Supplementary Materials for "Pleiotropy Analysis of Quantitative Traits at Gene Level by Multivariate Functional Linear Models"

Appendix A Information Of the Eight European Cohorts

For each of the eight European cohorts, we performed analysis for four lipid traits and 22 genes. The information of the 22 genes is given in Table S.1. The sample sizes of each trait are presented in Table S.2.

Table S.1: **Summary of 22 Genes and the Number of Genetic Variants in Each Gene Region by Mar. 2006 (NCBI36/hg18).** The number of variants is the number of genetic variants in a region of **Start (-5Kb) – End (+5Kb) Positions**. * The gene region of *PCSK9* is (55277737, 55303114), and (55271537, 55286109) is the region in the database.

Gene	Chromosome Region	Gene Positions (bp)	Start (-5Kb) – End (+5Kb) Positions	Number of Variants
*PCSK9**	1	55277737 – 55303114	55271537 – 55286109	74
APOB	2	21077806 – 21120450	21072806 – 21125450	223
IGF2BP2	3	186844221 – 187025521	186839221 – 187030521	231
CDKAL1	6	20642667 – 21340613	20637667 – 21345613	560
JAZF1	7	27836718 – 28186962	27831718 – 28191962	384
LPL	8	19840862 – 19869050	19835862 – 19874050	212
CDKN2B	9	21992902 – 21999312	21987902 – 22004312	64
CDC123	10	12277971 – 12332593	12272971 – 12337593	265
IDE	10	94201421 – 94323832	94196421 – 94328832	327
KIF11	10	94342805 – 94405132	94337805 – 94410132	216
HHEX	10	94439661 – 94445388	94434661 – 94450388	30
TCF7L2	10	114699999 – 114917426	114694999 – 114922426	258
KCNQ1	11	2422797 – 2826916	2417797 – 2831916	660
MTNR1B	11	92342437 – 92355596	92337437 – 92360596	106
HMGA2	12	64504507 – 64646338	64499507 – 64651338	214
TSPAN8	12	69805144 – 69838046	69800144 – 69843046	54
HNF1A	12	119900932 – 119924697	119895932 – 119929697	71
OASL	12	119942478 – 119961428	119937478 – 119966428	108
FTO	16	52295376 – 52705882	52290376 – 52710882	191
LDLR	19	11061038 – 11105505	11056038 – 11110505	43
APOE	19	50100879 – 50104490	50095879 – 50109490	35
GIPR	19	50863342 – 50877557	50858342 – 50882557	37

Table S.2: **Sample Sizes of the Four Lipid Traits for Each of the Seven Studies.**

Study	HDL	LDL	TG	CHOL
D2d-2007	2075	2074	2075	2075
DIAGEN	1470	1454	1470	1471
DPS	412	410	412	412
DRs EXTRA	1157	1157	1157	1157
FUSION Stage 2	2496	1892	2062	2500
METSIM	1346	1345	1346	1346
Norway	2484	2320	2487	2476

Appendix B Simulation Results

In this section of the **Supplementary Materials**, more empirical power results are presented based on the approximate F-distribution tests of Pillai-Bartlett trace. In the Figures S.1, S.2, S.3, and S.4, all causal variants had positive effects for the trait y_1. In the Figures S.5, S.6, S.7, and S.8, 50%/50% causal variants had negative/positive effects for the trait y_1.

