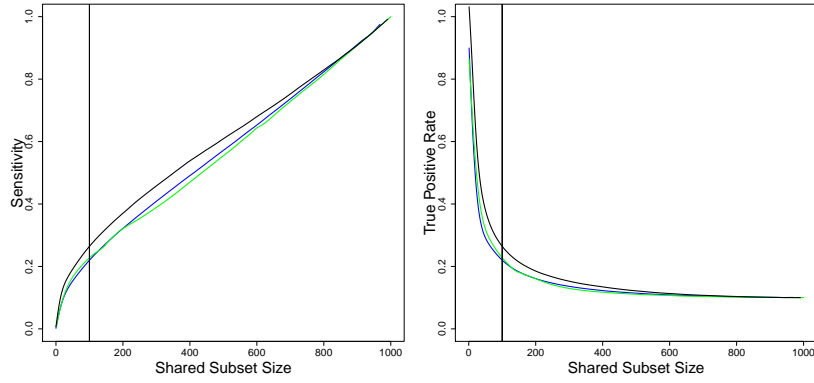


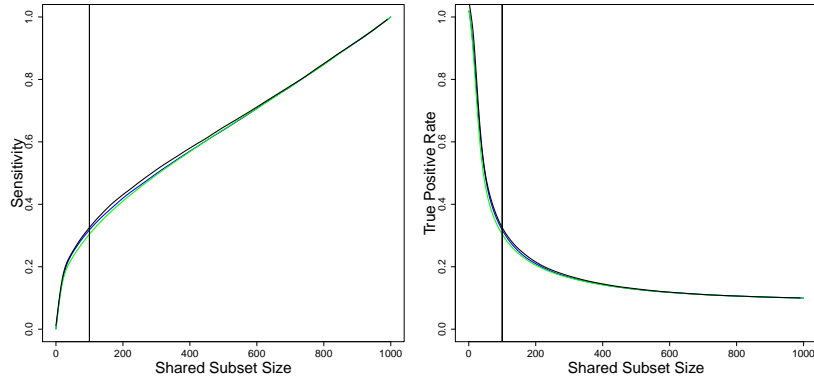
1. Supplementary file for simulations studying the effect of flipped signs of the true underlying shared SNPs, on the methods

This supplementary file contains more detailed results related to the simulation study presented in subsection 5.3. The goal of the simulation study in subsection 5.3 was to understand the impact of having opposite signs for the true underlying shared-SNP-effects, on the three approaches considered in this paper based on QRR, Lasso and RO. To clarify further, a shared SNP with flipped signs means a SNP with a positive effect on the phenotype from one GWAS and a negative effect on the phenotype from the other GWAS. For all simulations in this study, we flipped the signs for 50% of the true underlying (ground-truth) SNPs. There were two overarching simulations designs: one with 1000 SNPs and a second design based on 10,000 SNPs. In both cases, between-SNP correlations were incorporated in blocks of 10 SNPs, with two correlation ranges (0.05, 0.15) and (0.40, 0.60) yielding two separate simulation scenarios. For the design based on 1000 SNPs, the sample sizes considered were 300 and 3000. The only sample size considered for the design with 10,000 SNPs, was ($N =$) 3000. The number of true underlying shared SNPs incorporated in all scenarios with 1000 SNPs was ($M_c =$) 100, and in scenarios with 10,000 SNPs was ($M_c =$) 500. Thus, 50 true shared SNPs had flipped signs in the first case and 250 true shared SNPs had flipped signs in the second case.

