

**USING RANDOM-EFFECTS PROPORTIONAL HAZARDS METHODS TO IDENTIFY SUSCEPTIBILITY
LOCI FOR COMPLEX DISORDERS**

Mariza de Andrade and Susan Slager

Mayo Clinic, United States

In this paper we present a method to perform variance component analyses under general random effects proportional hazards models, and we also investigate the effect of ascertainment in the estimates of the random effects. The method is based on a Laplace approximation, and makes computation for correlated time-to-event data feasible. The correlated frailty models described here can be used to perform genetic analyses on age-at-onset data in a manner analogous to standard variance components methods for quantitative traits. We illustrate the use of the method by performing variance components linkage analyses on simulated data, and further examine the performance of this method for linkage analysis on lung cancer data. While it is well known in genetic analysis for quantitative traits that ascertainment may have an effect in the genetic variance components estimates, no study has been performed to investigate the effect of ascertainment in the estimates of the genetic random-effects. We will show results using simulated data when the families were selected either at random or by correcting by other ascertainment schemes.