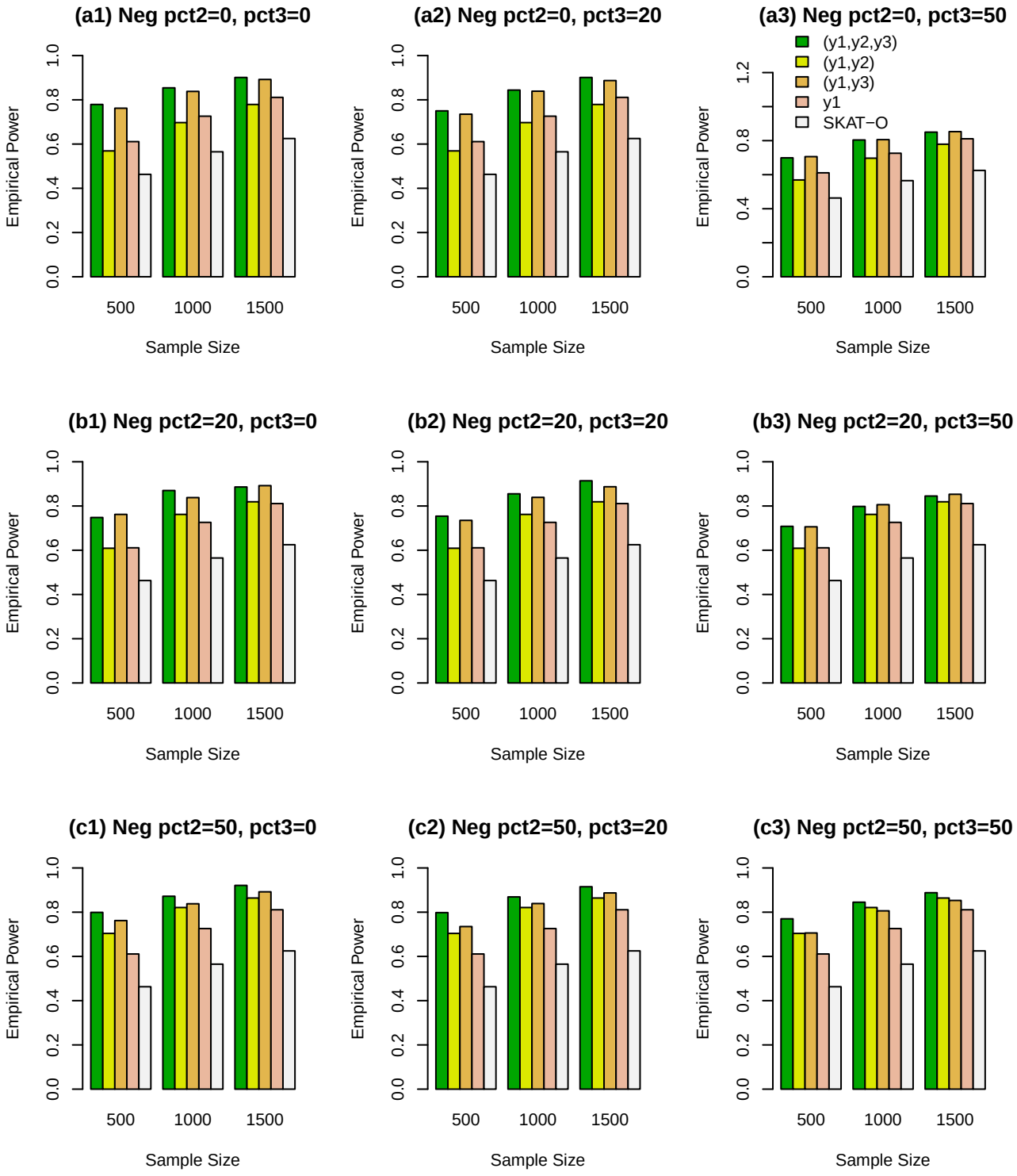

Figure S.1: **The Empirical Power of the Approximate F-distribution Test of Model (3) Using B-spline Basis Based on Pillai-Bartlett Trace and SKAT-O at $\alpha = 0.01$, When Causal Variants Were Only Rare and 10% of the Variants Were Causal.** For the trait y_1, all causal variants had positive effects; pct2 represents the percentage of negative effect causal variants for trait y_2; and pct3 represents the percentage of negative effect causal variants for trait y_3.

