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Supplemental Data

Transethnic Genetic-Correlation Estimates from Summary Statistics

Brielin C. Brown, Asian Genetic Epidemiology Network Type 2 Diabetes Consortium, Chun Jimmie Ye, Alkes L. Price, and Noah Zaitlen

Supplemental Figures and Tables

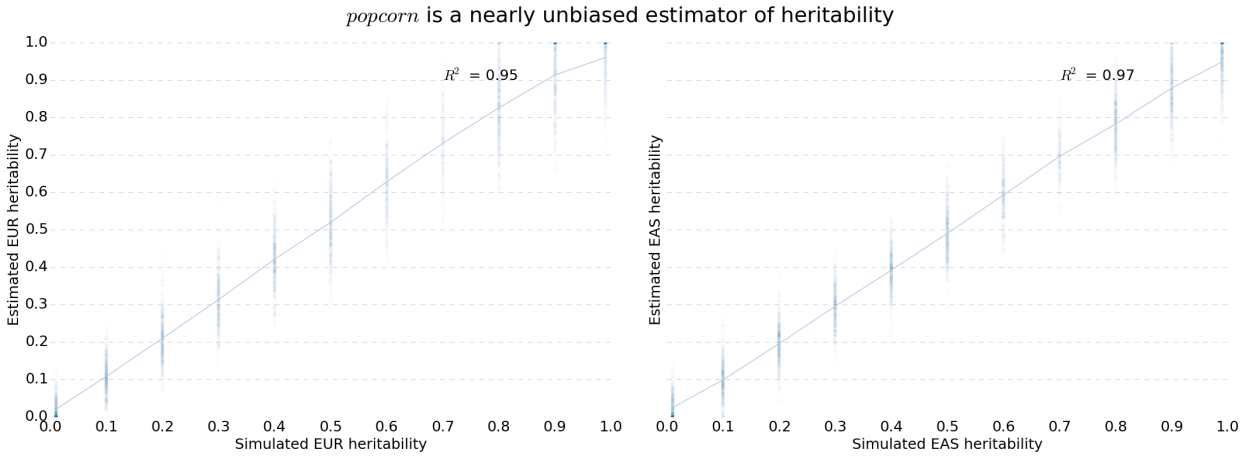

Figure S1: True and estimated heritability for simulated EUR and EAS populations as the heritability varies. All simulations conducted with simulated EUR and EAS genetic effect correlation of 0.5 using 4499 simulated EUR- and 4836 simulated EAS individuals at 248,953 SNPs.

