Supplemental Figures

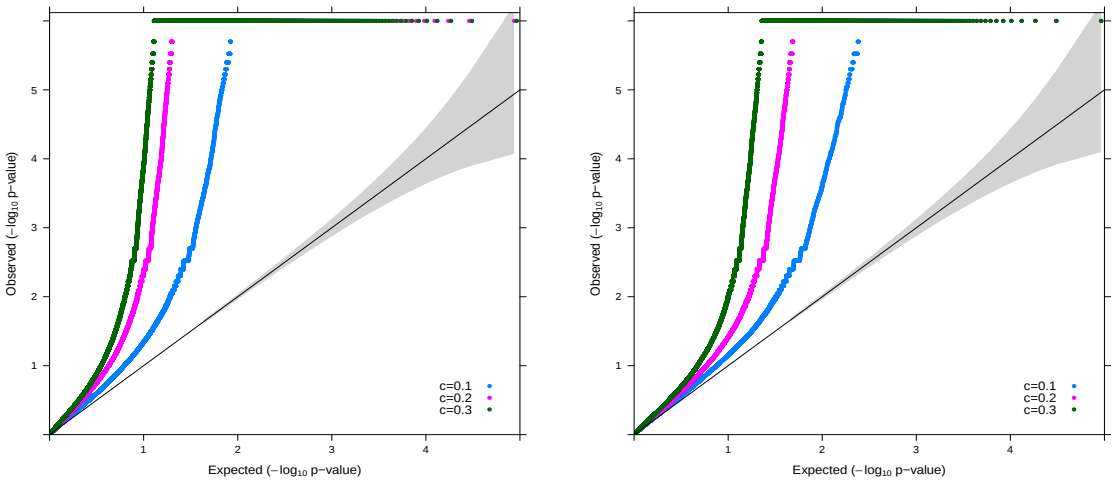

Figure S1: **QQ plots of non-causal genes on the simulated data.** We simulated both one causal SNP (left panel) or two causal SNPs (right panel) in one causal gene per locus. c is the causal effect size. The shaded part is 95% confidence interval for the null model.

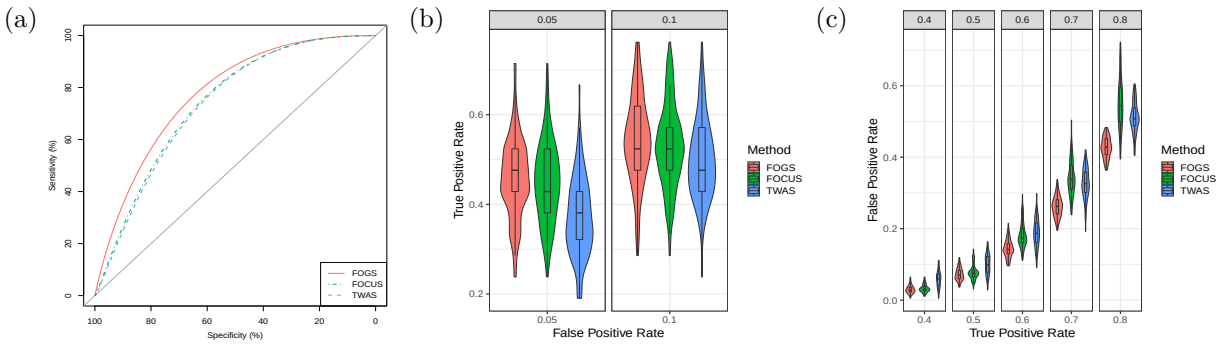

Figure S2: **Assessment of different methods performance under one causal SNP per locus situations.** The effect size was $c = 0.1$ and the estimated hertibability was about 0.1%. **a**, AUC comparison between different methods. **b**, True positive rate (Power) comparison under some specified false positive rates. **c**, False positive rate comparison under some specified true positive rates. The violin plot and box plot inside display the false/true positive rates of different methods under specified true/false positive rates.