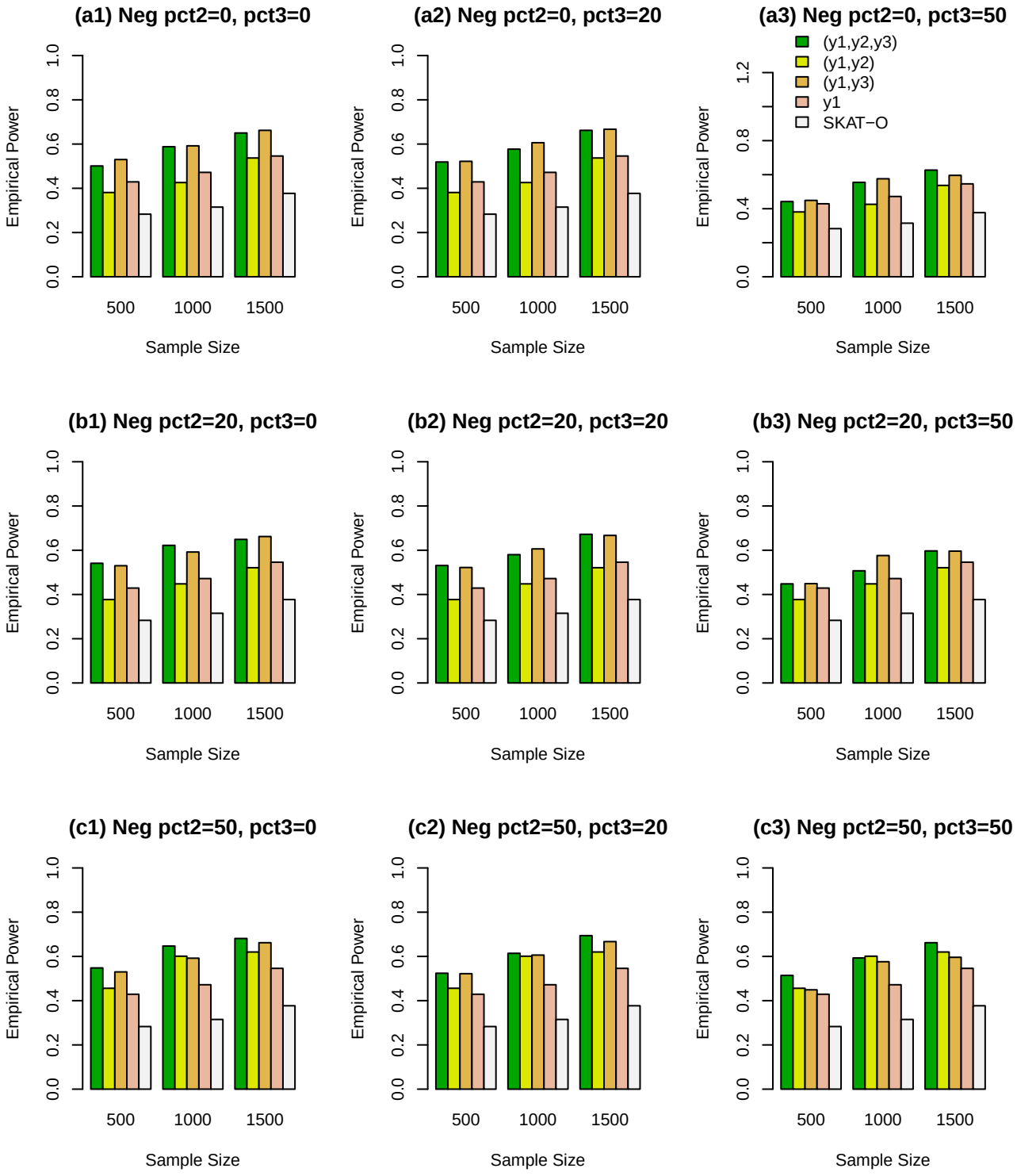

Figure S.2: **The Empirical Power of the Approximate F-distribution Test of Model (3) Using B-spline Basis Based on Pillai-Bartlett Trace and SKAT-O at $\alpha = 0.01$, When Causal Variants Were Only Rare and 5% of the Variants Were Causal.** For the trait y_1, all causal variants had positive effects; pct2 represents the percentage of negative effect causal variants for trait y_2; and pct3 represents the percentage of negative effect causal variants for trait y_3.

