

Supplementary Information

A Clustering Linear Combination Approach to Jointly Analyze Multiple Phenotypes for GWAS

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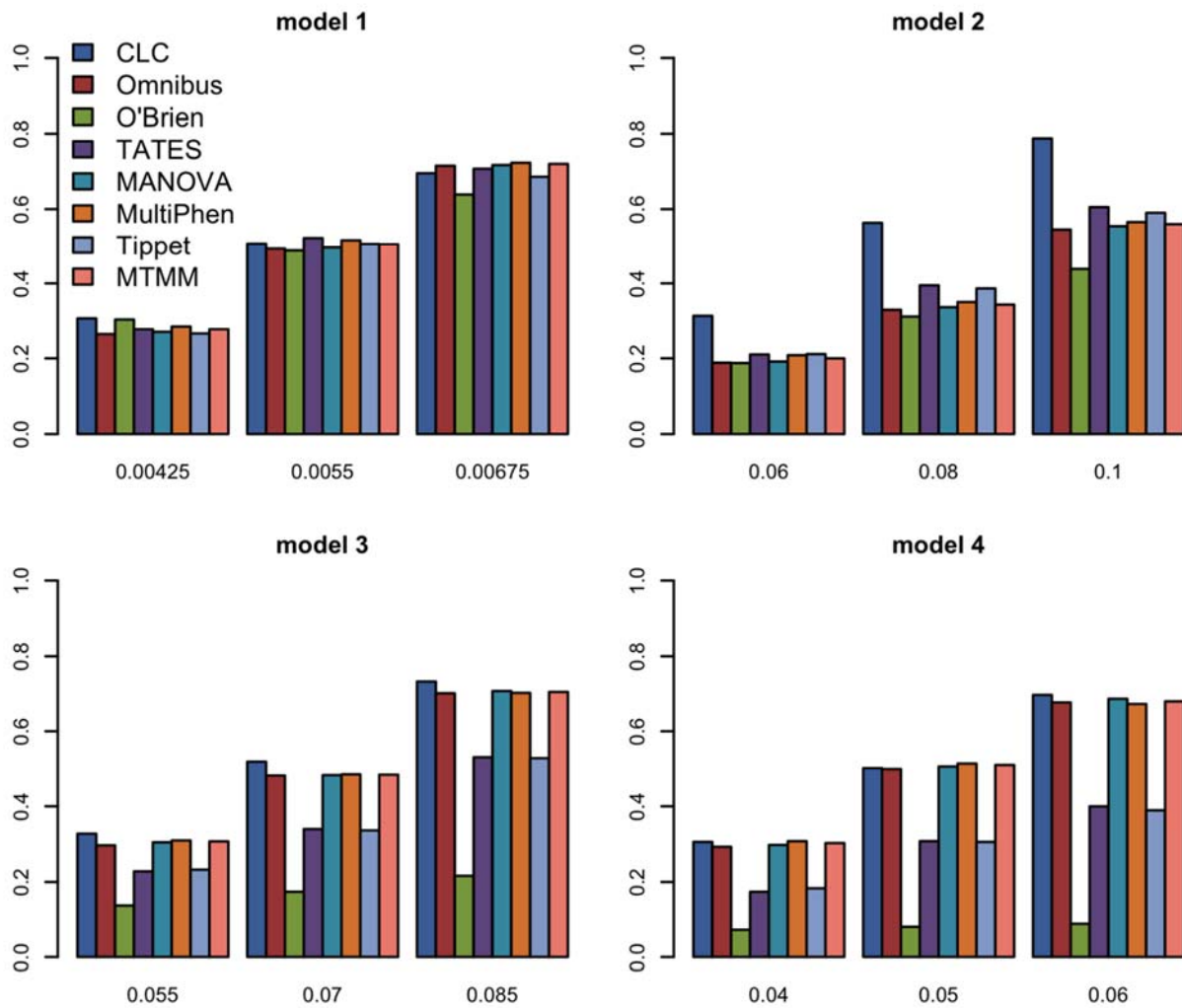


Fig. S1. Power comparisons of the eight tests (O'Brien, Omnibus, CLC, TATES, MANOVA, MultiPhen, Tippet, and MTMM) for the power as a function of effect size β for 20 phenotypes with half quantitative phenotypes and half qualitative phenotypes. The sample size is 1000. The between-factor correlation is 0.15 and the within-factor correlation is 0.25.

