

The use of disease propensity to reduce heterogeneity in nested genetic association studies of complex conditions

M. Fazil Baksh

Quantitative Biology and Applied Statistics, University of Reading, UK

Identification of genetic influences in studies of complex conditions is often contingent on the ability to minimize heterogeneity due to effects of non-genetic factors. Within a large prospective cohort, a procedure for reducing heterogeneity based on a measure of propensity for disease has recently been implemented in the design stage of a nested population-based genetic association study of obesity. In this talk, both theory and simulations are used to evaluate the potential of this procedure under various scenarios. In addition we present theoretical results showing that, under certain conditions, an artefactual genetic effect may be detected by current analysis methods and consider and evaluate a new analysis method appropriate for studies where these conditions prevail. Finally, the methodology is illustrated in a test for gene-environment effects using data obtained in the obesity study. Many genetic association studies are nested in established cohorts and it is inarguably pragmatic that the existing cohort data be used to improve efficiency of these studies. Researchers considering this approach should find our findings useful.