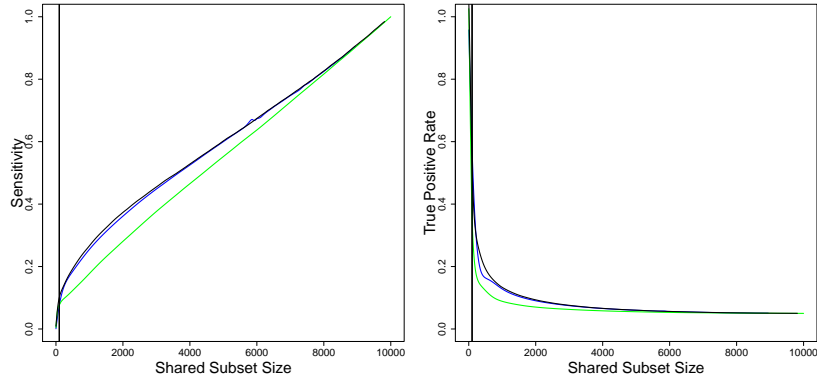
The results are plotted in figures 1 to 4. Figures 1 and 2 plot the results for between-SNP correlation range (0.05-0.15), and figures 3 and 4 plot the results for the correlation range (0.40-0.60). Figures 1 and 3 are the main figures. Figures 2 and 4 essentially repeat some of the information presented in figures 1 and 3, respectively, but now narrowing the focus to a smaller range of shared-subset-size on the x -axis, and plotting the pooled results with 95% confidence intervals, for bins of shared subsets. Thus the results in Table 2, essentially corresponds to one bin in figures 2 and 4. All figures contain three subplots labelled (a) to (c). Within each subplot, there are two panels, a left panel and a right panel. The left panel plots sensitivity against shared subset size detected at a given λ -threshold, while as the right panel plots true positive rate against the shared subset size. Within each panel the blue curve corresponds to QRR, green corresponds to Lasso and black corresponds to RO. A vertical line is plotted at the x -axis value corresponding to a shared subset size of 100. The first two subplots ((a),(b)) in each figure correspond to the simulation design with 1000 SNPs (i.e. M) and 100 underlying true shared SNPs (i.e. M_c). The last subplot (c) in each figure plots the results for the simulation design with 10,000 SNPs and 500 underlying true shared SNPs. Subplots (a) and (b) correspond to sample sizes of 300 and 3000, respectively. As mentioned previously, only one sample size ($N =$) 3000 was considered for the design with 10,000 SNPs. The results are based on 1000 iterations in the design scenarios with 1000 SNPs, and 100 iterations for the design with 10,000 SNPs. The curves plotted in all figures were obtained from the loess scatter-smooth plotter applied across the curves from all iterations. Since the λ -grid that we chose was fine enough and large enough, figures 1 and 3 plot the results for the entire range of possible shared subset sizes that can be selected - that is, 0-1000 for subplots (a) and (b) and 0-10000 for the subplot (c). In figures 2 and 4, we narrow the focus to shared subset size range of 0-300 because in practice selecting a shared subset of size larger than 300 is often not feasible.