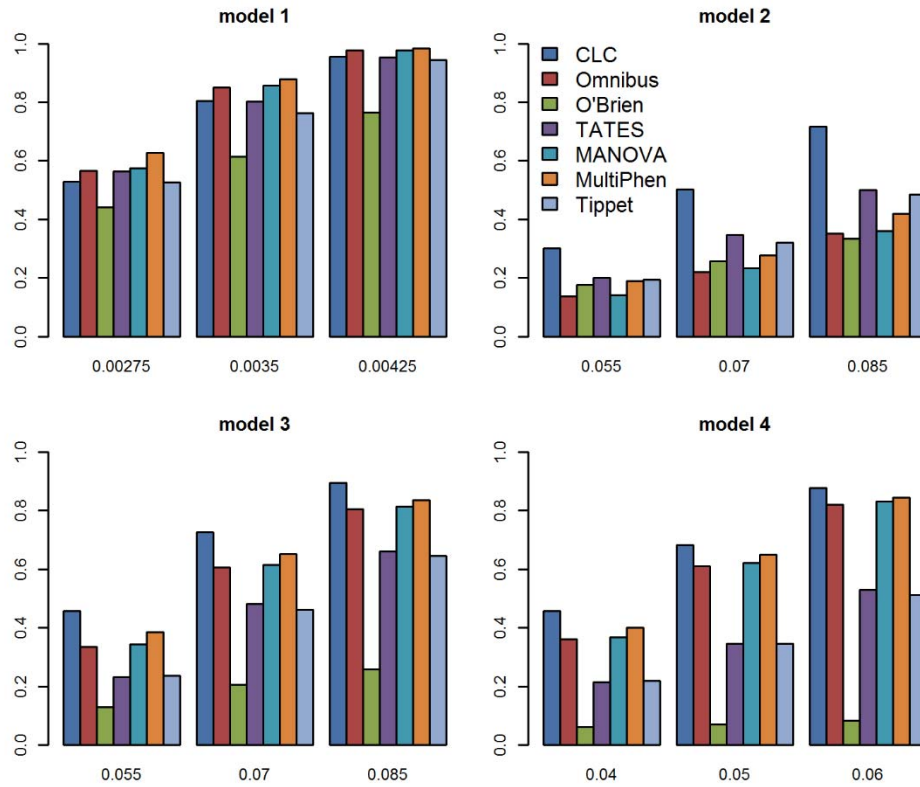


Fig. S2. Power comparisons of the seven tests (O'Brien, Omnibus, CLC, TATES, MANOVA, MultiPhen, and Tippet) for the power as a function of effect size β for 40 phenotypes with half quantitative phenotypes and half qualitative phenotypes. The sample size is 1000. The between-factor correlation is 0.15 and the within-factor correlation is 0.25.

