

The basic MMTM extends this impairment model, through joint modeling, to address the critical issue of survivorship. It is known that the presence of HAND, at least prior to the use of cART, is strongly associated with risk of death. Joint modeling allows us to incorporate the information provided by survival times to better reconstruct impairment trajectories—and vice-versa—and to address the complications derived from attrition due to death [3]. Following Chapter 6 of [3], and [2], we introduce a survival time s_i for each individual i , and expand the trajectory model for that individual to be

$$p(y_i, s_i | Age, \mathbf{g}_i) = \left[\sum_{k=1}^K g_{ik} d_k(y_i | Age) \right] \left[\sum_{k=1}^K g_{ik} h_k(s_i) \right], \quad (1)$$

where $h_k(s_i)$ is the density of the survival distribution for the k -th canonical profile, and the outcome is censored if $Age > s_i$. This model builds critically on two assumptions. First, we assume that each canonical profile comprises both an idealized trajectory to severe impairment, and an idealized mortality distribution; i.e. canonical profiles describe both impairment and survival. Second, given an individual's membership vector, $\mathbf{g}_i$, survival times and cognitive classification are independent. This is last assumption, sometimes referred to as local independence, is common and well-studied in factor analysis models, latent class models, and latent variable modeling generally [1]. Impairment and survival are dependent in the observed data, but the assumption of local independence forces $\mathbf{g}_i$ to be rich enough to fully explain this dependence when we condition on it. We deal with the problem of right censoring—people who do not survive long enough to determine their final cognitive disposition—through a data-augmentation scheme at the time of estimation via Markov Chain Monte Carlo Simulation.