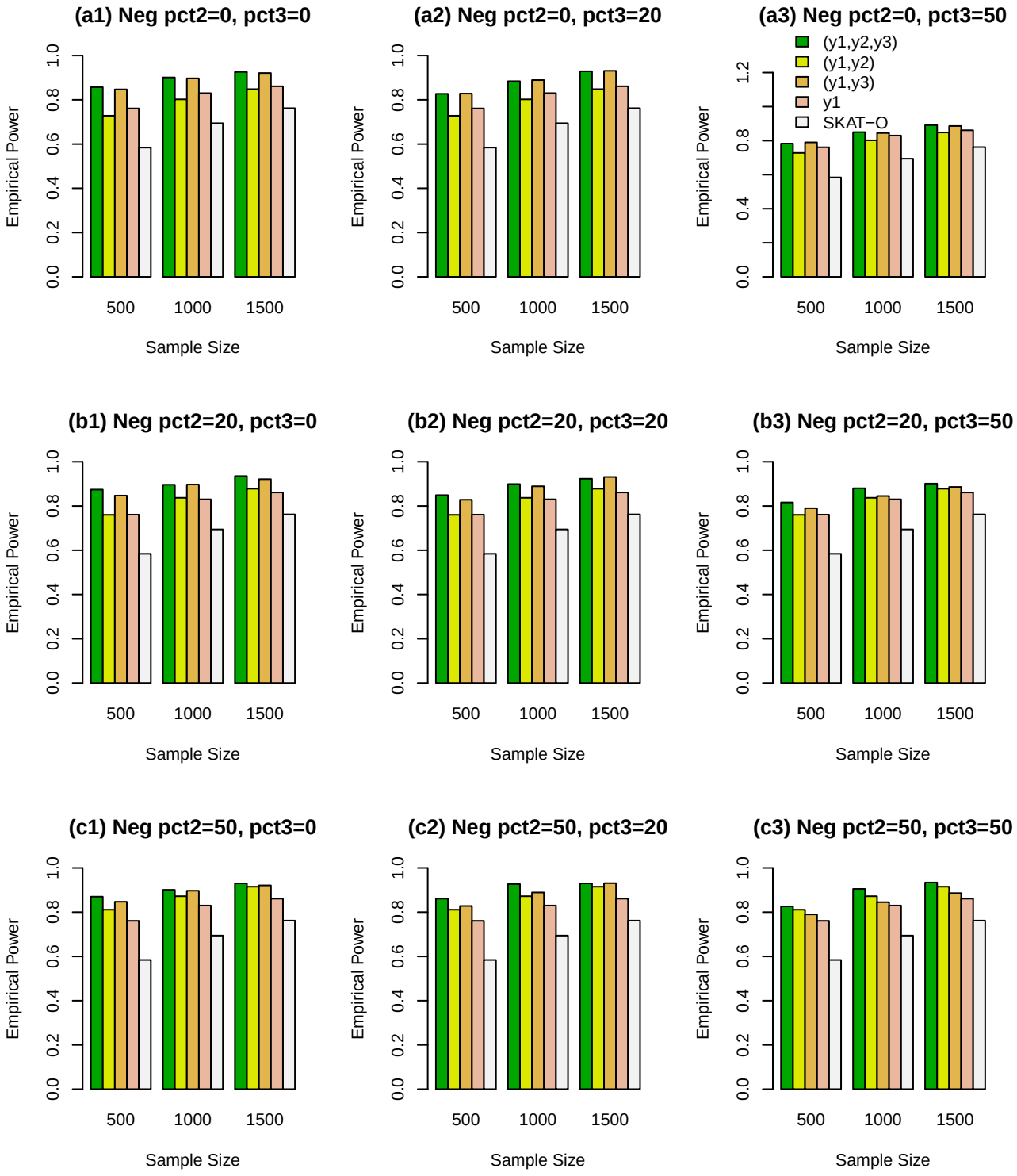

Figure S.3: **The Empirical Power of the Approximate F-distribution Test of Model (3) Using B-spline Basis Based on Pillai-Bartlett Trace and SKAT-O at $\alpha = 0.01$, When Causal Variants Were Both Rare and Common and 10% of the Variants Were Causal.** For the trait y_1, all causal variants had positive effects; pct2 represents the percentage of negative effect causal variants for trait y_2; and pct3 represents the percentage of negative effect causal variants for trait y_3.