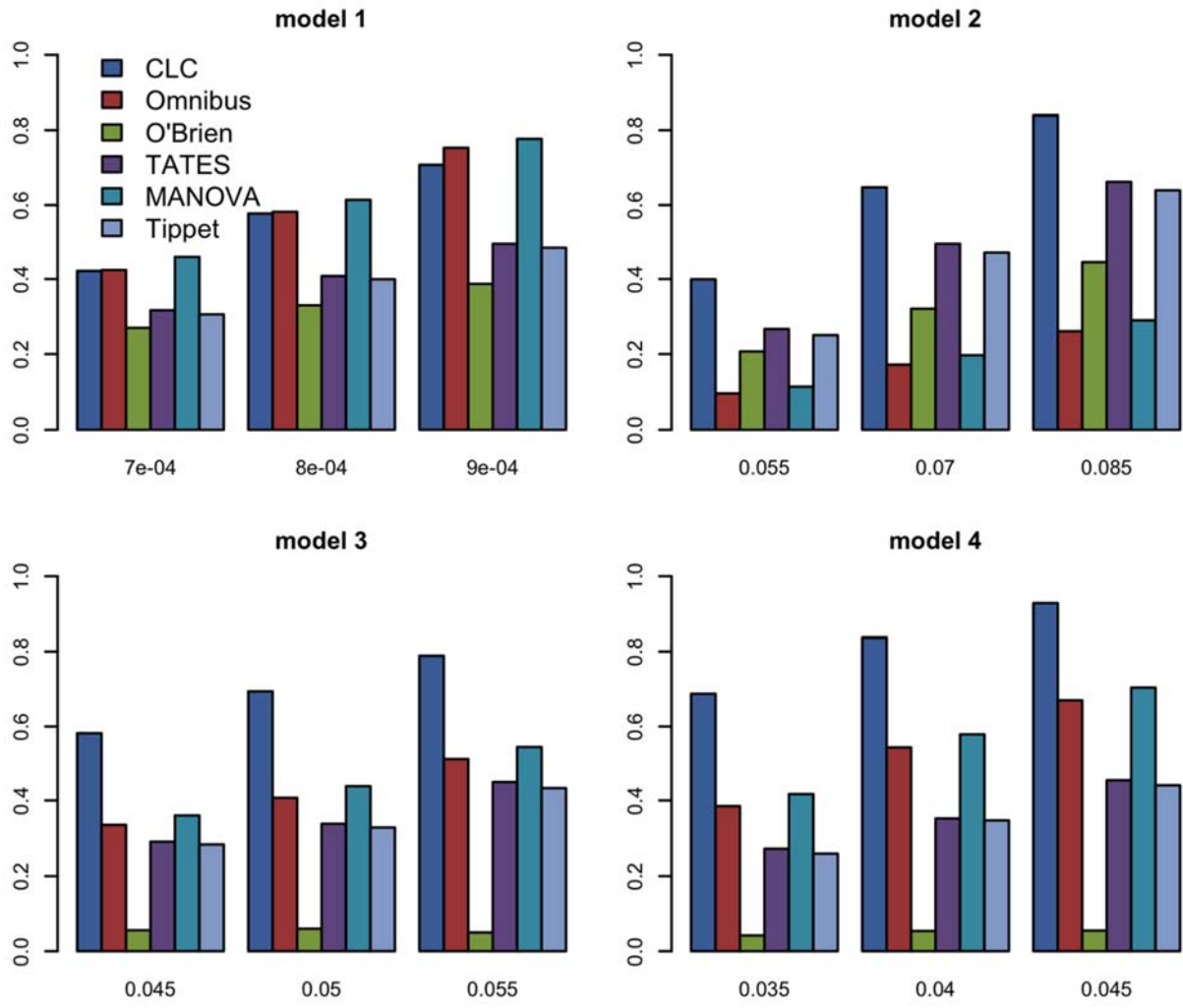


Fig. S3. Power comparisons of the six tests (O'Brien, Omnibus, CLC, TATES, MANOVA, and Tippet) for the power as a function of effect size β for 100 quantitative phenotypes. The sample size is 1000. The between-factor correlation is 0.15 and the within-factor correlation is 0.25.

