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# Frailty Models and the Analysis of Recurrent Events

Chair: Katherine Davies (University of Manitoba)

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**AVIK HALDER**, Queen's University

*Bayesian Semiparametric Inference of Frailty Model Using Lévy Process Priors*

Lee and Kim (2003) first proposed the use of a Levy process prior for Bayesian inference of the cumulative hazard function in a proportional hazard model. We extend this model by incorporating a frailty component for heterogeneity among the cumulative intensity processes for different subjects. The Lévy process prior generalizes that used by Sinha (1993) and Sinha et al.(1998), who do consider frailty models. It is assumed that random effects are Gamma with mean one and variance  $\theta$  which makes our model semi-parametric. We characterize the joint posterior and use blocked Gibbs sampling for sampling from the joint posterior.

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**CHRISTIAN BOUDREAU**, University of Waterloo

*Multivariate Frailty Models for Competing Risks*

In this talk we extend Fine and Gray's model for the subdistribution of a competing risk to include multivariate frailties that are assumed to have a joint log-normal distribution. This extension allows for the modelling of situations where a more complex frailty structure is needed than the usual shared frailty. For example, when multiple frailty terms occur within each cluster, or when frailties are nested. Estimation is done using a penalized partial likelihood approach in combination with a Laplace approximation of the partial likelihood. The proposed method is then illustrated using bone-marrow transplantation data for acute myeloid leukemia.

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**BALAKUMAR SWAMINATHAN**, University of Western Ontario

*Ascertainment Corrected Penetrance Estimate for Bivariate Event Time Outcomes using Frailty Model*

In the analysis of complex diseases, affecteds may experience successive events as a consequence of a primary event. We aim to quantify the dependence between sequential event times and estimate the age dependent penetrance. Shared gamma frailty model with Weibull baseline is used and adjusted for family based study design. Using 12 Lynch Syndrome families from Newfoundland, penetrance of first colorectal cancer by age 70 was 99% for male mutated gene carriers and 86% for female carriers. Penetrance to develop a second colorectal cancer in 5 years following first event was 20% for male carriers and 11% for female carriers.

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**LIQUN DIAO**, University of Waterloo

*Analysis of Recurrent Exacerbations in Chronic Disease via Vine Copula Models*

In some chronic disease settings recurrent events have a non-ignorable duration and are characterized as episodes. We formulate models in which the onset times are generated according to a Markov time scale and the durations of the episodes are governed by a semi-Markov process. To reflect multiple dependencies, we consider a construction according to vine copula models in which the multivariate joint density is decomposed into a cascade of pairwise conditional density functions. We propose candidate models, study properties of them, assess treatment effects, and examine the biases arising from simple analyses which ignore some dependencies.

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**HUA SHEN**, University of Waterloo

*A Sequential Mover-Stayer Model for Recurrent Events with "Burn-out"*

Patients with affective disorder experience repeated exacerbations but some researchers in psychiatry think this process may "burn-out" after which patients will not experience any new exacerbations. We describe a sequential mover-stayer process to

model such recurrent events. “Movers” follow a continuous-time multistate Markov model with non-zero transition intensity. When an individual becomes a “stayer” they enter a subject-specific absorbing state and hence acquire a null transition intensity. An EM algorithm is developed to estimate the parameters for the dynamic mover-stayer process as well as the transition intensities for the hidden Markov model.