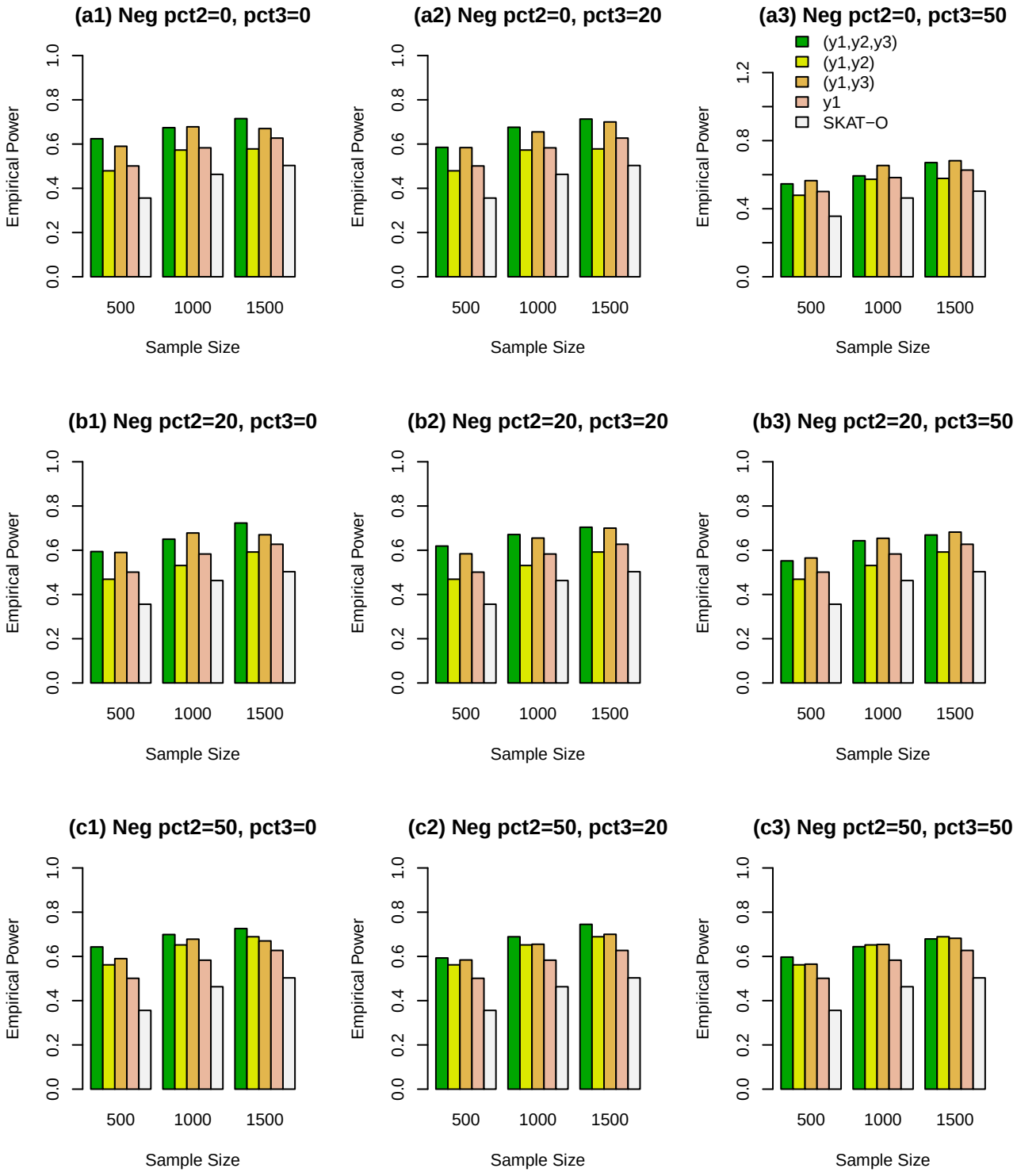

Figure S.4: **The Empirical Power of the Approximate F-distribution Test of Model (3) Using B-spline Basis Based on Pillai-Bartlett Trace and SKAT-O at $\alpha = 0.01$, When Causal Variants Were Both Rare and Common and 5% of the Variants Were Causal.** For the trait y_1, all causal variants had positive effects; pct2 represents the percentage of negative effect causal variants for trait y_2; and pct3 represents the percentage of negative effect causal variants for trait y_3.