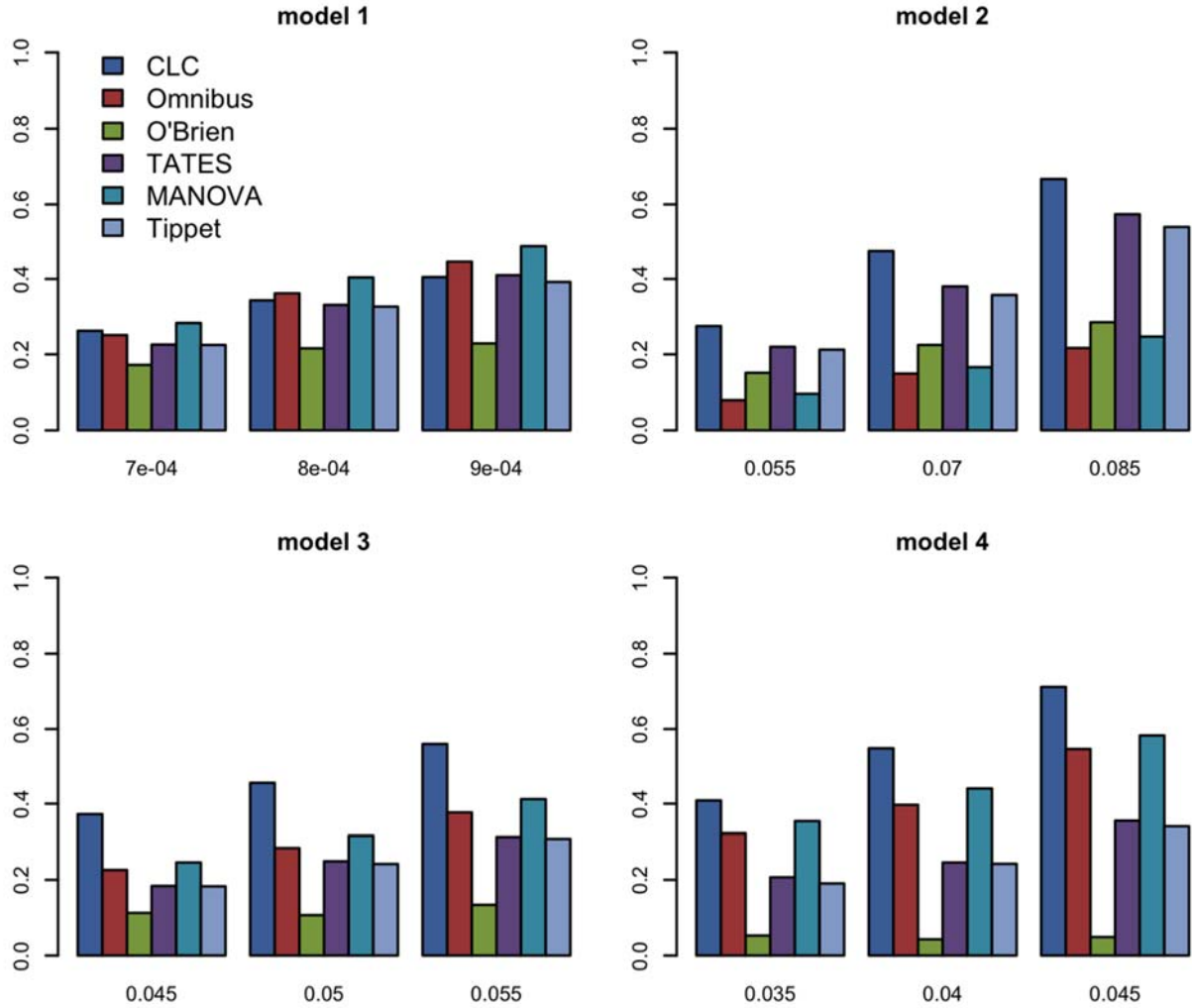


Fig. S4. Power comparisons of the six tests (O'Brien, Omnibus, CLC, TATES, MANOVA, and Tippet) for the power as a function of effect size β for 100 phenotypes with half quantitative phenotypes and half qualitative phenotypes. The sample size is 1000. The between-factor correlation is 0.15 and the within-factor correlation is 0.25.