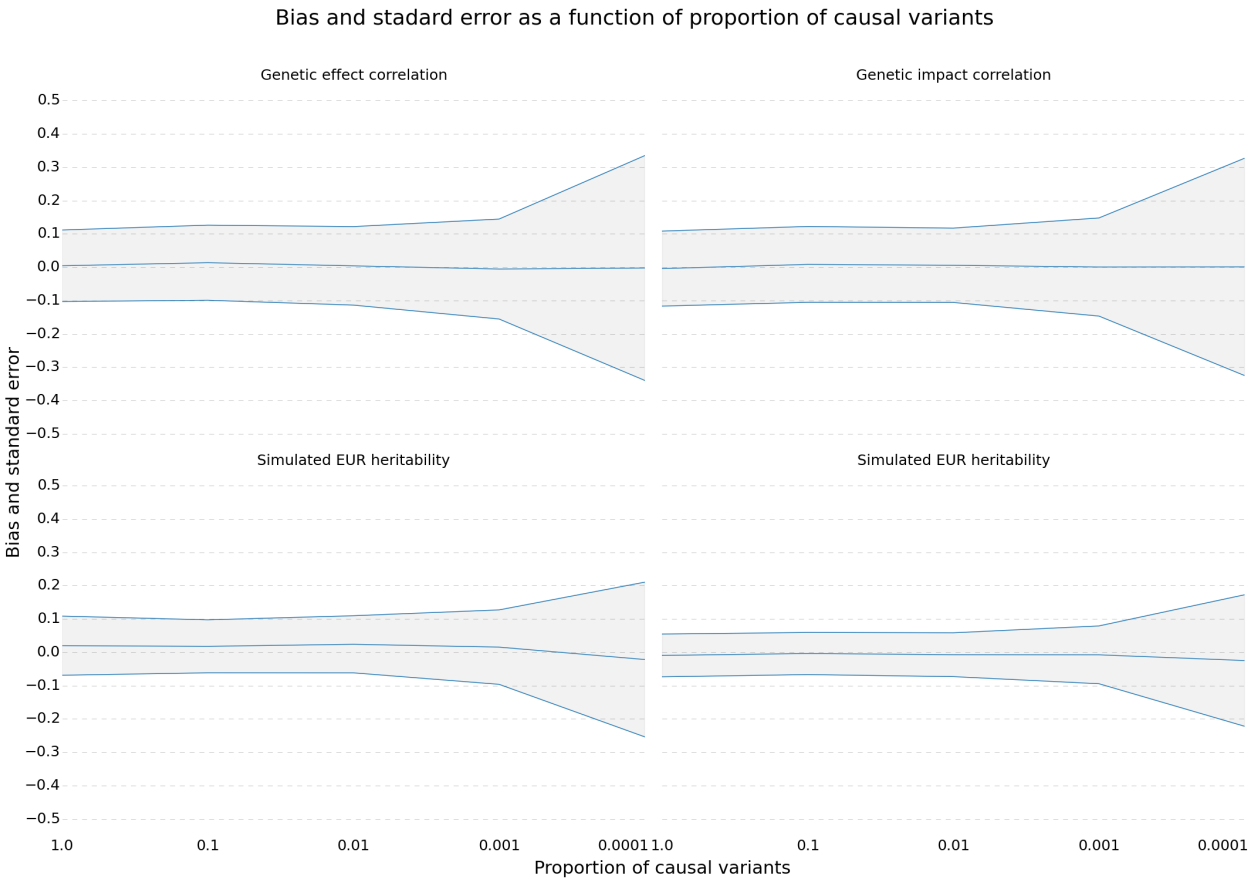

Figure S2: Bias and standard error as the proportion of causal variants is decreased from 1.0 (all variants causal, the infinitesimal model) to 0.0001 (one in ten thousand variants causal, or approximately 25 total causals). All simulations conducted using simulated phenotypes with $h_1^2 = 0.5$, $h_2^2 = 0.5$, $\rho_{gi,e} = 0.5$.

