	0.0016	-0.0001	0.0034
LMM	**COJO**	0.0016	-0.0001	0.0032
PRS.PSS	**0.01**	0.0011	0.0000	0.0022
PRS.PSS	**0.05**	0.0011	0.0000	0.0022
PRS.PSS	**0.1**	0.0012	0.0000	0.0023
PRS.PSS	**COJO**	NA	NA	NA
PRS.SS	**0.01**	0.0010	-0.0001	0.0022
PRS.SS	**0.05**	0.0010	-0.0001	0.0022
PRS.SS	**0.1**	0.0010	-0.0001	0.0022
PRS.SS	**COJO**	0.0012	0.0001	0.0023
PRS	**0.01**	0.0010	-0.0001	0.0022
PRS	**0.05**	0.0010	-0.0001	0.0022
PRS	**0.1**	0.0010	-0.0001	0.0022
PRS	**COJO**	0.0012	0.0000	0.0023
MLR	**0.01**	0.0025	0.0013	0.0036
MLR	**0.05**	0.0025	0.0013	0.0036
MLR	**0.1**	0.0025	0.0013	0.0036
MLR	**COJO**	0.0024	0.0012	0.0035
MLR1.adj	**0.01**	0.0017	0.0005	0.0028
MLR1.adj	**0.05**	0.0017	0.0005	0.0028
MLR1.adj	**0.1**	0.0017	0.0005	0.0028
MLR1.adj	**COJO**	0.0016	0.0005	0.0027
MLR2.adj	**0.01**	0.0016	0.0005	0.0027
MLR2.adj	**0.05**	0.0016	0.0005	0.0027
MLR2.adj	**0.1**	0.0016	0.0005	0.0027
MLR2.adj	**COJO**	0.0016	0.0004	0.0027

Supplementary Table 9: Shows h^2_{GWAS} estimates and their 95% confidence intervals using different methods for pulse rate trait.

Group	Prune	her	Lower band	Upper band
SLR.HWE	**0.01**	0.0288	0.0268	0.0308
SLR.HWE	**0.05**	0.0319	0.0298	0.0340
SLR.HWE	**0.1**	0.0350	0.0328	0.0372
SLR.HWE	**COJO**	0.0302	0.0281	0.0323
SLR.SS	**0.01**	0.0292	0.0258	0.0327
SLR.SS	**0.05**	0.0324	0.0287	0.0360
SLR.SS	**0.1**	0.0356	0.0317	0.0394
SLR.SS	**COJO**	0.0307	0.0271	0.0342
LMM	**0.01**	0.0274	0.0173	0.0375
LMM	**0.05**	0.0278	0.0182	0.0375
LMM	**0.1**	0.0287	0.0192	0.0381
LMM	**COJO**	0.0288	0.0183	0.0392
PRS.PSS	**0.01**	0.0276	0.0229	0.0322
PRS.PSS	**0.05**	0.0289	0.0241	0.0337
PRS.PSS	**0.1**	0.0287	0.0239	0.0335
PRS.PSS	**COJO**	NA	NA	NA
PRS.SS	**0.01**	0.0277	0.0234	0.0324
PRS.SS	**0.05**	0.0281	0.0238	0.0328
PRS.SS	**0.1**	0.0273	0.0230	0.0319
PRS.SS	**COJO**	0.0279	0.0236	0.0326
PRS	**0.01**	0.0273	0.0230	0.0319
PRS	**0.05**	0.0275	0.0232	0.0322
PRS	**0.1**	0.0270	0.0227	0.0316
PRS	**COJO**	0.0279	0.0236	0.0326
MLR	**0.01**	0.0311	0.0266	0.0360
MLR	**0.05**	0.0327	0.0280	0.0377
MLR	**0.1**	0.0340	0.0293	0.0391
MLR	**COJO**	0.0323	0.0276	0.0372
MLR1.adj	**0.01**	0.0279	0.0236	0.0326
MLR1.adj	**0.05**	0.0289	0.0245	0.0337
MLR1.adj	**0.1**	0.0298	0.0253	0.0346
MLR1.adj	**COJO**	0.0289	0.0245	0.0337
MLR2.adj	**0.01**	0.0275	0.0232	0.0321
MLR2.adj	**0.05**	0.0283	0.0240	0.0331
MLR2.adj	**0.1**	0.0286	0.0242	0.0333
MLR2.adj	**COJO**	0.0283	0.0239	0.0330

Supplementary Table 10: Shows h^2_{GWAS} estimates and their 95% confidence intervals using different methods for reaction time trait.