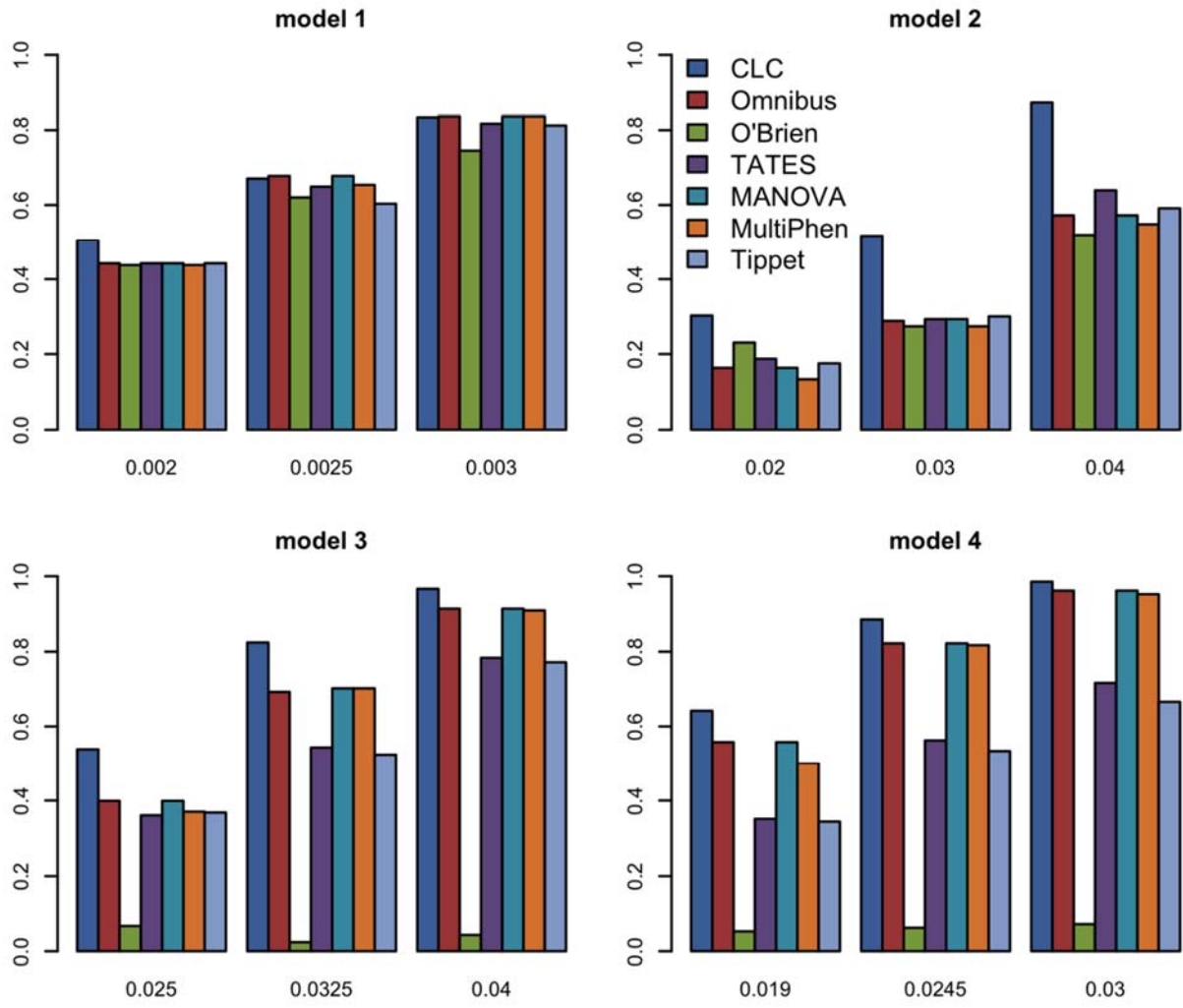


Fig. S5. Power comparisons of the seven tests (O'Brien, Omnibus, CLC, TATES, MANOVA, MultiPhen, and Tippet) for the power as a function of effect size β for 20 quantitative phenotypes. The sample size is 5000. The between-factor correlation is 0.15 and the within-factor correlation is 0.25.

