Multi-Variant Risk Reporting in the Coriell Personalized Medicine Collaborative (CPMC®) Research Study

APPENDIX: Glaucoma

Single Nucleotide Polymorphism (SNP) Identification

To be considered for use in multigenic risk reporting for glaucoma we required each SNP to: 1) show statistically significant association with glaucoma after correction for multiple testing and be replicated in at least one independent population sample, 2) be unlinked with all other SNPs in the final model ($R^2 < 0.2$), 3) be captured in the current version of the Affymetrix 6.0 Genotyping Array, 4) pass Coriell's internal SNP genotyping quality controls, and 5) be approved by the ICOB.

SNPs associated with glaucoma were initially identified in the NIH GWAS catalog (www.genome.gov/gwastudies). References from this catalog were then used in parallel with PubMed searches to explore the extent of the literature support for association.

Model

The CPMC model of glaucoma relative risk (RR), calculated via REGENT, includes two ICOB-approved, CLIA-validated SNPs captured by the current Affy 6.0 Genotyping Platform: rs7049105 and rs7518099 (also see Table 1 for input parameters). We used a prevalence of 0.019. Odds ratios from the listed citations were converted to relative risk (RR) values as described in the white paper.

Table 1.

SNP	MAF	Ncase	Ncontrol	RR_het	RR_hom	Citation
rs7049105	0.49	3146	3487	1.40	1.80	Wiggs et al. 2012
rs7518099	0.12	892	4582	1.48	1.95	Burdon et al. 2011

Evaluation

Figure 1 displays excellent consistency of categorical boundaries determined by REGENT.model across 100 simulations. Figure 2 displays excellent consistency of the proportion of individuals assigned to a given category by REGENT.model.

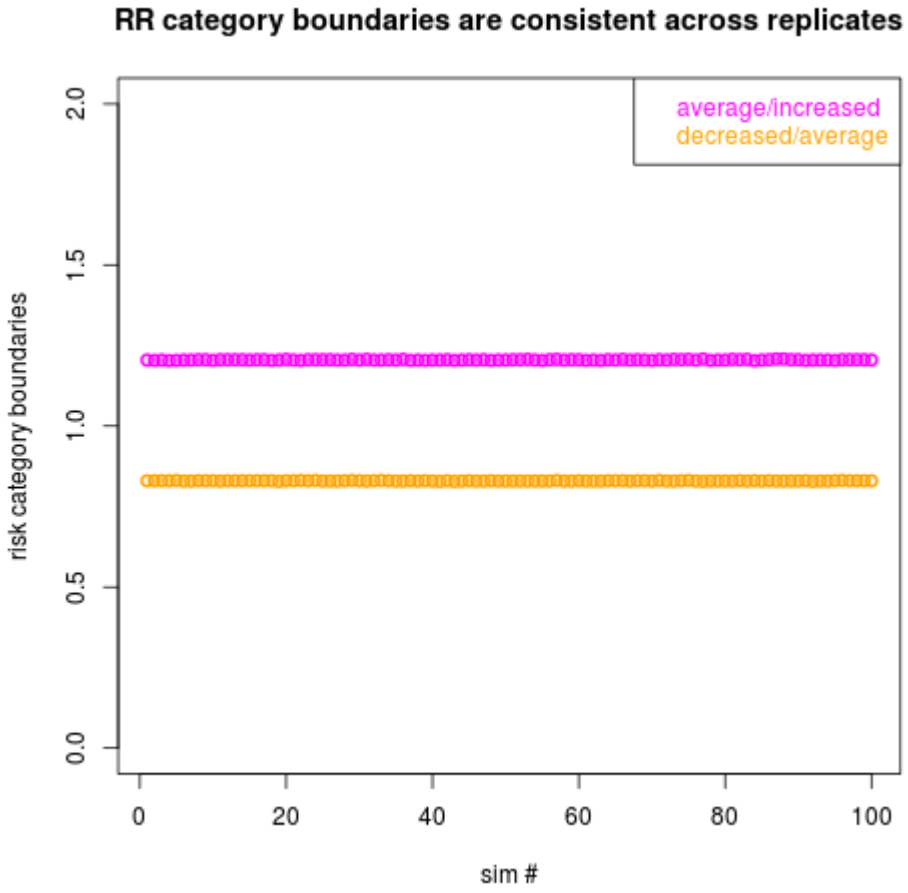

Figure 1.

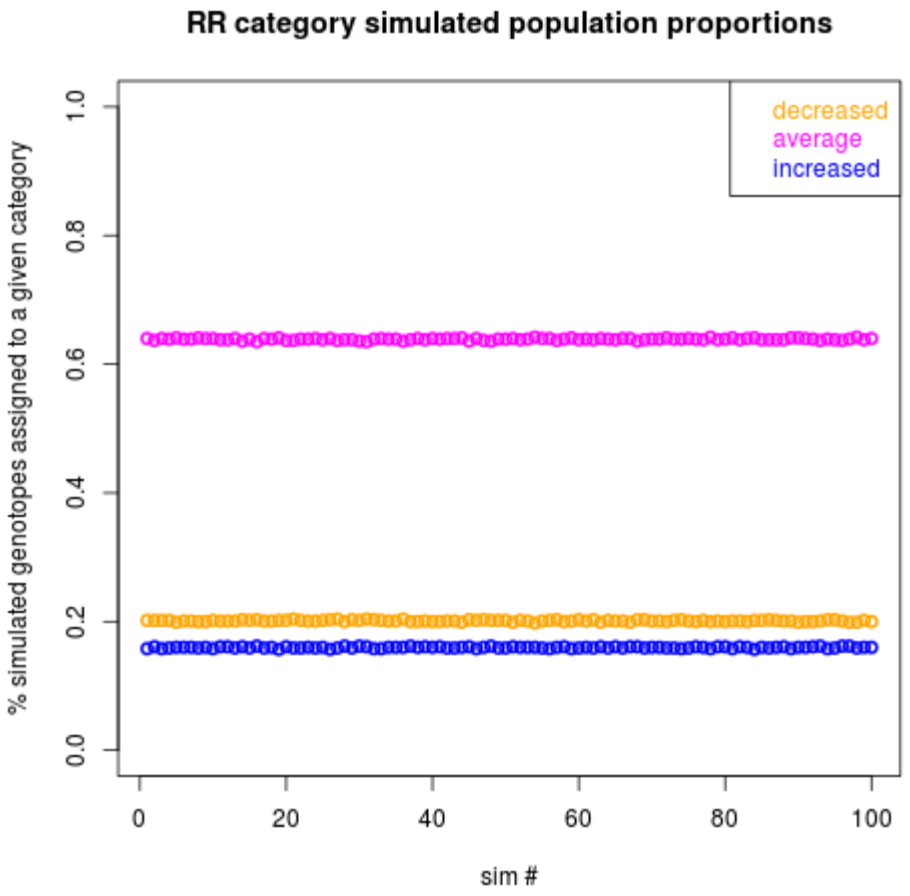

Figure 2.

References

Burdon et al. Genome-wide association study identifies susceptibility loci for open angle glaucoma at *TMCO1* and *CDKN2B-AS1*. Nature Genetics. 2011;43(6):574-8.

Wiggs, et al. Common variants at 9p21 and 8q22 are associated with increased susceptibility to optic nerve degeneration in glaucoma. *PloS Genetics.* 2012;8(4):e1002654.