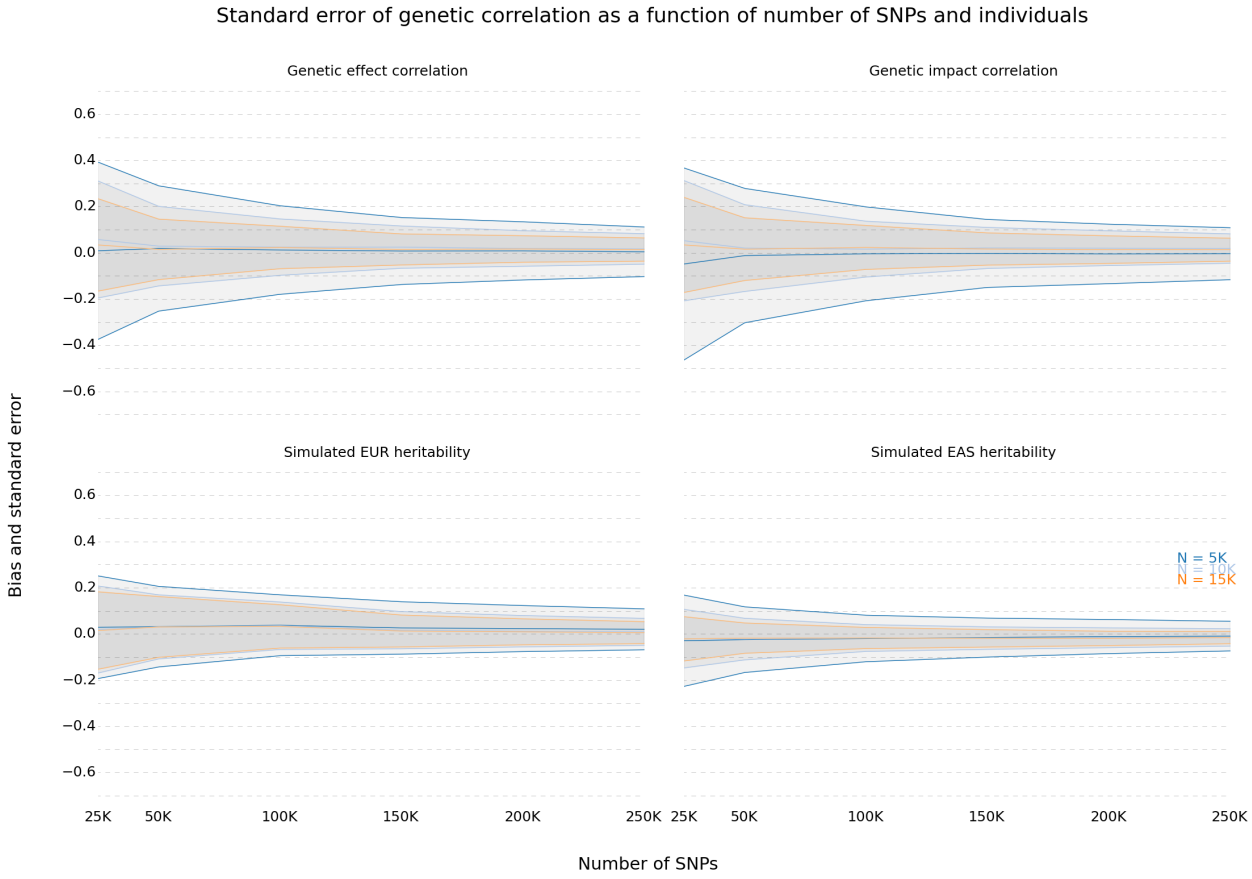

Figure S3: Bias and standard error of the heritability estimator in popcorn as a function of the number of SNPs and individuals. All simulations conducted using simulated phenotypes with $h_1^2 = 0.5$, $h_2^2 = 0.5$, $\rho_{gi,e} = 0.5$. To increase the number of individuals, we increased the relatedness cutoff to 0.075 resulting in 9838 EAS-like and 9603 EUR like samples, and again to 0.1 resulting in 15601 EAS-like and 15388 EUR-like individuals. In each case, 500 individuals were chosen uniformly at random to serve as a reference panel.

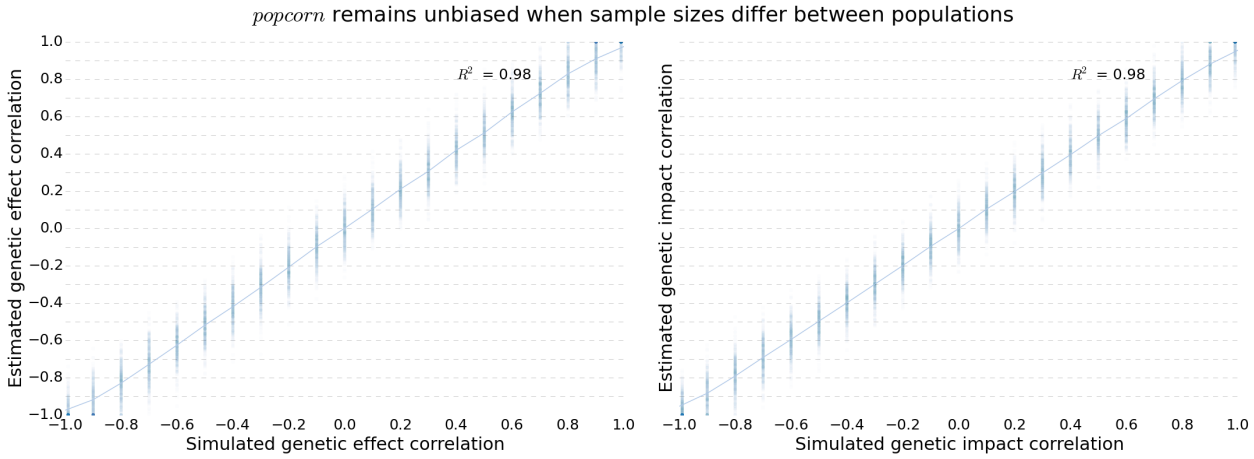

Figure S4: True and estimated genetic impact and effect correlation when the studies have very different sample sizes. All simulations conducted with simulated EUR and EAS heritability of 0.5 using 4,499 simulated EUR and 15,101 simulated EAS individuals at 248,953 SNPs.