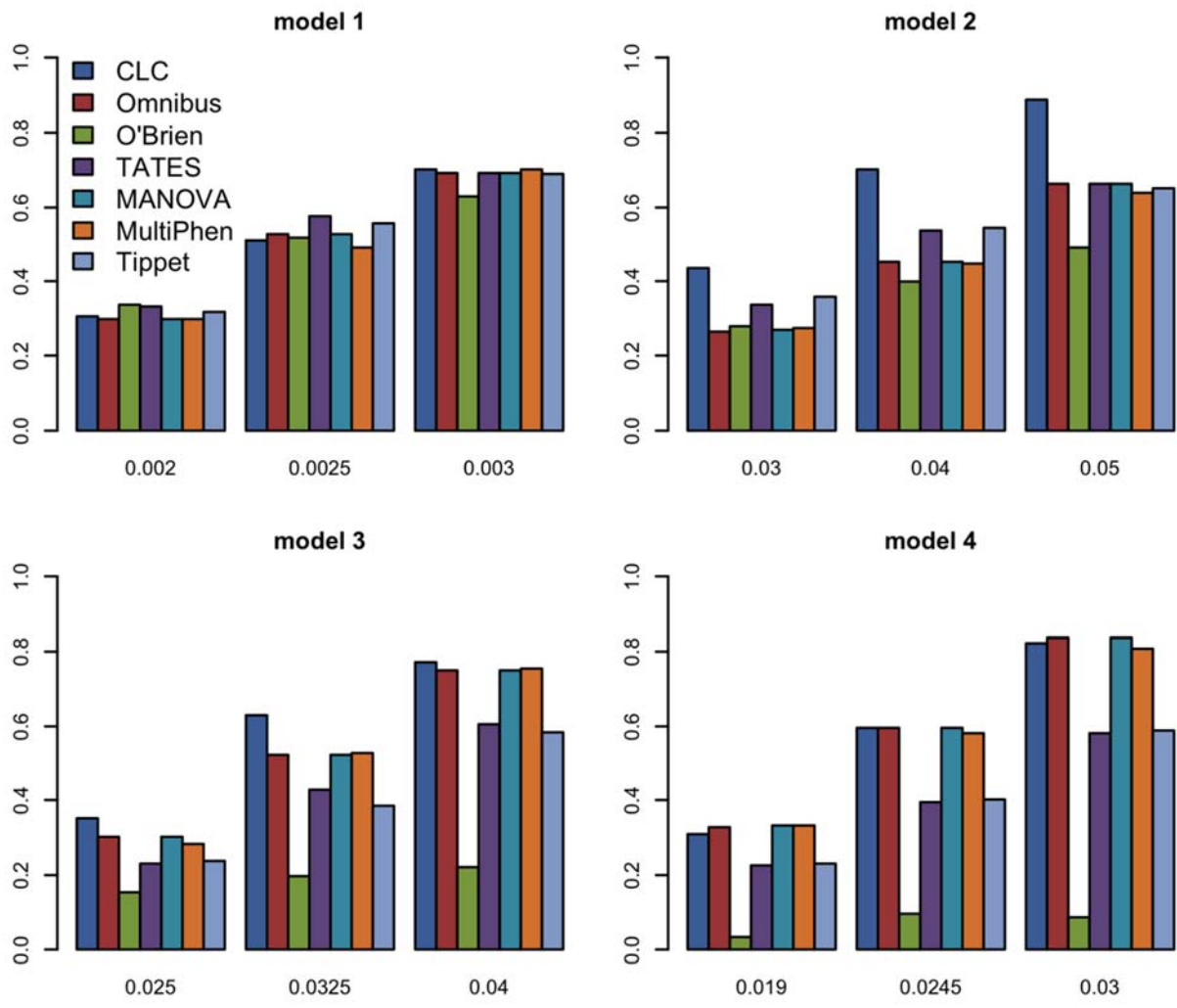


Fig. S6. Power comparisons of the seven tests (O'Brien, Omnibus, CLC, TATES, MANOVA, MultiPhen, and Tippet) for the power as a function of effect size β for 20 phenotypes with half quantitative phenotypes and half qualitative phenotypes. The sample size is 5000. The between-factor correlation is 0.15 and the within-factor correlation is 0.25.