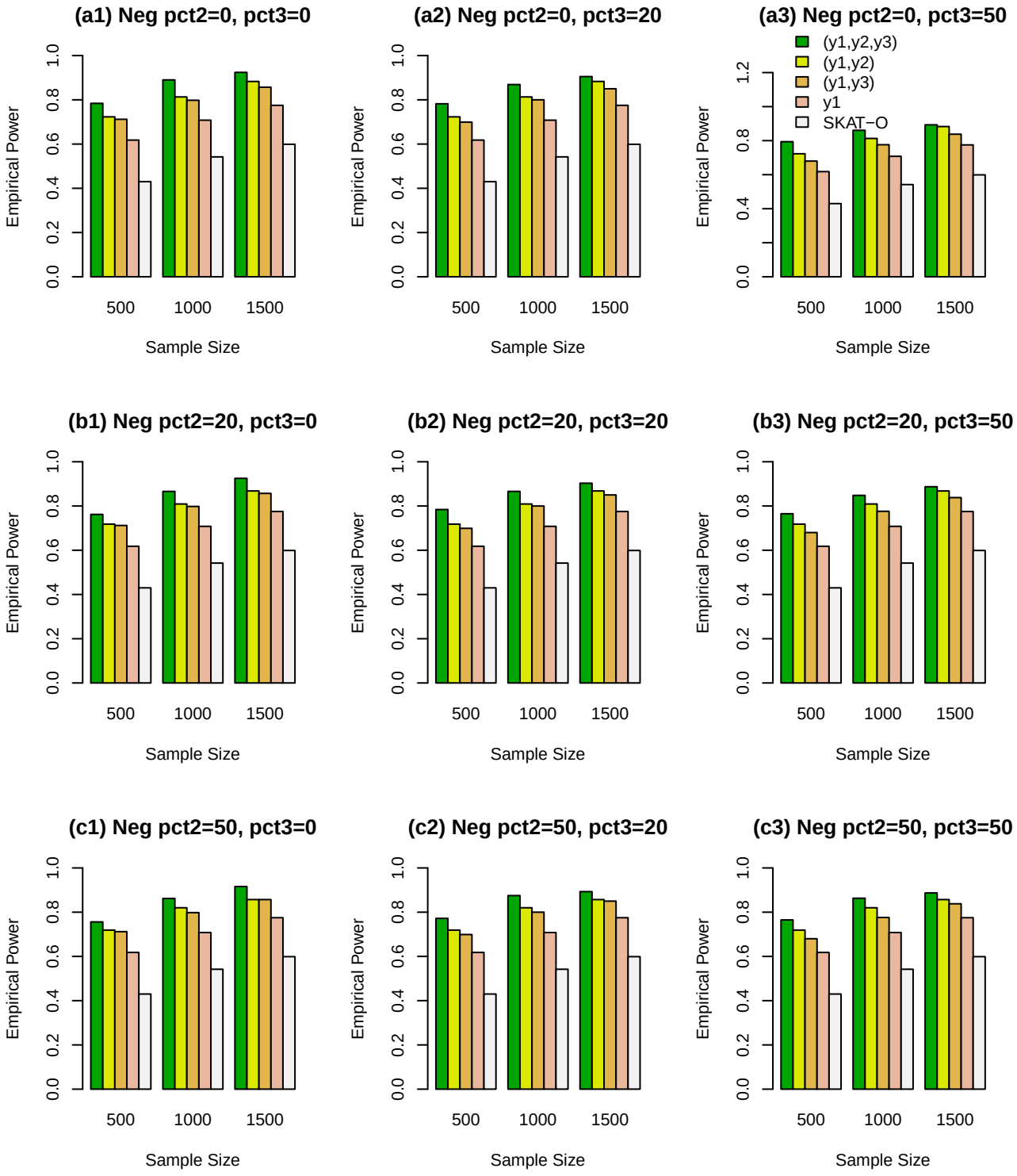

Figure S.5: **The Empirical Power of the Approximate F-distribution Test of Model (3) Using B-spline Basis Based on Pillai-Bartlett Trace and SKAT-O at $\alpha = 0.01$, When Causal Variants Were Only Rare and 10% of the Variants Were Causal.** For the trait y_1, 50%/50% causal variants had negative/positive effects; pct2 represents the percentage of negative effect causal variants for trait y_2; and pct3 represents the percentage of negative effect causal variants for trait y_3.