(a) $M = 1000, M_c = 100, N = 300$

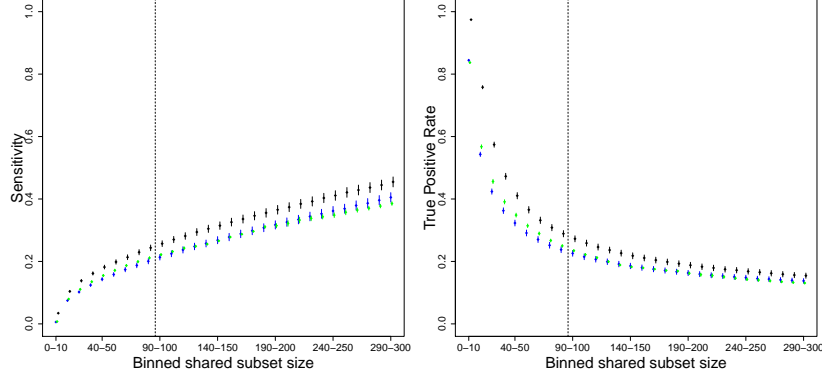


(b) $M = 1000, M_c = 100, N = 3000$

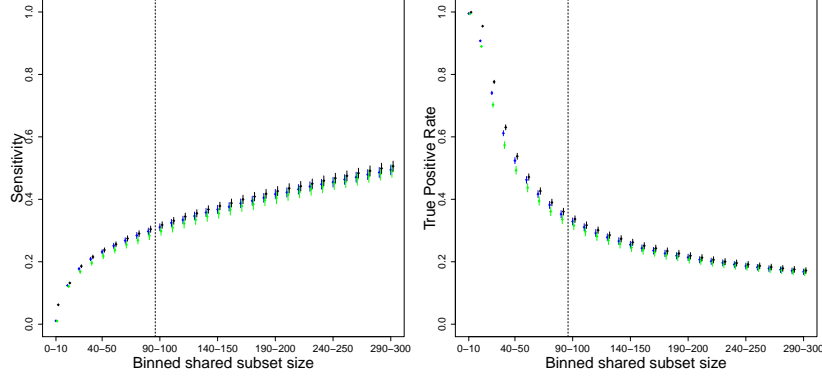


(c) $M = 10000, M_c = 500, N = 3000$

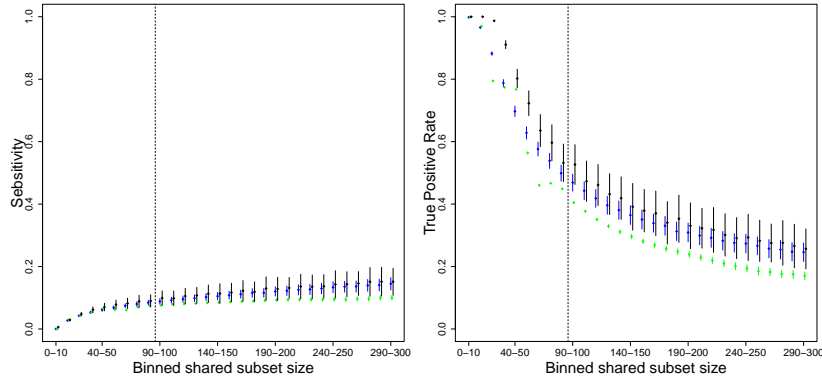
Figure 1: Impact of flipped signs for true shared SNP-effects, on performance of the methods. QRR: blue, Lasso: green, RO: black. Between-SNP correlation range: 0.05-0.15. x -axis in each panel plots the entire range of sizes for possible sizes shared subsets that may be selected. See page 1 for more description.



(a) $M = 1000$, $M_c = 100$, $N = 300$

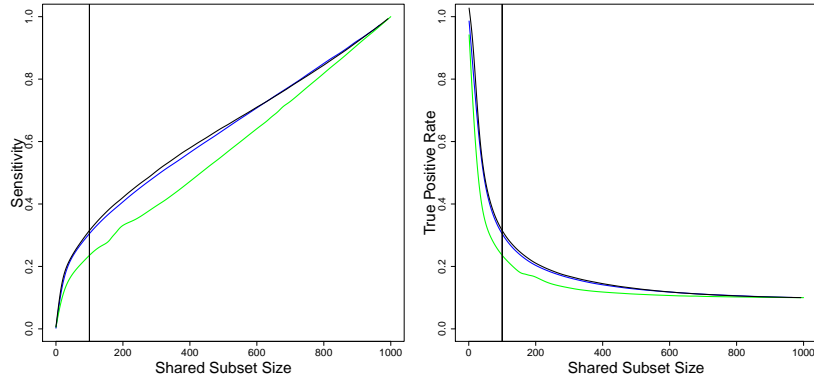


(b) $M = 1000$, $M_c = 100$, $N = 3000$

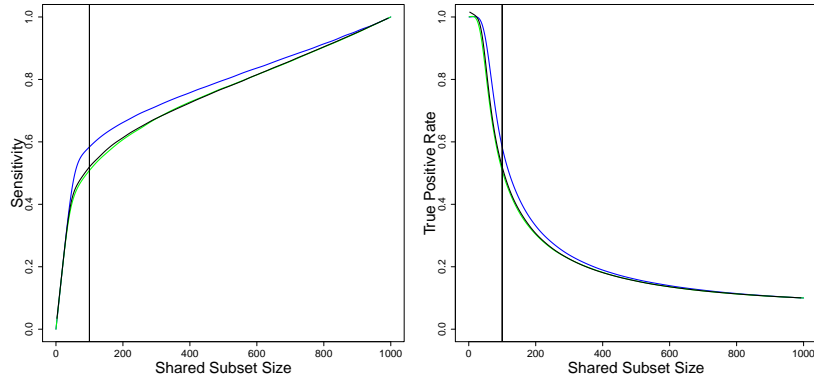


(c) $M = 10000$, $M_c = 500$, $N = 3000$

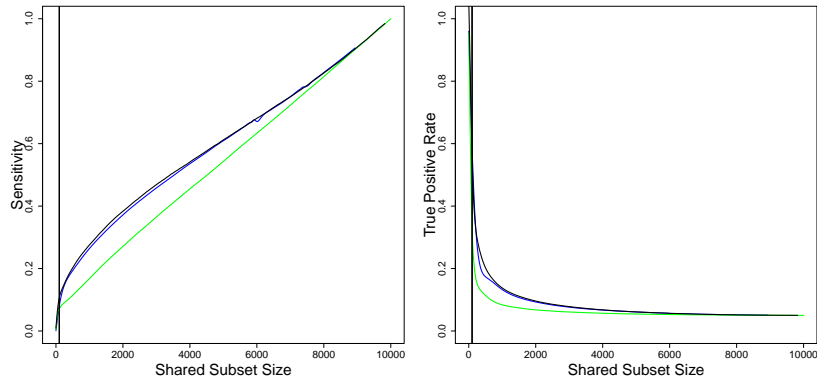
Figure 2: Impact of flipped signs for true shared SNP-effects, on performance of the methods. QRR: blue, Lasso: green, RO: black. Between-SNP correlation range: 0.05-0.15. x -axis in each panel corresponds to bins of size 10 for shared subsets. Thus, this figure presents the same information as in Figure 1, but pooled within each bin. The range of shared subset sizes on the x -axis is limited to 0-300. The vertical ‘error’ bars correspond to 95% confidence intervals. In figure (c) the vertical ‘error’ bars are longer because only 100 iterations were used. See page 1 for more description.