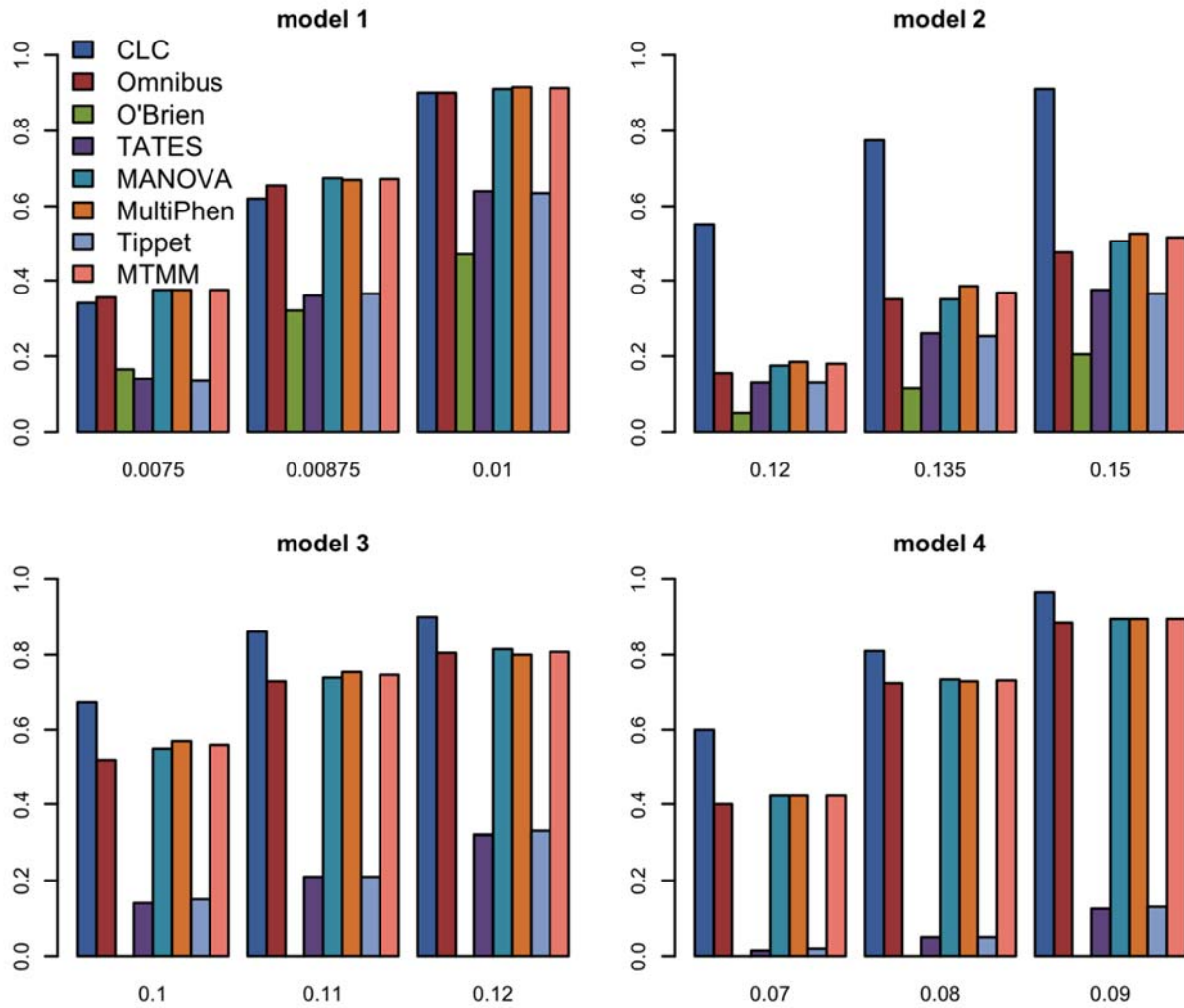


Fig. S7. Power comparisons of the eight tests (O'Brien, Omnibus, CLC, TATES, MANOVA, MultiPhen, Tippet, and MTMM) for the power as a function of effect size β for 20 quantitative phenotypes. The sample size is 1000. The between-factor correlation is 0.15 and the within-factor correlation is 0.25. The p-values of CLC are evaluated using 10^6 simulations; the p-values of Tippet are evaluated using 10^6 permutations; and the power is evaluated using 1,000 replicated samples at a significance level of 10^{-4} .

Fig. S8. The correlation matrix plot of the seven COPD-related phenotypes.

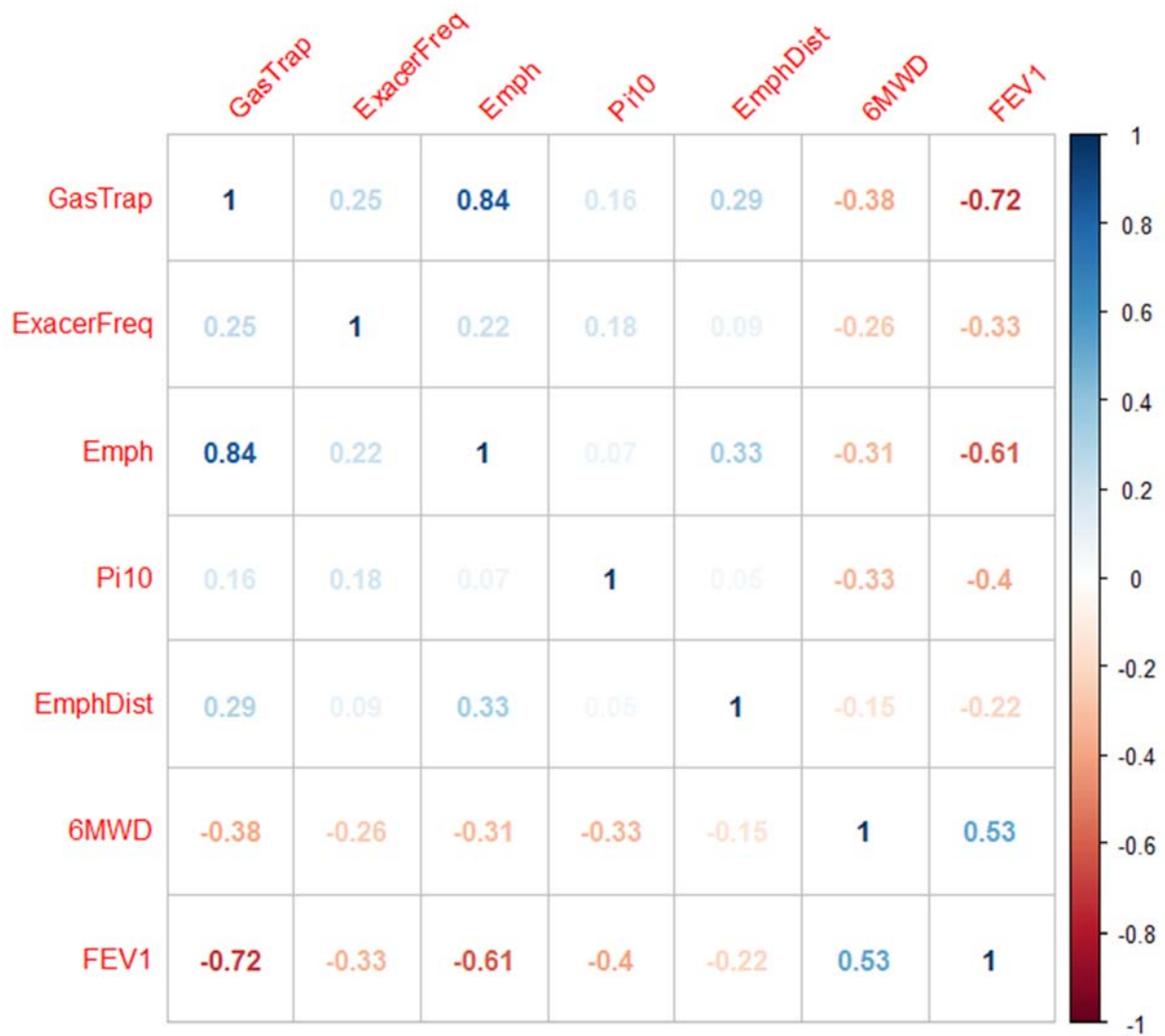


Table S1. The estimated type I error rates divided by the nominal significance level of O'Brien, Omnibus, TATES, MANOVA, and MultiPhen for 100 phenotypes and 1000 individuals under four models by using their analytic p-values. The type I error rates of significance level 10^{-4} are evaluated by 10^6 replicates. The 95% CI for type I error rate divided by the nominal significance level 10^{-4} for 10^6 replicates is (0.80,1.20).