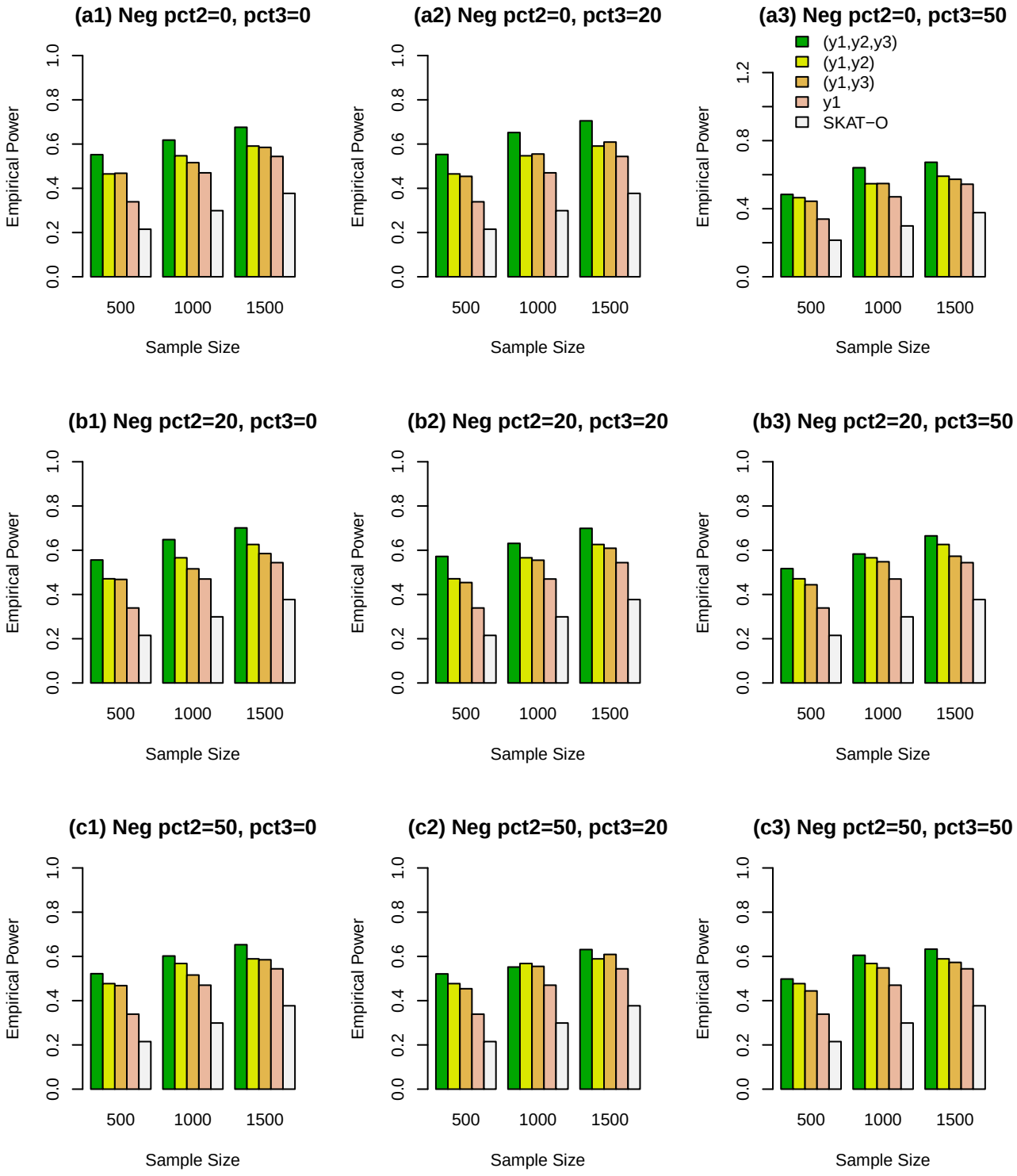

Figure S.6: **The Empirical Power of the Approximate F-distribution Test of Model (3) Using B-spline Basis Based on Pillai-Bartlett Trace and SKAT-O at $\alpha = 0.01$, When Causal Variants Were Only Rare and 5% of the Variants Were Causal.** For the trait y_1, 50%/50% causal variants had negative/positive effects; pct2 represents the percentage of negative effect causal variants for trait y_2; and pct3 represents the percentage of negative effect causal variants for trait y_3.

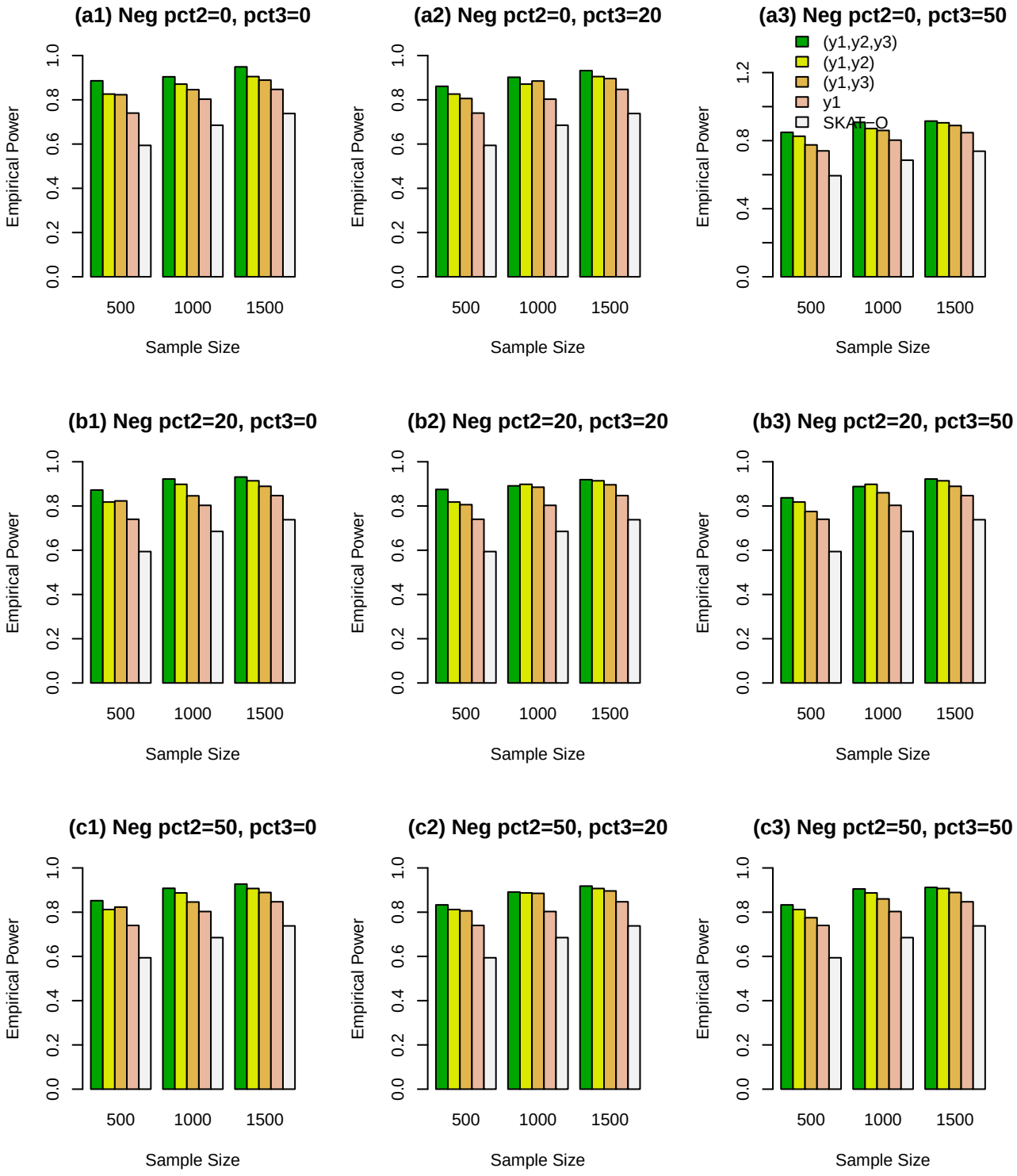

Figure S.7: **The Empirical Power of the Approximate F-distribution Test of Model (3) Using B-spline Basis Based on Pillai-Bartlett Trace and SKAT-O at $\alpha = 0.01$, When Causal Variants Were Both Rare and Common and 10% of the Variants Were Causal.** For the trait y_1, 50%/50% causal variants had negative/positive effects; pct2 represents the percentage of negative effect causal variants for trait y_2; and pct3 represents the percentage of negative effect causal variants for trait y_3.

