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Supplementary Information for

The Essentiality of Reporting Hardy-Weinberg Equilibrium Calculations in Population-Based Genetic Association Studies

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This PDF file includes:

Materials and Methods
Appendix 1

Materials and Methods

Article selection

Using the archive database of Cell Journal$_{\text{(Yakhteh)}}$ (Cell J), we scoured through articles using the keywords "polymorphism", "association", "SNP" and "genotype". We identified eleven articles reporting association studies of which one did not provide genotypic data in full and was thus removed from further analysis (1). Also, when combined genotypic frequencies were available for more than one SNP, raw frequencies for each SNP were obtained by analyzing their tabulated data.

Data analysis

Ten articles reporting detailed genotypic data were reviewed (see Appendix 1). One study did not conform to the typical case-control association study by not having a control group. However, since identifying deviation in the case group is also meaningful, we did not exclude this study from analysis. A total of 16 diallelic single nucleotide polymorphisms (SNPs) were reported for which HWE calculations were undertaken using Chi-square goodness-of-fit test (R function *HWE.chisq*) or an exact test (R function *HWE.exact*) when any genotype count was below 5. Also, relative excess heterozygosity (REH) and its 95% CI, as a direct measure of HWE compatibility, was calculated to compare to the result of goodness-of-fit tests and confirm incompatibility (2). Re-analysis of genetic associations at the allelic level was undertaken using Fisher's exact test. These analyses were implemented in the R environment (v 3.0.2) (3) using the 'genetics' and 'stats' packages. Furthermore, Wright's inbreeding coefficient (F) (4) was estimated from $F=1-Ho/He$ where Ho and He are the observed and expected heterozygosity for a SNP in a given group. The statistical significance level was set to $P<0.05$.

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Appendix 1. References with Eligible Data

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