Group	Prune	her	Lower band	Upper band
SLR.HWE	**0.01**	0.0025	0.0019	0.0030
SLR.HWE	**0.05**	0.0025	0.0019	0.0030
SLR.HWE	**0.1**	0.0025	0.0019	0.0030
SLR.HWE	**COJO**	0.0025	0.0019	0.0030
SLR.SS	**0.01**	0.0025	0.0016	0.0033
SLR.SS	**0.05**	0.0025	0.0016	0.0033
SLR.SS	**0.1**	0.0025	0.0016	0.0033
SLR.SS	**COJO**	0.0025	0.0016	0.0033
LMM	**0.01**	0.0003	-0.0004	0.0011
LMM	**0.05**	0.0003	-0.0004	0.0011
LMM	**0.1**	0.0003	-0.0004	0.0011
LMM	**COJO**	0.0003	-0.0004	0.0011
PRS.PSS	**0.01**	0.0007	-0.0004	0.0018
PRS.PSS	**0.05**	0.0007	-0.0004	0.0018
PRS.PSS	**0.1**	0.0007	-0.0004	0.0018
PRS.PSS	**COJO**	NA	NA	NA
PRS.SS	**0.01**	0.0004	-0.0007	0.0016
PRS.SS	**0.05**	0.0004	-0.0007	0.0016
PRS.SS	**0.1**	0.0004	-0.0007	0.0016
PRS.SS	**COJO**	0.0004	-0.0007	0.0016
PRS	**0.01**	0.0004	-0.0007	0.0016
PRS	**0.05**	0.0004	-0.0007	0.0016
PRS	**0.1**	0.0004	-0.0007	0.0016
PRS	**COJO**	0.0004	-0.0007	0.0016
MLR	**0.01**	0.0011	-0.0001	0.0022
MLR	**0.05**	0.0011	-0.0001	0.0022
MLR	**0.1**	0.0011	-0.0001	0.0022
MLR	**COJO**	0.0011	-0.0001	0.0022
MLR1.adj	**0.01**	0.0004	-0.0007	0.0015
MLR1.adj	**0.05**	0.0004	-0.0007	0.0015
MLR1.adj	**0.1**	0.0004	-0.0007	0.0015
MLR1.adj	**COJO**	0.0004	-0.0007	0.0015
MLR2.adj	**0.01**	0.0004	-0.0008	0.0015
MLR2.adj	**0.05**	0.0004	-0.0008	0.0015
MLR2.adj	**0.1**	0.0004	-0.0008	0.0015
MLR2.adj	**COJO**	0.0004	-0.0008	0.0015

Supplementary Table 11: Shows h^2_{GWAS} estimates and their 95% confidence intervals using different methods for systolic blood pressure trait.

Group	Prune	her	Lower band	Upper band
SLR.HWE	**0.01**	0.0182	0.0168	0.0196
SLR.HWE	**0.05**	0.0187	0.0173	0.0202
SLR.HWE	**0.1**	0.0201	0.0186	0.0216
SLR.HWE	**COJO**	0.0196	0.0181	0.0210
SLR.SS	**0.01**	0.0183	0.0160	0.0207
SLR.SS	**0.05**	0.0188	0.0164	0.0212
SLR.SS	**0.1**	0.0202	0.0177	0.0227
SLR.SS	**COJO**	0.0197	0.0172	0.0221
LMM	**0.01**	0.0129	0.0076	0.0181
LMM	**0.05**	0.0129	0.0077	0.0181
LMM	**0.1**	0.0127	0.0077	0.0178
LMM	**COJO**	0.0133	0.0080	0.0186
PRS.PSS	**0.01**	0.0122	0.0093	0.0150
PRS.PSS	**0.05**	0.0124	0.0095	0.0152
PRS.PSS	**0.1**	0.0124	0.0095	0.0152
PRS.PSS	**COJO**	NA	NA	NA
PRS.SS	**0.01**	0.0118	0.0090	0.0150
PRS.SS	**0.05**	0.0120	0.0092	0.0152
PRS.SS	**0.1**	0.0114	0.0087	0.0145
PRS.SS	**COJO**	0.0109	0.0083	0.0140
PRS	**0.01**	0.0118	0.0090	0.0150
PRS	**0.05**	0.0120	0.0092	0.0152
PRS	**0.1**	0.0114	0.0087	0.0146
PRS	**COJO**	0.0106	0.0079	0.0136
MLR	**0.01**	0.0165	0.0132	0.0202
MLR	**0.05**	0.0167	0.0134	0.0204
MLR	**0.1**	0.0170	0.0136	0.0207
MLR	**COJO**	0.0169	0.0136	0.0207
MLR1.adj	**0.01**	0.0128	0.0099	0.0160
MLR1.adj	**0.05**	0.0129	0.0100	0.0162
MLR1.adj	**0.1**	0.0128	0.0099	0.0161
MLR1.adj	**COJO**	0.0128	0.0098	0.0160
MLR2.adj	**0.01**	0.0129	0.0099	0.0161
MLR2.adj	**0.05**	0.0130	0.0101	0.0163
MLR2.adj	**0.1**	0.0128	0.0099	0.0161
MLR2.adj	**COJO**	0.0127	0.0098	0.0160