CORIELL
PERSONALIZED MEDICINE
COLLABORATIVE

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

APPENDIX: Lung Cancer

Single Nucleotide Polymorphism (SNP) Identification

To be considered for use in multigenic risk reporting for lung cancer we required each SNP to: 1) show statistically significant association with lung cancer 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 lung cancer 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 lung cancer relative risk (RR), calculated via REGENT, includes two ICOB-approved, CLIA-validated SNPs captured by the current Affy 6.0 Genotyping Platform: rs938682 and rs2736100 (also see Table 1 for input parameters). We used a prevalence of 0.00129 (http://seer.cancer.gov/statfacts/html/lungb.html). Odds ratios from the listed citations were converted to relative risk (RR) values as described in the white paper.

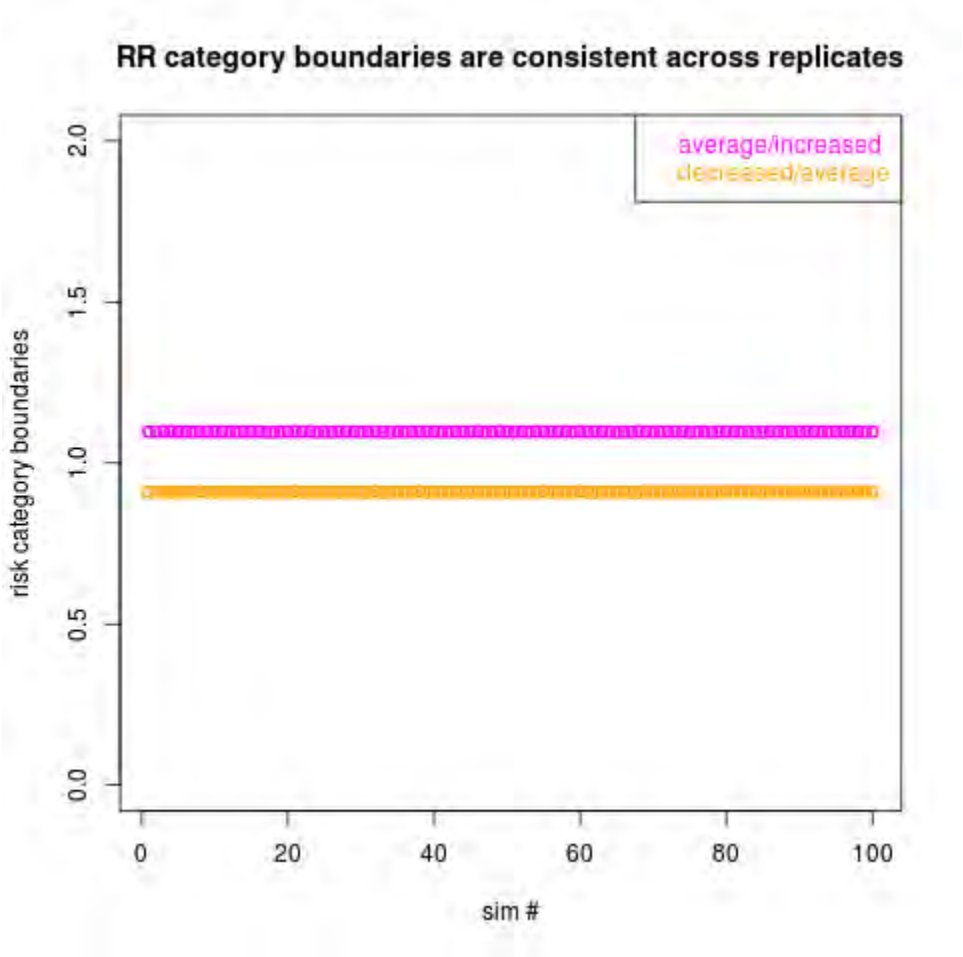
Table 1.

SNP	MAF	Ncase	Ncontrol	RR_het	RR_hom	Ncase	Ncontrol	Citation
rs938682	0.81	4417	4443	1.33	1.66	4417	4443	Broderick et al. 2009
rs2736100	0.48	49869	73464	1.23	1.46	49869	73464	Nie et al 2014

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



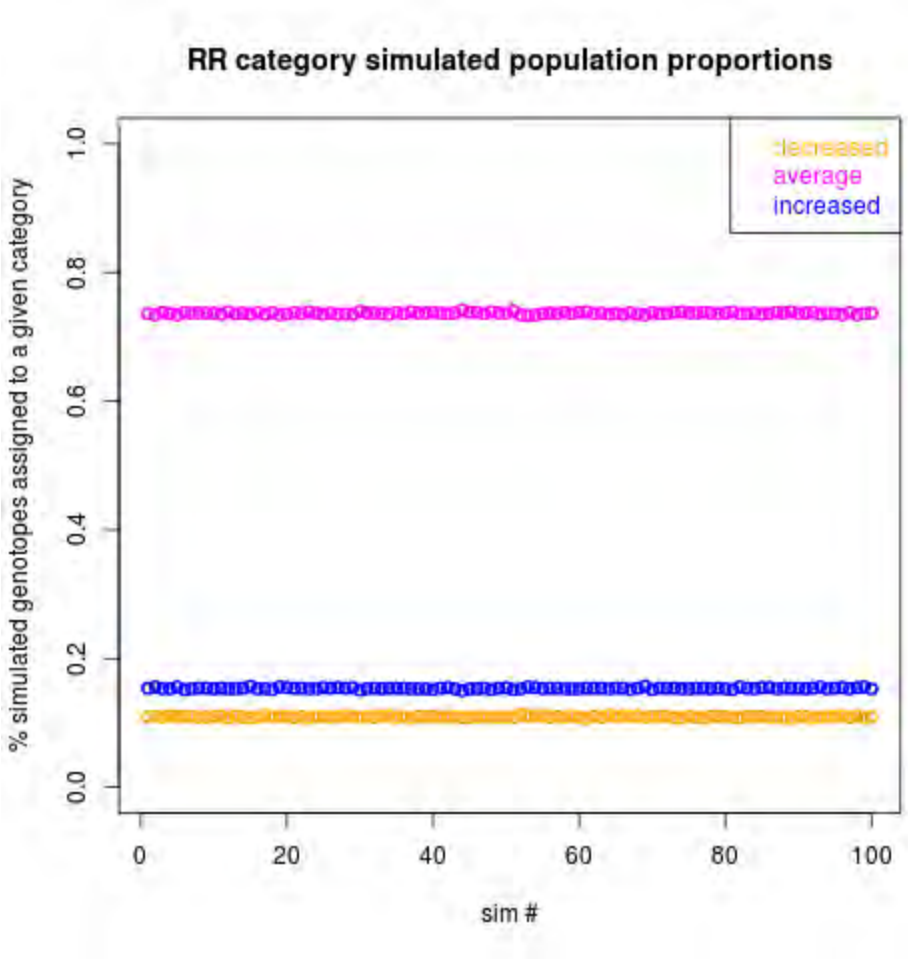


Figure 2

References

Broderick, et al. Deciphering the impact of common genetic variation on lung cancer risk: A genome-wide association study. *Cancer Res.* 2009;69(16):6633-41.

Nie, et al. TERT rs2736100 polymorphism contributes to lung cancer risk: a meta-analysis including 49,869 cases and 73,464 controls. *Tumor Biology.* 2014;35(6):5569-74.