
Empirical Comparison of A General Approach for Analyzing Sibling-Pair Data

FR Schumacher¹, DV Conti², JS Witte³

¹Case Western Reserve University, Cleveland, OH; ²University of Southern California, Los Angeles, CA; ³University of California San Francisco, CA

Family-based designs are commonly used for both genetic linkage and association in complex diseases in general and cardiovascular disease in particular. However, there remain important issues concerning the most powerful design and/or the best means for including all relevant information from existing data sets. When a study recruits a combination of concordant and discordant pairs, conventional linkage and association analyses do not optimally use all information on the subjects. For example, evaluating association with conditional logistic regression (CLR) will ignore concordantly affected sib-pairs. To address this problem one can use a general approach that separates genotype information into within- and between-family components (WBC; Fulkner, 1999; Abecasis, 2000). We present here the general theory underlying this approach, and illustrate its potential value with an application to association data from a study of candidate genes and prostate cancer. Specifically, we compare results from using the WBC approach to using CLR. Across the two methods of analysis the results for several candidate genes differed substantially. For example, when looking at a SNP in the candidate gene CYP3A4, the WBC approach yielded an OR= 2.14 (p-value= 0.07), whereas using CLR gave an OR= 1.70 (p= 0.26). However, the reverse situation occurred for other SNPs, whereby the WBC approach gave less statistically significant results. Since neither approach is sensitive to population stratification, the difference may be due to an increase in power for the WBC approach. This arises from the inclusion of concordant pairs in the analysis. The potential improved efficiency of the WBC approach may change drastically depending on the analysis, additional work will more fully compare (e.g. by simulation) this approach to conventional methods