Speaker: Dr. Chris Jackson

Title: Semi-Markov multi-state models for panel data: making them accessible and stable

Abstract:
Data on a discrete outcome, observed at arbitrary times, are commonly represented using a continuous-time multi-state model. These models can be challenging, since the full sequence of states and transition times is generally unknown. Models usually rely on the Markov assumption, that the time spent in one state, before moving to the next, is exponentially distributed. However, this is often implausible in applications. A range of approaches have been used previously to relax this, but they have generally been either computationally expensive, relied on specific state structures, or lacked software.

This talk presents a novel approach to computation of semi-Markov models, which makes them easily applicable for this kind of data. Phase-type approximations to standard time-to-event distributions are constructed using moment matching, which allows likelihoods to be evaluated efficiently. The `msmbayes` R package allows these to be implemented in any state transition structure. This package implements most of the features of the widely-used `msm` package for multi-state modelling, with the additional benefit of using Bayesian estimation. As well as enabling the use of background information, Bayesian estimation can stabilise computation in the common situation where some parameters are weakly identifiable. These developments are motivated by and illustrated with applications to jointly estimating the incidence and duration of an infection, and transitions between states of cognitive function and death in a study of ageing.

Speaker: Prof. dr Hein Putter

Title: Smooth estimation of transition hazards and probabilities in general interval-censored Markov multi-state models

Abstract:
Interval-censored multi-state models are relevant in longitudinal studies where individuals are not monitored continuously but scheduled to be inspected at certain times. Current approaches can be divided into non-parametric approaches, which are limited to the irreversible illness-death model, and (flexible) parametric models, often based on constant and piecewise constant transition hazards.

In this presentation, based on joint work with Paul Eilers and Jutta Gampe, we extend a recent approach for standard interval-censored data to multi-state models. I will explain and illustrate the approach for standard interval-censored data, and then discuss an extension of this approach for general interval-censored multi-state models. An illustration based on a reversible illness-death model using data from the AHEAD study is provided.

Speaker: Dr. Thomas Klausch

Title: Progressive multi-state semi-Markov models for screening data with censoring due to interventions

Abstract:
In many cancer screening and surveillance programs, such as colorectal cancer (CRC) screening, individuals are monitored at regular intervals for disease development. In CRC screening, for example, the targets are adenomas, which are precursors to CRC. Upon detection of an adenoma

(non-advanced or advanced) during a colonoscopy, the lesion is surgically removed, thereby interrupting its potential progression to CRC.

Researchers often aim to use health records collected in screening or surveillance programs to estimate the transition time distributions from cancer pre-states (e.g., adenomas) to cancer (CRC), and to relate these to background information (covariates). For statistical modelling, multi-state models are routinely applied, but these must account for the censoring structure that arises because disease progression is interrupted after surgical intervention.

We present our model and R package `BayesTSM` (Bayesian Three-State Survival Model), a semi-Markov model designed for this setting in progressive disease processes with three states (Ann. Appl. Stat. 17(2), 1285–1306). Specifically, `BayesTSM` employs a Bayesian Gibbs sampling algorithm to estimate two simultaneous accelerated failure time (AFT) models, tailored to handle informative censoring due to interventions through a combination of data augmentation and regularized parameter estimation. Our recent results further suggest that common alternative semi-Markov multi-state modelling approaches, such as the `cthmm` R package or the widely-used `msm` R package with a phase-type model, yield biased estimates of disease progression risks in settings with censoring due to interventions.

The main current limitation of `BayesTSM` is its assumption of perfect sensitivity and specificity of the screening test. In reality, imperfect sensitivity is a common issue, especially in cancer screening. For example, the FIT test (Faecal Immunochemical Test), routinely used in CRC screening, has a sensitivity of only about 40% for detecting advanced adenomas and may also produce false positives. In conclusion, we present our ongoing work on extending `BayesTSM` to incorporate imperfect test sensitivity and specificity.