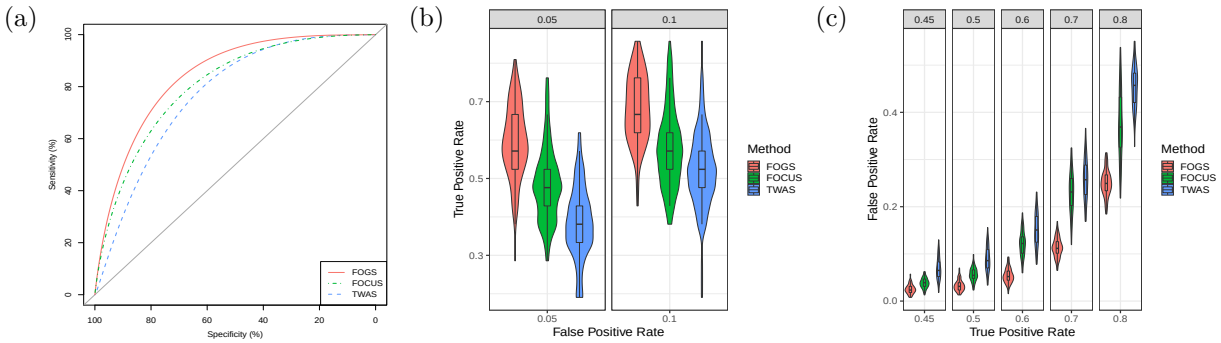

Figure S3: **Assessment of different methods performance under one causal SNP per locus situations.** The effect size was $c = 0.2$ and the estimated hertibability was about 1%. **a**, AUC comparison between different methods. **b**, True positive rate (Power) comparison under some specified false positive rates. **c**, False positive rate comparison under some specified true positive rates. The violin plot and box plot inside display the false/true positive rates of different methods under specified true/false positive rates.

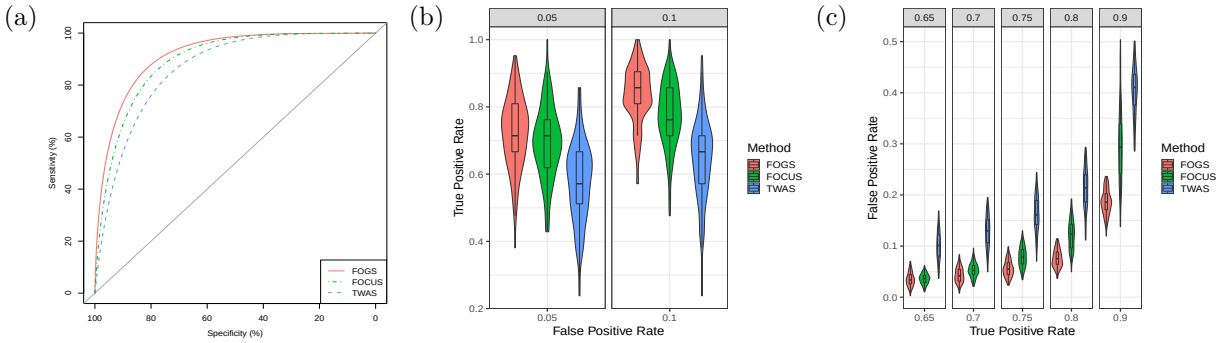

Figure S4: **Assessment of different methods performance under two causal SNPs per locus situations.** The effect size was proportional to the eQTL derived weights and magnitude parameter $c = 0.3$ (see Methods). The estimated hertibability was about 2.2%. **a**, AUC comparison between different methods. **b**, True positive rate (Power) comparison under some specified false positive rates. **c**, False positive rate comparison under some specified true positive rates. The violin plot and box plot inside display the false/true positive rates of different methods under specified true/false positive rates.