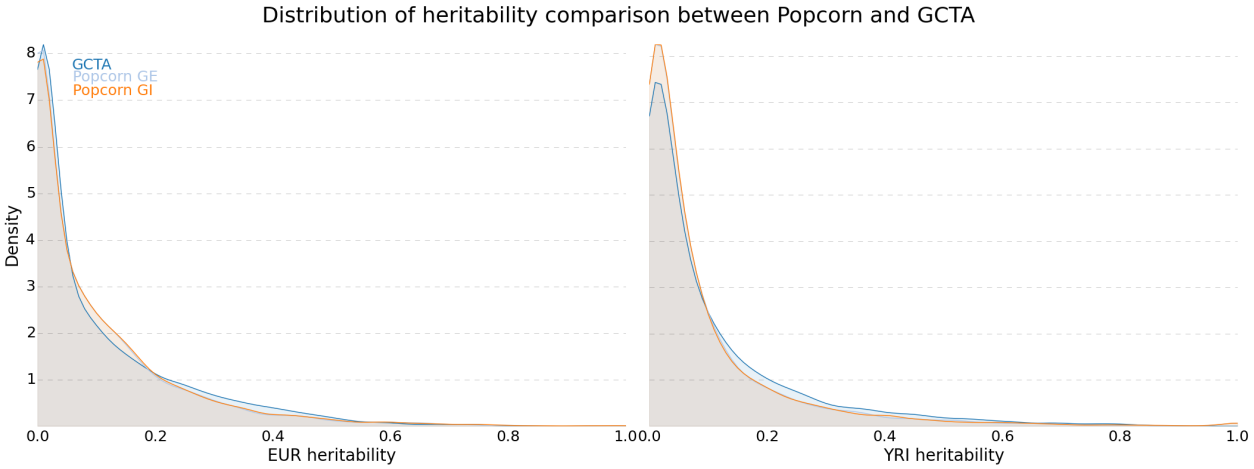

Figure S5: Density comparison between popcorn and GCTA as heritability estimators. Density was computed using the scipy statistics package gaussian_kde function on the set of heritability estimates.

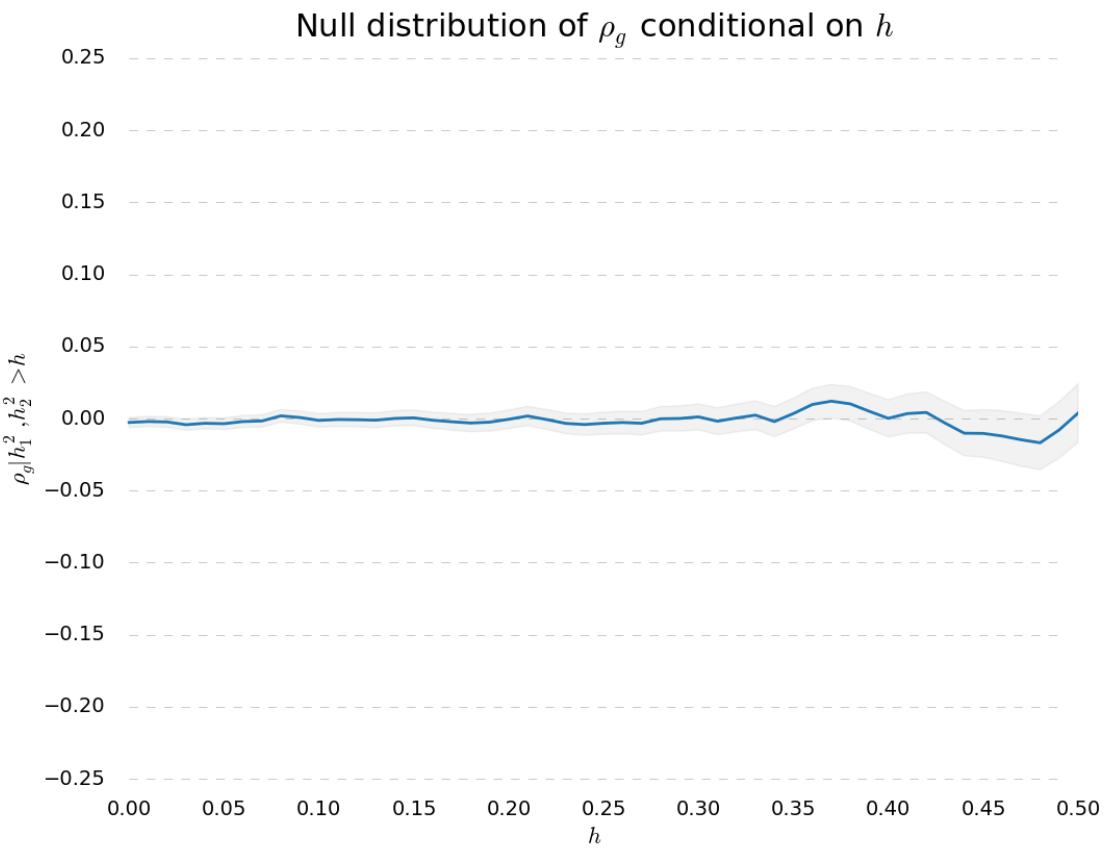

Figure S6: Null distribution of the conditional genetic correlation. Phenotypes were generated with heritability randomly sampled from the joint distribution of the gEUVADIS heritability estimates over randomly selected 4000 SNP regions from chromosome 1 of the true EUR and YRI genotypes and genetic correlation of 0. The mean and standard error of the genetic correlation of the set of genes with $\hat{h}_1^2$ and $\hat{h}_2^2$ exceeding threshold h in each analysis (y-axis) is plotted against h (x-axis)

