

# Linkage Analysis of Ordinal Traits for Pedigree Data

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## Abstract:

Linkage analysis is used routinely to map genes for human diseases and conditions. The existing linkage analysis methods require the corresponding traits to be binary or quantitative. However, many diseases and conditions, such as cancer and mental health conditions, are rated on ordinal scales. The objective of this study was to establish a framework to conduct linkage analysis for ordinal traits. We proposed a latent-variable proportional-odds model that relates inheritance patterns to the distribution of the ordinal trait. We used the likelihood-ratio test for testing evidence of linkage. Through simulation studies, we found that the power of our proposed model is substantially higher than that of the binary-trait-based linkage analysis and that our test statistic is robust with regard to certain parameter misspecifications. Using our proposed method, we performed a genome scan of the hoarding phenotype in a dataset with 53 nuclear families, collected by the Tourette Syndrome Association International Consortium for Genetics. Standard linkage scans were also performed using programs GeneHunter and Allegro and failed to reveal any marker significantly linked to the binary hoarding phenotypes. However, our method identified three markers at 4q34-35 ( $P=0.0009$ ), 5q35.2-35.3 ( $P=0.0001$ ), and 17q25 ( $P=0.0005$ ) that manifest significant allele sharing.