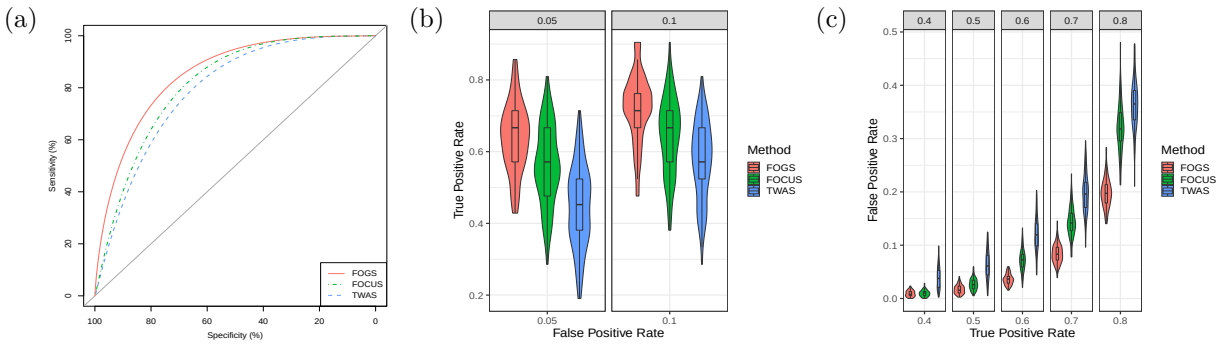

Figure S5: **Assessment of different methods performance under one causal gene per locus situations.** All the eSNPs from the causal genes were causal. The effect size was proportional to the eQTL derived weights and magnitude parameter $c = 0.2$ (see Methods). The estimated hertibability was about 0.4%. **a**, AUC comparison between different methods. **b**, True positive rate (Power) comparison under some specified false positive rates. **c**, False positive rate comparison under some specified true positive rates. The violin plot and box plot inside display the false/true positive rates of different methods under specified true/false positive rates.

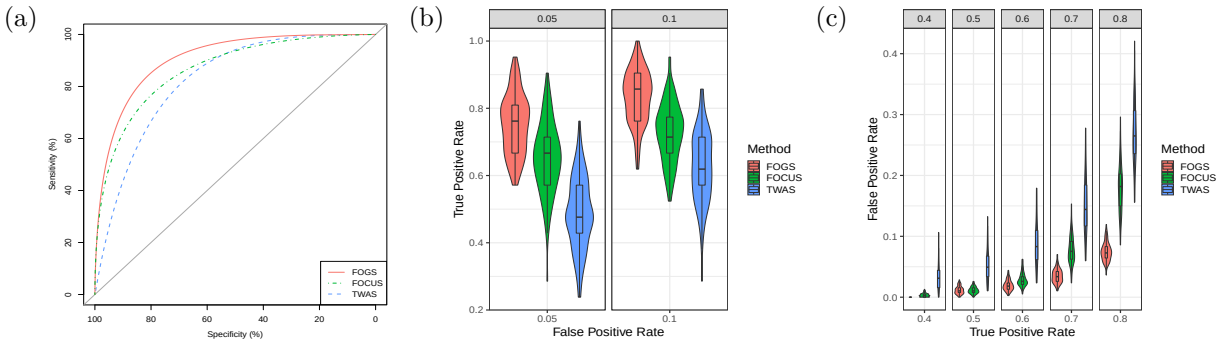

Figure S6: **Assessment of different methods performance under one causal gene per locus situations.** All the eSNPs from the causal genes were causal. The effect size was proportional to the eQTL derived weights and magnitude parameter $c = 0.3$ (see Methods). The estimated hertibability was about 1%. **a**, AUC comparison between different methods. **b**, True positive rate (Power) comparison under some specified false positive rates. **c**, False positive rate comparison under some specified true positive rates. The violin plot and box plot inside display the false/true positive rates of different methods under specified true/false positive rates.

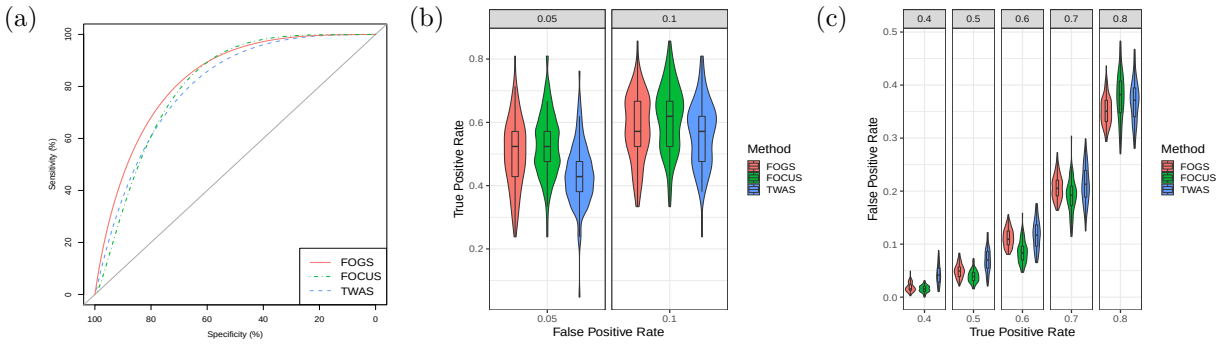

Figure S7: **Assessment of different methods performance under one causal gene per locus situations.** We randomly selected two SNPs in one gene to be causal, and the effect size was $c = 0.1$. Importantly, one of the selected causal SNP regulates at least two genes in the same locus. The estimated hertibability was about 2.5%. **a**, AUC comparison between different methods. **b**, True positive rate (Power) comparison under some specified false positive rates. **c**, False positive rate comparison under some specified true positive rates. The violin plot and box plot inside display the false/true positive rates of different methods under specified true/false positive rates.