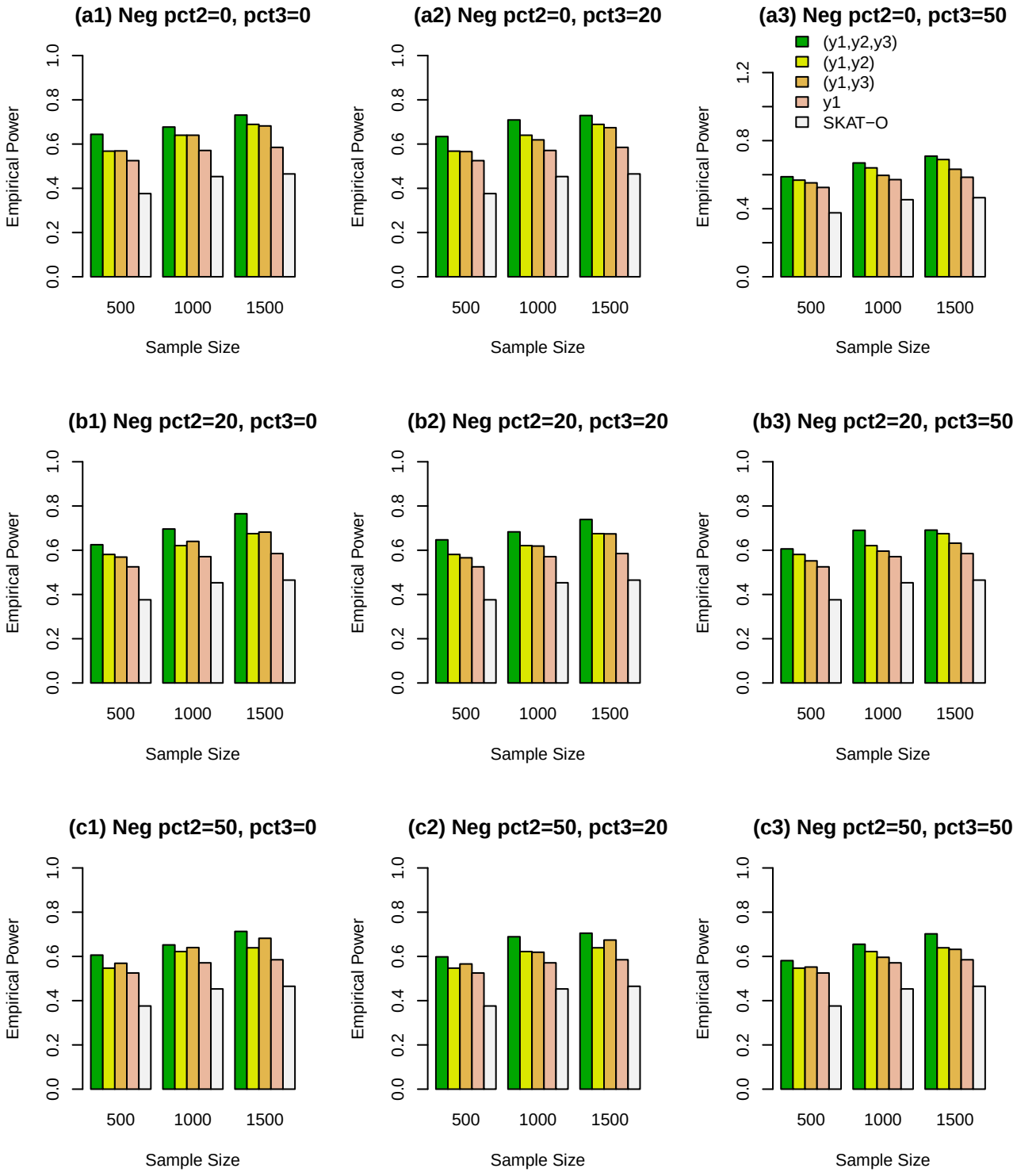

Figure S.8: **The Empirical Power of the Approximate F-distribution Test of Model (3) Using B-spline Basis Based on Pillai-Bartlett Trace and SKAT-O at $\alpha = 0.01$, When Causal Variants Were Both Rare and Common and 5% of the Variants Were Causal.** For the trait y_1, 50%/50% causal variants had negative/positive effects; pct2 represents the percentage of negative effect causal variants for trait y_2; and pct3 represents the percentage of negative effect causal variants for trait y_3.