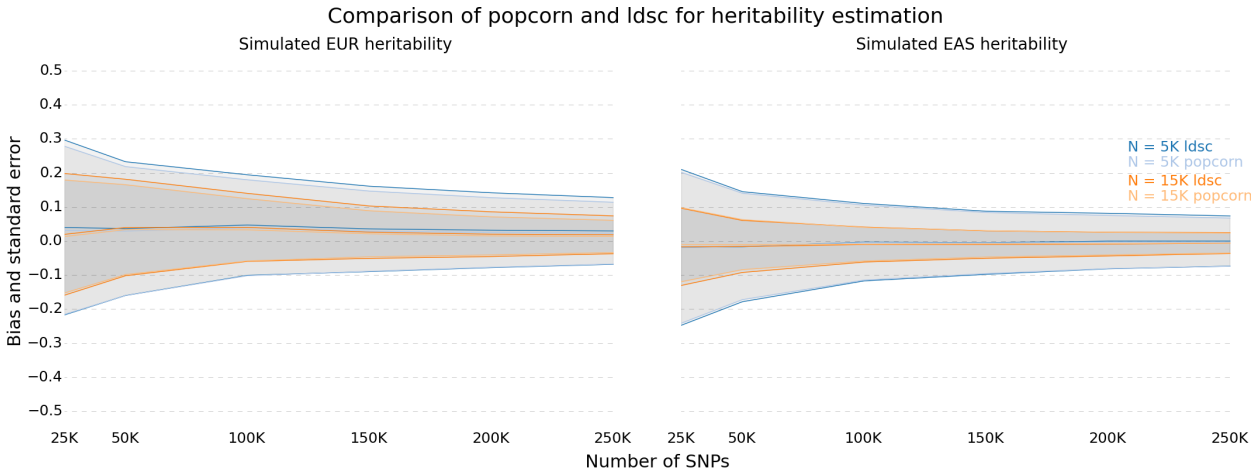

Figure S7: Comparison of the mean and standard error of popcorn and ldsc as heritability estimators as the number of SNPs and individuals in each study varies. All simulations conducted using simulated phenotypes with $h_1^2 = 0.5$, $h_2^2 = 0.5$, $\rho_{gi,e} = 0.5$.

Prevalence	N	$\hat{h}_1$	$\hat{h}_2$	$\hat{\rho}_g$
0.03	1000	0.31	0.31	0.28
0.05	1700	0.30	0.30	0.31
0.1	3400	0.31	0.30	0.30
0.25	5000	0.31	0.31	0.29

Table S1: Average heritability and genetic correlation over 1000 simulations with varying levels of ascertainment. All simulations contained exactly N cases and controls for a study prevalence of 0.5. Phenotypes were simulated with liability scale heritability of 0.3 for both phenotypes and genetic correlation of 0.3.

Phenotype	popcorn	ldsc	GCTA	$p_{popcorn \neq ldsc}$	$p_{popcorn \neq GCTA}$
Height	0.999 (0.000)	0.972 (0.022)	1.02 (0.023)	0.219	0.361
BMI	0.999 (0.000)	0.927 (0.038)	1.01 (0.064)	0.058	0.863

Table S2: Genetic correlation between male and female Europeans for height and BMI. Estimates from *popcorn* and *ldsc* were computed using scores computed from variants with allele frequency above 5% in 1000 genomes and all unambiguous variants with allele frequency above 5% in HapMap3. Summary statistics of height and BMI were obtained from the GIANT consortium.[1] Genotype-level results computed with *GCTA* were obtained from Yang et al.[2] p-values that our estimate did not differ significantly from the estimates of *ldsc* and *GCTA* were computed using a Wald test. Note that because our estimator is bounded from above by 1.0, the *popcorn* estimate and it's standard error are biased.

References

[1] Randall, J. C., Winkler, T. W., Kutalik, Z., Berndt, S. I., Jackson, A. U., Monda, K. L., Kilpeläinen, T. O., Esko, T., Mägi, R., Li, S., et al. (2013). Sex-stratified genome-wide association studies including 270,000 individuals show sexual dimorphism in genetic loci for anthropometric traits. PLoS Genetics *9*, e1003500.

[2] Yang, J., Bakshi, A., Zhu, Z., Hemani, G., Vinkhuyzen, A. A. E., Nolte, I. M., van Vliet-Ostaptchouk, J. V., Snieder, H., Study, T. L. C., Esko, T., et al. (2015). Genome-wide genetic homogeneity between sexes and populations for human height and body mass index. Human Molecular Genetics *24*, 7445–7449.