	Model	OB	OMI	TATES	MANOVA	MultiPhen
Quantitative	1	0.92	0.81	0.92	0.86	1.60
	2	0.89	0.83	0.99	0.90	1.51
	3	0.98	0.92	0.90	1.12	1.46
	4	0.92	0.84	1.04	1.01	1.59
Half quantitative and half qualitative	1	0.87	0.86	0.99	0.97	1.64
	2	0.87	0.81	0.87	0.98	1.57
	3	0.96	0.82	1.06	0.90	1.70
	4	0.98	0.93	0.89	1.20	1.63

Table S2. Significant SNPs, the corresponding adjusted (Bonferroni correction for multiple testing) p-values for testing each of the seven phenotypes individually, and the minimum p-values over all phenotypes after adjustment for the number of phenotypes (Min-P) in the analysis of COPDGene.

Chr	Position	Variant identifier	Gas Trapping	Exacerbation Frequency	Emphysema	Airway Wall Area	Emphysema Distribution	Six-minute walk distance	FEV1	Min-P
4	145431497	rs1512282	2.81×10^{-4}	6.06×10^{-3}	1.64×10^{-4}	5.92	6.74×10^{-9}	6.12×10^{-3}	4.53×10^{-3}	4.72×10^{-8}
4	145434744	rs1032297	1.17×10^{-5}	7.33×10^{-3}	1.24×10^{-5}	5.26	7.64×10^{-13}	2.06×10^{-3}	2.99×10^{-5}	5.35×10^{-12}
4	145474473	rs1489759	1.51×10^{-5}	3.40×10^{-2}	8.82×10^{-6}	5.32	1.20×10^{-18}	3.55×10^{-4}	3.96×10^{-5}	8.40×10^{-18}
4	145485738	rs1980057	1.92×10^{-5}	2.82×10^{-2}	1.82×10^{-5}	4.93	1.40×10^{-19}	6.22×10^{-4}	7.18×10^{-5}	9.80×10^{-19}
4	145485915	rs7655625	1.45×10^{-5}	2.92×10^{-2}	1.29×10^{-5}	4.94	2.40×10^{-16}	4.41×10^{-4}	4.13×10^{-5}	1.68×10^{-15}
15	78882925	rs16969968	4.88×10^{-4}	3.09	1.82×10^{-7}	5.13	3.13×10^{-8}	2.23	4.03×10^{-6}	2.19×10^{-7}
15	78894339	rs1051730	3.66×10^{-4}	3.28	1.82×10^{-7}	4.92	2.77×10^{-8}	2.15	3.54×10^{-6}	1.94×10^{-7}
15	78898723	rs12914385	4.77×10^{-5}	1.76	2.14×10^{-7}	1.91	5.32×10^{-10}	2.42×10^{-1}	1.49×10^{-7}	3.72×10^{-9}
15	78911181	rs8040868	1.07×10^{-4}	1.02	4.66×10^{-7}	2.55	2.43×10^{-9}	3.37×10^{-1}	8.23×10^{-8}	1.70×10^{-8}
15	78878541	rs951266	5.86×10^{-4}	3.19	1.67×10^{-7}	5.38	5.42×10^{-8}	2.77	6.39×10^{-6}	3.79×10^{-7}
15	78806023	rs8034191	2.45×10^{-3}	3.06	1.61×10^{-6}	4.40	1.03×10^{-7}	3.21	2.80×10^{-5}	7.21×10^{-7}
15	78851615	rs2036527	3.35×10^{-3}	3.49	3.00×10^{-6}	4.45	1.64×10^{-7}	2.14	2.09×10^{-5}	1.15×10^{-6}
15	78826180	rs931794	1.39×10^{-2}	3.70	4.84×10^{-6}	3.76	1.23×10^{-7}	2.38	5.94×10^{-5}	8.61×10^{-7}
15	78740964	rs2568494	3.40×10^{-2}	6.46	3.08×10^{-5}	6.79	2.01×10^{-4}	1.67	1.97×10^{-4}	2.16×10^{-4}