Evaluation on the effect size of rare variants based on genome-wide association studies in WTCCC data

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Genome-wide association studies (GWASs) have identified hundreds of susceptibility genetic variants which were associated with complex diseases, however, most common variants explain only a modest proportion of heritability of these diseases. There are many causes for so-called missing heritability, and one reason is the ignorance of the impact of rare variants. Currently, many statistical tests developed for common variants in GWASs may not be directly applicable for rare variants due to low power. Hence, novel and powerful statistical method is needed for rare variants. In this presentation, we estimate the effect size of rare variants based on odds ratio and Cohen's h. In addition, the relationship between the threshold of MAF, the magnitude of effect size, the sample size and the power will be examined. We utilize the coronary artery disease (CAD) case-control data from the Wellcome Trust Case Control Consortium (WTCCC) to provide an evaluation of type I error rate for each effect size. Using a total of 413,059 genetic markers on Chromosomes 1~22, the results indicated that larger variation was found for odds ratio than that of Cohen's h. In particular, for rare SNPs, the values of type one error rates are higher than the nominal level 0.05, regardless of effect sizes.

Keyword: Cohen's *h*, Effect size, Genome-wide association study, Type I error.