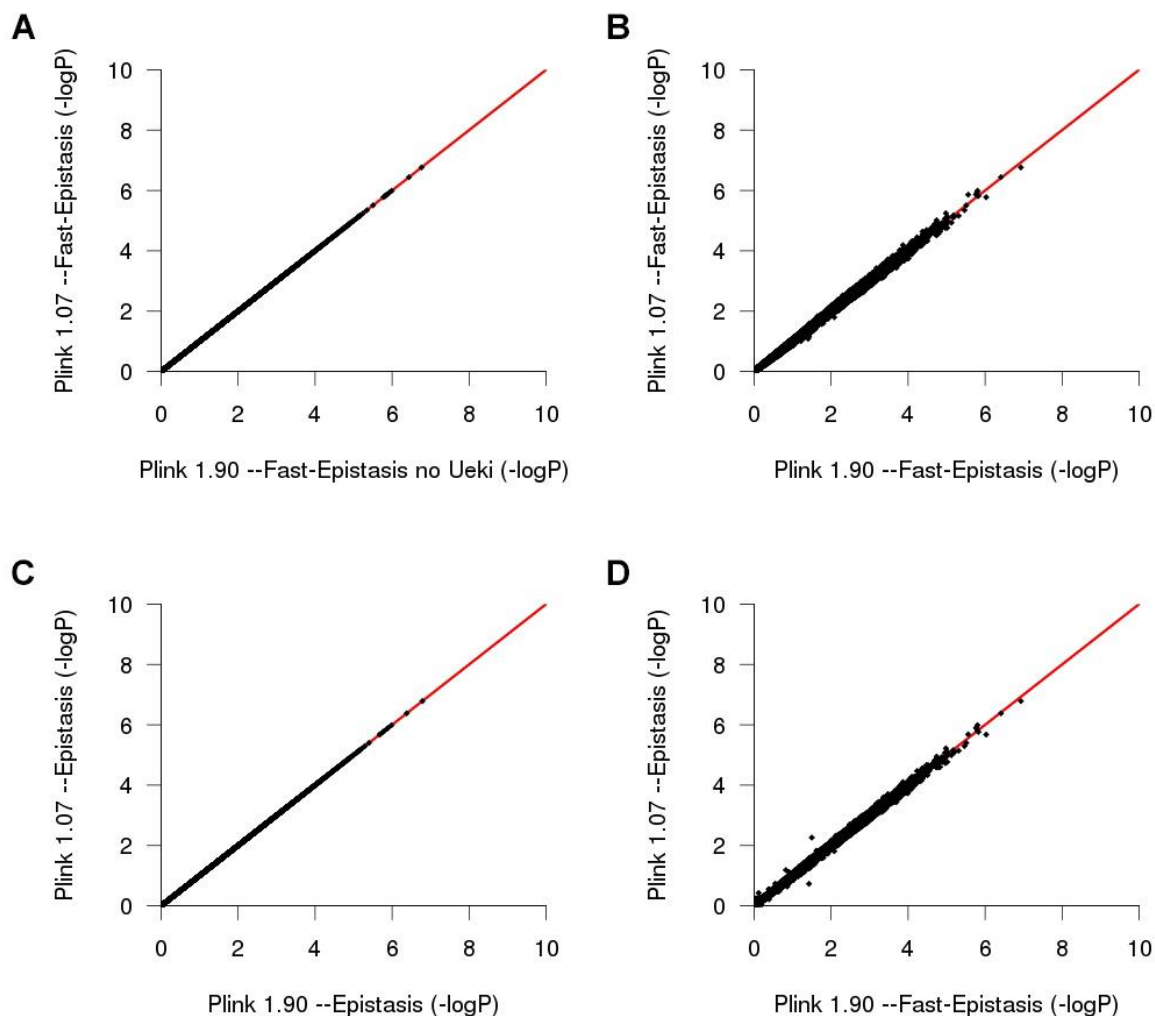


**Figure S-2. Comparison of epistasis analysis results derived from Plink 1.07 and Plink 1.90.**



Since Plink 1.90 (the software used to conduct genome-wide SNP-SNP interaction analyses in the present study) was in beta testing at the time of study, we sought to verify the accuracy of its results. To do this, we compared four different analyses conducted in Plink 1.90 to similar analyses conducted in Plink 1.07 (the latest stable release of the original Plink toolset), as follows: **(A)** Plink 1.07 FastEpistasis vs. Plink 1.90 FastEpistasis with the “no Ueki” option. This option disables corrections made to the FastEpistasis algorithm implemented in Plink 1.90, in order to allow exact comparisons with FastEpistasis as implemented in Plink 1.07 (see <https://www.cog-genomics.org/plink2/epistasis>). **(B)** Plink 1.07 FastEpistasis vs. Plink 1.90 FastEpistasis without the “No Ueki” option. Slight differences in results from the two packages are due to known corrections made using the Ueki method. **(C)** Plink 1.07 Epistasis vs. Plink 1.90 Epistasis. Here, both packages used logistic regression to evaluate epistatic effects. **(D)** Plink 1.07 Epistasis vs. Plink 1.90 FastEpistasis. Slight differences are due to the known fact that FastEpistasis is designed as an approximate method to search for epistatic effects. To conduct all of these comparisons,  $N = 2,012$  SNPs were randomly selected from the discovery dataset (for type 2 diabetes) and all possible combinations of these SNPs were subjected to the various analyses for SNP-SNP interactions ( $N = 2,023,066$  interactions tested for each analysis).  $-\text{Log}_{10}$  P-values from these tests are plotted above. Red lines indicate 1:1 correlation.

#### References:

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Purcell S, Neale B, Todd-Brown K, Thomas L, Ferreira MAR, Bender D, Maller J, Sklar P, de Bakker PIW, Daly MJ & Sham PC (2007). PLINK: a toolset for whole-genome association and population-based linkage analysis. *American Journal of Human Genetics*, 81.