(a) $M = 1000, M_c = 100, N = 300$

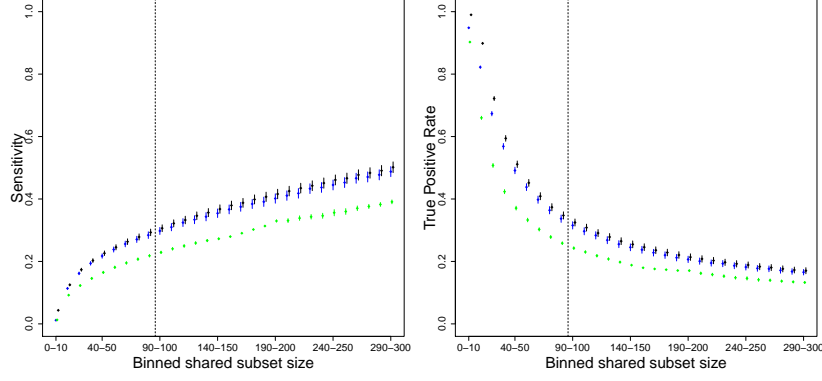


(b) $M = 1000, M_c = 100, N = 3000$

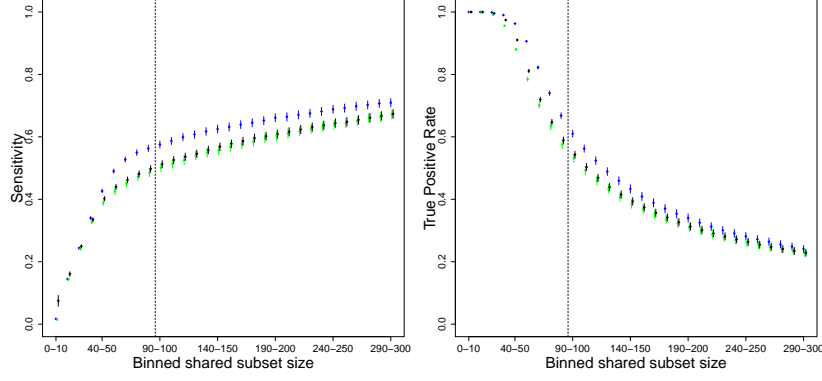


(c) $M = 10000, M_c = 500, N = 3000$

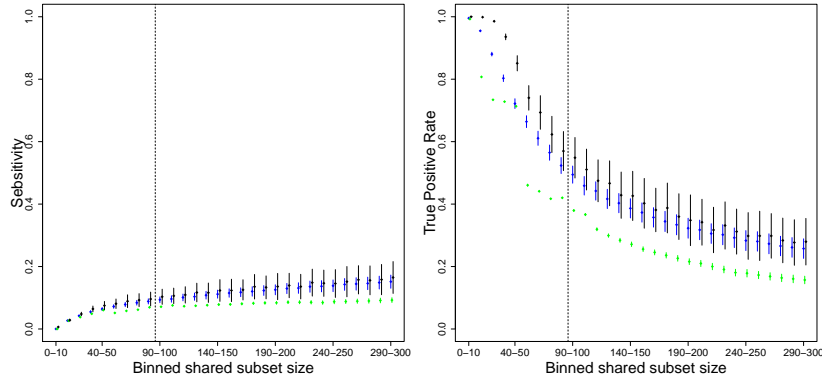
Figure 3: Impact of flipped signs for true shared SNP-effects, on performance of the methods. QRR: blue, Lasso: green, RO: black. Between-SNP correlation range: 0.40-0.60. x -axis in each panel plots the entire range of sizes for possible shared subsets that may be selected. See page 1 for more description.



(a) $M = 1000, M_c = 100, N = 300$



(b) $M = 1000, M_c = 100, N = 3000$



(c) $M = 10000, M_c = 500, N = 3000$

Figure 4: Impact of flipped signs for true shared SNP-effects, on performance of the methods. QRR: blue, Lasso: green, RO: black. Between-SNP correlation range: 0.40-0.60. x -axis in each panel corresponds to bins of size 10 for shared subsets. Thus, this figure presents the same information as in Figure 1, but pooled within each bin. The range of shared subset sizes on the x -axis is limited to 0-300. The vertical ‘error’ bars correspond to 95% confidence intervals. In figure (c) the vertical ‘error’ bars are longer because only 100 iterations were used. See page 1 for more description.