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A haplotype generalized linear model to combine case-control and triads with accounting for population stratification in genetic association studies

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Combining data when data are collected under different study designs, such as family triads and unrelated case-control samples, gains more power and is cost-effective than analyzing each data separately. However, a potential concern is population stratification (PS) among unrelated case-control samples and analysed integrating data should address this confounding effect. In this paper, a method that tests and estimates haplotype effects on disease risk and allows for modification against PS for combining both data types as family and unrelated samples is developed.A haplotype generalized linear model (HGLM) based on haplotype weighted-count data estimated from either data type was advocated. Furthermore, a framework of analysis of variance based on haplotype weighted-count for detecting whether it is appropriate to combine two data sources, as well as the modified HGLM with clustering methodsfor addressingPS when calculating haplotype weighted-count was presented. The statistical properties in terms of accuracy, false positive rate (FPR) and empirical power by analyzing simulated data were evaluated. The simulation studies with various disease risks, sample sizes, and combination schemes have uniformly shown that the proposed method significantly improves the power of detecting haplotype-specific risk compared with existing approaches. Simulation results indicate that the proposed model competes well with the likelihood-based haplotype association analysis, and gives unbiased estimate and achieves more power gain, particularly when the sample size is small with mild or moderate effect. In the presence of PS, the modified HGLM remains valid and has satisfactory nominal level and small bias.

Biography

Shu-Hui Wen has completed her PhD in Biostatistics at the age of 28 years from National Taiwan University, Taipei, Taiwan.She has published more than 15 papers in reputed journals and has been serving as a reviewer for academic journals.

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