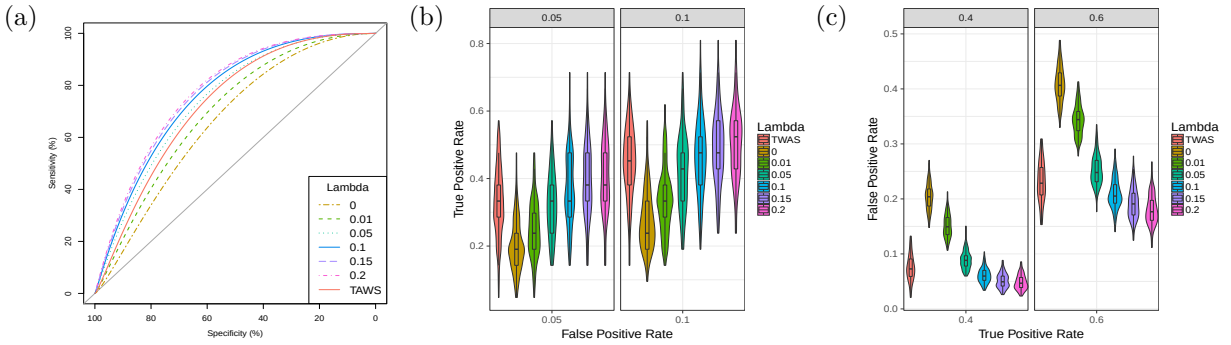

Figure S8: **Sensitive analysis of ridge penalty parameter λ of FOGS with simulated data.** We randomly selected two SNPs in one gene to be causal and the effect size was $c = 0.1$. We further randomly selected 1,000 subjects to construct the reference panel. **a**, AUC comparison between different methods. **b**, True positive rate (Power) comparison under some specified false positive rates. **c**, False positive rate comparison under some specified true positive rates. The violin plot and box plot inside display the false/true positive rates of different methods under specified true/false positive rates.

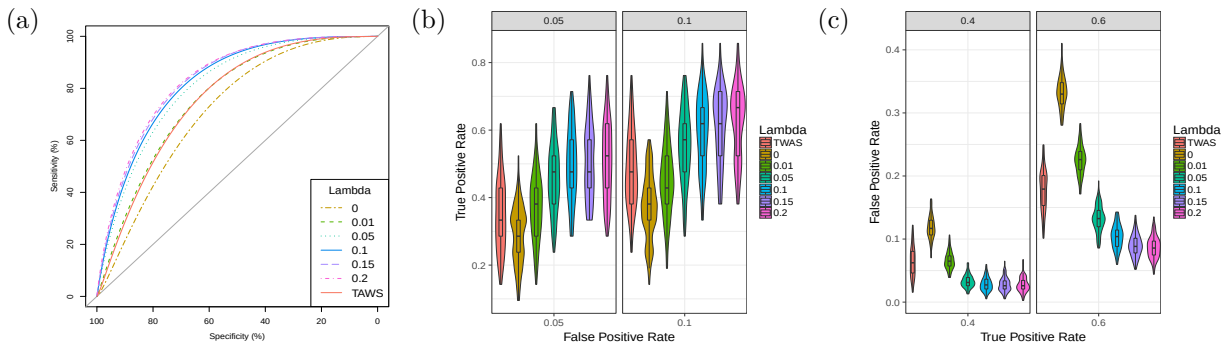

Figure S9: **Sensitive analysis of ridge penalty parameter λ of FOGS with simulated data.** We randomly selected two SNPs in one gene to be causal and the effect size was $c = 0.1$. We further randomly selected 2,000 subjects to construct the reference panel. **a**, AUC comparison between different methods. **b**, True positive rate (Power) comparison under some specified false positive rates. **c**, False positive rate comparison under some specified true positive rates. The violin plot and box plot inside display the false/true positive rates of different methods under specified true/false positive rates.

