Three-state frailty model for age at onset of dementia and death in Swedish twins

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We present a frailty model to estimate the relative importance of genetic and environmental factors on age at onset of dementia in a twin design. We use modern survival methodology to define a model that accounts simultaneously for longitudinal aspects, e.g., left truncation and right censoring in data, and the bivariate nature of twin data. Additionally, we present a three-state frailty model, with nondemented, demented, and dead states, describing variation in the onset of disease and mortality simultaneously in one model, while accounting for possible dependence for the two competing events. The frailty structure, i.e., the latent random effects structure, mimics the traditional twin model for continuous variables used in quantitative genetics, and as such describes within-pair dependence. This in turn leads to estimates for intrapair correlations, as well as for additive genetic, and shared and nonshared environmental components of variance. A hierarchical Bayesian model formulation and Gibbs sampling are used to estimate posterior distributions of the parameters.

The models are applied to Swedish Twin Registry data on the onset of dementia in elderly twins. We conclude with a discussion on extensions of the setup to both measured genetic markers and repeated measures of cognitive data.