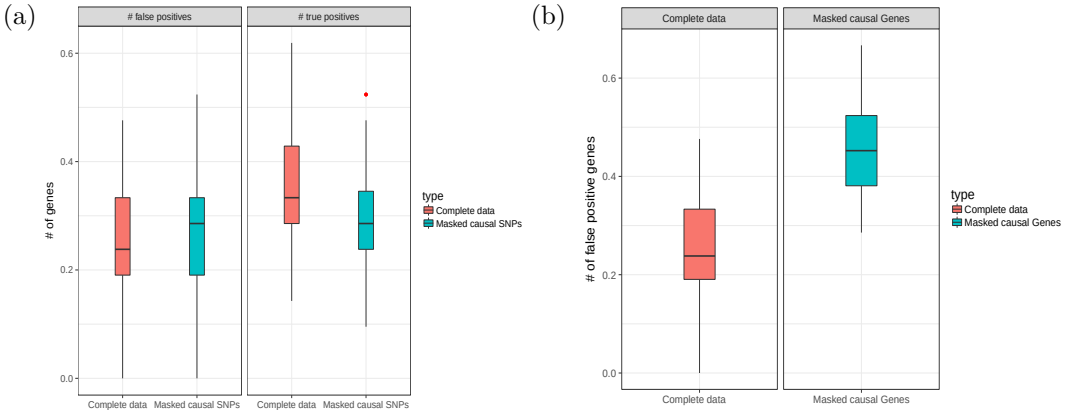

Figure S10: **FOCUS performance under situations with causal SNPs missing.** We considered the following two cases: **a**, the two causal SNPs were missing; **b**, the causal gene (with all its SNPs) was missing (see main text for details). **a**, Numbers of false positives and true positives per locus for FOCUS with either complete data or data with causal SNPs missing. **b**, Number of false positives per locus for FOCUS with either complete data or data with the causal gene missing.

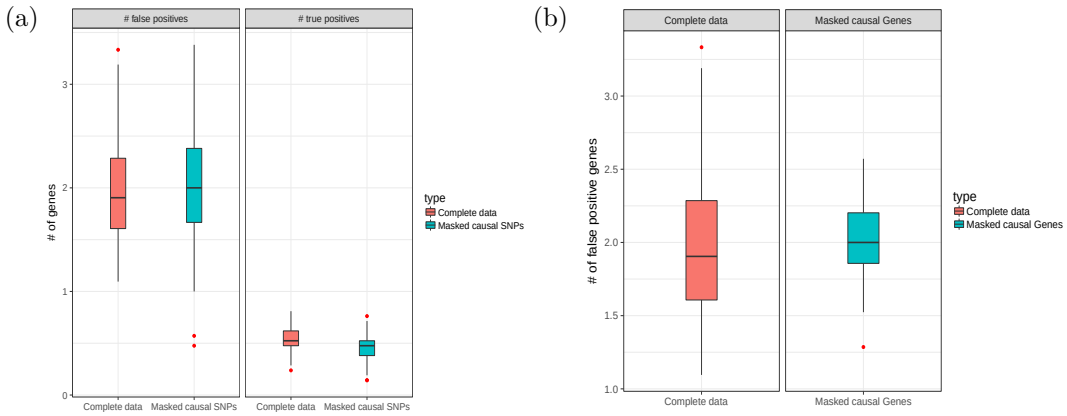

Figure S11: **TWAS ranking performance under situations with causal SNPs missing.** We considered the following two cases: **a**, the two causal SNPs were missing; **b**, the causal gene (with all its SNPs) was missing (see main text for details). **a**, Numbers of false positives and true positives per locus for TWAS ranking with either complete data or data with causal SNPs missing. **b**, Number of false positives per locus for TWAS ranking with either complete data or data with the causal gene missing.

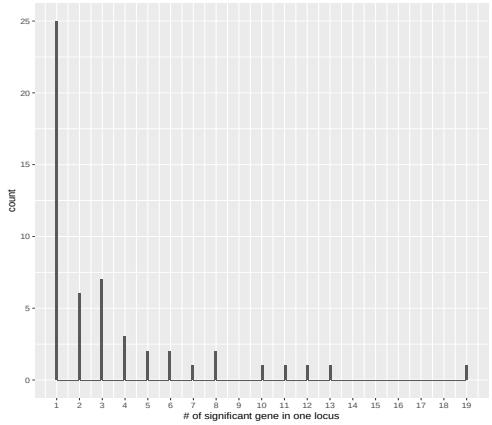

Figure S12: **Number of significant genes identified by TWAS in each risk locus.** For illustration, we removed 75 risk loci that contained no significant gene identified by TWAS.